Synthesis, Characterization and Antibacterial Properties of Complex [Ag(SCN)(2-NH2py)]

Dewi Mariyam¹, I Wayan Dasna¹²*, Husni Wahyu Wijaya¹², Danar¹

¹Department of Chemistry, Faculty of Mathematics and Natural Sciences, State University of Malang, Semarang road 5 Malang 65145, Indonesia
²Centre of Advanced Material for Renewable Energy, State University of Malang, Semarang road 5 Malang 65145, Indonesia
*Corresponding author: idasna@um.ac.id

Abstract. The reaction of AgSCN with 2-aminopyridine in ammonia solution produces the colorless crystal of catena-poly [Ag(SCN))(C6H5N2)]n. The crystals were characterized by FTIR analysis and single crystal X-Ray diffraction. The silver(I) ion bind to one N atom of 2-aminopyridine, one N atom of thiocyanate and two S atoms of two thiocyanates to form a pseudo-tetrahedral complex. The presence of thiocyanates bridge ligand give an one-dimensional polymer. Complex [Ag(SCN)(2-NH2py)] crystallizes in monoclinic lattice and P21 space group with a=9.122(3) Å, b=4.1506(15) Å, c=11.269(4) Å, α= γ= 90°, β= 109.214(8)°, R= 0.0287. Intermolecular hydrogen bonds between amino group and thiocyanate NH–H…N–CS (2.389 Å) are also found in this structure. In vitro antibacterial screening complex was evaluated against two bacteria (Escherichia coli and Staphylococcus aureus). The results show that complex has higher antibacterial activity than 2-aminopyridine and KSCN. This is due to central ion and the ability of the ligand to interact with membrane proteins.

Keywords: Ag(I) complex, 2-aminopyridine, KSCN, characterization, antibacterial activity.

1 Introduction

Complexes of heterocyclic nitrogen ligands are one of the coordination compound types that have been widely developed because of their potential as antimicrobials [1–4]. Replacing the -CH group with an N atom in the cyclic has a significant effect on the chemical properties and interactions which can influence the pharmacological properties of the compound [5]. Heterocyclic nitrogen ligands such as pyridine and its derivatives are known to permanently damage cell membranes through the activation of oxidative stress in the cell membrane. Then, heterocyclic nitrogen ligands can enter the genetic material and inhibit or modify the genetic replication process leading to cell damage and death [6]. Furthermore, pyridine derivative can modify the DNA of E. coli bacteria and change the spatial structure of lipopolysaccharides in their cell membranes. One of the frequently used N-heterocyclic pyridine derivative ligands is aminopyridine (x-NH2py, x= 2,3, or 4). x-NH2py has potential...
as a bidentate ligand through the formation of coordinating covalent bonds with the N of the pyridine ring and the N in the –NH2 group.

Complexes with 2-, 3-, or 4-NH2py ligands show that NH2py tends to act as a monodentate ligand by binding to the central atom via the N pyridine ring. Complexes that have been reported such as [Ni(NCS)2(2-NH2py)2.C4H10O] [7], {∞[Cd(µ-SCN)2(4-NH2py)2]} [8], [Cu(SCN)2(x-NH2py2)] (x=2, 3, or 4) [4], and [M(3-NH2py2)(dca)]2 (M=Mn2+, Cu2+, Cd2+, or Co2+; dca = dicyanamide) [1,9–11], [AgL(x-NH2py)2] [12–16] demonstrated the formation of polymer complexes via bridge formation by bidentate ligands such as dicyanamide, thiocyanate and azide. Several other complexes with monodentate ligands such as Cl– such as [CoCl2(4-NH2py)2] [17], [ZnCl2(2-NH2py)2] [18], [CoCl2(3-NH2py)2] [19], [ZnCl2(3-NH2py)2] [20] forms a molecular complex with a coordination number of 4 with a distorted tetrahedral geometry. Based on these facts, anion ligands that coordinate covalent bonds with the central atom influence the formation of complex compound structures with ligands either 2-, 3- or 4- NH2py, both polymeric and molecular.

Silver(I) is one of the ions that are widely used in the development of polymer coordination compounds because of the various geometries and types of coordination that could be formed. The development of silver(I) complex compounds with pyridine and its derivatives has become an interesting topic because their structures allow them to form monomers, dimers and even polymers, as well as their biological activity which are quite extensive. Silver complexes with 2,3 and 4 aminopyridines have been reported to form complexes with various geometries such as, linear [12,13,16,21], trigonal geometry [15,21,22], square-planar geometry [23], tetrahedral [24] and etc. In general, the aminopyridines are bonded to central ions through the N atoms of the pyridine ring, but Golder et al., 2010 showed the formation of 1-dimensional polymers through 4-aminopyridine bridge ligand in their complex. The complexes of silver(I) with bidentate anion ligands such as WO42-, [N(CN)2]-, SCN-, NCO- allow the formation of polymer complexes in either 1-dimensional, 2-dimensional, or 3-dimensional. Therefore, Ag(I) polymer complexes with bridging ligands need to be studied both in terms of their structure and application potential.

Since the 18th century, silver(I) and its compounds have been used as antimicrobial agents. Silver compounds have been used in a variety of medicinal applications, especially those related to infectious diseases, such as antiseptic and for the treatment of burns. The mechanism of silver complexes as antibacterials is related to the slow release of Ag+ ions and reactions with thiol functional groups on proteins or with functional groups on enzymes. Ligands in the Ag(I) complex generally work as carriers/carriers for Ag(I) ions. In addition, silver ions can also produce reactive oxygen species that target lipids, DNA, RNA, and proteins, thereby causing damage to membranes, proteins, and DNA. Therefore, structure determination and antibacterial activity tests of the complex [Ag(SCN)(2-NH2py)] need to be carried out to determine the structure and potential application of the complex as an antibacterial agent.

2 Experimental Details

2.1 Synthesis of Complex

AgNO3 Merck, p.a, Na[N(CN)2] sigma aldrich, p.a, 2-aminopyridine Merck, p.a, acetonitril J.t Baker, p.a, and demineralized water were used without further purification. Complex was synthesized according to previous report Yu-Guang Li, et al. (2005) [16]. 1 mmol (0,1539 g) of AgNO3 and 1 mmol (0,0972 g) of KSCN were dissolved in demineralized water. Then, the solution of KSCN was slowly added to the AgNO3 solution. The solution was stirred
continuously for 1 hour. The white solid was filtered and dried. The procedures were repeated until filtrate doesn't produce white precipitate. The white solid of AgSCN solid (1 mmol) was dissolved in ammonia solution. 1 mmol (0.0941 gram) of 2-aminopyridine was dissolved in acetonitrile. [Ag(NH3)2]SCN solution was slowly added to 2-aminopyridine and stirred for 24 hours in room temperature. After a week of slow evaporation solution, colorless crystals were obtained.

2.2 Characterization Technique

Melting point temperature was measured in the 30-300 °C range using the Fisher-John Melting Point Apparatus. The electrical conductivity of complex solutions was measured using Cyberscan CON 11/110 conductivity meter. The infrared spectra were recorded using Shimadzu spectrophotometer type IRPrestige21 on KBr pellets in the 4000-400 cm\(^{-1}\) range.

2.3 Single Crystal X-Ray Structure Determination

Intensity data were gathered at 236 K using XRD single crystal Bruker, D8 Quest Diffractometer equipped with a CCD area detector, and Mo K\(\alpha\) source (\(\lambda = 0.71073 \text{ Å}\)) monochromated by layered confocal mirrors. Data reduction and scaling were performed using Bruker APEX 4 suite, and absorption correction was performed using SADABS. SHELXT was used to solve the initial structure, revealing non-hydrogen atom's positions, which was refined using the SHELXL program on a ShelXle user interface. Anisotropic refinement was performed on non-hydrogen atoms. Hydrogen atoms were placed in the calculated positions using a riding model.

2.4 Antibacterial Activity Test

The antibacterial tests were conducted in the Laboratory of Microbiology, State University of Malang. The tests were done on different types of pathogen bacteria, gram-positive-Staphylococcus aureus and gram-negative- Escherichia coli. The reference antibacterial drug chloramphenicol was evaluated for its antibacterial activity, and the results were compared with those of the free ligands and the complexes. Samples were dissolved in the DMSO 0.5% to obtain 1 mg/mL solutions. The method used is the disc diffusion method [25,26]. The disc containing antimicrobial agents or compounds was applied to the MHA plate within 20 min after inoculating it with the bacteria. Three discs were coated per petri dish. The plates were inverted and incubated at 37 °C for 24 h. After that, the zones of complete inhibition were measured.

3 Results and Discussion

3.1 Synthesis of Complex

The reaction between AgSCN and 2-NH2py in ammonia solution and acetonitrile produces needle-shaped and colorless crystals. The reaction of its formation is illustrated in Figure 1. Ammonia solution used to dissolve the AgSCN reactant to form a complex [Ag(NH3)2]SCN which can be dissolved in water [27]. The melting point measurement result shows that complexes begin to decompose at 108 °C, marked by a change in crystal color from colorless
to white. The results of the electrical conductivity test show that complex have an electrical conductivity value 74.6 µS (<100 µS). This result shows that complex is non-electrolyte compounds [28]. Based on these references, complex [Ag(SCN)(2-NH2py)]n in methanol solvent is molecular complex.

![Fig. 1. Reaction of formation complex [Ag(SCN)(2-NH2py)]n](image)

### 3.2 FTIR Analysis

A shift in the wavenumber towards a smaller direction indicates that the group is directly involved in the bond formation [4] and it is generally known that the NH2 stretching vibration undergo bathochromic/red shift when the N atom of the amino group is directly involved in the formation of coordination bonds. (Δλ = 150-200 cm⁻¹) [29,30]. The bathochromic shift is caused by a change in hybridization due to the formation of coordination bonds through lone pair nitrogen and a change in NH2 geometry, resulting in a decrease in the stretching and bending vibration energy constants in the -NH2 group [30]. Based on Table 1, it can be seen that the symmetric and asymmetric stretching vibrations of –NH2 do not experience a significant shift in the IR spectra of the four complexes, so it can be seen that the 4-NH2py ligand is not bound through the N atom of the –NH2 group. Hypsochromic shift in wavenumber in ring breathing vibrations indicates the formation of coordination bonds using lone pair electrons from N endocyclic pyridine [30].

The nature of the thiocyanate anion which is able to form bonds via the S atom or N atom can also be observed through the IR spectrum. If the thiocyanate anion bonds through the N atom, then the C-N vibration will shift towards a smaller wavenumber (bathochromic/red shift) and the peak of the S-C stretching vibration will shift to a larger wavenumber (hypochoromatic/blue shift) and vice versa [4]. The thiocyanate ligand has a coordination bond with Ag⁺ via the S atom, supported by a decrease in the S-C stretching vibration wavenumber.
Fig. 2. FTIR spectra of complex, KSCN, and 2-NH2py

<table>
<thead>
<tr>
<th>Vibration</th>
<th>2-NH2py</th>
<th>KSCN</th>
<th>[Ag(4-NH2py)(SCN)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\nu_{as}(\text{NH}_2)$</td>
<td>3453s</td>
<td></td>
<td>3451s</td>
</tr>
<tr>
<td>$\nu_{s}(\text{NH}_2)$</td>
<td>3306s</td>
<td></td>
<td>3348s</td>
</tr>
<tr>
<td>$\nu(\text{C=N} \text{ ring})$</td>
<td>1503s</td>
<td></td>
<td>1487s</td>
</tr>
<tr>
<td>VCN</td>
<td>2108s</td>
<td></td>
<td>2106s</td>
</tr>
<tr>
<td>VSC</td>
<td>743s</td>
<td></td>
<td>732s</td>
</tr>
</tbody>
</table>

3.3 Crystal Structure Determination

Determination of the structure of complex compounds was carried out using APEX 3 software after obtaining intensity data from the single crystal XRD instrument. The refinement process has been completed if data is obtained with an R factor value $< 5\%$. The results of the refinement of complex compounds obtained crystallographic data as shown in Table 2.

<table>
<thead>
<tr>
<th>Complex</th>
<th>[Ag(SCN)(2-NH2py)]$_{n}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. CCDC</td>
<td>2234646</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>C$_6$H$_6$AgN$_3$S</td>
</tr>
<tr>
<td>Empirical mass</td>
<td>260.07</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>$P2_1$</td>
</tr>
</tbody>
</table>
The Ag$^+$ ion binds to one N atom from the pyridine ring, one N from the thiocyanate and 2 S atoms from the SCN$^-$ bridge ligand to form a pseudo-tetrahedral complex (Figure 3). The asymmetric unit of complex consists of one Ag$^+$ central ion, one 2-NH$_2$py ligand and one thiocyanate ligand. The Ag-N NH$_2$py bond length (Table 3) shows a longer bond compared to the Ag-N 2-NH$_2$py bond length in complexes [Ag(2-NH$_2$py)$_3$(NO$_3$)] (Ag-N 2.141-2.179 Å) [15] and [Ag(2-NH$_2$py)$_2$(NO$_3$) (Ag-N 2.1406-2.1413 Å) [13]. This is due to the formation of polymers which causes the molecules to be close each other and the bond angles are distorted in a smaller direction. As a result, the steric effect generated in the polymer molecule becomes greater, so the Zn-N 2-NH$_2$py bond lengthens. Two Ag-S bonds show slightly different bond lengths, due to differences in steric effects from the environment around the Ag-S bond.

![Fig. 3. Structure of complex [Ag(SCN)(2-NH$_2$py)]$_n$

Table 3. Geometric parameters (Å, °) of complex [Ag(SCN)(2-NH$_2$py)]$_n$

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length (Å)</th>
<th>Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ag1—N1</td>
<td>2.257 (4)</td>
<td>118.60 (16)</td>
</tr>
<tr>
<td>N1—Ag1—N2</td>
<td>2.296 (4)</td>
<td>122.45 (12)</td>
</tr>
<tr>
<td>Ag1—N2</td>
<td>2.257 (4)</td>
<td>118.60 (16)</td>
</tr>
<tr>
<td>N1—Ag1—S1$^i$</td>
<td>2.296 (4)</td>
<td>122.45 (12)</td>
</tr>
</tbody>
</table>
Through the a-axis, the expanded of the complex structure forms a staircase-like structure that extends infinitely along the b-axis (Figure 4a). Complex crystallizes in a monoclinic lattice with space group P21 (Figure 4b). There are two molecules in each unit cell, where one complex 5 molecule comes from the results of the screw axis symmetry operation 21 (-x,½+y,-z). Hydrogen bonds between the H of the amino group and the N of the thiocyanate (NH—H···N—CS 2.389 Å) are also found in the crystal packing.

### 3.4 Antibacterial Properties

The antibacterial activity test of compounds was carried out using the Kirby-bauer disk diffusion method against 2 types of bacteria, each representing gram-positive bacteria (S.aureus) and gram-negative bacteria (E.coli). After incubation for 24 hours, a clear zone was obtained (Figure 5) which shows the zone of bacterial growth inhibition by complex. The bacterial inhibition zone of compounds is shown in Table 4. Based on the test results, complex has higher antibacterial activity than KSCN and 2-aminopyridine. This is related to decrease in the polarity of the metal ion due to the sharing of some of the charge of the central positive atom with the ligand donor atom, resulting in delocalization of electrons in the metal complex. Reducing the polarity of the complex increases the hydrophobic and lipophilic character of the metal complex, allowing it to permeate the lipid layer of the bacterial membrane [25]. However, the antibacterial activity of the complex was lower than that of silver salt and chloramphenicol. The activity of silver-based complexes is strictly connected to their water solubility and stability, lipophilicity, redox ability and rate of release silver ions [31]. Silver salts tend to dissolve more easily in water, and the release of silver(I) ions is faster from the complex, so that silver(I) ions diffuse more easily and bind to active protein groups in bacteria.
4 Conclusion

The complex [Ag(SCN)(2-NH2py)]ₙ was synthesized using direct method by mixing solution of AgSCN: 2-NH2py with ratio 1:1 at room temperature. The complex has a distorted pseudo-tetrahedral geometry and crystallizes in the P2₁ monoclinic crystal system. Ag⁺ ion bind through N atom of the pyridine ring. The SCN⁻ ligand in the complex becomes a bridge ligand through the N atom and S atom to form one dimensional polymeric complex. The results of the antibacterial activity test showed that the complex had antibacterial activity at an intermediate level, and showed better antibacterial activity than the free ligand, but was weaker than silver salt and chloramphenicol.

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