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SYNTHESIS, STRUCTURAL AND MICROSCOPIC ANALYSIS OF LOW VALENT COBALT CHELATES WITH N, O-DONOR LIGANDS

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ABSTRACT

The synthesis and characterization of low-valent cobalt chelates with N,O-donor ligands were investigated to explore their structural features and potential biomedical relevance. Cobalt(II) chloride was reacted with glycine and 8-hydroxyquinoline (oxine) under varying solvent conditions, followed by reduction attempts using sodium borohydride. The resulting complexes were analyzed through elemental analysis, FTIR spectroscopy, gravimetric halide determination, and single-crystal X-ray diffraction. The study revealed solvent-dependent coordination behavior: glycine yielded $Co(gly)Cl_3$ *with selective amine coordination, oxine in aqueous media produced* $[Co(oxine)_2(H_2O)_2]Cl_2$ *with classical chelation, while oxine in* $THF/SOCl_2$ *formed* $[CoCl_4]^-[C_9H_7NOH]^+$*, where protonated oxine acted as a counter ion. Structural analysis confirmed distorted tetrahedral geometries and extensive hydrogen bonding interactions stabilizing the crystal lattice. Attempts to stabilize cobalt(I) complexes were inconclusive, highlighting the challenges of achieving square planar geometries in low-valent cobalt systems. These findings underscore the critical role of solvent environment and reaction conditions in dictating cobalt coordination chemistry and provide insights for future efforts to design cobalt-based complexes with potential anticancer properties analogous to platinum drugs.*

KEYWORD

Cobalt chelates, N,O-donor ligands, Coordination chemistry, Structural characterization, Anticancer metal complexes

INTRODUCTION

The discovery of the platinum-based pharmaceutical *cis-platin* approximately four decades ago stimulated extensive research in medicinal inorganic chemistry, which continues to thrive today (1). *Cis-platin* remains one of the most widely used antitumor drugs, more than thirty years after its approval as a chemotherapeutic agent. Over the past three decades, numerous coordinated metal complexes have been synthesized, characterized, and tested for antitumor activity in both cell culture and animal models (2). However, platinum complexes remain the only ones in routine clinical use.

Cis-platin, also known as cis-diamminedichloridoplatinum(II) (CDDP), is employed in the treatment of various cancers including breast, cervical, testicular, ovarian, bladder, lung, and prostate malignancies. Its mechanism of action involves binding to DNA and inducing cross-links, thereby interfering with replication and transcription (3). Despite its success, *cis-platin* therapy is limited by severe side effects such as nephrotoxicity, bone marrow suppression, nausea, and vomiting (4).

Other metal complexes have shown promise in medicine. Gold complexes such as Auranofin are used in the treatment of rheumatoid arthritis (5), while technetium and rhenium complexes are applied in imaging and radiotherapy (6). Ruthenium complexes have demonstrated antitumor activity (7), and cobalt(III) complexes have exhibited antibacterial and antiviral properties (8). Cobalt is particularly attractive as a candidate for drug development because it is an essential element in the body, present in vitamin B12 complexes, and is less likely to cause severe side effects compared to platinum.

Most platinum-based anticancer complexes adopt square planar geometry, which is crucial for their biological activity. In contrast, cobalt complexes typically exhibit tetrahedral or octahedral geometries, with square planar arrangements being rare in its common oxidation states (+2 and +3). The objective of this study was to synthesize and characterize low-valent cobalt(I) complexes with N,O-donor ligands, with the aim of achieving square planar geometry. Such complexes could potentially mimic the anticancer properties of Pt(II) complexes while reducing toxicity (9). This represents one of the first attempts to synthesize square planar cobalt(I) chelates capable of triggering apoptosis.

Materials and Methods

General Procedures

All preparations were carried out under an atmosphere of dry, oxygen-free nitrogen. Organic solvents were freshly distilled prior to use. Dichloromethane was refluxed over phosphorus pentoxide and distilled under nitrogen to remove residual water. Tetrahydrofuran (THF) was refluxed over sodium metal until the benzophenone indicator turned deep purple, then distilled under inert atmosphere. Methanol and ethanol were treated with anhydrous magnesium sulfate, refluxed over calcium oxide, and distilled under nitrogen. Single-crystal X-ray diffraction (XRD) for the oxine complex was performed. Elemental analysis (C/H/N/O) was conducted using a Perkin Elmer 2400 CHN analyzer. Infrared spectra were recorded in the range of 4000–400 cm^{-1} on a Shimadzu FTIR-8400 spectrometer. Solid samples were prepared as KBr discs. XRD data were collected using a Bruker APEX II 4K CCD detector at 100(2) K, employing Cu Kα radiation (10).

Analytical Techniques

Gravimetric determination of halides: Halogens were determined gravimetrically as silver halides (11). Samples containing chloride ions were digested with concentrated nitric acid, precipitated with $AgNO_3$, and coagulated by gentle heating. The precipitate was filtered, washed with dilute HNO_3, dried at 140 °C, and weighed until constant mass was achieved.

Preparative Work

Reaction of cobalt(II) chloride with glycine: Glycine (0.05 mol) was dissolved in hot methanol and added to a solution of cobalt(II) chloride (0.025 mol) in ethanol. The mixture was stirred at 40 °C for 2–3 hours, cooled, and treated with diethyl ether to precipitate a purple solid. Needle-like crystals formed upon standing overnight.

Reaction of cobalt(II) chloride with oxine in THF: Cobalt(II) chloride (0.025 mol) was dissolved in THF and dried with $SOCl_2$. Oxine (0.025 mol) was added gradually, and the mixture refluxed for 2–3 hours. A blue precipitate formed, which was filtered, dried, and analyzed.

Reaction of cobalt(II) chloride with oxine in water: Hydrated cobalt(II) chloride (0.025 mol) was dissolved in water and mixed with oxine (0.025 mol) in ethanol. The solution was stirred at 65 °C for 2–4 hours, yielding a yellow precipitate that was filtered, washed, and dried.

Reduction of $Co(gly)Cl_3$ with $NaBH_4$: A suspension of $NaBH_4$ in ethanol was added dropwise to a solution of $Co(gly)Cl_3$ in ethanol. The mixture turned dark purple, was stirred for 2–3 hours, and the product was filtered, washed, and recrystallized.

Reduction of $CoCl_2 \cdot 6H_2O$ with $NaBH_4$ in the presence of oxine: $NaBH_4$ was added dropwise to a suspension of cobalt(II) chloride and oxine in benzene/ethanol. The mixture changed color from blue to orange, producing dark crystals that were filtered, washed, and dried.

Single-crystal XRD analysis: Crystals suitable for XRD were obtained by slow solvent evaporation. Data were collected using Mo Kα radiation, and structures were solved by direct methods with SHELXTL software (12).

RESULTS

In this chapter, the results of the study on the reaction between cobalt (II) chloride with two chelating ligands, glycine and 8-hydroxyquinoline (oxine) in different solvent systems are presented and discussed. Reaction of hydrated CoCl2 with glycine was conducted in mixed solvents, ethanol/methanol. Reaction of hydrated CoCl2 with oxine was conducted in three different solvents i.e. water, ethanol and tetrahydrofuran. The compounds were characterized by; elemental analysis, FTIR spectroscopy and single crystal X-ray crystallography.

Elemental analysis

Table 1: Elemental analysis for glycine and oxine cobalt complexes

Compound	C % found(cal)	N % found(cal)	H % found(cal)	O % found(cal)
$Co(gly)Cl_3$	10.57(9.95)	5.88(5.80)	3.68(2.51)	13.10(13.26)
$[CoCl_4]^-[C_9H_7NOH]^+$	30.04(30.4)	3.79(3.95)	2.33(2.02)	-
$CoCl_2(Oxine)_2(H_2O)_2$	56.07(56.41)	7.58(7.31)	4.17(4.21)	16.35(16.70)

Reaction of cobalt(II) chloride with glycine

Reaction of $CoCl_2$ with glycine in 1:2 mole ratios in methanol/ethanol at 40 °C resulted in the formation of a purple solid identified as $Co(gly)Cl_3$, in which only one glycine ligand was coordinated to the metal centre. This formulation was determined on the basis of elemental analysis and gravimetric analysis. The solid precipitated out of solution upon cooling to room temperature and melted without decomposition at 128–141 °C.

The IR spectrum showed broad bands in the region 3550–3050 cm^{-1} assignable to N–H stretching of the amine coordinated to the cobalt centre. In the free ligand, this band occurs in the region 3050–2675 cm^{-1}. The infrared spectrum of the complex was measured in the region 400–700 cm^{-1} to identify frequencies of M–O and M–N. The spectrum showed a band at 606 cm^{-1} assigned to M–O, while M–N frequencies were identified at 501 cm^{-1}. A weak band was observed at around 2822 cm^{-1} corresponding to the CH_2 symmetric stretch. The strongest absorption bands in the glycine spectrum were N–H stretching at 3170 cm^{-1}, C=O stretching at 1650 cm^{-1}, and N–H deformation at 1540 cm^{-1}.

Table 2: Comparing the IR spectra of free glycine ligand and $Co(gly)Cl_3$

Glycine ligand		$Co(gly)Cl_3$	
Wave number(cm^{-1})	Assignment	Wave number(cm^{-1})	Assignment
3050-2675	NH_2 broad bands	3550-3050	NH_2 broad bands
1410	Symmetric COO- stretch	1395	Symmetric COO- stretch

Reaction of cobalt(II) chloride with oxine in THF using $SOCl_2$ Reaction of $CoCl_2$ with oxine in a 1:1 mole ratio in THF at 87 °C resulted in the formation of a blue solid identified as $[CoCl_4]^-[C_9H_7NOH]^+$. The molecular structure was confirmed by single-crystal X-ray diffraction. The solid was soluble in THF and recrystallized at room temperature. It melted without decomposition at 217–242 °C. The compound crystallized in a monoclinic system and was refined to an R value of 0.0226. The IR spectrum showed strong bands at 1662 cm^{-1}, 1495 cm^{-1}, and 1268 cm^{-1} corresponding to aromatic C=N, C=C, and C–O stretching modes. Compared to the free oxine ligand, strong bands were observed at 1602 cm^{-1}, 1496 cm^{-1}, and 1275 cm^{-1}. Bands at 405 cm^{-1} and 504 cm^{-1} due to M–N and M–O stretching vibrations were absent.

Reaction of cobalt(II) chloride with oxine in water Reaction of $CoCl_2$ with oxine in a 1:1 mole ratio in water at 65 °C produced a yellow solid identified as $[Co(oxine)_2(H_2O)_2]Cl_2$ based on elemental and gravimetric analysis. The solid was soluble in water at room temperature and melted without decomposition at 187–197 °C. The IR spectrum of the complex showed new bands at 450 cm^{-1} corresponding to ν(M–O) and 503 cm^{-1} corresponding to ν(M–N). Carbon–oxygen vibration bands were observed at 1104 cm^{-1}. Additional vibration bands were recorded in the region of 1650–1400 cm^{-1} for C=N and C=C stretching. Ring skeleton ν(C–C) and ν(C–N) bands were observed around 1600 cm^{-1}, 1450 cm^{-1}, and 1370 cm^{-1}. A band in the range of 750–830 cm^{-1} attributable to rocking and wagging modes of vibration of water (H_2O) was present in the coordination complex but absent in the free oxine ligand.

Structural characterization of [CoCl4]-[C9H7NOH] +

Crystals of [CoCl4]-[C9H7NOH] +were obtained as blue-green blocks that crystallized in the monoclinic C2/c space group, with one anion and two cations in the asymmetric unit.

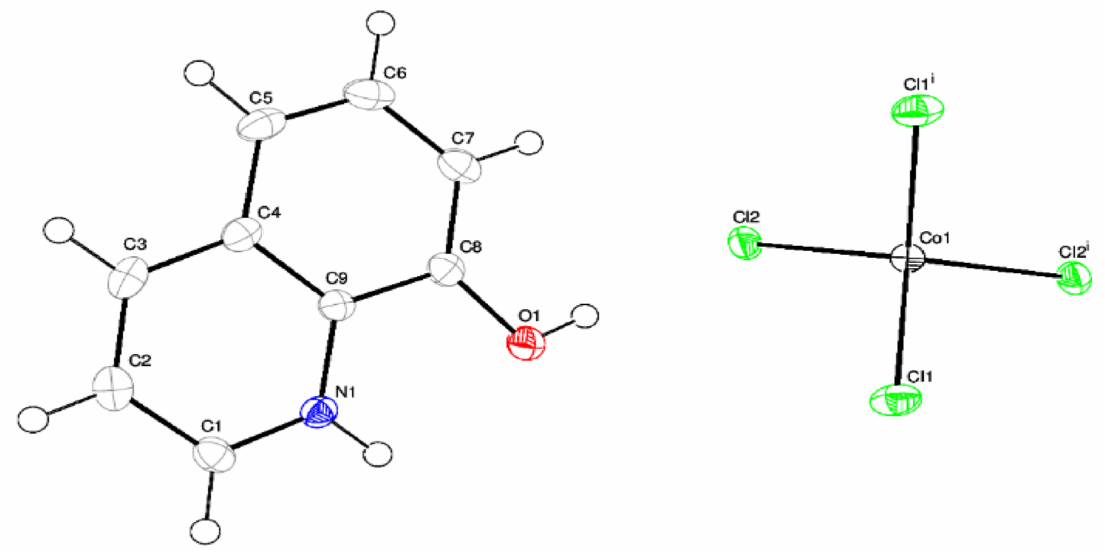


Figure 1: ORTEP diagram of [CoCl4]-[C9H7NOH]+

The bond angles around the cobalt center, specifically Cl(1)–Co(1)–Cl(2) at 112.65°, show a slight deviation from the ideal tetrahedral angle of 109°, resulting in a distorted tetrahedral geometry.

Figure 2 illustrates the packing arrangement of the molecules in the crystal when viewed along the *b* axis. The molecules are organized in layers, with asymmetric units alternating in orientation along the *c* axis. In this arrangement, pairs of cations adopt a staggered orientation, with their hydroxyl (OH) groups directed in opposite directions.

Figure 3 depicts the hydrogen bonding interactions between cations and anions within the structure. Each anion is surrounded by four cation pairs arranged in staggered orientations. Two chloride atoms form hydrogen bonds with the OH groups of the cations, while the remaining two chloride atoms are hydrogen-bonded to the NH groups. Additionally, four other cations establish hydrogen bonds with four surrounding [CoCl$_4$]$^-$ chlorides, reinforcing the stability of the crystal lattice.

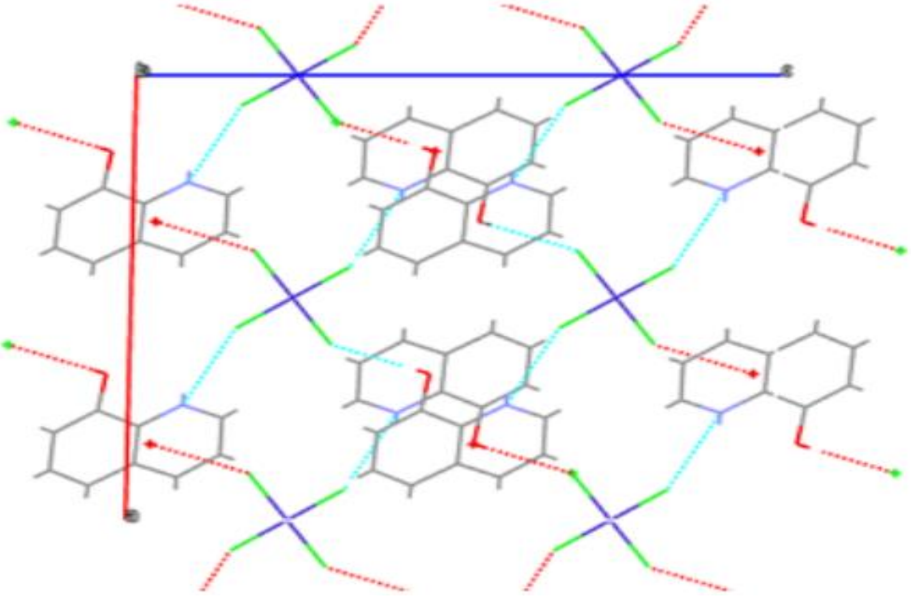


Figure 2: The parking diagram for [CoCl4]-[C9H7NOH]+ viewed along b axis

Figure 4.3 shows the hydrogen bonds between the cations and anions in the structure. Each anion is surrounded by four cation pairs which are in staggered orientation such that the anion is hydrogen-bonded to four different cations from the four pairs i.e. two Cl atoms are hydrogen-bonded to the OH groups while the remaining two are hydrogen-bonded to the NH groups of the cations. The remaining four cations are hydrogen bonded to four of the surrounding [CoCl4]-chlorides.

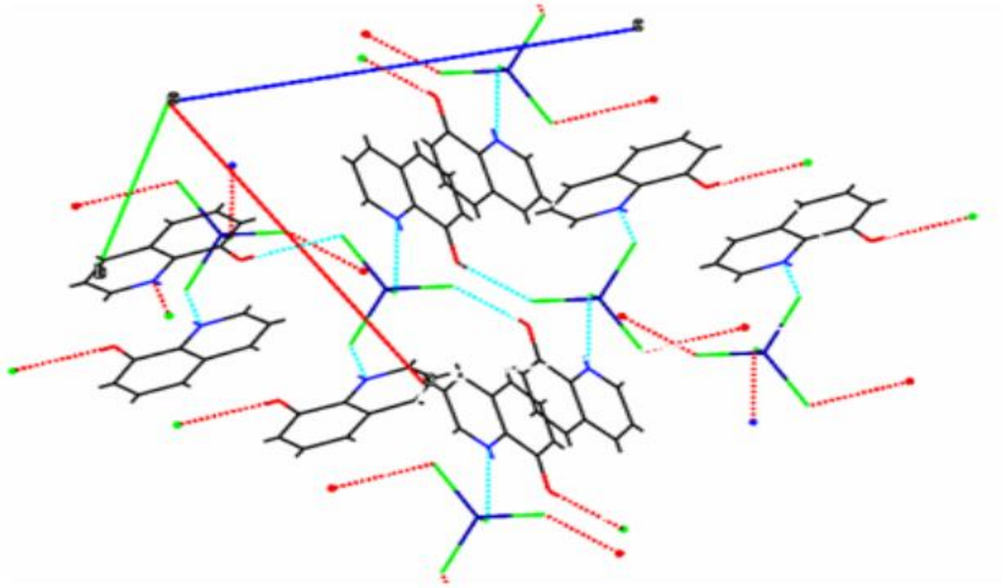


Figure 3: The parking diagram for [CoCl4]-[C9H7NOH]+ showing H-bonds

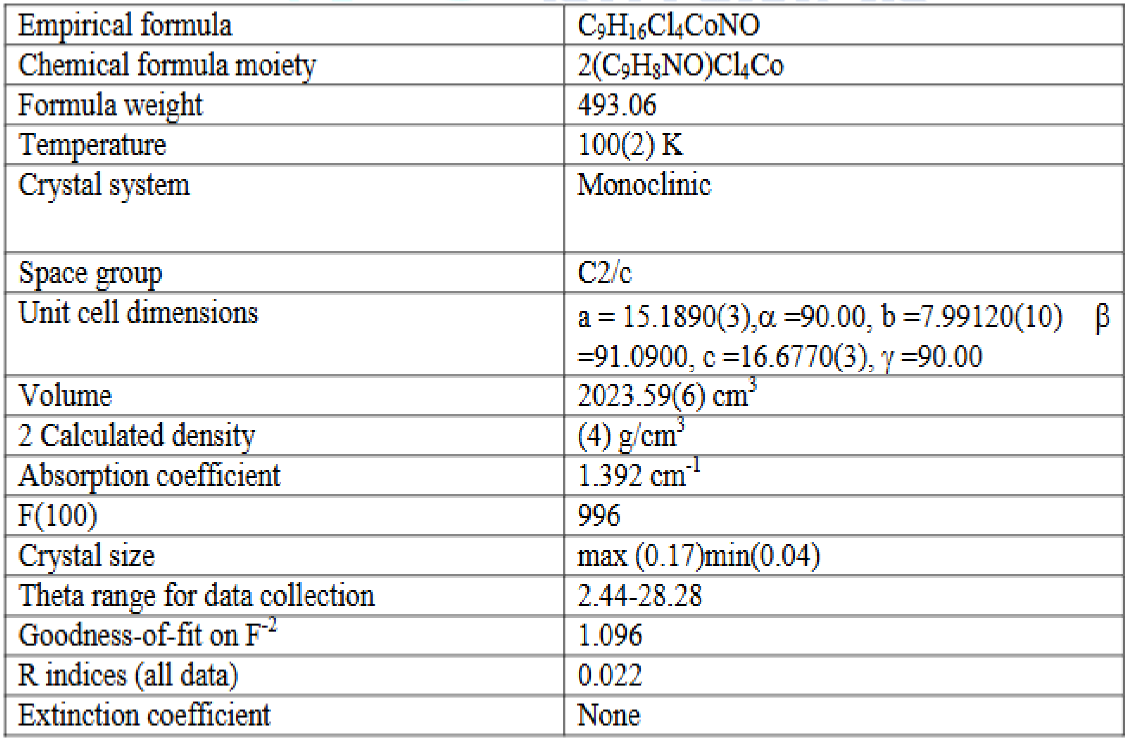
The bond distances and angles are given in table 2 and the parameters for crystal data in Table 2.

The Co1-Cl1 bond lengths are notably longer than Co1-Cl2.

Table 3: Bond lengths (Å) and angles (°) for [CoCl4]-

Bond	Length(Å)	Bond	Angles(°)
C1-N1	1.3263(18)	N1-C1-C2	120.30(13)
CI-C2	1.395(2)	N1-C1-H1	119.9
C1-H1	0.9500	C2-C1-H1	119.9
C2-C3	1.369(2)	C3-C2-H2	120.4
C2-H2	0.9500	C1-C2-H2	120.4
C3-C4	1.413(2)	C2-C3-C4	121.03
C3-H3	0.9500	C2-C3-H3	119.5
C4-C9	1.4111(18)	C4-C3-H3	119.5
C4-C5	1.4170(19)	C9-C4-C3	117.67(13)
C5-C6	1.371(2)	C9-C4-C5	118.51(13)
C5-H5	0.9500	C3-C4-C5	123.82(13)
C6-C7	1.410(2)	C6-C5-C4	119.41
C6-H6	0.9500	C6-C5-H5	120.3
C7-C8	1.3730(19)	C4-C5-H5	120.3
C7H7	0.9500	C5-C6-C7	121.58(13)
C8-O1	1.3579(17)	C5-C6-H6	119.2
C8-C9	1.4145(18)	C7-C6-H6	119.2
Cl1-Co1	2.2731(3)	Cl1-Co1-Cl1	104.64(12)
Cl2-Co1	2.2835(3)	Cl1-Co1-Cl2	107.59(12)
Co1-Cl1	2.2731(3)	Cl1-Co1-Cl2	112.65(12)
Co1-Cl2	2.2835	Cl1-Co1-Cl2	112.65(12)
O1-H1	0.8400	C8-O1-H1	109.5

Table 4: Crystallographic data for [CoCl4]-[C9H7NOH] +



Empirical formula	$C_9H_{16}Cl_4CoNO$
Chemical formula moiety	$2(C_9H_8NO)Cl_4Co$
Formula weight	493.06
Temperature	100(2) K
Crystal system	Monoclinic
Space group	C2/c
Unit cell dimensions	a = 15.1890(3),α =90.00, b =7.99120(10) β =91.0900, c =16.6770(3), γ =90.00
Volume	2023.59(6) cm^3
2 Calculated density	(4) g/cm^3
Absorption coefficient	1.392 cm^{-1}
F(100)	996
Crystal size	max (0.17)min(0.04)
Theta range for data collection	2.44-28.28
Goodness-of-fit on F^{-2}	1.096
R indices (all data)	0.022
Extinction coefficient	None

Discussion

The results demonstrate that cobalt(II) chloride readily forms chelates with N,O-donor ligands, but the coordination outcome is highly dependent on the solvent environment and reaction conditions. The formation of $Co(gly)Cl_3$ in methanol/ethanol suggests that glycine coordinates selectively through its amine group, stabilizing cobalt in the +3 oxidation state rather than the expected +2. This highlights the oxidative susceptibility of cobalt under certain conditions and the role of ligand environment in dictating oxidation state (13, 14).

The reaction of $CoCl_2$ with oxine in water produced $[Co(oxine)_2(H_2O)_2]Cl_2$, confirming successful chelation through both nitrogen and oxygen donor sites. The presence of characteristic M–O and M–N stretching frequencies in the IR spectrum supports coordination, while the water bands indicate hydration within the lattice. This complex illustrates the stabilizing effect of aqueous media in promoting classical chelation (15).

In contrast, the THF/$SOCl_2$ system yielded $[CoCl_4]^-[C_9H_7NOH]^+$, an unusual product where oxine acted as a protonated counter ion rather than a ligand. The absence of M–N and M–O bands in the IR spectrum confirmed the lack of coordination. This outcome can be attributed to the generation of HCl from $SOCl_2$ hydrolysis, which protonated oxine and prevented its binding to cobalt (16). The distorted tetrahedral geometry observed in the crystal structure further emphasizes the unique coordination behavior under strongly acidic conditions (17).

Attempts to reduce Co(III) and Co(II) precursors with $NaBH_4$ produced dark solids, but inconclusive analytical data suggest either incomplete reduction or formation of mixed-valence species. Future work should focus on optimizing reduction conditions and solvent systems to stabilize cobalt(I) complexes, which are hypothesized to adopt square planar geometry and mimic the anticancer properties of Pt(II) complexes (18, 19).

Conclusion

Cobalt(II) chloride salts readily react with chelating ligands to yield high amounts of cobalt chelates; however, the nature of the resulting complexes is strongly dependent on the synthesis conditions. When hydrated cobalt(II) chloride was reacted with oxine in THF in the presence of thionyl chloride, the unexpected complex $[CoCl_4]^-[C_9H_7NOH]^+$ was obtained, where protonated oxine acted as a counter anion rather than a coordinating ligand. In contrast, the reaction of cobalt(II) chloride with oxine in a water/ethanol mixture produced $[Co(oxine)_2(H_2O)_2]Cl_2$, in which the ligand successfully coordinated to the metal while retaining its +2 oxidation state.

Similarly, the reaction of cobalt(II) chloride with glycine in THF resulted in the formation of the Co(III) complex, $Co(gly)Cl_3$, rather than the expected Co(II) complex, $Co(gly)Cl_2$. These complexes were synthesized for the first time in this study. Attempts to reduce $Co(gly)Cl_3$ and $CoCl_2·6H_2O$ in the presence of oxine using $NaBH_4$ produced dark solids; however, elemental analysis of these products was inconclusive.

Recommendation

Optimization of solvent systems to enable successful NMR characterization of the synthesized complexes.

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