Synthesis, characterization, anti-microbial and anti-fungal activity studies of four novel 2-aminopyridine and 2,4-dichloro-5-sulfamoylbenzoic acid salts and their Cu(II) complexes

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Abstract

Four novel proton transfer compounds (1-4) obtained between 2-aminopyridine (**1**), 2-amino-4-methylpyridine (2), 2-amino-5-methylpyridine (3), 2-amino-6-methylpyridine (4) and 2,4-dichloro-5-sulfamoylbenzoic acid (Hsba) and their Cu(II) complexes (6-10) have been synthesized. The structures of powdery salts (1-4) and complexes (6-10) have been suggested by spectral (^{1}H-NMR, FT-IR and UV–Vis), elemental analysis, AAS, molar conductivity and magnetic susceptibility techniques of 6-10 have also been reported. The structures of metal complexes (6-10) were observed octahedral according to spectroscopic analysis results. Additionally, anti-microbial and anti-fungal activities of all compounds have been tested against *Escherichia coli* (ATCC 25922) (Gram negative), *Enterococcus faecalis* (*ATCC 29212*) (Gram positive), *Staphylococcus aureus* (ATCC 29213) (Gram positive), and *Candida Albicans* (ATCC 14053) (yeast), *Candida parapisilosis* (ATCC 22019) (yeast), and *Candida krusei* (ATCC 6258) (yeast). The results were comparisoned with the antibiotics, Fluconazole as anti-fungal agent and Cefepime, Levofloxacin, Vancomycin as anti-microbial agents. Activity against all compounds bacteria and yeasts was observed. Therefore, all compounds may be utilized for the synthesis of new anti-microbial and anti-fungal. Compounds with the best activity are 2 (15.60 µg/mL) for *S. aureus*, 2, 8 and 11 (31.25 µg/mL) for *E. Faecalis*, 2a5mp, 1, 2 and 9 (31.25 µg/mL) for E. Coli, $Cu(OAc)_2.2H_2O$, 1, 2 and 9 (31.25 µg/mL) for *C. Parapsilosis*, Hsba (15.60 µg/mL) for *C. Albicans* and Hsba and 8 (31.25 µg/mL) for *C. Krusei*.

Keywords: 2-Aminopyridine; anti-microbial and anti-fungal activities; Cu(II) complexes; 2,4-dichloro-5-sulfamoylbenzoic acid; proton transfer salt.

1. Introduction

It is known that 2,4-dichloro-5-sulfamoylbenzoic acid derivatives (Hsba) have biological activities such as diuretic (Xia *et al.,* 1991, Latosinska *et al.,* 2012), antiviral (Latosinska *et al.,*

2009), anticonvulsant (Marona and Kiec-Kononowicz,1998), fungicidal, anti-inflammatory (Gaidukevich *et al.,* 1984), anti-microbial and anti-fungal (Meena *et al.,* 2020, Ilkimen and Gülbandılar , 2022) and antiglaucoma (Arslan *et al.,* 2002, Yenikaya *et al.,* 2010, 2011a, Slawinski *et al.,* 2014, Matulis *et al.* 2017, Zakšauskas *et al.,* 2022). There are also few reports on the simple transition metal complexes {Na(I) (Latosinska *et al.,* 2012), Fe(III) (Ilkimen *et al.,* 2020) and Mg(II), Fe(II), Co(II), Ni(II), Cu(II) and Cd(II) (Ilkimen and Gülbandılar, 2022)}, proton transfer salts {2-aminomethylpyridine (Yenikaya *et al.,* 2010), 2-amino-3-methylpyridine and ethylenediamine (Yenikaya *et al.,* 2011a)} and mixed ligand metal complexes {2-aminomethylpyridine (Yenikaya *et al.,* 2010), 2-amino-3,5-dibromopyridine, 2-amino-3-bromo-5-nitropyridine, 2-amino-3-hydroxypyridine, (Ilkimen and Yenikaya, 2021), 2-aminomethylpyridine, 4,4'-bipyridine (Liu *et al.,* 2015) and 1,3-bis(4-pyridyl)propane (Zhao *et al.,* 2015)} of Hsba have been synthesized.

2-Aminopyridine and derivatives have biological activities such as anti-alzheimer's, anti-inflammatory, anti-convulsant, anti-microbial, anti-viral, anti-histaminic, analgesic, cardiotonic, anti-fungal, anti-parasitic and anti-diabetic, (Marinescu, 2017). 2-Aminopyridine derivatives can coordinate with the metal ions with N or NH_2 (Yenikaya *et al.,* 2009, Yenikaya *et al.,* 2011b).

In this study, four new salts (1-4) obtained from between 2-aminopyridine (1), 2-amino-4-methylpyridine (2), 2-amino-5-methylpyridine (3), 2-amino-6-methylpyridine (4), 2-amino-3-methylpyridine (5) (Yenikaya *et al.,* 2011a) and 2,4-dichloro-5-sulfamoylbenzoic acid (Hsba), their Cu(II) complexes (6-10) have been synthesized and illuminated by spectral (^{1}H NMR, FT-IR and UV–Vis), AAS, elemental analysis, molar conductivity and magnetic susceptibility techniques of 6-10 have also been reported. Furthermore, all compounds were tested for their anti-microbial and anti-fungal activities against *Escherichia coli* (ATCC 25922) (Gram negative), *Enterococcus faecalis* (*ATCC 29212*) (Gram positive), *Staphylococcus aureus* (ATCC 29213) (Gram positive), and *Candida parapisilosis* (ATCC 22019) (yeast), *Candida Albicans* (ATCC 14053) (yeast) and *Candida krusei* (ATCC 6258) (yeast) cultures.

2. Experimental section

2.1. General methods and materials

General methods and materials are given Supplementary File.

2.2. Synthesis of compounds 1-4 and 6-11.

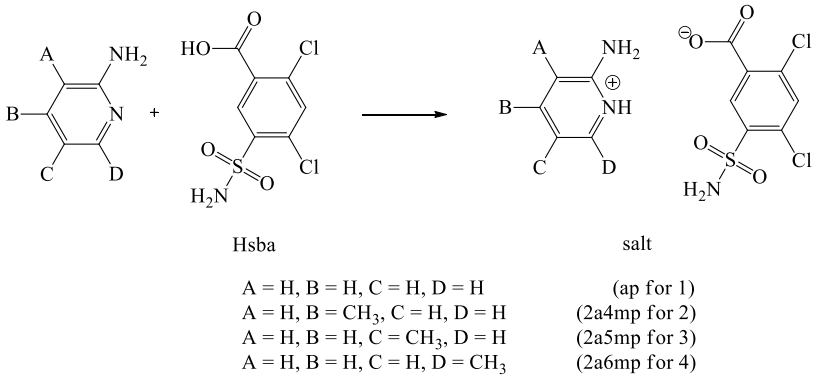
10 mmol Hsba (2.7009 g, 10 mmol) and 10 mmol base solution (ap for 1, 2a4mp for 2, 2a5mp for 3, 2a6mp for 4) dissolved in 50 mL of pure ethanol. The white powdery solid proton transfer salts were obtained by stirring for one day. Some selected physical properties of salts (1-4) are given in Table 1.

1 mmol $Cu(CH_3COO)_2.H_2O$ and 1 mmol proton transfer salt {1 for 6, 5 for 7, 2 for 8, 3 for 9 and 4 for 10) was dissolved in technical ethanol (50%) (20 mL) with stirring two hours. The reaction mixture was kept to give turquoise powdery solid (Figure 1). Some selected physical properties of complexes (6-10) are given in Table 1.

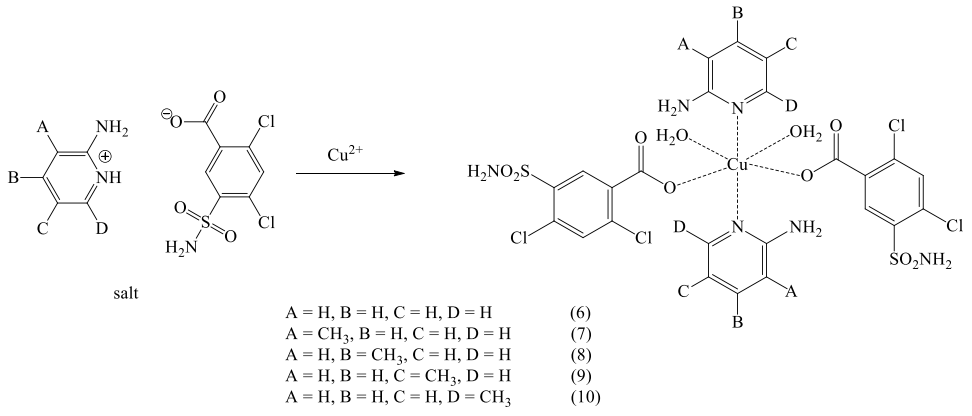
Table 1. Some physical properties of 1-4.

Compound	Formula	Color	MW* (g/mol)	Yield (%)
1	$C_{12}H_{11}Cl_2N_3O_4S$	White	364.20	95
2	$C_{13}H_{13}Cl_2N_3O_4S$	White	378.23	90
3	$C_{13}H_{13}Cl_2N_3O_4S$	White	378.23	85
4	$C_{13}H_{13}Cl_2N_3O_4S$	White	378.23	90
5	$C_{13}H_{13}Cl_2N_3O_4S$	Turquoise	825.97	65**
6	$C_{24}H_{24}Cl_4CuN_6O_{10}S_2$	Turquoise	854.02	68
7	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	Turquoise	854.02	85
8	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	Turquoise	854.02	64
9	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	Turquoise	854.02	68
10	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	Turquoise	854.02	50

*Estimated MW, **(Yenikaya *et al.,* 2011a)



a



b

Fig. 1. Syntheses of compounds 1-4 and 6-10 (a for 1-4, b for 6-10).

Table 2. Elemental analysis for 1-10 and AAS results for 6-10.

Compound	Formula	% Anal. Calcd. (% Found)				
		C	H	N	S	Cu
1	$C_{12}H_{11}Cl_2N_3O_4S$	39.55(39.57)	3.05(3.04)	11.50(11.54)	8.80(8.80)	-
2	$C_{13}H_{13}Cl_2N_3O_4S$	41.30(41.28)	3.50(3.46)	11.10(11.11)	8.50(8.48)	-
3	$C_{13}H_{13}Cl_2N_3O_4S$	41.25(41.28)	3.45(3.46)	11.10(11.11)	8.45(8.48)	-
4	$C_{13}H_{13}Cl_2N_3O_4S$	41.29(41.28)	3.48(3.46)	11.15(11.11)	8.52(8.48)	-
5*	$C_{13}H_{13}Cl_2N_3O_4S$	41.29(41.28)	3.48(3.46)	11.15(11.11)	8.52(8.48)	-
6	$C_{24}H_{24}Cl_4CuN_6O_{10}S_2$	34.92(34.90)	2.95(2.93)	10.15(10.17)	7.78(7.76)	7.70(7.69)
7	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	36.55(36.57)	3.33(3.30)	9.85(9.84)	7.50(7.50)	7.45(7.44)
8	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	36.60(36.57)	3.35(3.30)	9.80(9.84)	7.45(7.50)	7.40(7.44)
9	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	36.56(36.57)	3.32(3.30)	9.81(9.84)	7.48(7.50)	7.47(7.44)
10	$C_{26}H_{28}Cl_4CuN_2O_{17}S_2$	36.59(36.57)	3.34(3.30)	9.82(9.84)	7.52(7.50)	7.46(7.44)

*(Yenikaya *et al.,* 2011a)

2.3 Anti-microbial Assay

In this study, microorganisms of *Escherichia coli* (ATCC 25922) (Gram negative), *Enterococcus faecalis* (*ATCC 29212*) (Gram positive), *Staphylococcus aureus* (ATCC 29213) (Gram positive), and *Candida Albicans* (ATCC 14053) (yeast), *Candida parapisilosis* (ATCC 22019) (yeast), and *Candida krusei* (ATCC 6258) (yeast) were used.

2.3.1. Determination of Anti-microbial Effect by Microdilution Method

MICs (minimum inhibitory concentrations) of the starting materials Hsba, ap, 2a3mp, 2a4mp, 2a5mp, 2a6mp and $Cu(CH_3COO)_2.H_2O$), proton transfer salts (1-5) and Cu(II) complexes (6-11) against yeasts (*C. Parapsilosis, C. Albicans* and *C. krusei*) and bacterial strains (*E. Faecalis, S. Aureus* and *E. coli,*) were determined. The MIC of reference antibiotics Levofloxacin, Cefepime, Vancomycin and Fluconazole were compared with all compounds. For this purpose, U-shaped 96-well microplates were used in the microdilution method.

2.3.2. Microdilution method

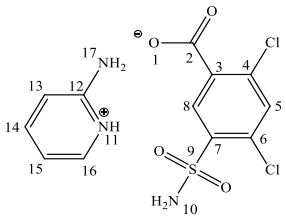
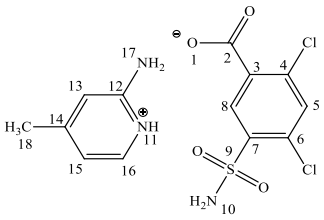
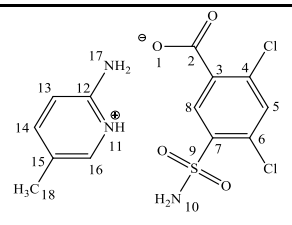
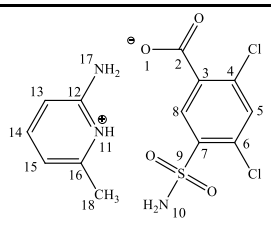
MHB medium was prepared as single and double force. The all compounds (4 mg) and antibiotics (4 mg) were dissolved in 2 mL of DMSO solution. The bacterial and fungal species used were incubated overnight on single-strength MHB medium and their fresh cultures were prepared. Suspensions of the cultures were prepared, and cell densities were adjusted to 0.5 Mc Farland tube turbidity ($1.0x10^8$ (kob)/mL).

3. Results and discussion

3.1. ^{1}H NMR studies of 1-4.

In ^{1}H NMR spectra of 1-4 (Figures S1a-S4a, respectively, Table 3), protons of sba^{-} were observed as 1H singlet at 7.85-7.88 ppm (H^{5} and H^{6}) and 2H singlet at 7.70-7.81 ppm (H^{10}) for for 1-4.

Table 3. ^{1}H-NMR results for compounds 1-4.

			
	1		2
H^{5}	7,85 (1H, s)	H^{5}	7,87 (1H, s)
H^{8}	8,31 (1H, s)	H^{8}	8,28 (1H, s)
H^{10}	7,81 (2H, s)	H^{10}	7,79 (2H, s)
H^{11}	-	H^{11}	-
H^{13}	6,65 (1H, d) [$^{3}J_{H13-H14}$ = 8,557 Hz]	H^{13}, H^{15}	6,48 (2H, d+d) [$^{4}J_{H13-H15}$ = 2,920 Hz, $^{3}J_{H15-H16}$ = 8,991 Hz]
H^{14}	7,57 (1H, txd) [$^{3}J_{H14-H13/H15}$ = 7,800 Hz, $^{4}J_{H14-H16}$ = 1,754 Hz]	H^{16}	7,79 (1H, d) [$^{3}J_{H16-H15}$ = 5,132 Hz]
H^{15}	6,60 (1H, t) [$^{3}J_{H15-H14}$ = 6,364 Hz]	H^{17}	7,50 (H, s)
H^{16}	7,92 (1H, d) [$^{3}J_{H16-H15}$ = 4,578 Hz]	H^{18}	2,22 (3H, s)
H^{17}	7,10 (1H, s)		
			
	3		4
H^{5}	7,88 (1H, s)	H^{5}	7,85 (1H, s)
H^{8}	8,29 (1H, s)	H^{8}	8,28 (1H, s)
H^{10}	7,80 (2H, s)	H^{10}	7,70 (2H, s)
H^{11}	-	H^{11}	-
H^{13}	7,45 (1H, d) [$^{3}J_{H13-H14}$ = 8,622 Hz]	H^{13}	6,53 (1H, d) [$^{3}J_{H13-H14}$ = 8,576 Hz]
H^{14}	6,60 (1H, d) [$^{3}J_{H14-H13}$ = 8,618 Hz]	H^{14}	7,57 (1H, t) [$^{3}J_{H14-H13}$ = 7,465 Hz]
H^{16}	7,92 (1H, d) [$^{3}J_{H16-H15}$ = 4,578 Hz]	H^{15}	6,51 (1H, d) [$^{3}J_{H15-H14}$ = 7,228 Hz]
H^{17}	-	H^{17}	7,35 (1H, s)
H^{18}	2,13 (3H, s)	H^{18}	2,34 (3H, s)

The protons of the aminopyridinium ring were observed 6.65 ppm (H^{13}, doublet, $^3J_{H13-H14}$ = 8.557 Hz) and 7.82 ppm (H^{16}, doublet, $^3J_{H16-H15}$ = 4.578 Hz), 7.57 ppm (H^{14}, triplet-double, $^3J_{H14-H13/H15}$ = 7.800 Hz, $^4J_{H14-H16}$ = 1.754 Hz) and 6.60 ppm (H^{15}, triplet, $^3J_{H15-H14}$ = 6.364 Hz) with 1H intensity for 1; 6.48 ppm (H^{13} and H^{15}, doublet + doublet, $^4J_{H13-H15}$ = 2.920 Hz ve $^3J_{H15-H16}$ = 8.991 Hz, with 2H intensity) and 7. 97 ppm (H^{16}, doublet, $^3J_{H16-H15}$ = 5.132 Hz with 1H intensity) for 2; 7.45 ppm (H^{13}, doublet, $^3J_{H13-H14}$ = 8.622 Hz), 6.60 ppm (H^{14}, doublet, $^3J_{H14-H13}$ = 8,618 Hz) and 7.92 ppm (H^{16}, doublet, $^3J_{H16-H15}$ = 4,578 Hz) with 1H intensity for 3; 6.53 ppm (H^{13}, doublet, $^3J_{H13-H14}$ = 8,576 Hz), 7.57 ppm (H^{14}, triplet, $^3J_{H14-H13}$ = 7,465 Hz) and 6.51 ppm (H^{15}, doublet, $^3J_{H15-H14}$ = 7,228 Hz) with 1H intensity for 4. H^{17} proton of 1, 2 and 4 were observed as 2H singlet at between 7.10 ppm and 7.50 ppm while of 3 were not observed in the spectrum. In addition, H^{18} protons of 2-4 were observed as 3H singlet at between 2.13 ppm and 2.34 ppm. The protons (H^{10}, H^{11} and H^{17}) of 1-4 were not showed in spectra obtained in DMSO-d_6 with D_2O (Figures S1b-S4b).

The ratio of acid (Hsba) and base (ap, 2a3mp, 2a4mp, 2a5mp and 2a6mp) was found to be 1:1 from the spectra data of the salts (1-4). These results support the proposed constructs in Figure 1.

3.2 FT-IR measurements

The FT-IR spectral data of the all compounds {Tables S1-S3, Figures S5-S14 (1-10)} are given in supplementary file. The broad absorption bands the ν(OH) group coordinated water molecules for the complexes 6-10 observed in the range of 3567-3430 cm^{-1}. The absorption bands of NH_2 group of free ligands (Hsba, ap, 2a3mp, 2a4mp, 2a5mp and 2a6mp) (Tables S1) are slightly shifted from those found 3382, 3341, 3235 and 3172 cm^{-1} for 1, 3476, 3332 and 3165 cm^{-1} for 2, 3408, 3344, 3262 and 3162 cm^{-1} for 3, 3309, 3267, 3197 and 3191 cm^{-1} for 4, 3465, 3358 and 3212 cm^{-1} for 6, 3476, 3361, 3319 and 3278 cm^{-1} for 7, 3432 and 3351 cm^{-1} for 8, 3334, 3294 and 3186 cm^{-1} for 9, 3444, 3392, 3352 and 3290 cm^{-1} for 10 due to the weak intermolecular interactions. The weak bands at 2792-2550 cm^{-1} are attributed to the ν(N^+-H) vibration for 1-4 (Cook, 1961) while are not observed for 6-10 due to the deprotonation of the salt during the complex formation (Figure 1). The carboxylate groups exhibit strong carbonyl bands are reflected by IR spectrum of the asymmetric (ν_{as}) and symmetric (ν_s) stretching vibrations at 1701 and 1456 cm^{-1} (Tables S3). The differences (Δυ) between the asymmetric and symmetric stretches of the carboxylate groups of 6-10 are 188, 192, 189, 200, 210 and 200, respectively, which suggests a monodentate binding of the carboxylate group to the metal ion in all complexes (Nakamoto, 1997). The bands at the region of 3109-3072, 3012-2725, 1641-1425, 1402-1043, 1257-1100, 794-763, 474-454 cm^{-1} and 597-564 cm^{-1} are attributed to the aromatic C-H, methyl groups (expect, ap, 1 and 6), *ν*(C=N) (expect Hsba) and *ν*(C=C), *ν*(C-O) (expect aminopyridine derivatives), *ν*(S=O) (expect aminopyridine derivatives), pyridine groups (expect Hsba), M-N and M-O (expect 11) vibrations for all compounds.

3.3 UV/Vis measurements

The electronic spectra of the free ligands Hsba, ap, 2a3mp, 2a4mp, 2a5mp, 2a6mp, $Cu(OAc)_2.2H_2O$ and compounds 1-10 (Figures S16-S25) were recorded in DMSO ($1x10^{-3}$ *M*) (Table S4). Characteristic π- π* transitions are observed at are observed 257 (35120 $Lmol^{-1}cm^{-1}$) and 285 (11230 $Lmol^{-1}cm^{-1}$) nm for Hsba, 313 (32610 $Lmol^{-1}cm^{-1}$) nm for ap, 296 (34190 $Lmol^{-1}cm^{-1}$) nm for 2a3mp, 309 (33120 $Lmol^{-1}cm^{-1}$) and 291 (26230 $Lmol^{-1}cm^{-1}$) nm for 2a4mp, 325 (28780 $Lmol^{-1}cm^{-1}$) and 295 (29280 $Lmol^{-1}cm^{-1}$) nm for 2a5mp, 321 (32150 $Lmol^{-1}cm^{-1}$) and 308 (31940 $Lmol^{-1}cm^{-1}$) nm for 2a6mp, 256 (36270 $Lmol^{-1}cm^{-1}$) nm for $Cu(OAc)_2.2H_2O$, 300 (34370 $Lmol^{-1}cm^{-1}$) nm for 1, 318 (41190 $Lmol^{-1}cm^{-1}$) and 290 (29140 $Lmol^{-1}cm^{-1}$) nm for 2, 306 (38640 $Lmol^{-1}cm^{-1}$) and 295 (26270 $Lmol^{-1}cm^{-1}$) nm for 3, 306 (37760 $Lmol^{-1}cm^{-1}$) and 298 (21240 $Lmol^{-1}cm^{-1}$) nm for 4, 304 (29090 $Lmol^{-1}cm^{-1}$) and 296 (29540 $Lmol^{-1}cm^{-1}$) nm for 5, 301(22870 $Lmol^{-1}cm^{-1}$) nm for 6, 300 (30610 $Lmol^{-1}cm^{-1}$) and 290 (32060 $Lmol^{-1}cm^{-1}$) nm for **7**, 312 (38640 $Lmol^{-1}cm^{-1}$) and 309 (38640 $Lmol^{-1}cm^{-1}$) nm for 8, 308 (38640 $Lmol^{-1}cm^{-1}$) nm for 9 and 295 (35390 $Lmol^{-1}cm^{-1}$) and 291 (32490 $Lmol^{-1}cm^{-1}$) nm for 10. The bands for the d-d transitions are observed at 760 (140 $Lmol^{-1}cm^{-1}$) nm for $Cu(OAc)_2.2H_2O$, 792 (270 $Lmol^{-1}cm^{-1}$) nm for 6, 791 (230 $Lmol^{-1}cm^{-1}$) nm for **7**, 790 (240 $Lmol^{-1}cm^{-1}$) nm for 8, 791 (340 $Lmol^{-1}cm^{-1}$) nm for 9 and 797 (100 $Lmol^{-1}cm^{-1}$) nm for 10.

3.4 Magnetic susceptibility measurements

The result magnetic moments of Cu(II) complexes (6-10) are between 1.65 BM and 1.75 BM per metal ion, showing the presence of one (d^9) unpaired electron.

3.5. Molar conductivity measurements

The result molar conductivity of 6-10 are 7.9 for 6, 7.8 for 7, 8.4 for 8, 1.8 for 9 and 6.3 for 10 in DMSO, showing that the complexes 6-10 are non-ionic (Geary, 1971).

The very powerful single-crystal X-ray diffraction method cannot be applied to identify the structures of compounds 6-10 due to their dust form. Formulae for the complexes were proposed using spectral (FT-IR and UV–Vis), elemental analysis, AAS, molar conductivity and magnetic susceptibility techniques methods (Figure 1b).

3.6. Anti-microbial Activity Results

In this work, anti-microbial and anti-fungal activity of the free ligand (Hsba, ap, 2a3mp, 2a4mp, 2a5mp, 2a6mp and $Cu(OAc)_2.2H_2O$), proton transfer salts (1-5) and Cu(II) complexes (6-11) were tried by microdilution method. Flucanazole was used as an anti-fungal agent, whereas Cefepime, Vancomycin and Levofloxacin were used as standard anti-microbial agents. MIC values of the all compounds are given in Table 4. According to MIC values it was showed that most of the compounds have anti-microbial and anti-fungal activity properties.

When the MIC values of antibacterial agents and compounds are compared, all compounds are active against *Staphylococcus aureus;* $Cu(OAc)_2.2H_2O$ (31.25 µg/mL), 2 (15.60 µg/mL), 3 (31.25 µg/mL), 4 (31.25 µg/mL) and 9 (31.25 µg/mL) demonstrated strong activity according to Levofloxacin while demonstrated similar activity ap, 2a3mp, 2a4mp, 2a6mp, 1, 5-8 and 11 (62.50 µg/mL). 2 (15.60 µg/mL) showed strong activity according to Vancomycin and Cefepime while showed similar activity $Cu(OAc)_2.2H_2O$, 3, 4 and 9 (31.25 µg/mL). The other compounds showed less activity according to Vancomycin and Cefepime. Hsba, 2a5mp and 10 (125.00 µg/mL) showed less activity according to standard anti-microbial agents for *S aureus*. *Enterococcus faecalis;* 2, 8 and 11 (31.25 µg/mL) showed strong activity according to Vancomycin and Levofloxacin while showed similar activity (62.50 µg/mL) other compounds (except Hsba, 2a5mp, 3, 6 and 10). 2, 8 and 11 (31.25 µg/mL) indicated similar activity according to Cefepime while indicated less activity other compounds. *Escherichia coli;* 2a5mp, 1, 2, and 9 (31.25 µg/mL) showed strong activity according to Cefepime and Levofloxacin while showed similar activity other compounds (62.50 µg/mL) (except Hsba). Hsba (125.00 µg/mL) showed less activity according to standard anti-microbial agents. 2a5mp, 1, 2, and 9 (31.25 µg/mL) observed similar activity according to Levofloxacin while observed less level of activity other compounds.

Table 4. MIC results of the compounds (µg/mL).

Compound	*S.aureus*	*E.faecalis*	*E.coli*	*C.parapsilosis*	*C.albicans*	*C.krusei*
Vancomycin	31.25	62.50	62.50		-	-
Levofloxacin	62.50	62.50	31.25		-	-
Cefepime	31.25	31.25	62.50		-	-
Fluconazole	-	-	-	62.50	31.25	-
Hsba	125.00	125.00	125.00	62.50	15.60	31.25
ap	62.50	62.50	62.50	62.50	31.25	62.50
2a3mp	62.50	62.50	62.50	62.50	62.50	62.50
2a4mp	62.50	250	62.50	62.50	62.50	62.50
2a5mp	125.00	125.00	31.25	62.50	62.50	62.50
2a6mp	62.50	62.50	62.50	62.50	62.50	62.50
$Cu(OAc)_2.2H_2O$	31.25	62.50	62.50	31.25	125.00	125.00
1	62.50	62.50	31.25	125.00	62.50	62.50
2	15.60	31.25	31.25	31.25	62.50	62.50
3	31.25	250	62.50	62.50	62.50	125.00
4	31.25	62.50	62.50	31.25	62.50	125.00
5	62.50	62.50	62.50	62.50	125.00	125.00
6	62.50	125.00	62.50	62.50	62.50	62.50
7	62.50	62.50	62.50	62.50	62.50	125.00
8	62.50	31.25	62.50	31.25	31.25	31.25
9	31.25	62.50	31.25	31.25	62.50	62.50
10	125.00	125.00	62.50	62.50	62.50	62.50
11	62.50	31.25	62.50	31.25	62.50	125.00

When the mic values of antibacterial agents and compounds are compared, all compounds are active against *Candida parapisilosis;* $Cu(OAc)_2.2H_2O$, 2, 4, 8, 9 and 11 (31.25 µg/mL) showed strong activity according to Fluconazole while showed similar activity (62.50 µg/mL) other compounds. *Candida albicans;* Hsba (15.60 µg/mL) indicated strong activity according to Fluconazole while indicated similar activity ap and 8 (31.25 µg/mL). The other compounds demonstrated less activity according to Fluconazole {2a3mp, 2a4mp, 2a5mp, 2a6mp, 1-4, 6, 7 and 9-11 (62.50 µg/mL) > $Cu(OAc)_2.2H_2O$ and 5 (125.00 µg/mL)}. *Candida krusei;* all compounds demonstrated strong activity according to Fluconazole {Hsba and 8 (31.25 µg/mL) > ap, 2a3mp, 2a4mp, 2a5mp, 2a6mp, 1, 2, 6, 9 and 10 (62.50 µg/mL) > $Cu(OAc)_2.2H_2O$, 3-5, 7 and 11 (125.00 µg/mL)}.

4. Conclusions

In this study, four new proton transfer salts (1-4) and five Cu(II) complexes (6-10) of 2-aminopyridine derivatives and 2,4-dichloro-5-sulfamoylbenzoic acid have been obtained for the first time. The structures of proton transfer salts (1-4) have been suggested by evaluating the data obtained from elemental analysis, FT-IR and NMR spectra (Figure 1a). As a result of the evaluation of the data obtained from elemental analysis, AAS, FT-IR, UV-Vis, magnetic susceptibility and molar conductivity studies, the formulas of the complexes (6-10) were proposed as in Figure 1b. The acid:base ratio was found to be 1:1 in proton transfer salts. The metal:acid:base ratio was found to be 1:2:2 in the complexes. The structures of the synthesized metal complexes were observed to octahedral for 6-10 results of analyses results.

Activity against all compounds bacteria and yeasts was observed. Compounds with the best activity are 2 (15.60 µg/mL) for *S. aureus*, 2, 8 and 11 (31.25 µg/mL) for *E. Faecalis*, 2a5mp, 1, 2 and 9 (31.25 µg/mL) for E. Coli, $Cu(OAc)_2.2H_2O$, 1, 2 and 9 (31.25 µg/mL) for *C. Parapsilosis*, Hsba (15.60 µg/mL) for *C. Albicans* and Hsba and 8 (31.25 µg/mL) for *C. Krusei*. Therefore, the obtained compounds (1-10) can be evaluated for the compound of new antibacterials.

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