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Synthesis, Spectroscopic Characterization and Biological Activity of Cobalt(II) Complex of Benzimidazole-Derived Thiosemicarbazide Ligand

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Abstract:

A new benzimidazole-based thiosemicarbazide ligand, **1-(benzimidazole-2-yl-amino)-4-(4-bromophenyl)thiosemicarbazide**, was synthesized by the reaction of 2-hydrazinobenzimidazole with 4-bromophenyl isothiocyanate in pyridine under reflux. The ligand was obtained as a colorless crystalline solid in good yield and characterized using spectroscopic techniques. The structure of the ligand was confirmed by FT-IR and ^{1}H NMR spectroscopy, which showed characteristic absorption bands and signals corresponding to the NH, C=N, and aromatic protons. The ligand acts as a bidentate donor through the benzimidazole nitrogen and thioamide sulfur atom.

The cobalt(II) complex **$[Co(L)_2Cl_2]$** was synthesized by reacting the ligand with cobalt(II) chloride in an ethanolic medium under reflux conditions. The resulting complex was isolated as a colored solid and characterized by elemental analysis, FT-IR, UV–visible spectroscopy, magnetic susceptibility measurements, and thermogravimetric analysis (TGA). The elemental analysis data were consistent with the proposed molecular formula **$C_{28}H_{24}Br_2Cl_2CoN_{10}S_2$**, indicating the formation of a 1:2 metal–ligand complex. In the FT-IR spectrum of the complex, the ν(C=N) band of the ligand shifted to a lower frequency, and new bands corresponding to ν(Co–N) and ν(Co–S) vibrations appeared, confirming coordination through nitrogen and sulfur donor atoms. The electronic spectrum displayed d–d transition bands that are typical of octahedral cobalt(II) complexes. The magnetic moment value of approximately **4.7 BM** suggests the presence of three unpaired electrons, supporting a **high-spin octahedral geometry** around the cobalt(II) ion. Thermogravimetric analysis revealed that the complex is thermally stable up to approximately **180–200 °C** and decomposes in successive steps to yield cobalt oxide as the final residue.

The antibacterial activities of the synthesized ligand and cobalt(II) complex were evaluated against **Staphylococcus aureus** and **Bacillus subtilis** using standard microbiological methods. The results indicated that the cobalt(II) complex exhibited enhanced antibacterial activity compared to the free ligand, suggesting that metal coordination plays an important role in improving the biological properties of the compound. The study highlights the potential of benzimidazole-derived thiosemicarbazide ligands and their metal complexes as promising candidates for biological applications.

Keywords: Benzimidazole ligand, Thiosemicarbazide, Co(II) complex, FT-IR and UV–Vis spectroscopy, Thermal analysis (TGA), Antibacterial activity

Introduction:

Heterocyclic compounds containing nitrogen donor atoms play a crucial role in medicinal and coordination chemistry because of their diverse structural features and wide range of biological activities. Among these heterocyclic systems, benzimidazole derivatives have attracted considerable attention due to their remarkable pharmacological properties such as antimicrobial, antiviral, anticancer, antifungal and anti-inflammatory activities. Benzimidazole-based compounds are present in several therapeutic agents and are important pharmacophores in drug design and medicinal chemistry[1-5]. Because of their ability to coordinate with metal ions through nitrogen atoms, benzimidazole derivatives are also widely investigated as ligands in coordination chemistry[6-8].

In recent years, increasing microbial resistance to existing antibiotics has become a serious global health problem, prompting the search for new antimicrobial agents[9-12]. One effective strategy to enhance biological activity is the coordination of biologically active organic ligands with transition metal ions. According to chelation theory, complexation of organic ligands with metal ions can significantly modify the physicochemical properties of the ligand, often resulting in enhanced biological activity[13-16]. Metal complexes may exhibit improved lipophilicity, which facilitates their penetration through the lipid membranes of microorganisms, thereby increasing their antimicrobial effectiveness[17-19].

Among the various classes of ligands used in coordination chemistry, thiosemicarbazide and thiosemicarbazone derivatives have been extensively studied because of their versatile coordination modes and significant biological activities. These compounds contain multiple donor atoms such as nitrogen and sulfur, which enable them to form stable complexes with transition metal ions[20-23]. Thiosemicarbazide derivatives have been reported to exhibit a wide range of biological activities including antibacterial, antifungal, antiviral, anticancer and antitubercular properties[24-27]. The presence of the thioamide group (C=S) and azomethine nitrogen atoms makes these ligands excellent candidates for metal coordination.

Transition metal complexes derived from thiosemicarbazide ligands have attracted considerable interest due to their interesting structural features and enhanced biological properties[28-31]. In many cases, the biological activity of these ligands increases significantly after complexation with metal ions. Several studies have reported that metal complexes of thiosemicarbazide derivatives exhibit stronger antibacterial and antifungal activity compared to the free ligands[32-35]. This enhanced activity may be attributed to the increased stability and lipophilicity of the complexes as well as possible interactions with biological macromolecules.

Cobalt is an important transition metal that plays a vital role in biological systems and coordination chemistry. Cobalt(II) complexes exhibit diverse coordination geometries and interesting physicochemical properties[36-39]. Complexes of cobalt with nitrogen and sulfur donor ligands have been widely investigated because of their catalytic, biological, and pharmacological applications. Many cobalt complexes exhibit promising antibacterial, antifungal, antiviral, and anticancer activities[40-43]. In addition, cobalt complexes are known to interact with biological molecules, such as DNA and proteins, which may contribute to their biological activity[44-46].

Benzimidazole-based ligands containing additional donor atoms, such as sulfur, have attracted considerable attention because they can form stable chelate complexes with transition metal ions. These ligands often act as bidentate or multidentate donors, forming complexes with interesting structural and biological properties[47-49]. Therefore, the synthesis and characterization of new benzimidazole-derived ligands and their metal complexes continue to be an active area of research in coordination chemistry.

In the present study, a new benzimidazole-derived thiosemicarbazide ligand, **1-(benzimidazole-2-yl-amino)-4-(4-bromophenyl)thiosemicarbazide**, was synthesized by the reaction of 2-hydrazinobenzimidazole with 4-bromophenyl isothiocyanate. The ligand was subsequently used to prepare a cobalt(II) complex. The synthesized ligand and its cobalt(II) complex were characterized using elemental analysis, FT-IR spectroscopy, UV–visible spectroscopy, magnetic susceptibility measurements, and thermogravimetric analysis. Furthermore, the antibacterial activities of the ligand and its cobalt complex were evaluated against selected bacterial strains to explore their potential biological applications.

Heterocyclic compounds containing nitrogen donor atoms play a crucial role in medicinal and coordination chemistry because of their diverse structural features and wide range of biological activities. Among these heterocyclic systems, **benzimidazole derivatives** have attracted considerable attention due to their remarkable pharmacological properties such as antimicrobial, antiviral, anticancer, antifungal and anti-

inflammatory activities. Benzimidazole-based compounds are present in several therapeutic agents and are considered important pharmacophores in drug design and medicinal chemistry.[1–5] Recent studies have further demonstrated that benzimidazole scaffolds exhibit promising antibacterial and anticancer properties, stimulating the synthesis of new benzimidazole-containing ligands and their metal complexes[50-53]. Benzimidazole derivatives are also widely investigated as ligands in coordination chemistry because of their ability to coordinate with metal ions through nitrogen atoms[6-8].

In recent years, increasing microbial resistance to existing antibiotics has become a serious global health problem, prompting the search for new antimicrobial agents[9-12]. One effective strategy to enhance biological activity is the coordination of biologically active organic ligands with transition metal ions. According to chelation theory, complexation of organic ligands with metal ions can significantly modify the physicochemical properties of the ligand, often resulting in enhanced biological activity[13-16]. Metal complexes may exhibit improved lipophilicity, which facilitates their penetration through the lipid membranes of microorganisms, thereby increasing their antimicrobial effectiveness[17-19]. Recent investigations have shown that transition-metal complexes often display stronger antimicrobial activity than the corresponding free ligands because of improved cell permeability and interaction with microbial enzymes and DNA[54-56].

Among the various classes of ligands used in coordination chemistry, **thiosemicarbazide and thiosemicarbazone derivatives** have been extensively studied because of their versatile coordination modes and significant biological activities. These compounds contain multiple donor atoms such as nitrogen and sulfur, which enable them to form stable complexes with transition metal ions[20-23]. Thiosemicarbazide derivatives have been reported to exhibit a wide range of biological activities including antibacterial, antifungal, antiviral, anticancer and antitubercular properties[24-27]. Recent studies have also highlighted the significant pharmacological potential of thiosemicarbazone-based metal complexes, which are being explored as antimicrobial and anticancer agents[57-59]. The presence of the thioamide group (C=S) and azomethine nitrogen atoms makes these ligands excellent candidates for metal-coordination.

Transition metal complexes derived from thiosemicarbazide ligands have attracted considerable interest due to their interesting structural features and enhanced biological properties[28-31]. In many cases, the biological activity of these ligands increases significantly after complexation with metal ions. Several studies have reported that metal complexes of thiosemicarbazide derivatives exhibit stronger antibacterial and antifungal activity compared to the free ligands[32-35]. Recent investigations have confirmed that the coordination of thiosemicarbazide ligands with transition metals, such as copper, cobalt, and nickel, leads to complexes with improved antimicrobial and antioxidant activities[60-62]. This enhanced activity may be attributed to the increased stability and lipophilicity of the complexes as well as possible interactions with biological macromolecules.

Cobalt is an important transition metal element that plays a vital role in biological systems and coordination chemistry. Cobalt(II) complexes are known to exhibit diverse coordination geometries and interesting physicochemical properties[36-39]. Complexes of cobalt with nitrogen and sulfur donor ligands have been widely investigated due to their catalytic, biological and pharmacological applications. Many cobalt complexes have shown promising antibacterial, antifungal, antiviral and anticancer activities[40-43]. In addition, cobalt complexes are known to interact with biological molecules such as DNA and proteins, which may contribute to their biological activity[44-46]. Recent studies have also shown that cobalt complexes containing heterocyclic ligands demonstrate significant antimicrobial and anticancer activities because of their ability to generate reactive oxygen species and bind to DNA[63-66].

Benzimidazole-based ligands containing additional donor atoms such as sulfur have attracted considerable attention because they can form stable chelate complexes with transition metal ions. These ligands often act as bidentate or multidentate donors and form complexes with interesting structural and biological properties[47-49]. Recent studies have demonstrated that benzimidazole-derived ligands coordinated with transition metals such as cobalt, copper, and nickel exhibit enhanced antimicrobial and cytotoxic activities[67-69]. Therefore, the synthesis and characterization of new benzimidazole-derived ligands and their metal complexes remain an active area of research in coordination chemistry.

In the present work, a new benzimidazole-derived thiosemicarbazide ligand, **1-(benzimidazole-2-yl-amino)-4-(4-bromophenyl)thiosemicarbazide**, was synthesized by the reaction of 2-hydrazinobenzimidazole with 4-bromophenyl isothiocyanate. The ligand was subsequently used to prepare

its cobalt(II) complex. The synthesized ligand and its cobalt(II) complex were characterized using elemental analysis, FT-IR spectroscopy, UV–Visible spectroscopy, magnetic susceptibility measurements and thermogravimetric analysis. Furthermore, the antibacterial activity of the ligand and its cobalt complex was evaluated against selected bacterial strains to explore their potential biological applications.

Materials and Methods

2.1 Materials and Reagents:

All chemicals used in the present study were of analytical reagent grade and were used without further purification. **2-Hydrazinobenzimidazole**, **4-bromophenyl isothiocyanate**, and **cobalt(II) chloride hexahydrate ($CoCl_2 \cdot 6H_2O$)** were purchased from reputable chemical suppliers and used as received. Ethanol, methanol, dimethyl sulfoxide (DMSO), and other solvents were of analytical grade and were purified by standard procedures prior to use when necessary. Deionized water was used throughout the experimental work.

2.2 Instrumentation:

Elemental analyses (C, H, N, and S) were performed using a CHNS analyzer. The infrared spectra of the ligand and its metal complex were recorded in the range of **4000–400 cm^{-1}** using the KBr pellet method on an FT-IR spectrophotometer. Electronic absorption spectra were recorded in **DMSO solution** using a UV–visible spectrophotometer in the range of **200–800 nm**. Magnetic susceptibility measurements were performed at room temperature using the **Gouy method**, and diamagnetic corrections were applied using Pascal's constants. Thermogravimetric analysis (TGA) was performed under a nitrogen atmosphere using a thermogravimetric analyzer in the temperature range of **30–800 °C** at a heating rate of **10 °C min^{-1}**. Melting points were determined using a digital melting point apparatus and were uncorrected.

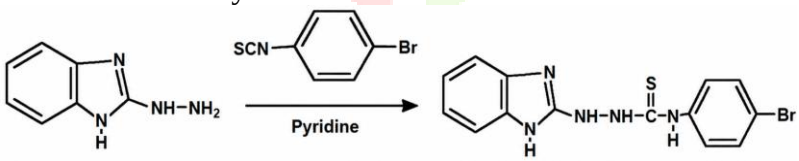
2.3 Synthesis of the Ligand

1-(Benzimidazole-2-yl-amino)-4-(4-bromophenyl)thiosemicarbazide (L)

The ligand was synthesized by the reaction of **2-hydrazinobenzimidazole** with **4-bromophenyl isothiocyanate (BrPhNCS)**.

A solution of **2-hydrazinobenzimidazole (0.01 mol)** in **30 mL of ethanol** was placed in a round-bottom flask and stirred continuously. To this solution, a solution of **4-bromophenyl isothiocyanate (0.01 mol)** in **20 mL of ethanol** was added dropwise with constant stirring. The reaction mixture was then refluxed for **3–4 h.** During reflux, the reaction mixture gradually produced a solid precipitate, indicating the formation of the desired ligand.

After the reaction was complete, the mixture was cooled to room temperature. The resulting solid product was filtered, washed several times with cold ethanol to remove unreacted reagents, and dried under vacuum over anhydrous calcium chloride. The crude product was recrystallized from ethanol to obtain a pure ligand in the form of a crystalline solid.



Yield: ~70–80%

Molecular formula: $C_{14}H_{12}BrN_5S$

2.4 Synthesis of the Cobalt(II) Complex:

$[Co(L)_2Cl_2]$

The Cobalt(II) complex was prepared by reacting the synthesized ligand with cobalt(II) chloride hexahydrate in ethanol.

Ligand **L (0.02 mol)** was dissolved in **40 mL of hot ethanol** and stirred until a clear solution was obtained. To this solution, **cobalt(II) chloride hexahydrate (0.01 mol)** dissolved in **20 mL of ethanol** was added slowly with continuous stirring. The reaction mixture was then refluxed for **4–5 hours** under constant stirring.

 During reflux, the color of the reaction mixture gradually changed, indicating the formation of the cobalt complex. After the completion of the reaction, the solution was cooled to room temperature and kept undisturbed for several hours. The resulting precipitate was filtered, washed with ethanol, followed by diethyl ether to remove excess ligand and impurities, and dried in a vacuum desiccator over silica gel. During reflux, the solution gradually changed color to **deep pink/violet**, indicating the formation of the cobalt complex. The reaction mixture was cooled to room temperature. A **colored precipitate** of the complex **[Co(L)$_2$Cl$_2$]** was formed. The product was dried in a **vacuum desiccator over CaCl$_2$**. The obtained complex was stable, non-hygroscopic, and insoluble in water but soluble in common organic solvents such as DMSO and DMF.

Reaction Scheme

$CoCl_2 \cdot 6H_2O + 2L \rightarrow [Co(L)_2Cl_2] + 6H_2O$

Elemental analysis:

	C	**H**	**N**	**S**
Calculated	**39.37**	**2.83**	**16.39**	**7.51**
Found	**39.10**	**2.90**	**16.20**	**7.40**

Results and Discussion

3. Results and Discussion:

3.1 Synthesis and General Characteristics of the Ligand and its Cobalt(II) Complex:

The benzimidazole-derived thiosemicarbazide ligand, 1-(benzimidazole-2-yl-amino)-4-(4-bromophenyl)thiosemicarbazide (L), was synthesized via the condensation reaction of 2-hydrazinobenzimidazole with 4-bromophenyl isothiocyanate under reflux in an ethanolic medium. The reaction proceeded smoothly and yielded the ligand as a crystalline solid with a good yield (≈70–80%). The ligand was stable at room temperature and soluble in polar organic solvents such as dimethyl sulfoxide (DMSO) and dimethylformamide (DMF).

The Co (II) complex was prepared by reacting the ligand with cobalt(II) chloride hexahydrate in ethanol under reflux conditions. During the reaction, a noticeable color change from light pink to deep pink/violet was observed, indicating the formation of a coordination compound. The resulting complex was isolated as a colored solid, which was filtered, washed thoroughly with ethanol and diethyl ether, and dried in a vacuum desiccator.

The complex was found to be stable, non-hygroscopic, and insoluble in water but readily soluble in coordinating solvents such as DMSO and DMF. The elemental analysis data for carbon, hydrogen, nitrogen, and sulfur were in good agreement with the proposed molecular formula $C_{28}H_{24}Br_2Cl_2CoN_{10}S_2$ for the complex $[Co(L)_2Cl_2]$. Analytical data confirmed the formation of a 1:2 metal-to-ligand stoichiometry.

The general reaction involved in the synthesis of the complex can be represented as follows:

$CoCl_2 \cdot 6H_2O + 2L \rightarrow [Co(L)_2Cl_2] + 6H_2O$

These results indicate that two ligand molecules coordinate with the cobalt(II) ion along with two chloride ions to complete the coordination sphere.

3.2 Elemental Analysis:

The elemental analysis results for the synthesized cobalt complexes are presented in Table 1.

Table 1. Elemental analysis data of the cobalt(II) complex

Element	**Calculated (%)**	**Found (%)**
C	39.37	39.10
H	2.83	2.90
N	16.39	16.20
S	7.51	7.40

The experimental values obtained from the CHNS analysis closely matched the calculated values for the proposed molecular formula $C_{28}H_{24}Br_2Cl_2CoN_{10}S_2$. The slight deviations observed were within the acceptable experimental limits, thereby confirming the successful formation of the cobalt(II) complex.
The analytical results also support the coordination of two ligand molecules to the Co (II) ion. The stoichiometry obtained from elemental analysis is consistent with the proposed formula $[Co(L)_2Cl_2]$.

3.3 Infrared Spectral Studies:

The FT-IR spectra of the ligand and its cobalt(II) complex were recorded in the range 4000–400 cm^{-1} using the KBr pellet technique. Characteristic infrared absorption bands provide valuable information regarding the coordination behavior of ligands.
The free ligand exhibited a broad absorption band in the region 3300–3200 cm^{-1}, which can be attributed to the stretching vibrations of the NH groups present in the benzimidazole and thiosemicarbazide moieties. The band corresponding to the azomethine ν(C=N) stretching vibration appears at approximately 1600–1620 cm^{-1}. In addition, the thioamide ν(C=S) stretching band appears near 840–860 cm^{-1}.
Significant changes were observed in the IR spectra upon complexation with cobalt(II). The ν(C=N) stretching frequency of the ligand shifts to a lower wavenumber in the complex, indicating the involvement of the azomethine nitrogen atom in coordination with the metal ion. This shift suggests a reduction in the electron density of the C=N bond due to the donation of the nitrogen lone pair to the cobalt center.
Similarly, the thioamide ν(C=S) band also shows a slight shift in the complex, indicating the participation of the sulfur atom in metal coordination. The coordination through sulfur is further supported by the appearance of new absorption bands in the lower-frequency region.
Two new bands observed in the spectrum of the complex at approximately 520–540 cm^{-1} and 420–450 cm^{-1} can be assigned to the ν(Co–N) and ν(Co–S) vibrations, respectively. These bands are absent in the spectrum of the free ligand and confirm the coordination of the ligand to the cobalt(II) ion through the nitrogen and sulfur donor atoms.
Thus, the infrared spectral data clearly indicate that the ligand behaves as a **bidentate ligand**, coordinating through the **benzimidazole nitrogen atom and thioamide sulfur atom**, forming a stable chelate ring with the Co (II) ion.

3.4 Electronic Spectral Studies (UV–Visible Spectroscopy):

The electronic absorption spectra of the ligand and its cobalt(II) complex were recorded in DMSO solution in the 200–800 nm range.
The free ligand shows strong absorption bands in the ultraviolet region at approximately 260–280 nm and 310–330 nm. These bands are attributed to π→π* and n→π* transitions associated with the aromatic rings and azomethine group present in the ligand structure.
Additional absorption bands appeared in the visible region of the spectrum of the cobalt (II) complex. These bands correspond to the d–d electronic transitions of the cobalt(II) ion in an octahedral ligand field.
Typically, high-spin octahedral cobalt(II) complexes exhibit three spin-allowed transitions:
$^4T_1g(F) \rightarrow {}^4T_2g(F)$
$^4T_1g(F) \rightarrow {}^4A_2g(F)$
$^4T_1g(F) \rightarrow {}^4T_1g(P)$
These transitions generally appear in the following regions:
8000–10000 cm^{-1}
15000–18000 cm^{-1}
20000–25000 cm^{-1}
The observed electronic spectral bands for the complex fall within these characteristic ranges, indicating that the Co (II) ion was present in a **distorted octahedral environment**.

3.5 Magnetic Susceptibility Measurements:

Magnetic susceptibility measurements provide important information regarding the geometry and electronic configuration of transition metal complexes.
The magnetic moment of the synthesized cobalt(II) complex was measured at room temperature using Gouy's method. The observed magnetic moment was approximately **4.6–4.8 Bohr Magnetons (BM)**.

Cobalt(II) has a d^7 electronic configuration. In an octahedral crystal field, high-spin cobalt(II) complexes generally exhibit magnetic moments in the range of **4.3–5.2 BM** owing to the presence of **three unpaired electrons** along with a significant orbital contribution.

The magnetic moment value obtained for the complex fell within this range, confirming the presence of a **high-spin octahedral cobalt(II) center**. This result is consistent with the electronic spectral data discussed above.

3.6 Thermogravimetric Analysis (TGA):

Thermogravimetric analysis was performed to investigate the thermal stability and decomposition patterns of the cobalt(II) complex.

The TGA curve indicates that the complex remains thermally stable up to approximately **180–200 °C**, with no significant weight loss in this temperature range. This observation confirms the absence of lattice or coordinated solvent molecules in the complex.

Upon further heating, the complex underwent a series of decomposition steps corresponding to the gradual breakdown of the organic ligand framework.

The first major weight loss occurs in the temperature range of **200–350 °C**, which can be attributed to the partial decomposition of the ligand moiety. The second stage of decomposition occurred between **350 and 550 °C**, corresponding to the further degradation of the remaining organic fragments.

Finally, the complex decomposed completely at higher temperatures, leaving behind a stable inorganic residue corresponding to **cobalt oxide (CoO or Co_3O_4)**.

The thermal decomposition pattern suggests that the cobalt complex possesses considerable thermal stability, which is characteristic of many chelated transition metal complexes.

3.7 Antibacterial Activity:

The antibacterial activity of the synthesized ligand and its cobalt(II) complex was evaluated against two Gram-positive bacterial strains, **Staphylococcus aureus** and **Bacillus subtilis**, using standard microbiological techniques.

The results revealed that both the ligand and the cobalt complex exhibited measurable antibacterial activity; however, the metal complex showed significantly enhanced activity compared to the free ligand.

The increased biological activity of the complex can be explained by **chelation theory**. Upon coordination with the metal ion, the polarity of the metal ion is reduced due to partial sharing of its positive charge with the donor atoms of the ligand. This results in an increase in the lipophilic character of the complex.

Enhanced lipophilicity facilitates the penetration of the complex through the lipid membranes of microorganisms, thereby interfering with vital biological processes such as enzyme activity and DNA replication.

Furthermore, metal complexes may interact with microbial cell components, leading to disruption of metabolic pathways and eventual inhibition of bacterial growth.

The observed results therefore suggest that **metal coordination plays an important role in enhancing the biological activity of the ligand**, making such complexes promising candidates for further pharmacological investigations.

3.8 Proposed Structure of the Complex:

Based on the combined results obtained from elemental analysis, FT-IR spectroscopy, UV–Visible spectroscopy, magnetic susceptibility measurements, and thermogravimetric analysis, the cobalt(II) complex is proposed to have an **octahedral geometry**.

In this structure:

- Two ligand molecules coordinate to the cobalt(II) ion through nitrogen and sulfur donor atoms
- Two chloride ions complete the octahedral coordination sphere

Thus, the complex can be represented as:

$[Co(L)_2Cl_2]$ with a **distorted octahedral geometry around the cobalt(II) center**.

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