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Methyl-substituted 2-aminothiazole–based cobalt(II) and silver(I) complexes: synthesis, X-ray structures, and biological activities

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Abstract: 2-Aminothiazole derivatives bear three nucleophilic centers, i.e. endocyclic N, exocyclic NH_2, and S atom in the ring system. In addition to these centers there are π-electrons in the ring system which can also expectedly be involved in some sort of coordination. To the best of our knowledge the solid state coordination chemistry of such ligands has not been fully presented in the literature. These ligands (2-amino-4-methylthiazole and 2-amino-5-methylthiazole) were coupled with $CoCl_2$ under aerobic conditions to form tetrahedral complexes, bis(2-amino-4-methylthiazole)dichlorocobalt(II) (**1**) and bis(2-amino-5-methylthiazole)dichlorocobalt(II) (**2**). Reaction of 2-amino-5-methylthiazole with $AgNO_3$ led to an expected two-coordinated, bis(2-amino-5-methylthiazole)silver(I) nitrate (**3**) as crystalline material. In all complexes the coordination behavior of the aminothiazole derivatives was identical, coordinating to the metal center through endocyclic N atom. The structures of these complexes were confirmed by single-crystal X-ray analysis. Compounds (**1**–**3**) were screened for their antimicrobial potency against gram-negative (*E. sakazkii*, *E. coli*, *K. pneumoniae*) and a gram-positive bacteria (*S. aurus*). Additionally, their role as enzyme inhibitors (acetylcholinesterase, AChE, and butyrylcholinesterase, BChE) and their free radical scavenging ability (2,2-Diphenyl-1-picrylhydrazyl, DPPH, and 2,2'-azino-*bis*(3-ethylbenzothiazoline-6-sulphonic acid, ABTS) were studied. These ligands bear additional nucleophilic centers (S and NH_2) and can be involved in secondary interactions as confirmed by their solid-state structures. These interactions make the molecules biologically important and thus play a pivotal role in establishing the supramolecular network. We report here the coordination chemistry and selected biological applications of complexes **1**–**3**.

Key words: 2-Aminomethylthiazole, cobalt complexes, enzyme inhibition, antimicrobial agents, antioxidant agents

1. Introduction

There are numerous coordination compounds in the literature wherein metal ions are stabilized by monodentate heterocyclic organic ligands.[1–4] Most of the organic ligands containing noncarbon atom(s) are commercially available. They form complexes with several metal ions and play a key role in a number of useful applications. Among metal ions, Co(II) and Ag(I) ions are important owing to their presence in biological systems.[5–7] Five-membered heterocylic ring systems such as pyrazol,[1] thiophen,[8] oxazole[9] and their derivatives are well-known

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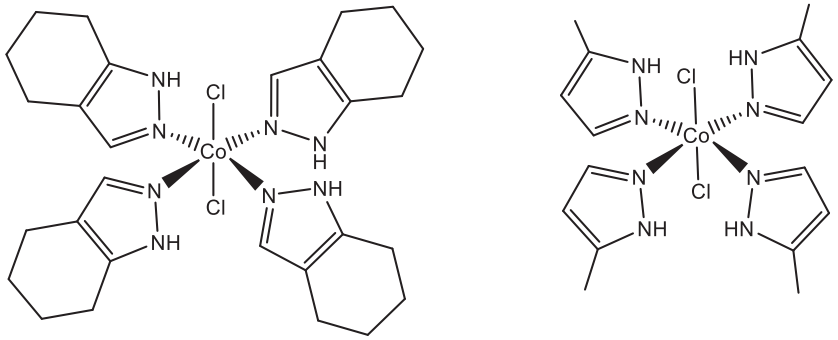
ligands in coordination chemistry. Thiazole is a monodentate five-membered heterocyclic ligand (terminal) containing N and S as heteroatoms and is a part of vitamin B1.[10,11] Compounds derived from thiazole have gained greater attention in synthetic coordination chemistry,[12−14] biological,[15,16] and nonbiological applications.[17,18] 2-Amino-4-methylthiazole and 2-amino-5-methylthiazole feature several commercial applications and act as starting precursors in a number of chemicals.[19−22]

Our research focuses on simple organic derivatives as ligands, particularly those containing more than one nucleophilic centers (either endocyclic or exocyclic) (Scheme 1).[1,23] 2-Amino-4-methylthiazole and 2-amino-5-methylthiazole are more attractive in terms of nucleophilic centers to act as ligand but a comprehensive literature survey indicates that coordination chemistry of these compounds as ligands is unexplored, particularly with Co(II) ion. Reacting these ligands with $CoCl_2$ led to tetrahedral bis(2-amino-4-methylthiazole)dichlorocobalt(II) (**1**) and bis(2-amino-5-methylthiazole)dichlorocobalt(II) (**2**), respectively. Reaction of 2-amino-5-methylthiazole with $AgNO_3$ formed, as expected, a two-coordinated, bis(2-amino-5-methylthiazole)silver(I) nitrate (**3**) complex as crystalline material. The coordination behavior of ligand was identical with both metal ions where only endocyclic N atom gets coordinated to the metal center in a similar manner as reported for Zn(II)[24] and Cd(II)[25] metal ions. All complexes were structurally characterized by X-ray diffraction and their antimicrobial, antioxidant, and enzyme inhibitory efficiency were studied.



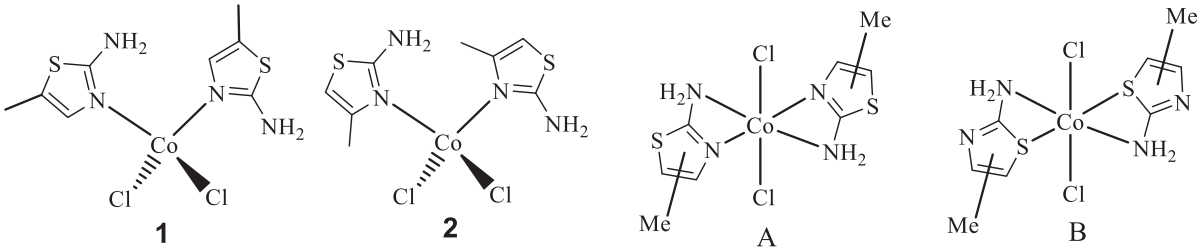
Scheme 1. Coordination compounds of Co(II) and N-donor pyrazolyl derivatives. Both ligands possess two nucleophilic centers.

2. Results and discussion

2.1. Chemistry and X-ray diffraction

There are no reports regarding coordination chemistry of 2-amino-4-methylthiazole and 2-amino-5-methylthiazole with Co(II) and Ag(I) metal ions. These compounds possess three possible nucleophilic centers, i.e. S, N (endocyclic), and NH_2 (exocyclic). The coordination chemistry of these derivatives as ligands can be interesting owing to the presence of these coordinating centers. Thus, the ligands were expected to afford 4-membered metallacycles (Scheme 2, structures A and B). Theoretical calculations reveal that both the N centers can be potential coordination sites owing to greater Mulliken charges and structure A would be the probable chelate.[26] However, reaction of the corresponding ligand with $CoCl_2$ in 2:1 stoichiometric ratios, respectively, instead afforded tetrahedral complexes (**1** and **2**) where the ligands were coordinated via endocyclic-N atom in a terminal fashion. These observations are also in contrast to our previously reported results[1,23] where the same metal afforded 6-coordinated complexes (Scheme 1). The resultant structures indicate that the basicity of the three centers is widely different; therefore, coordination with cobalt ion was highly selective through *endo*-N. This

behavior of the ligand is already reported for structurally analogous ligands with a number of metal ions.[27,28] In some reports[29,30], both nitrogen atoms of the thiazole ring gave two isomers with different biological activities.



Scheme 2. Structure of complexes **1** (2-amino-4-methylthiazole based) and **2** (2-amino-5-methylthiazole based), **A** and **B** are the proposed chelates of ligands (not obtained) with the same metal ion.

2.1.1. Description of compound 1

The molecular structure of compound **1** was confirmed by single-crystal diffraction analysis and is shown in Figure 1. The data pertinent to crystal structure determination and refinements are summarized in Table 1. The solid state structure shows that the compound crystallizes in monoclinic crystal system having the space group of $P2_1/n$. Ligands are arranged in distorted tetrahedral manner around the central metal atom. In the complex, two thiazole derived ligands are coordinated to cobalt through endocylic N-atoms. The average bond lengths for Co-N, and Co-Cl are 2.018Å, and 2.270Å, respectively. The bond angles around Co(II) ion ∠N1-Co1-Cl1, ∠N1-Co1-N1^i, ∠N1^i -Co1-Cl1, and ∠Cl1-Co1-Cl^i vary slightly from each other, 108.16°, 111.60°, 112.48° and 103.78°, respectively. Other angles around the metal ion are within the range as expected for a tetrahedral geometry with slight distortions.[31] Monodentate ligands (C1–C3, N1, S1) and (C5–C7, N3, S2) are planar with a slight RMS deviation of 0.0107 and 0.0043 Å, respectively. The dihedral angle between A and B is 71.61 (8)°. The plane C (Co1/Cl1/Cl2) is of course planar. The dihedral angle between A, C and B, C is 54.99 (6)° and 53.41 (5)°, respectively. Supramolecular structure of the compound in solid state is stabilized by short contacts and intramolecular (N-H – – – Cl 2.46Å), as well as intermolecular hydrogen bonding was observed, as depicted in Figure 2.

2.1.2. Structural description of complex 2

Crystals of complex **2** were isolated from the ethanolic solution and the structure of the compound was determined by single-crystal analysis, shown in Figure 3. Compound **2** crystallizes in trigonal system with space group $P3_112$ where the geometry around cobalt ion is distorted tetrahedral. Metal ion is coordinated with two 2-amino-5-methylthiazole ligands through endocyclic nucleophilic center (N atom) and two chloro ligands, in the same manner as in complex **1**. The average bond lengths for Co-N and Co-Cl were observed to be 2.015 Å, 2.013 Å and 2.255 Å, 2.263 Å, respectively. The bond angles ∠N3-Co1-N1, ∠Cl1-Co1-Cl2, ∠N1-Co1-Cl1, and ∠N1-Co1-Cl2 are 108.58°, 116.27°, 106.78° and 109.36°, respectively, which are in the expected range as reported for analogous tetrahedral compounds.[32] In comparison to octahedral cobalt complexes stabilized by relatively simple ligands, the effect of coordination number is obvious to cause bond contraction in tetrahedral complexes.[1] The molecules of compound **2** exhibit intramolecular as well as intermolecular N-H—Cl hydrogen bonding. The average separation between NH and Cl is 2.48 Å. Detailed hydrogen bond geometries found in complex **1** and **2** are summarized in Table 2.

Table 1. Crystal data and structure refinements of compounds **1**–**3**.

	Complex **1**	Complex **2**	Complex **3**
Empirical formula	$C_{16}H_{24}Cl_4Co_2N_8S_4$	$C_8H_{12}Cl_2CoN_4S_2$	$C_8H_{12}Cl_2AgN_5S_2O_3$
Formula weight	716.33	358.17	398.22
Temperature (K)	296	296	133
Wavelength (Å)	0.71073	0.71073	0.71069
Crystal system	Monoclinic	Trigonal	Monoclinic
Space group	$P2_1$/n	$P3_112$	$P2_1$/c
a,b,c (Å)	8.412(14), 13.462(19), 13.072(17)	8.864(3), 8.864(3), 16.792(6)	9.363(5), 5.754(3), 25.043(13)
apo (°)	90, 102.36(7), 90	90, 90, 120	90, 97.75(4), 90
Volume Å^3	1446.0(4)	1142.4(10)	1336.85(12)
μ(mm^{-1})	1.83	1.74	1.83
Z	2	3	4
Density (Mg m^{-3})	1.645	1.562	1.979
F (000)	724	543	792
(h, k, l) min	(–9, –17, –16)	(–7, –10, –20)	(–11, –7, –30)
(h, k, l) max	(10, 9, 16)	(11, 9, 9)	(11, 6, 30)
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.034, 0.094, 1.03	0.030, 0.067, 0.98	0.025, 0.063, 1.09
No. of measured, independent and observed $[I > 2\sigma(I)]$ reflections	9197, 3137, 2454	4064, 1659, 1398	17956, 2625, 2450
No. of Reflections/ Restrains/Parameters	3137/0/156	1659/0/79	2625/1/190

Table 2. Hydrogen-bond geometry (Å, °) pertaining to complexes **1** and **2**.

	D—H $\cdots$ A	D—H	H $\cdots$ A	$D \cdots A$	D—H $\cdots$ A
Complex 1	N2—H2A $\cdots$ Cl2	0.86	2.48	3.269(3)	153.4
	N2—H2B $\cdots$ Cl1^{i}	0.86	2.51	3.329(3)	159.6
	N4—H4D $\cdots$ Cl2	0.86	2.49	3.288(3)	154.2
	N4—H4E $\cdots$ Cl1^{ii}	0.86	2.52	3.320(3)	155.1
	Symmetry codes: (i) x+ 1/2, –y+ 1/2, z+ 1/2; (ii) x+ 1, y, z.				
Complex **2**	N2—H2A $\cdots$ Cl1^{i}	0.86	2.46	3.276(3)	159.0
	N2—H2B $\cdots$ Cl1^{ii}	0.86	2.61	3.361(3)	147.0
	C2—H4B $\cdots$ Cl1	0.96	2.94	3.729(7)	140.4
	Symmetry codes: (i) $x, x-y, -z+2$; (ii) $-y, -x, -z+5/3$.				

2.1.3. Structure of complex 3

The interaction of the ligand with Ag ion in its complex did not show remarkable changes as compared to complexes **1** and **2** (discussed above). An expected two-coordinated complex was obtained where the

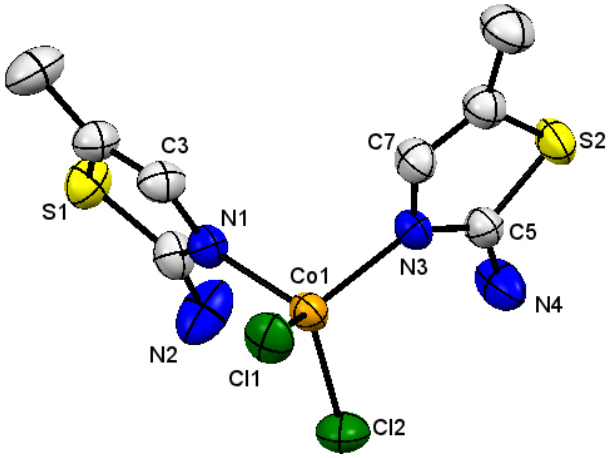


Figure 1. Molecular structure of compound **1** with partial numbering scheme, thermal ellipsoids are drawn at 50% probability level; hydrogen atoms are omitted for clarity reasons. Selected bond lengths (Å) and angles (°): Co1-N1 2.015(2), Co1-N3 2.013(2), Co1-Cl1 2.255(8), Co1-Cl2 2.255(8); Cl1-Co1-Cl2 116.27(3), N3-Co1-Cl1 106.78(7), N1-Co1-Cl2 109.36(8), N3-Co1-N1 108.58(8).

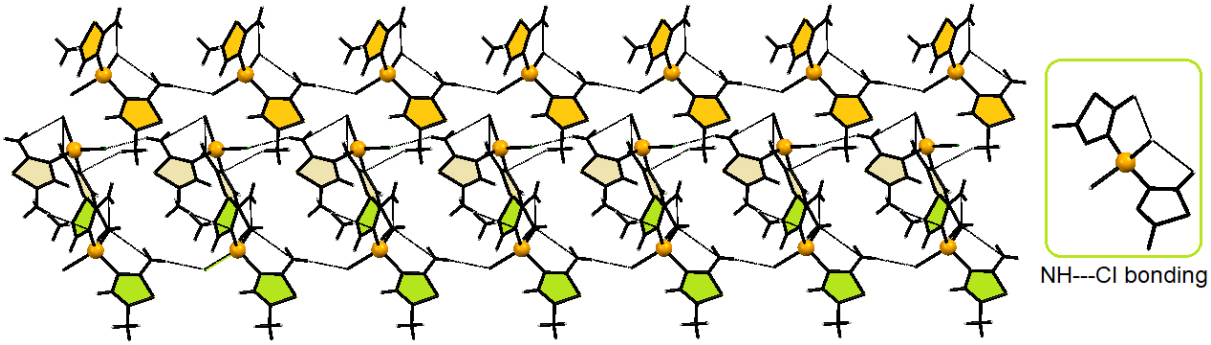


Figure 2. Intramolecular (right inserted) and intermolecular interaction in compound **1**, in both types of interactions the N-H and Cl are involved. Only three parallel layers of molecules are shown; suspended contacts are deleted.

coordination behavior of the ligands was similar to that observed for complexes **1** and **2**. The bond distances between Ag and N atoms were slightly different for the two ligands, i.e. Ag-N1 2.128 Å and Ag-N2 2.117 Å and are shorter than the reported complexes.[33] The linearity of the molecule considerably deviates from the perfect structure, ∠N1-Ag-N2 171°. Such type of deviation has been observed in Ag complexes with multifunctional ligands capable of making secondary interactions with the metal center.[34] The deviation from the linear geometry is because of the short-ranged interactions found in molecules of the compound. Thus, Ag ion is pseudo 5-coordinated, as depicted in Figure 4, inserted. Besides two nitrogen atoms (shown in Figure 4) of the coordinated ligands, Ag ion is also attached to S and C (through π-electrons) of the neighboring molecules and to an oxygen atom of the NO_3^- moiety, with observed distances of 3.388, 3.347, and 3.004 Å, respectively. The impact of Ag—O bond on the structure of the resultant complex is dominant as compared to Ag—S and Ag—C interactions (Figure 4) and causes a slight contraction (~ 10°) in the N-Ag-N bond. The NH_2 hydrogens are involved in hydrogen bonding with oxygen of NO_3^- group which makes both the thiazole rings coplanar with negligible deviation with respect to each other. Intermolecular argentophilic[35,36] or S—S interactions[37] were not observed as it had already been reported for Ag and other related complexes.

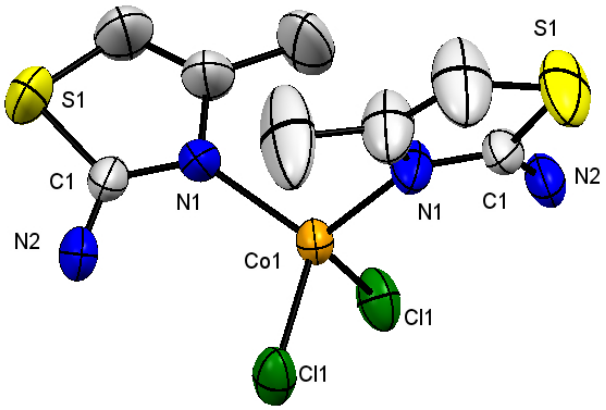


Figure 3. Molecular structure of compound **2** with partial numbering scheme, 50% thermal ellipsoids, hydrogen atoms are omitted for clarity. In some parts, the molecule shows disorder but connectivities can be established. Selected bond lengths (Å) and angles (°): Co1-N1 2.018(3), Co1-N1^{i} 2.018(3), Co1-Cl1 2.270(14), Co1- Cl1^{i} 2.270(13); N1-Co1-N1^{i} 111.60(2), N1-Co1-Cl1 108.16 (12), N1^{i}-Co1-Cl1 112.48(10), Cl1-Co1-Cl1^{i} 103.78(6).

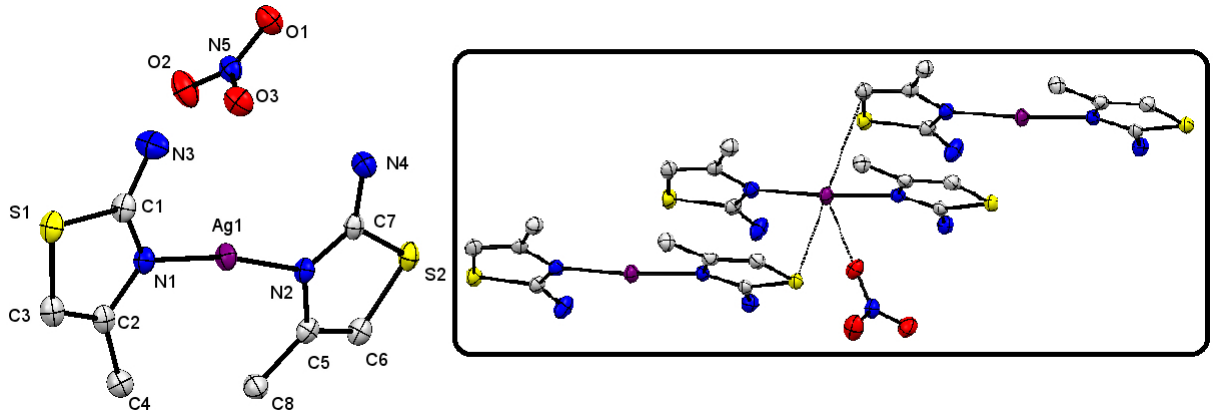


Figure 4. Molecular structure of compound **3** (Left) with numbering scheme, thermal ellipsoids drawn at 50% probability level, hydrogen atoms are omitted for clarity reasons. Right inserted shows secondary interactions wherein Ag is involved; such interactions bend the N-Ag-N bond by ca. 10°. Selected bond lengths (Å) and angles (°): Ag1- N2 2.1164(16), Ag1-N1 2.1277(16), S1-C3 1.734(2), S1-C1 1.737(2), N2-C7 1.319(3), N2-C5 1.401(3), N4-C7 1.333(3); N2-Ag1-N1 170.98(7), C6-S2-C7 89.43(10), C7-N2-Ag1 127.35(14), C5-N2-Ag1 121.45(13), C5-N2-C7 111.19(16).

2.2. Biological activities

2.2.1. DPPH and ABTS free radical scavenging activity of the synthesized complexes (1 and 2)

Scientific community is always interested to search for better reagents against certain ailments. Bioinorganic/coordination chemistry plays an active role to serve the humanity and has the credit of having pioneer anticancer agent.[38] In coordination compounds both ligand(s) and metal ion are equally important and while designing a drug for specific purpose, the compatibility of both these entities should critically be considered for a biological system. Free radicals produced in living cells are responsible for damaging tissues and cause certain disorders including cancer. The prevention of these reactive species are controlled by natural sources but the overproduction has to be cured by certain supplements. Transition metal complexes play important role as antioxidants.[1] Scavenging of a thermally robust and well-known free radical, 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-*bis*(3-ethylbenzothiazoline-6-sulphonic acid (ABTS) is a possible measure of antioxidant

potency of a particular reagent.[39,40] They show maximum absorption at 517 and 734 nm, respectively.[41,42] Change in the resultant absorbance of DPPH/ABTS and test compound is an indicator of radical scavenging activity. Percentages of radical scavenging activities for complexes **1**, **2** are summarized in Table 3 and the same results are graphically represented in Figures **5** and **6**, which shows similar gradation in a dose dependent manner as we have reported recently.[43]

Table 3. Percentages of DPPH and ABTS radical scavenging potentials of compounds **1,2***.

	Complex **1**		Complex **2**		Standard (gallic acid)	
	DPPH	ABTS	DPPH	ABTS	DPPH	ABTS
1000 ppm	67.21	65.42	62.31	59.42	84.51	87.66
500 ppm	63.90	59.91	58.32	52.49	77.84	81.64
250 ppm	57.09	55.29	42.89	39.74	73.50	76.01
125 ppm	51.23	45.20	33.10	29.78	65.74	70.46
62.5 ppm	41.21	25.36	27.34	24.30	61.56	64.50
IC_{50} value (µg/mL)	**114**	**165**	341	437	23.20	17.47

*The activities shown by complex **3** were negligible and have not been considered to be published.

It is evident from the table above that the sample solutions show significant antioxidant activities by showing considerable decrease in absorbance at 517 or 734 nm with increasing concentration of the respective compound. Although complexes **1** and **2** are structurally very close, their activity is quite different from each other. Compound **1** is a much more active antioxidant (67% and 65% against DPPH and ABTS, respectively) than compound **2** (62% and 59%, respectively), which can probably be attributed to the difference in the extent of hydrogen bonding existing in both the compounds. In compound **1**, a chloro ligand is involved in intramolecular hydrogen bonding with nitrogen of the amino group on both sides and the other chloro ligand is involved in intermolecular hydrogen bonding (Figure 2). In compound **2**, however, the situation is different where one chloro ligand is involved in intramolecular hydrogen bonding with nitrogen of the amino group on only one side and the other chloro ligand is involved in intermolecular hydrogen bonding. In compound **1**, the free rotation of thiazolyl ligands is restricted by intramolecular Cl– – –HN interaction which is the probable reason for the difference in activities of both the compounds.

2.2.2. Antibacterial activity of the synthesized complexes (1 and 2)

The antibacterial activities of the synthesized complexes (**1** and **2**) against four different bacterial strains, i.e. *E. sakazkii*, *E. coli*, *K. pneumoniae* (gram-negative), and *S. aurus* (gram-positive) were measured by agar disc diffusion method. Both complexes showed least activity compared to standard (Ceftriaxone) against the selected bacterial strains. Complexes **1** and **2** were comparatively more active against gram positive strain, i.e. *S. aurus,* by inhibiting growth in zones of 15 and 16 mm, respectively. The observed values for zones of inhibition are given in Table 4. Complex **3** was more active against *E. coli* and up to 17 mm of inhibition was observed. A comparison of these complexes with our recently published data[23] indicates that complexes **1**–**3** are relatively more efficient than tetrahydroindazole-based complexes of Co(II).

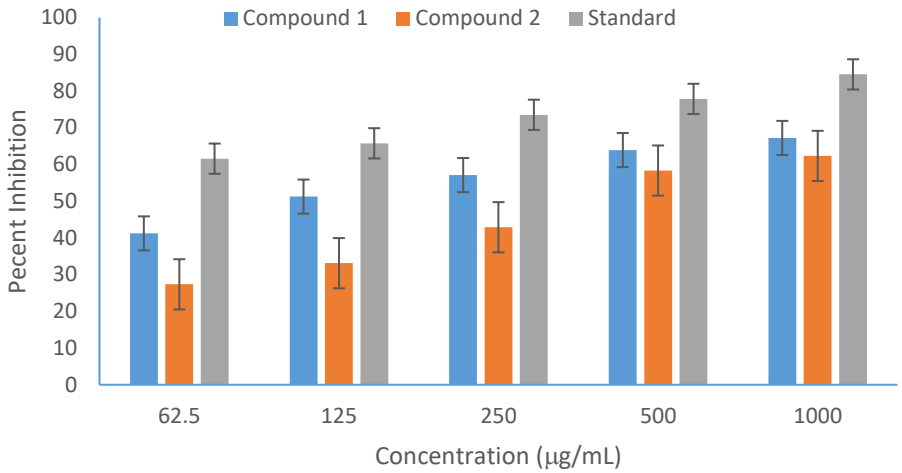


Figure 5. Graphical representation of percent inhibition of compounds **1** and **2** against DPPH, IC_{50} values are 114, 341, and 23.2 µg/mL for compounds **1**, **2**, and standard (gallic acid), respectively.

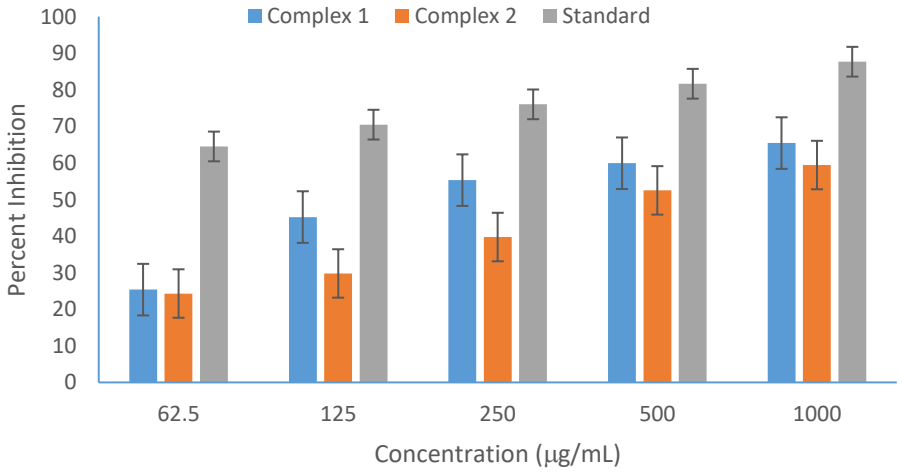


Figure 6. Graphical representation of percent inhibition of compounds **1** and **2** against ABTS, IC_{50} values are 165, 437, and 17.47 µg/mL for compounds **1**, **2**, and standard (gallic acid), respectively.

Table 4. Zone of inhibition of complexes **1**–**3** (mm) against selected strains.

S. No	*E. sakazkii*	*E. coli*	*K. pneumoniae*	*S. aureus*
1	09	06	09	15
2	12	11	13	16
3	15	17	05	12
Ceftriaxone	27	35	28	31

2.2.3. Enzyme inhibition

Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) enzymes interrupt certain biological processes which are the main cause of Alzheimer's disease (AD). In the treatment of this disease certain agents are able to restore the level of acetylcholine by inhibiting AChE and BChE. For a long time, several reagents have been tested but their use as medicine has been questioned due to side effects and low efficacy. In order to address

this challenge, the search for an efficient agent with least side effects, easy availability, and economic feasibility is always of interest. Compounds **1**–**3** were tested as inhibitors against AChE and BChE by following the reported procedure.[23] Complex **1** was more active in inhibiting AChE with a comparatively low IC_{50} value of 89.21 µg/mL. The same complex showed less efficiency against BChE with IC_{50} value = 191.65 µg/mL. Complex **2** was least active against these enzymes IC_{50} = 294.71 µg/mL (AChE), 193.06 µg/mL (BChE). Silver complex showed reasonable activity against both enzymes, i.e. 148.40 µg/mL (AChE) and 147.63 µg/mL (BChE) (Table 5).

Table 5. AChE and BChe inhibition studies of complexes 1–3*.

Compound	Conc. µg/mL	AChE % inhibition	IC_{50} µg/mL	BChE %inhibition	IC_{50} µg/mL
1	1000	71.23	89.21	67.34	191.65
	500	63.31		58.23	
	250	54.81		51.21	
	125	53.76		49.22	
	62.5	45.22		39.49	
	31.625	39.00		25.22	
2	1000	75.32	294.71	69.90	193.06
	500	64.11		57.31	
	250	47.22		54.23	
	125	46.10		41.21	
	62.5	32.21		28.70	
	31.625	21.03		15.40	
3	1000	74.32	148.40	74.32	147.63
	500	63.23		63.23	
	250	59.32		59.32	
	125	46.90		46.90	
	62.5	31.02		31.02	
	31.625	27.31		27.31	

*Galantamine was used as standard with an IC_{50} value of 12.65 (AChE) and 24.99 (BChE).

2.3. Conclusions

Straightforward synthesis of cobalt(II) complexes with nitrogen donor ligands namely 2-amino-4-methylthiazole and 2-amino-5-methylthiazole, was carried out. The complexes crystallize in monoclinic (**1**,**3**) and trigonal (**2**) crystal systems and the geometrical parameters (bond lengths and angles) are quite close to each other. The geometry around the cobalt metal center is essentially tetrahedral. Slight deviations in cobalt complexes are because of different types of ligands attached to the same metal center. The solid-state intramolecular and intermolecular interactions are the probable reason of this deviation in complexes.

The synthesized complexes were evaluated for their antioxidant and antibacterial potentials. The compounds show moderate activity against selected bacterial strains (*E. sakazkii*, *E. coli*, *S. aurus*, and *K. pneumoniae*). Free radical scavenging potentials were tested against DPPH/ABTS free radical but unfortunately the results were not satisfactory. Cobalt complex **1** is a better AChE inhibitor with a considerable lower IC_{50} value of 89.21 µL/mL), Silver complex **3** showed reasonable AChE and BChE inhibition, IC_{50} value 148.40

and 147.63 µL/mL, respectively. Compound **2** is a poor inhibitor for AChE as well as BChE. The activity against gram-positive bacteria can be improved by further modification of the coordinated ligands. Compared to the available standards, these complexes have moderate antibacterial, antioxidant, and enzyme inhibition potentials.

3. Experimental

3.1. General

Ethanol (analytical grade), 2-amino-4-methylthiazole, 2-amino-5-methylthiazole, silver nitrate, and cobalt(II) chloride are commercial products and were used without further purification. The melting points of the synthesized complexes were determined with the help of Stuart-SMP10 (Japan) melting point apparatus and are uncorrected. ^{1}H- and ^{13}C-NMR spectra (Ag complex) were recorded on VARION INOVA 300 MHz using deuterated DMSO in 5-mm o.d. NMR tubes.

3.2. X-ray structure determination

The single-crystal X-ray diffraction data (Mo-Kα, λ = 0.71073 Å) were collected by using Bruker kappa APEXII CCD diffractometer (complexes **1** and **2**) and STOE-IPDSII/STADIVARI (**3**), the later fitted with a low temperature unit. A single-crystal of suitable dimensions of complex **3** was selected in perfluorinated oil at room temperature[44] and diffraction data were measured at 133K. Crystal structures were refined with the help of SIR97,[45] SHELXL97,[46,47] WinGX,[48] and PLATON.[49]

3.3. Syntheses of complexes 1–3

Complex **1** was synthesized by drop wise addition of an ethanolic solution of 2-amino-4-methylthiazole (0.5 g, 4.3 mmol) to an ethanolic solution of $CoCl_2.6H_2O$ (0.52 g, 2.2 mmol) with continuous stirring. The reaction mixture was stirred for 24 h and upon removal of the solvent under reduced pressure the volume of the reaction mixture was reduced to one-third. After a few days, dark green crystals appeared. Melting point = 310–313 °C.

Complex **2** was synthesized by mixing 2-amino-5-methylthiazole (0.5 g, 4.3 mmol) and $CoCl_2.6H_2O$ (0.52 g, 2.2 mmol) in the same way as discussed above. Melting point = 315–218 °C.

Complex **3** was obtained in 10 mL of EtOH, by the reaction of 2-amino-4-methylthiazole (0.5 g, 4.3 mmol) and silver nitrate (0.37 g, 2.1 mmol). The solid residue obtained was separated and crystals were obtained in MeOH at room temperature. Melting point = 211–214 °C. ^{1}H-NMR (300 MHz): δ (ppm) = 2.17 (s, 6H, Me), 6.32 (s, 2H, CH), 7.76 (br, 4H, NH_2); ^{13}C-NMR (75 MHz): δ (ppm) = 18.2, 101.8, 145.4, 171.5.

3.4. Antibacterial, enzyme inhibition, and antioxidant activities of compounds 1–3

Antibacterial efficiency against selected bacterial strains, *E. coli* (gram-negative), *E. sakazkii* (gram-negative), *K. pneumoniae* (gram-negative) and *S. aureus* (gram-positive) was studied. Enzyme inhibition (AChE and BChE) and antioxidant potential (DPPH and ABTS) of complexes **1–3** were studied by following the procedure discussed in our recently published article.[23]

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Supplementary material

Crystallographic data for the structure have been deposited to the Cambridge Crystallographic Data Center, CCDC No. 1825355–1825357 (**1**–**3**). These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.