Synthesis and structural characteristics of silver(I) complex with *N*-benzylthiabendazole

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Abstract: Thiabendazole (TBZH) is well known for its antifungal and antihelmintic effects without exhibiting toxicity to humans. Different studies have shown that substitution with various alkyl or aryl groups at different positions on the benzimidazole or thiazole rings of TBZH can significantly influence its biological activity. Furthermore, replacing the hydrogen atom of the N–H group in TBZH with a benzyl substituent has been reported to increase its lipophilicity. In the present study, *N*-benzylthiabendazole (*N*-BzTBZ) was used as a ligand for the synthesis of a new silver(I) complex, $[Ag(N\text{-}BzTBZ)_2]CF_3SO_3$. The reaction between the *N*-BzTBZ ligand and $AgCF_3SO_3$ was carried out in an equimolar ratio in ethanol by stirring at room temperature for 24 h. The resulting complex, $[Ag(N\text{-}BzTBZ)_2]CF_3SO_3$, was structurally characterized using various spectroscopic methods, including IR and ^1H NMR spectroscopy, and its crystal structure was determined by single-crystal X-ray diffraction analysis. Moreover, the solution stability of the synthesized complex was evaluated by UV-Vis spectroscopy, cyclic voltammetry, and molar conductivity measurements.

Keywords: silver(I) complexes, *N*-benzylthiabendazole, spectroscopic and electrochemical methods

1. Introduction

The continuous development of new potential drugs with desired biological properties is essential for the successful treatment of infectious and degenerative diseases [1]. Metal-based drugs have been recognized as promising candidates for reducing mortality and preserving global health, as the incorporation of transition metal ions into organic compounds can significantly enhance their biological activity [1]. The successful use of silver and its compounds in treating microbial infections has been known since ancient times [2]. One of the most notable examples of silver use in medicine is its complex with sulfadiazine (AgSD), formulated as a cream for preventing wound infections after burns [2]. Since the discovery of antimicrobial action of AgSD, many other silver(I) complexes have been synthesized and investigated for the treatment of microbial infections [2].

Therefore, in this study, we used *N*-benzylthiabendazole (*N*-BzTBZ) as a ligand for the synthesis of a new silver(I) complex, [Ag(*N*-BzTBZ)$_2$]CF_3SO_3. The synthesized complex was characterized using spectroscopic and electrochemical methods.

2. Methodology

2.1 Materials and measurements

Silver(I) trifluoromethanesulfonate, ethanol, acetonitrile, dimethyl sulfoxide (DMSO), and deuterated dimethyl sulfoxide (DMSO-d_6) were purchased from Sigma-Aldrich. All chemicals were of analytical reagent grade and used without further purification. IR spectra were recorded using a Perkin-Elmer Spectrum Two spectrometer in the range of 4000–450 cm^{-1}, prepared as KBr pellets. ^1H NMR spectra were obtained at room temperature on a Bruker Avance 300 spectrometer operating at 300 MHz. For NMR analysis, 5.0 mg of the compound was dissolved in 0.6 mL of DMSO-d_6 and transferred into a 5 mm NMR tube. Chemical shifts (δ) are reported in parts per million (ppm), and coupling constants (J) in Hertz (Hz). UV–Vis spectra were recorded on a Shimadzu UV-1800 spectrophotometer over a wavelength range of 1100–200 nm. The concentration of the complex solution was 3.2×10^{-5} M. Molar conductivity measurements were performed using a Crison Multimeter MM 41 digital conductivity meter. The solution of the complex in DMSO had a concentration of 1.0×10^{-3} M. Cyclic voltammetry (CV) measurements were carried out using an AutoLab PGSTAT204 potentiostat/galvanostat. A three-electrode cell (5.0 mL) was employed, consisting of a glassy carbon (GC) working electrode, a Ag/AgCl (saturated KCl) reference electrode, and a platinum wire counter electrode. The complex was dissolved in DMSO at a concentration of 1.0×10^{-3} M for electrochemical analysis.

2.2 Synthesis of silver(I) complex with N-benzylthiabendazole

The silver(I) complex, [Ag(*N*-BzTBZ)$_2$]CF_3SO_3, was synthesized by adding 1.0 mmol of $AgCF_3SO_3$ (256.9 mg) to a solution of the *N*-BzTBZ ligand (277.3 mg, 1.0 mmol) in ethanol. The reaction mixture was stirred at room temperature in the dark for 24 h. The resulting white precipitate was collected and then dissolved in 10.0 mL of acetonitrile, from which colorless crystals of the complex were obtained upon slow evaporation.Yield (calculated based on the *N*-BzTBZ ligand): 218.3 mg (52%).

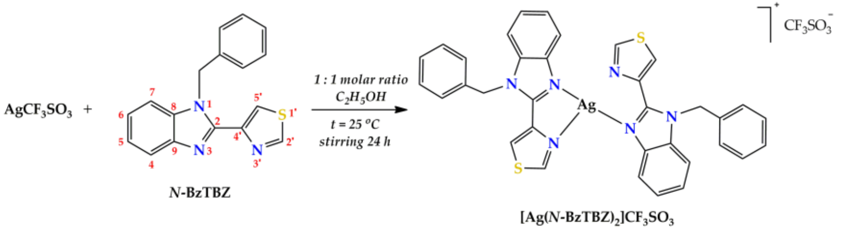
Anal. Calc. = $C_{35}H_{26}AgF_3N_6O_3S_3$ (MW = 839.68): C, 51.70; H, 3.77; N, 9.52. Found: C, 51.89; H, 3.65; N, 9.37%. ^1H NMR (300 MHz, DMSO-d_6): δ = 6.04 (*s*, –CH_2–), 7.08-7.41 (*m*, $H_{\text{phenyl group}}$), 7.70 (*s*, H4 and H7), 7.82 (*s*, H5 and H6), 8.63 (*s*, H5′), 9.39 (*s*, H2′) ppm. IR (KBr, ν, cm^{-1}): 3089m, 3066w, 3032w ($\nu(C_{ar}–H)$), 2979w (ν(C–H)), 1619w, 1497w, 1468w, 1439s, 1424m, 1392w ($\nu(C_{ar}=C_{ar})$ and $\nu(C_{ar}=N)$), 1283s, 1270s, 1250s, 1228vs, 1221vs

(ν_{as}(SO_3)), 1195m (ν_s(CF_3)), 1153vs (ν_{as}(CF_3)), 1084m, 1021vs (ν_s(SO_3)), 739s (γ(C_{ar}–H)). UV-Vis (DMSO, λ_{max}, nm): 302.0 ($\varepsilon = 2.6 \times 10^4$ $M^{-1}cm^{-1}$). Λ_M (DMSO): 39.4 $\Omega^{-1}cm^2mol^{-1}$.

3. Results and Discussion

3.1 Synthesis of silver(I) complex with N-benzylthiabendazole

The silver(I) complex was synthesized according to the route presented in Scheme 1. The reaction of $AgCF_3SO_3$ with an equimolar amount of *N*-benzylthiabendazole (*N*-BzTBZ) in ethanol at ambient temperature yielded the mononuclear [Ag(*N*-BzTBZ)$_2$]CF_3SO_3 complex. ^{1}H NMR, IR and UV-Vis spectroscopy, and cyclic voltammetry were applied for characterization of the synthesized complex, while a single-crystal X-ray diffraction analysis was used for the determination of its structure.



Scheme 1. Schematic presentation of the synthesis of silver(I) complex. Atom numbering in the *N*-BzTBZ ligand was used for ^{1}H NMR characterization.

3.2 Description of the single crystal structure

The [Ag(*N*-BzTBZ)$_2$]$^+$ cation of the complex exhibits a distorted trigonal planar coordination geometry, in which the coordination sphere of the Ag(I) ion consists of two *N*-BzTBZ ligands. One ligand is bidentately coordinated to the Ag(I) ion, while the other is coordinated through a benzimidazole nitrogen atom. The triflate anion is incorporated into the crystal lattice as a counterion (Figure 1).

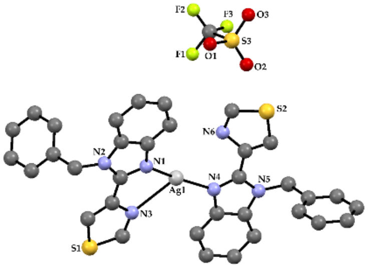


Figure 1. Crystal structure of the silver(I) complex. Hydrogen atoms are not shown.

3.3 Spectroscopic characterization

The IR spectrum of the complex shows the bands attributable to the vibrations of the coordinated *N*-BzTBZ ligand, as well as strong absorptions in the 1300-1000 cm^{-1} region originating from the triflate as a counterion.

In the ^{1}H NMR spectrum of the complex all proton resonances are shifted upfield compared to those of the free ligand, confirming its coordination to the Ag(I) ion.

3.4 Solution stability

The solution behavior of the silver(I) complex in DMSO was examined by recording the UV-Vis spectra immediately after its dissolution, as well as after 48 h. Since no significant changes in the intensity or position of the absorption maximum were observed in the UV-Vis spectra during this period, it can be proposed that the *N*-BzTBZ ligand remains coordinated to the Ag(I) ion in solution.

The measured molar conductivity of the synthesized complex is consistent with a 1:1 electrolyte type [3].

To confirm the redox stability of the complex, its cyclic voltammogram (CV) was recorded at a glassy carbon (GC) electrode in DMSO under the following conditions: $E_{\text{begin}} = -2.0$ V and $E_{\text{end}} = 2.0$ V. No oxidation or reduction peaks of the Ag(I) ion were observed, indicating the stability of the complex due to the coordination of the *N*-BzTBZ ligands to the Ag(I) ion.

4. Conclusions

We have demonstrated that the reaction between equimolar amounts of *N*-benzylthiabendazole (*N*-BzTBZ) and $AgCF_3SO_3$ in ethanol leads to the formation of a mononuclear silver(I) complex, $[Ag(N\text{-BzTBZ})_2]CF_3SO_3$. Crystallographic analysis revealed that the complex adopts a distorted trigonal planar geometry, with two *N*-BzTBZ ligands coordinated to the Ag(I) ion, while the $CF_3SO_3^-$ anion functions solely as a counterion. The synthesized complex remains stable in DMSO solution for up to 48 h.

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