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Synthesis, characterization, anti-microbial activity studies of 2-methoxy-5-sulfamoylbenzoic acid and 2-aminopyridine derivatives salts and their Cu(II) complexes

2-Metoksi-5-sülfamoilbenzoik asit ve 2-aminopiridin türevlerinin tuzları ve bunların Cu(II) komplekslerinin sentezi, karakterizasyonu, antimikrobiyal aktivite çalışmaları

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Abstract

*Two new salts (**4** and **5**) obtained between 2-methoxy-5-sulfamoylbenzoic acid (**1**) and 2-aminopyridine (**2**) or 2-amino-4-methylpyridine (**3**), and their Cu(II) complexes (**6** and **7**) have been obtained. The structures of the salts (**4** and **5**) were suggested by elemental analysis, NMR, FT-IR and UV-Vis, while the structures of Cu(II) complexes (**6** and **7**) were suggested by elemental analysis, AAS, UV-Vis and magnetic susceptibility techniques. While the acid:base ratio was 2:1 for **4** and 1:1 for **5** salts, the metal:acid:base ratio was 1:2:2 for **6** and **7**. According to the results of spectroscopic analysis, the structures of **6** and **7** compounds were proposed as octahedral. Additionally, antimicrobial activities of all compounds were studied against Pseudomonas aeruginosa (ATCC 27853), Staphylococcus aureus (NRRL B-767), Bacillus subtilis, Enterococcus faecalis (ATCC 29212), Escherichia coli (ATCC25922) and Listeria monocytogenes (ATCC 7644) bacteria and Candida albicans (F89) yeast. The results were comparisoned with the antibiotics (Fluconazole, Vancomycin, Cefepime and Levofloxacin). All compounds showed activity against bacteria and yeasts.* Compounds *$Cu(OAc)_2.2H_2O$ (31.25 µg/mL) for C. Albicans, **1** and **7** (31.25 µg/mL) for L. monocytogens, all compounds (except **6**) (7.60 µg/mL) for B. subtilis, **2** (31.25 µg/mL) for E. Coli, **7** (15.60 µg/mL) for S. aureus, **7** (31.25 µg/mL) for E. Faecalis, and **3** (15.60 µg/mL) for* P. aeruginoa have the best activity.

Keywords: 2-Aminopyridine, 2-Methoxy-5-sulfamoylbenzoic Acid, Salt, Cu(II) Complexes, Anti-microbial Activity.

Öz

*2-Metoksi-5-sülfamoilbenzoik asit (**1**) ve 2-aminopiridin (**2**) veya 2-amino-4-metilpiridin (**3**) reaksiyonundan iki yeni tuz (**4** ve **5**) ve bunların Cu(II) kompleksleri (**6** ve **7**) elde edildi. Tuzların (**4** ve **5**) yapıları element analizi, NMR, FT-IR ve UV-Vis ile aydınlatılırken, Cu(II) komplekslerinin (**6** ve **7**) yapıları element analizi, AAS, UV-Vis ve manyetik duyarlılık teknikleri ile önerildi. Asit:baz oranı **4** tuz için 2:1 ve **5** tuz için 1:1 iken, metal:asit:baz oranı **6** ve **7** için 1:2:2 'dir. Spektroskopik analiz sonuçlarına göre **6** ve **7** bileşik oktahedral olarak önerildi. Ayrıca tüm bileşiklerin antimikrobiyal aktiviteleri Pseudomonas aeruginosa (ATCC 27853), Staphylococcus aureus (NRRL B-767), Bacillus subtilis, Enterococcus faecalis (ATCC 29212), Escherichia coli (ATCC25922) ve Listeria monocytogenes (ATCC 7644) bakterilerine ve Candida albicans (F89) mayası. Sonuçlar antibiyotiklerle (Flukonazol, Vankomisin, Sefepim ve Levofloksasin) karşılaştırıldı. Tüm bileşikler bakteri ve mayalara karşı aktivite gösterdi. Bileşiklerde en iyi aktivite C. Albicans için $Cu(OAc)_2.2H_2O$ (31,25 µg/mL), L. monocytogens için **1** ve **7** (31,25), B. subtilis için tüm bileşikler (**6** hariç) (7,60 µg/mL), E. Coli için **2** (31,25 µg/mL), S. aureus için **7** (15,60 µg/mL), E. Faecalis için **7** (15,60 µg/mL) ve P. aeruginoa için **3** (15,60 µg/mL) sahiptir.*

Anahtar kelimeler: 2-Aminopiridin, 2-Metoksi-5-sülfamoilbenzoik Asit, Tuz, Cu(II) Kompleksleri, Anti-mikrobiyal Aktivite.

1 Introduction

Proton transfer reactions between an acid and a base appear in many natural phenomena, from the presence of salts to the zwitterionic nature of common amino acids in habitats or interactions between proteins and substrates [1,2]. Proton transfer salts are compounds that contain positive and negative charges by transferring the unshared electron of the base and the proton of the acid. The ionization of active pharmaceutical ingredients in salts plays a crucial role in the formulation of drugs [2,3]. Salts and metal complexes from salts are generally more soluble than their corresponding non-ionized forms, thus providing drugs with improved pharmacokinetics [4]. In recent years, there has been a need for new chemical substances that are active against diseases due to the decrease in the sensitivity of microorganisms causing diseases to the drugs used. There is a need for more effective new chemicals, which can be obtained inexpensively, to eradicate diseases that can be fatal to human health.

This study has biological activity studies of basic component 2-aminopicoline derivatives such as anti-convulsant, anti-histaminic, anti-bacterial, anti-fungal, anti-parasitic, anti-diabetic, cardiotonic, analgesic, anti-viral, anti-alzheimer's and anti-inflammatory [5]. 2-Aminopicoline derivatives can coordinate with N or NH_2 with Cu(II) [6,7].

This study has biological activity studies of the acid compound 2-methoxy-5-sulfamoylbenzoic acid (Hsba) derivatives have

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biological properties such as enzyme inhibitor, meniscus, infection treatment, rheumatism treatment, analgesic, antimicrobial, antidiabetic and anti-inflammatory [8-15].

In the literature, simple metal complexes of 2-methoxy-5-sulfamoylbenzoic acid [16,17], 2-amino-3-picoline [15], 2,3-diamino-5-(Cl/H)pyridine [18], 2-aminonitropyridine derivatives [19], 2-amino-5-(Br/Cl/CN)pyridine [20], 2-amino-6-(C_2H_5/I)pyridine and 2-amino-4,6-dimethylpyridine [21] with salts and their Cu(II) complexes and 2,3-diamino-5-(Br/Cl/H)pyridine, 2-amino-3-(OH/CH_3/$OCH_2C_6H_5$)pyridine, 2-amino-3-methyl-6-ethylpyridine and 2-amino-3-nitro-6-methylpyridine with mixed ligand Cu(II) complexes [16] were synthesized.

In this study, two new salts (**4** and **5**) obtained between 2-methoxy-5-sulfamoylbenzoic acid (**1**) and 2-aminopyridine (**2**) or 2-amino-4-methylpyridine (**3**), and their Cu(II) complexes (**6** and **7**) have been obtained. The structures of the salts (**4** and **5**) were suggested by elemental analysis, NMR, FT-IR and UV-Vis, while the structures of Cu(II) complexes (**6** and **7**) were suggested by elemental analysis, AAS, UV-Vis and magnetic susceptibility techniques. According to the results of spectroscopic analysis, the structures of **6** and **7** compounds were proposed as octahedral. Additionally, antimicrobial activities of all compounds were studied against *Candida albicans* (F89) yeast *and P. aeruginosa*, *S. aureus*, *B. subtilis*, E. faecalis, *E. coli* and *L. monocytogenes* bacteria. The results were comparisoned with the antibiotics. All compounds showed activity against bacteria and yeasts.

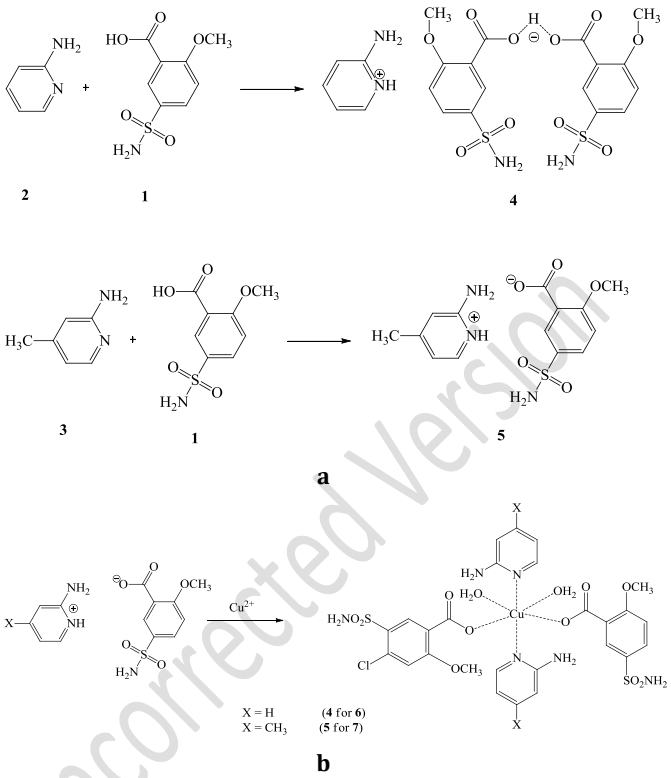


Figure 1. *Syntheses of compounds* ***4-7*** *(**a** for **4** and **5**, **b** for **6** and **7**).*

2 Experimental section

2.1 Preparation of salts and Cu(II) complexes

5 mmol **1** (2.3123 g) and 5 mmol 2-aminopyridines (**2** for **4** and **3** for **5**) dissolved in 40 mL of ethanol (99.99%). The white amorphous solids were procured by stirring for three hours (90% yield for **4** and 85 yield for **5**) (Fig. 1a).

5 mmol salt {**4** for **6** and **5** for **7**) and 5 mmol $Cu(CH_3COO)_2.H_2O$ was dissolved in ethanol:water solution (3:1) (50 mL) with stirring one week. Purple amorphous solids (60% yield for **6** and 78% yield for **7**) were obtained from the mixtures (Fig. 1b).

Anal. Calcd. for **4** ($C_{21}H_{24}N_4O_{10}S_2$): C, 45.32%; H, 4.35%; N, 10.07%; S, 11.52%. Found: C, 45.302%; H, 4.375%; N, 10.04%; S, 11.53%; for **5** ($C_{14}H_{17}N_3O_5S$): C, 45.32%; H, 4.35%; N, 10.07%; S, 11.52%. Found: C, 45.35%; H, 4.30%; N, 10.10 %; S, 11.50%; Anal. Calcd. for **6** ($C_{26}H_{32}CuN_6O_{12}S_2$): C, 41.73%; H, 4.31%; Cu, 8.49%; N, 11.23%; S, 8.57%. Found: C, 41.75%; H, 4.30%; Cu, 8.50%; N, 11.23%; S, 8.58%; Anal. Calcd. for **7** ($C_{28}H_{36}CuN_6O_{12}S_2$): C, 43.32 %; H, 4.67%; Cu, 8.19%; N, 10.83%; S, 8.26%. Found: C, 43.25%; H, 4.70%; Cu, 8.20%; N, 10.90%; S, 8.28%.

2.2 Anti-microbial Assay

In this study, Eskişehir Osmangazi University's Faculty of Medicine provided the *E. faecalis* and *E. coli* bacteria utilized and the biology department of Eskişehir Technical University provided the *C. albicans*, *B. subtilis*, *L. monocytogenes*, *S. aureus* and *P. aeruginosa* microorganisms. All compounds had their antibacterial activity assessed using a microdilution susceptibility test. In DMSO solution, the sample solutions had previously been separated.

The compounds' antibacterial investigation was conducted using a microbroth dilution susceptibility test. The samples' stock solutions in DMSO were created. In 4 mL of DMSO solution, synthesized substances (8 mg) and antibiotics (8 mg) were dissolved. Using McFarland No. 0.5 standard solution, overnight-grown bacterial and yeast suspensions in double-strength Mueller-Hinton broth were standardized to 10^8 Colony Forming Units/mL. The wells then received 100 µL of each microbe suspension. As a negative control, the last well chain without a microorganism was employed. The medium and sterile distilled water acted as a positive growth control. The first well without turbidity was chosen as the MIC following an 18–24 h incubation period at 37 °C.

3 Results and discussion

3.1 ^{1}H ve ^{13}C NMR studies of 4 and 5.

In ^{1}H ve ^{13}C NMR spectra and the chemical shift values of **4** and **5** are given Figures S1-S4, respectively, and Table 1.

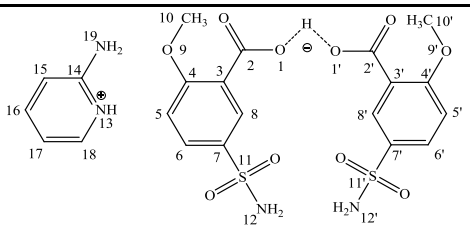
In the ^{1}H NMR spectra of **4** and **5** (Figs S1 and 3), the protons of **1** of **4** and **5** were observed 7.30 ppm (H^5, singlet), 7.93 ppm (H^6, doublet-doublet, $^3J_{H6\text{-}H5}$ = 5.798 Hz, $^4J_{H6\text{-}H8}$ = 2.465 Hz), 8.10 ppm (H^8, doublet, $^4J_{H8\text{-}H6}$ = 2.46 Hz) with 2H intensity and 3.90

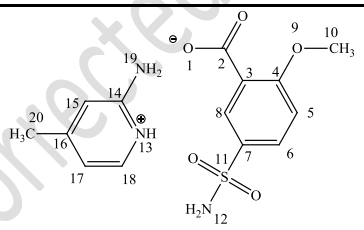
ppm (H^{10}, singlet) with 6H intensity for **4** and 7.30 ppm (H^5, singlet), 7.92 ppm (H^6, doublet-doublet, $^3J_{H6-H5}$ = 8.807 Hz, $^4J_{H6-H8}$ = 2.487 Hz for **5**), 8.10 ppm (H^8, doublet, $^4J_{H8-H6}$ = 2.459 Hz for **5**) with 1H intensity for **5** and 3.90 ppm (H^{10}, singlet) with 3H intensity for **4** and **5**, 7.33-7.35 ppm (H^{12}, singlet) with 4H for **4** and 2H for **5**. In protons of **2** for **4** and **3** for **5**, respectively, were observed 6.48 ppm (H^{15}, doubletxdoublet,$^3J_{H15-H16}$ = 8.351 Hz, $^4J_{H15-H17}$ = 2.129 Hz), 7.37 ppm (H^{16}, tripletxdoublet, $^3J_{H16-H17/H15}$ = 7.745 Hz, $^4J_{H16-H18}$ = 1.909 Hz), 6.48 ppm (H^{17}, tripletxdoublet, $^3J_{H17-H15/H18}$ = 8.351 Hz, $^4J_{H17/H15}$ = 2.129 Hz) and 7.89 (H^{16}, dxd, $^3J_{H18-H17}$ = 4.872 Hz, $^4J_{H18-H16}$ = 1.378 Hz) with 1H intensity for **4** and 7.24 ppm (H^{15}, doublet, $^4J_{H15-H17}$ = 8.494 Hz), 6.47 ppm (H^{17}, doubletxdoublet, $^3J_{H17-H18}$ = 5.249 Hz, $^4J_{H17-H15}$ = 0.753 Hz) and 7.77 ppm (H^{18}, doublet, $^3J_{H18-H17}$ = 4.896 Hz) with 1H intensity for **5**. H^{19} proton of **4** and **5** were observed as 2H singlet at 5.98-6.08 ppm. H^{20} protons of **5** were observed as 3H singlet at 2.15 ppm. H^1 proton for **4** and H^{13} protons of **4** and **5** were not showed in spectra.

As expected, ^{13}C-NMR spectrum of **4** and **5** exhibits thirteen for **4** and fourteen for **5** signals (Figs. 2 and 8, Table 1). The carbon signals of **4** and **5** were observed at 167.409 and 169.351 (C^2), 122.621 and 125.958 (C^3), 160.590 and 159.939 (C^4), 112.218 and 112.542 (C^5), 130.631 and 129.295 (C^6), 135.954 and 135.798 (C^7), 128.890 and 128.164 (C^8), 56.656 and 56.114 (C^{10}), 159.117 and 158.762 (C^{14}), 109.739 and 109.717 (C^{15}), 139.005 and 143.882 (C^{16}), 113.018 and 113.90 (C^{17}), 145.337 and 150.258 (C^{18}) ppm, respectively, and 43.643 (C^{20}) ppm for **5**.

The ratio of **1** and base (**2** and **3**) was found to be 2:1 for **4** and 1:1 for **5** from the NMR spectra results of the salts (Fig. 1).

Table 1. *^{1}H-NMR results for compounds **4** and **5**.*





4				**5**			
^{1}H-NMR		**^{13}C-NMR**		**^{1}H-NMR**		**^{13}C-NMR**	
H^1	-	C^2, $C^{2'}$	167.409	H^5	7.30 (1H, d) [$^3J_{H5-H6}$ = 8.875 Hz]	C^2	169.351
H^5, $H^{5'}$	7.30 (2H, d) [$^3J_{H5-H6}$ = 8.879 Hz]	C^3, $C^{3'}$	122.621	H^6	7.92 (1H, dxd) [$^3J_{H6-H5}$ = 8.807 Hz, $^4J_{H6-H8}$ = 2.487 Hz]	C^3	125.958
H^6, $H^{6'}$	7.93 (2H, dxd) [$^3J_{H6-H5}$ = 5.798 Hz, $^4J_{H6-H8}$ = 2.465 Hz]	C^4, $C^{4'}$	160.590	H^8	8.10 (1H, d) [$^4J_{H8-H6}$ = 2.459 Hz]	C^4	159.939
H^8, $H^{8'}$	8.10 (2H, d) [$^4J_{H8-H6}$ = 2.46 Hz]	C^5, $C^{5'}$	112.218	H^{10}	3.90 (3H, s)	C^5	112.542
H^{10}, $H^{10'}$	3.90 (6H, s)	C^6, $C^{6'}$	130.631	H^{12}	7.35 (2H, s)	C^6	129.295
H^{12}, $H^{12'}$	7.33 (4H, s)	C^7, $C^{7'}$	135.954	H^{13}	-	C^7	135.798
H^{13}	-	C^8, $C^{8'}$	128.890	H^{15}	7.24 (1H, d) [$^4J_{H15-H17}$ = 8.494 Hz]	C^8	128.164
H^{16}	7.37 (1H, txd) [$^3J_{H16-H17/H15}$ = 7.745 Hz, $^4J_{H16-H18}$ = 1.909 Hz]	C^{10}, $C^{10'}$	56.656	H^{17}	6.47 (1H, dxd) [$^3J_{H17-H18}$ = 5.249 Hz, $^4J_{H17-H15}$ = 0.753 Hz]	C^{10}	56.114
H^{15}, H^{17}	6.48 (2H, txd+dxd) [$^3J_{H15-H16\ veya\ H17-H15/H18}$ = 8.351 Hz, $^4J_{H15-H17\ veya\ H17/H15}$ = 2.129 Hz]	C^{14}	159.117	H^{18}	7.77 (1H, d) [$^3J_{H18-H17}$ = 4.896 Hz]	C^{14}	158.762
H^{18}	7.89 (1H, dxd) [$^3J_{H18-H17}$ = 4.872 Hz, $^4J_{H18-H16}$ = 1.378 Hz]	C^{15}	109.739	H^{19}	6.08 (2H, s)	C^{15}	109.717
H^{19}	5.98 (2H, s)	C^{16}	139.005	H^{20}	2.15 (3H, s)	C^{16}	143.882
		C^{17}	113.018			C^{17}	113.90
		C^{18}	145.337			C^{18}	150.258
						C^{20}	43.643

3.2 IR measurements

The IR data of free ligands, the salts and Cu(II) complexes are given in Table 2 and Figures S5-S8. The bands the ν(O-H) group of water molecules for **6** and **7** observed in the range of 3431 and 3462 cm^{-1}. The bands of NH_2 group of free ligands (**1-3**) (Table 2) are slightly shifted from those found 3397, 3308, 3277 and 3206 cm^{-1} for **4**, 3445, 3320 and 3222 cm^{-1} for **5**, 3384, 3346, 3276, 3238 cm^{-1} for **6** and 3409 and 3226 cm^{-1} for **7**. The weak bands of ν(N^+-H) vibration for **4** and **5** observed at 2680-2441 cm^{-1} [22] while are not observed for **6** and **7** due to salt deprotonation during complex formation. Asymmetric (νas) and symmetrical (νs) stretch vibration wave numbers of carboxylate groups are given in Table 2. The difference in wave number (Δυ) shows how many teeth the group is attached to the metal. Δυ values for complexes **6** and **7** are 191 and 207, respectively, indicating monodentate binding of the carboxylate group to Cu(II) ion in the complexes [23]. It is seen in all compounds (**1-7**) as the strong absorption bands in the range of 1634-1410 cm^{-1} for ν(C=N) (except **1**) and (C=C), 1388-1086 cm^{-1} for (C-O) (except **2** and **3**), 1334-1119 cm^{-1} for (S=O) (except **2** and **3**) and 796-751 cm^{-1} for pyridine groups (except **1**). The weak vibration bands aromatic ν(C-H), aliphatic ν(C-H) (except **2**) all compounds, ν(M-O) and ν(M-N) for **6** and

7 observed at 3090-3070 cm^{-1}, 2995-2748cm^{-1}, 577 and 542 cm^{-1} and 489 and 491 cm^{-1}, respectively.

Table 2. *IR spectral data of compounds* ***4-7*** *(cm^{-1})*

	1	**2**	**3**	**4**	**5**	**6**	**7**
ν(OH)	2900(br)			-	-	3431(br)	3462(br)
	3425(m)	3443(m)	3317(m)	3397(m)	3445(m)	3384(m)	3409(m)
	3278(m)	3291(m)	3175(m)	3308(m)	3320(m)	3346(m)	3226(m)
				3277(m)	3222(m)	3276(m)	
				3206(m)		3238(m)	
$\nu(C\text{-}H)_{Ar}$	3090(w)	3070(w)	3072(w)	3089(w)	3080(w)	3085(w)	3082(w)
$\nu(CH)_{Alp.}$	2975(w)	-	2971(w)	2985(w)	2991(w)	2995(w)	2929(w)
	2835(w)		2855(w)	2851(w)	2951(w)	2875(w)	2858(w)
				2748(w)	2848(w)	2768(w)	2787(w)
$\nu(N^{+}H)$	-	-	2971(w)	2680(w)	2666(w)	-	-
			2855(w)	2441(w)	2522(w)		
ν(C=O)	1684(s)	-	-	1671(s)	1663(s)	1652(s)	1627(s)
						1461(s)	1407(s)
ν(C=N)	1430(s)	1622(s)	1580(s)	1623(s)	1624(s)	1634(s)	1610(s)
ν(C=C)	1401(s)	1593(s)	1460(s)	1573(s)	1584(s)	1612(s)	1559(s)
		1555(s)	1445(s)	1549(s)	1558(s)	1580(s)	1492(s)
		1483(s)		1492(s)	1477(s)	1505(s)	1474(s)
		1435(s)		1463(s)	1442(s)	1484(s)	
				1440(s)	1410(s)		
ν(C-O)	1352(s)	-	-	1381(s)	1388(s)	1382(s)	1386(s)
	1250(s)			1274(s)	1272(s)	1293(s)	1297(s)
	1169(s)			1086(s)	1086(s)	1090(s)	1095(s)
ν(S=O)	1373(s)	-	-	1334(s)	1329(s)	1270(s)	1297(s)
	1160(s)			1172(s)	1166(s)	1162(s)	1169(s)
				1119(s)	1120(s)	1120(s)	1137(s)
ν(py)	-	751(s)	768(s)	775(s)	782(s)	796(s)	778(s)
ν(M-N)	-	-	-	-	-	489(w)	491(w)
ν(M-O)	-	-	-	-	-	577(w)	542(w)

3.3 UV/Vis measurements

The electronic spectra of compounds **1-7** were registered in DMSO ($1x10^{-3}$ *M*) (Table 3). Characteristic π-π^* and n-π^* transitions are observed 302 and 291 nm for **1**, 313 nm for **2**, 309 and 291 nm for **3**, 309 and 290 nm for **4**, 316 and 303 nm for **5**, 364 and 295 nm for **6** and 395 and 293 nm for **7**. The d-d transitions bands, indicating an six coordinated metal ions, were found at 780 for **6** [24] and 762 nm for **7** [25].

Table 3. *Optical properties all compounds in DMSO ($nm(Lmol^{-1}cm^{-1})$).*

1	**2**	**3**	**4**	**5**	**6**	**7**
302(32160)	313(32610)	309(33120)	309(31400)	316(35870)	780(200)	762(240)
291(26530)		291(26230)	290(25970)	303(35870)	364(33260)	395(25240)
					295(14550)	293(32860)

3.4 Magnetic susceptibility measurements

Magnetic susceptibility results of Cu(II) complexes (**6** and **7**) were found 1.72 BM. These values say that there are unpaired electrons in the complexes. The magnetic values found are within the range typically found for Cu(II) complexes that are octahedral [26].

3.5 Anti-microbial Activity Results

The anti-microbial activity of anti-fungal agent (Flucanazole), anti-microbial agents (Levofloxacin, Cefepime and Vancomycin), $Cu(OAc)_2.2H_2O$ and **1-7** were investigated by microdilution method. All compounds showed activity against bacteria and yeast. MIC values of anti-fungal and anti-microbial agents, $Cu(OAc)_2.2H_2O$ and **1-7** all compounds are given in Table 5. Activity values are similar to 2-aminopicoline found in the literature [14-21].

The antifungal drug and substances have activity against *C. parapisilosis* when MIC values are compared; $Cu(OAc)_2.2H_2O$ (31.25 μg/mL) observed greater activity than according to Fluconazole while **2**, **4-7** showed equal effective (62.50 μg/mL). **1** and **3** were found to have a lower degree of action (125.00 μg/mL).

All antibacterial drugs and substances have activity against *L. monocytogens*; when MIC values are compared; all compounds indicated greater activity than according to Vancomycin

(125.00 µg/mL) {**1** and **7** (31.25 µg/mL) > $Cu(OAc)_2.2H_2O$ and **2-6** (62.50 µg/mL)}. **1** and **7** showed equal activity (31.25 µg/mL) according to Levofloxacin and Cefepime while indicated less activity other compounds (62.50 µg/mL).

B. subtilis; all compounds showed greater activity than according to Vancomycin (250.00 µg/mL) {$Cu(OAc)_2.2H_2O$, **1-5** and **7** (62.50 µg/mL) > **6** (125.00 µg/mL)}. $Cu(OAc)_2.2H_2O$, **1-5** and **7** showed equally effective (62.50 µg/mL) according to Levofloxacin and Cefepime while **6** was found to have a lower degree of according to Levofloxacin and Cefepime.

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

	C. albicans	***L. monocytogens***	***B. subtilis***	***E. coli***	***S. aureus***	***E. faecalis***	***P. aeruginoa***
Vancomycin	-	125.00	250	31.25	31.25	62.50	62.50
Levofloxacin	-	31.25	62.50	31.25	31.25	62.50	31.25
Cefepime	-	31.25	62.50	62.50	62.50	31.25	31.25
Fluconazole	62.50	-	-	-	-	-	-
$Cu(OAc)_2.2H_2O$	31.25	62.50	62.50	62.50	31.25	62.50	62.50
1	125.00	31.25	62.50	125.00	125.00	125.00	31.25
2	62.50	62.50	62.50	15.60	62.50	62.50	62.50
3	125.00	62.50	62.50	31.25	62.50	62.50	15.60
4	62.50	62.50	62.50	125.00	62.50	62.50	62.50
5	62.50	62.50	62.50	62.50	62.50	62.50	31.25
6	62.50	62.50	125.00	125.00	62.50	125.00	62.50
7	62.50	31.25	62.50	62.50	15.60	31.25	62.50

E. coli; **2** (15.60 µg/mL) and **3** (31.25 µg/mL) indicated greater activity than according to Cefepime while $Cu(OAc)_2.2H_2O$ **5** and **7** showed similar effective (62.50 µg/mL). Compounds **1**, **4** and **6** (125.00 µg/mL) were found to have a lower degree of according to Cefepime. **2** (15.60 µg/mL) indicated greater activity than according to Vancomycin and Levofloxacin while **3** showed equal effective (31.25 µg/mL). $Cu(OAc)_2.2H_2O$, **1** and **5-7** were found to have a lower degree of according to Vancomycin and Levofloxacin.

S. aureus; **7** (15.60 µg/mL) indicated greater activity than according to Vancomycin and Levofloxacin while $Cu(OAc)_2.2H_2O$ showed equally effective (31.25 µg/mL). Compound **2-6** (62.50 µg/mL) and **1** (125.00 µg/mL) was found to have a lower degree of according to Cefepime and Vancomycin. **7** (15.60 µg/mL) and $Cu(OAc)_2.2H_2O$ (31.25 µg/mL) showed greater activity than according to Cefepime while **2-6** (62.50 µg/mL) showed equally effective. Compound **1** (125.00 µg/mL) was found to have a lower degree of according to Cefepime.

E. faecalis; **7**(31.25 µg/mL) observed similar activity according to Cefepime while other compounds seen less level of activity {$Cu(OAc)_2.2H_2O$ and **2-5** (62.50 µg/mL) **> 1** and **6** (125.00 µg/mL)}. **7** (31.25 µg/mL) showed greater activity than according to Vancomycin and Levofloxacin while $Cu(OAc)_2.2H_2O$ and **2-5** showed equally effective (62.50 µg/mL. Compounds **1** and **6** were found to have a lower degree of according to Vancomycin and Levofloxacin.

P. aeruginoa; **3** (15.60 µg/mL), **1** and **5** (31.25 µg/mL) showed greater activity than according to Vancomycin while $Cu(OAc)_2.2H_2O$, **2**, **4**, **6** and **7** equally effective (62.50 µg/mL). **3** (15.60 µg/mL) showed greater activity than according to Cefepime and Levofloxacin while **1** and **5** showed equally effective (31.25 µg/mL). Other compounds were found to have a lower degree of according to Cefepime and Levofloxacin.

4 Conclusions

In this study, two new salts (**4** and **5**) and Cu(II) complexes (**6** and **7**) of 2-methoxy-5-sulfamoylbenzoic acid and 2-aminopyridines have been synthesized. The structures of **4** and **5** were proposed by NMR, FT-IR and elemental analysis spectra while the structures of **6** and **7** were suggested by AAS, elemental analysis, UV-Vis, FT-IR and magnetic studies. While the acid:base ratio was 2:1 for **4** and 1:1 for **5** salts, the metal:acid:base ratio was 1:2:2 for **6** and **7**. According to the analysis results, the structures of **6** and **7** were found to be octahedral. Compounds $Cu(OAc)_2.2H_2O$ (31.25 µg/mL) for *C. Albicans*, **1** and **7** (31.25) for *L. monocytogens*, all compounds (except **6**) (7.60 µg/mL) for *B. subtilis,* **2** (31.25 µg/mL) for E. Coli, **7** (15.60 µg/mL) for *S. aureus*, **7** (31.25 µg/mL) for *E. Faecalis*, and **3** (15.60 µg/mL) for *P. aeruginoa* have the best activity.

5 Author contribution statements

Author 1 and 2 took part in the study's experimental study process and writing phase and provided control and supervision and also in the literature research, construction, and writing of the experiments.

6 Ethics committee approval and conflict of interest statement

"There is no need to obtain permission from the ethics committee for the article prepared".

"There is no conflict of interest with any person/institution in the article prepared".

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Additionals

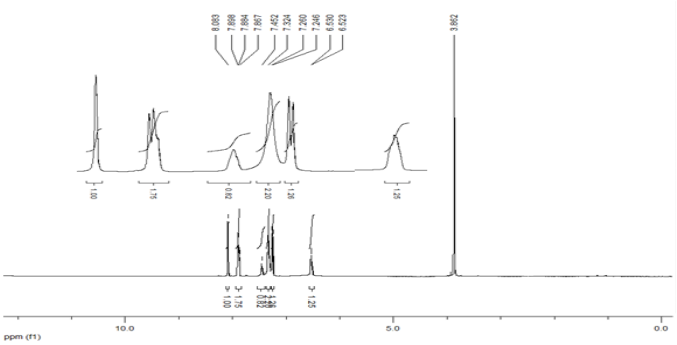

Figure S1. *^{1}H NMR spectra of compound **4**.*

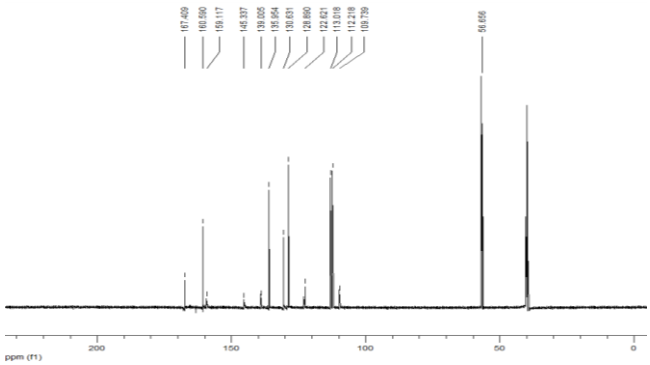

Figure S2. *^{13}C NMR spectra of compound **4**.*

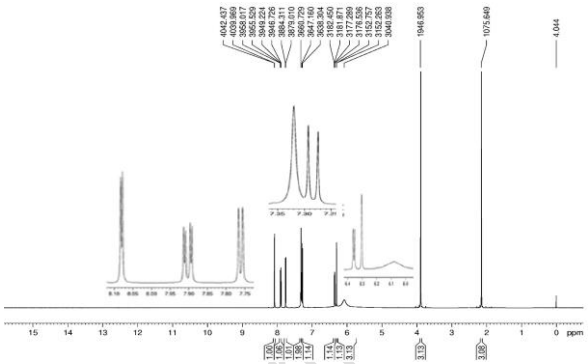

Figure S3. *^{1}H NMR spectra of compound **5**.*

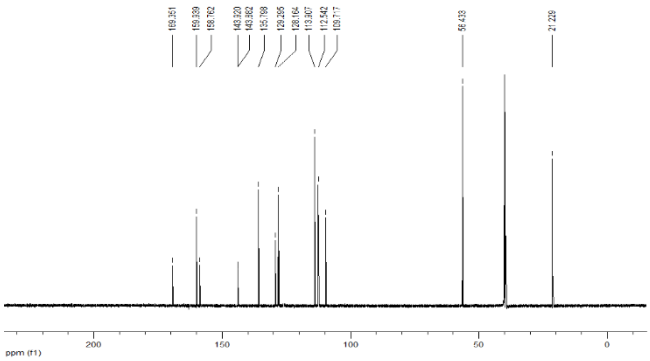

Figure S4. *^{13}C NMR spectra of compound **5**.*

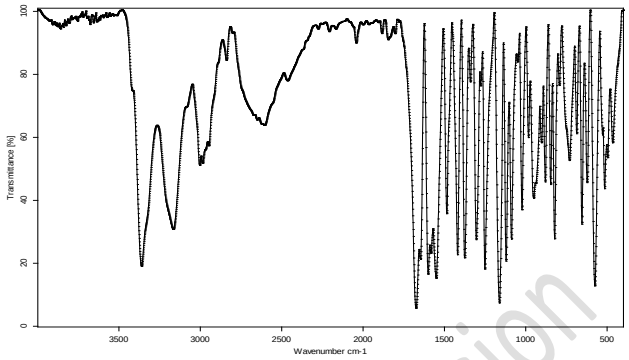

Figure S5. *IR spectrum of **4**.*

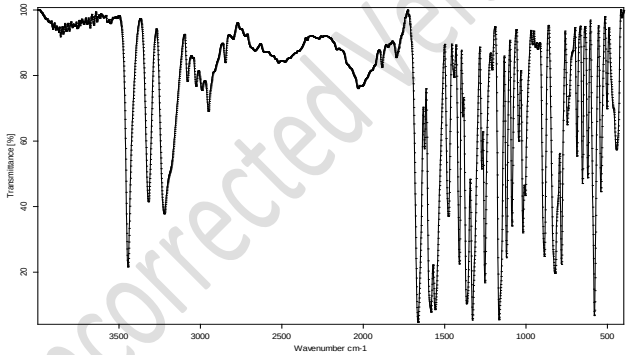

Figure S6. *IR spectrum of **5**.*

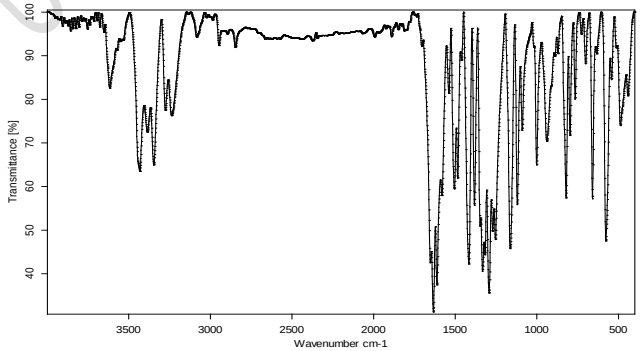

Figure S7. *IR spectrum of **6**.*

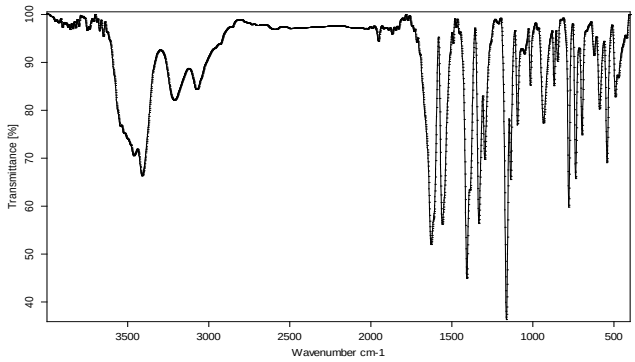

Figure S8. *IR spectrum of **7**.*