AN ABSTRACT OF THE THESIS OF

Jinjiang Zhu for the Master of Science Degree in Physical Science (Chemistry) Presented on November 01, 1996

Title: Cholesterylaminecobalto(III)-11-tungstoborate and Other Organoheteropoly-tungstate Preparations: Organic Ligand Substrate and Heteropoly Anion Syntheses

Abstract approved: Arthur M Lawless

Salts of the following heteropolytungstate anions (HPA), $[(H_2O)CoO_5SiO_4W_{11}O_{30}]^{6-}$, $[(H_2O)CoO_5SiO_4W_{11}O_{30}]^{5-}$, $[(H_2O)CoO_5BO_4W_{11}O_{30}]^{7-}$, and $[(H_2O)CoO_5BO_4W_{11}O_{30}]^{6-}$, have been prepared and analyzed by optical microscope, FTIR spectra, UV-visible spectra, and the characteristic reaction with Zn. Organic ligand substrates, cholesterylamine and 2-octylamine, have been synthesized by the Mitsunobu reaction. These organic ligand substrates were characterized by proton NMR, FTIR, thin layer chromatography (TLC), and some physical-chemical properties. Organoheteropolytungstates, $[(C_{27}H_{47}N)CoO_5BO_4W_{11}O_{30}]^{6-}$ and $[(C_9H_7N)CoO_5BO_4W_{11}O_{30}]^{6-}$, have been prepared and isolated by using a phase transfer catalysis (PTC) technique through

ligand substitution. The UV-visible spectra were used to monitor the formation of organoheteropoly-tungstates. A phase transfer catalysis cycle has been suggested as the mechanism in the ligand substitution of HPA via PTC. Some organic amine derivatives, pyridine, isoquinoline, quinoline, 8-methylquinoline, and 2-octyl-amine, have been used to investigate the steric and electronic effects. A geometric steric hindrance cavity has been suggested in the ligand substitution of HPA based on the structure-reactivity relationships.

Cholesterylaminecobalto(III)-11-tungstoborate and Other Organoheteropoly-tungstate Preparations: Organic Ligand Substrate and Heteropoly Anion Syntheses

A Thesis

Presented to

the Division of Physical Science

EMPORIA STATE UNIVERSITY

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

by

Jinjiang Zhu

November 1996

R. Wayne Barkhau 11-22-96
Approved for the Major Division

John D. Schuerman
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ACKNOWLEDGMENTS

I would like to express my sincere gratitude to my research advisor, Dr. Arthur M. Landis, for his direction, help and understanding during my formal study and the research upon which this thesis is based. I would like to express my sincere thanks to committee member: Dr. Charles Greenlief for his kind advice and assistance during my MS studies and research at Emporia State University; and Dr. Gaylen Neufeld for his assistance. I would also like to express my great appreciation to all of the faculty of the Chemistry Department for their advice and help during my course work, research, and career preparation. Finally, I thank Dr. Manli Zheng of CAChe Scientific for her help in making some of the structural models of our compounds using CAChe Scientific computer software in our research.

I am greatly indebted to my parents for their grace in bringing me up; my parents-in-law and my sister for their help to raise my daughter, Danqi Zhu, as I strive for my M.S. degree and career. I am deeply thankful to my friends, brothers, and relatives who encouraged and helped me to complete this degree. And I thank my wife for her help in my life and career.

CONTENTS

ACKNOWLEDGMENTS ii

CONTENTS iii

LIST OF FIGURES vii

LIST OF TABLE ix

CHAPTER I. INTRODUCTION 1

I-1. Definition of Heteropoly Anion (HPA) 1

I-2. Some Historical Perspectives of HPAs and Keggin Structure 2

I-3. Properties of HPAs 4

A. Stability 5

B. Solubility 6

C. Acidity 7

D. Redox Behavior 8

E. Lacunary HPAs 8

F. Photochemistry 9

I-4. Preparation of HPAs and Their Complexes 9

I-5. The Synthesis of Primary Amines from Alcohols 10

I-6. Phase Transfer Catalysis (PTC) and Ligand Substitution 10

I-7 The Purpose of this Study 12

CHAPTER II. EXPERIMENTAL 14

II-1. The Preparation of Heteropoly Tungstate 14

A. Potassium Aquocobalto(II)-11-tungstosilicate 14

B. Potassium Aquocobalto(III)-11-tungstosilicate 15

C. Potassium Aquocobalto(II)-11-tungstoborate 16

D. Potassium Aquocobalto(III)-11-tungstoborate 17

II-2. The Preparation of Amines 18

A. Preparation of 2-Octylamine 18

B. Preparation of Cholesterylamine 19

II-3. Ligand Substitution 21

A. Potassium Cobalto(III)-11-tungstoborate ($Co^{3+}B$) with 2-Octylamine 21

B. Potassium Isoquinolinecobalto(III)-11-tungstoborate 22

C. Potassium Cobalto-(III)-11-tungstoborate ($Co^{3+}B$) with cholesterylamine 23

D. Potassium Cobalto-(III)-11-tungstoborate ($Co^{3+}B$) with 8-methylquinoline 24

E. Potassium Cobalto-(III)-11-tungstoborate ($Co^{3+}B$) with quinoline and indole 25

CHAPTER III. RESULTS AND DISCUSSION 26

III-1. Ligand Substitution 26

A. Structure Activity Relationships 26

1. The Structures of Heteropoly Anions 26

2. The Structures of Organic Ligands 27

a. The structure of pyridine 27

b. The structures of isoquinoline, quinoline, and 8-methylquinoline 28

c. The structure of indole 28

d. The structures of 2-octylamine and cholesterylamine 29

3. Substitution Reactivities Between Organic Ligands and $Co^{3+}B$ 30

a. The reactivity of pyridine 31

b. The reactivity of isoquinoline 31

c. The reactivity of cholesterylamine 31

d. The reactivity of 2-octylamine 32

e. The reactivities of quinoline, 8-methylquinoline, and indole 32

f. The steric effects and geometric size 33

B. The Application of Phase Transfer Catalysis (PTC) 35

1. The Choice of Phase Transfer Agent, Polar Phase, and

Nonpolar Organic Phase 35

2. The Phase Transfer Catalysis and Ligand Substitution with HPA 36

C. The Preparation of Complexes by HPA Tungstate with Organic Amines 39

III-2. The Synthesis of Amines 40

A. The Reaction Mechanism 40

B. Chromatography and Spectral Analysis 41

1. 2-Octylamine Preparation 41

2. Cholesterylamine Preparation 42

a. Preparation of intermediate 42

b. Preparation of cholesterylamine 43

III-3. The Preparation of Heteropoly Tungstate 44

III-4. Conclusions and Further Considerations 45

BIBLIOGRAPHY 48

APPENDIX A. FIGURES 55

APPENDIX B. TABLE 79

LIST OF FIGURES

Figure 1. Keggin Structure (1:12 Heteropoly Anion) 56

Figure 2. Modified Keggin Structure 57

Figure 3. Reaction Formula of Modified Keggin Structure and Ligand Substitution 58

Figure 4. Mitsunobu Reaction and Gabriel Hydrolysis 59

Figure 5. FTIR Spectrum of Potassium Aquocobalto(II)-11-tungstosilicate ($Co^{2+}Si$) 60

Figure 6. FTIR Spectrum of 2-Octylamine 61

Figure 7. FTIR Spectrum of 2-Octanol 62

Figure 8. Proton NMR Spectrum of N-Cholesterylphthlimide 63

Figure 9. Proton NMR Spectrum of Cholesterylamine 64

Figure 10. Proton NMR Spectrum of Cholesterol 65

Figure 11. Visible Spectrum of Isoquinoline 66

Figure 12. Visible Spectrum of Cholesterylamine in Aqueous Phase (HPA:THAB = 1:2.5) 67

Figure 13. Visible Spectrum of Cholesterylamine in Toluene Phase (HPA:THAB = 1:2.5) 68

Figure 14. Visible Spectrum of Cholesterylamine in Aqueous Phase (HPA:THAB = 1:6) 69

Figure 15. Visible Spectrum of Cholesterylamine in Toluene Phase (HPA:THAB = 1:6) 70

Figure 16. Visible Spectrum of 8-Methylquinoline 71

Figure 17. Visible Spectrum of Quinoline 72

Figure 18. Visible Spectrum of Indole 73

Figure 19. Organic Ligands Used in this Research 74

Figure 20. The Geometric Size of the Conical Cavity of HPA 75

Figure 21. Phase Transfer Catalytic Cycle in Ligand Substitution of HPA 76

Figure 22. Models of Cholesterylamine-HPA Complexes 77

Figure 23. The Probable Mechanism of the Mitsunobu Reaction and Gabriel Hydrolysis 78

LIST OF TABLE

Table I. The Known Heteroatoms in Heteropolyanions 80

CHAPTER I. INTRODUCTION

I-1. Definition of Heteropoly Anion (HPA)

Aqueous metal cations, oxyions, and polymeric oxides are linked in a formal sense by a sequence of hydrolysis reactions to form polyoxometalate anions [1, 2, 3]. Although the overwhelming majority of metal oxides and polyoxoion salts are insoluble, or have a poorly defined or limited solution chemistry, the class of polyoxometalate anions, isopoly and heteropoly oxoanions (HPA), of the early transition elements forms an important exception [1]. The general definition for HPAs is represented by

$$[X_xM_mO_y]^{q-} \quad (x \leq m) \qquad (1)$$

The M atoms, called addenda atoms, are usually molybdenum (Mo) , tungsten (W), or vanadium (V), less frequently niobium (Nb) or tantalum (Ta), or mixtures of these elements in their highest oxidation states (d^o, d^1) [1, 4]. The X atoms, called heteroatoms, number more than seventy elements with a "coordination number" ranging from 3 to 12 from all groups of the Periodic Table (except the rare gases) [Table I] [1, 5]. M is limited to those elements with both a favorable combination of ionic radius and charge for octahedral coordination by oxygen and the ability to form $d\pi$-$p\pi$ M-O bonds; no such restrictions exist on X [1, 6].

Substantial differences exist between Mo, W, and V on the one hand and Ta and Nb on the other, mostly due to the very insoluble oxides that are formed with

Ta and Nb at relatively high pH. Vanadium, although in the same group as Ta and Nb, has a quite different solution chemistry which is much more like that of W and Mo [4].

I-2. Some Historical Perspectives of HPAs and Keggin Structure

The first report about a HPA dates back to 1826 when Berzelius described the yellow precipitate formed when ammonium molybdate was added to phosphoric acid. This is now known as the ammonium salt of dodecamolybdophosphoric acid [7]. In 1862 Marignac described the preparation and properties of dodecatungstosilic acid and correctly analyzed it as $SiO_2 \cdot 12WO_3 \cdot 2H_2O$, but did not propose a structure for the compound [8]. By the first decade of this century about 60 different types of heteropoly acids had been described [1, 9]. Determination of the structure was not possible until the advent of the X-ray diffraction technique.

In 1933 Keggin solved the structure of the heteropoly acid $[H_3PW_{12}O_{40}] \cdot 6H_2O$ by analysis of X-ray diffraction after Pauling had proposed a similar structure in 1929 [10, 11, 12]. Keggin showed that the anion was indeed based on 12 WO_6 octahedral units and these octahedra were linked by shared edges as well as corners surrounding a central PO_4 tetrahedron (Figure 1). This is called the "Keggin structure" with the general formula $[X^{n+}M_{12}O_{40}]^{(8-n)-}$. The anion structure was confirmed by Bradley and Illingworth's investigation of

$[H_3PW_{12}O_{49}]\cdot 29H_2O$ by analysis of powder photographs from X-ray diffraction in 1936 [13, 27]. At that time Anderson proposed a possible structure for 6-polyacids by consideration of atomic radii [14]. This structure of $[TeMo_6O_{24}]^{6-}$ now called "Anderson structure" was reported by Evans in 1948 by using X-ray crystallography [15]. As of 1950 only a few researchers were working on heteropoly research in Europe and the United States [1].

In 1962 Simmons and Baker reported the preparation of the first HPA that contained two different heteroatoms, cobalt and silicon, in combination with tungsten [16]. These authors also reported that one or more of the addenda atoms can be replaced by a second kind of octahedrally-coordinated heteroatom. Simmons's work established the identities of the constituents and showed that the cobalt atom is in the anion and that it was in an octahedral coordination. Figgis and Baker in 1970 reported that the species of Simmons really was a 1:1:11 HPA (not a 1:1:12 HPA) where the ratios were cobalt : silicon : tungsten in the anion (Figure 2). This structure with the general formula $[(Y^y)M'^{m'+}O_5X^{x+}O_4M_{11}O_{30}]^{(12-m'-x+y)-}$ is called the Baker-Figgis model or the modified Keggin structure [17, 18].

In 1977 Landis substantiated the 1 :1 : 11 formulation for analogous "dumbbell" complexes with bridging pyrazine and studied the octahedral trans effect of cobalt in a series of these 1 : 1 : 11 dihetero polytungstate salts [19]. He

prepared, isolated, purified, analyzed, and characterized 32 potassium salts of dihetero-11-tungsto HPAs.

In 1984 Katsoulis and Pope described that, when phase transfer agents were added to an aqueous-organic mixed solvent system, HPAs with the Baker-Figgis model can lose the coordinated water molecules leading to the coordinatively unsaturated sites on the surface of the HPA [20]. The anhydrous HPAs react with a variety of donors.

A survey of the literature indicated that the research and development of HPAs was slow prior to the end of the 1980s. The number of articles about HPAs compiled in Chemical Abstracts (C.A.) was about 67 during 1972-1976, 126 during 1977-1981, and 216 during the 1982-1986 period.

Subsequent developments in X-ray crystallographic hardware and software, in spectroscopic methods such as Raman, one- and two-dimensional metal and ^{17}O NMR, and ^{183}W NMR, and in new analytical techniques such as fast atom bombardment (FAB) mass spectrometry have expanded research on HPAs.[5]. Increased applications of HPAs in catalysis, chemical analysis, ion-exchange, biochemical applications, semiconductors, and other areas have also expanded research on HPAs. More than 1050 articles and patents were published during 1987-1991.

I-3. Properties of HPAs

The physical properties of HPAs as used in this thesis are all related to the Keggin-structure HPAs [1, 4, 21, 22, 23, 24]. The differences are principally related to the choice of metal atom (M), the central hetero atom (X) or the counter-ion.

A. Stability [1, 4, 5]

Many HPAs are thermally stable up to 300-400 °C with the tungsten HPAs being more stable than the molybdenum-based compounds. In the solid state, salts of HPAs are in almost all cases more stable than the acids because the first step in the decomposition sequence is the removal of a lattice oxygen atom by two protons. The central heteroatom (X) has a smaller influence; HPAs with phosphorus or arsenic as the heteroatom are more stable than those with silicon, germanium or boron.

In solution the stability is highest for heteroatoms with a valency of four. Thus, Si and Ge HPAs are more stable toward alkaline hydrolysis than phosphorus containing HPAs, while arsenic and boron give HPAs that are not stable in aqueous solution. The stability of HPAs is greater in organic media. The pH plays a decisive role. HPAs are only stable in an acidic environment. HPAs are decomposed by strongly basic solutions, for example,

$$[PW_{12}O_{40}]^{3-} + 23\ OH^- \text{---------->}\ HPO_4^{2-} + 12\ WO_4^{2-} + 11\ H_2O$$

and

$[CrMo_6O_{24}H_6]^{3-} + 9\ OH^- \text{-------}> Cr(OH)_3 + 6\ MoO_4^{2-} + 6\ H_2O.$

B. Solubility

The proton forms of all members of the Keggin series are very soluble in water, in lower alcohols, and in acetone. This often means that HPAs dissolve in their water of crystallization upon heating unless rigorously dried. In higher alcohols the solubility can also be quite high, especially at somewhat elevated temperature (e.g. $H_3PW_{12}O_{40}$, 100 g/L in 2-ethyl-hexanol, at 80 °C) [25].

The solubility of HPA salts in water is strongly dependent on the counter-ion that is present and on the charge of the HPA. The lithium (Li) and sodium (Na) salts of the relatively low-charged Keggin HPAs (PW_{12}, PMo_{12}, SiW_{12}) are very soluble, while the potassium (K), cesium (Cs), and ammonium (NH_4^+) salts are virtually insoluble. In general, the larger (and softer) the counter-ion is, the less soluble is the HPA salt.

However, the dependence on the total anion charge is marked. For example, from a mixture of compounds with different vanadium content, $[PV_nM_{(12-n)}O_{40}]^{(3+n)-}$, as obtained after synthesis, the potassium salts with different n can be crystallized selectively from water because of the progressively better solubilities of the salts with increasing n [26]. In the work presented here, potassium salts of $[(H_2O)CoO_5SiO_4W_{11}O_{30}]^{5-}$, and $[(H_2O)CoO_5BO_4W_{11}O_{30}]^{6-}$ with a

negative charge of five and six were soluble in water and the former had better solubility than the latter. No obvious solubility was observed in methanol and acetone for both HPA salts. The HPAs are considered as the large, symmetrical anions with a low-charge density. These characteristics make them very soft ions. Hence they have the strongest interactions with other soft ions and are soluble in soft solvents [26, 28].

C. Acidity

The acid strength of HPAs is much higher than that of the free acid of the hetero-atom [30, 31]. For example $H_3PW_{12}O_{40}$ is a stronger acid than H_3PO_4. The central atom is the most important factor for determining the acid strength. On the whole the acidity is more related to the total charge of the anion than to the type of metal atom in the shell of the HPA. In aqueous solution all protons of a HPA are fully dissociated [4].

Comparison with other inorganic acids can only be done in organic solvents. When this is done in acetic acid, it is found that HPAs are comparable to perchloric acid. The acid strength of HPAs is in the order [4]

$$PW_{12} > PMo_{12} > SiW_{12} > AsW_{12} > GeW_{12}.$$

In crystalline HPAs a number of molecules of water of hydration are always present (normally six per Keggin unit) that take part in proton localization. Protons do not bind directly to the anion until the HPA is fully dehydrated, which

is the case after heating to about 300 °C. At even higher temperatures two protons combine with an oxygen atom from the HPA and form water, leaving an HPA molecule with oxygen vacancies and thus destabilizing it [32].

D. Redox Behavior

HPAs can serve as multi-electron oxidants [33]. The oxidation potential is strongly dependent on the metal of the HPA and is not much influenced by the central atom. The reduced HPAs can be reoxidized without loss of structure [34]. This makes them interesting as catalysts, especially as the oxidation potential lies in such a range that reoxidation with molecular oxygen is feasible.

E. Lacunary HPAs

The lacunary HPAs, which can be formed by alkaline dissociation of other HPAs, form a special category [1, 4, 5]. Their properties differ from the other complete HPAs

1. They are not really acidic,
2. They are not soluble in organic solvents, but can be transferred by tetra-alkylammonium compounds to such solvents [4],
3. They have a buffering capacity.

An important difference between these compounds and the normal HPAs is their ability to coordinate cations. The stability of a HPA cation complex depends both on the HPA and the guest metal atom. Cations with a valency of +1 do not

form complexes, but only salts [4].

F. Photochemistry

A special feature of the HPAs of the Keggin types is the possibility of being used in photochemical oxidations. They can be activated by ultraviolet or visible light and in this excited state are able to dehydrogenate secondary alcohols or even alkanes. The reduced HPA can easily be reoxidized with oxygen [4, 35, 36, 37, 38, 39, 40, 41].

I-4. Preparation of HPAs and Their Complexes

In general the HPAs are synthesized by acidification of an aqueous solution of the metal and the hetero-atom in the appropriate ratio, or from other polyanions [5, 16, 17, 18, 19, 42-50]. The acidification leads to dehydrational polymerization of the metal-oxoanions and depending on the conditions (temperature, pH, and counter-ions) different structures are formed.

The reaction for the Keggin structure type anion can be represented as follows [4]:

$$pX^{x+}O_r + qM^{m+}O_n + zH^+ \text{<==>} X_pM_qO_y^{(px+mq-2y)} + z/2\ H_2O \qquad (1)$$

with M = addenda metals

X = hetero-atoms

m = valency of metal

x = valency of hetero-atom

and $y + z/2 = nq + rp$ (oxygen balance).

For example,

$$PO_4^{3-} + 12\ MoO_4^{2-} + 24\ H^+ <=======> PMo_{12}O_{40}^{3-} + 12\ H_2O \qquad (2)$$

The probable reactions of heteropolytungstate for the modified Keggin structure, or Baker-Figgis model [17, 19, 45, 46], and ligand substitution as used in this thesis are presented in Figure 3.

I-5. The Synthesis of Primary Amines from Alcohols

Synthesis of amines have probably received more attention than the preparation of any other functional group in organic chemistry [51]. Many methods have been devised [51-55]. Generally, the hydroxyl group of an alcohol is first converted to another functional group such as the halogens or sulfonic esters. These intermediates are then used subsequently for conversion to the amines [51, 52, 54, 56-63, 66]. The Mitsunobu reaction [56, 57, 58] provides a mild method to prepare amines from alcohol by the use of diethyl azodicarboxylate and triphenylphosphine, and utilizes the Gabriel hydrolysis. The steps in this reaction are shown in Figure 4.

I-6. Phase Transfer Catalysis (PTC) and Ligand Substitution

Bringing together two mutually insoluble reagents in sufficient concentration to attain conveniently rapid reaction rates usually is difficult. The classical laboratory approach to this problem is simply the use of a solvent which

can dissolve both reagents. Use of solvents is not always convenient, and on an industrial scale it frequently is expensive. The technique of phase transfer catalysis provides a method which avoids the use of special solvents.

The PTC technique has been effectively used for organic and some organometallic syntheses [64]. The basic premise of phase transfer catalysis of a two-phase reaction is that one can select a phase transfer agent that, used in catalytic quantities, can bring one of the reactants into the normal phase of the other reactant in such form that high reaction rates are observed. In the case of the transfer of an anion from the aqueous to the organic phase, the choice of phase transfer agent is determined by the properties of anions, aqueous phase, and organic phase.

Several factors affect the distribution of catalyst cations between aqueous and organic phases [65]. (1) The organic structure of the catalyst cation not only affects its ability to transport an anion from the aqueous to the organic phase, but also strongly affects the rate of the organic phase reaction. (2) The characteristic of the anion associated with the catalyst cation influences its tendency to transfer. The anions are hydrated to a different extent. This hydration depends mostly on the charge-to-volume ratio of the anion. The more the anion is hydrated, the more strongly it will be attracted to the aqueous phase and the more difficult it will be to transfer. Additionally, any organic structure of the anion adds to the total organic

structure of the cation-anion pair, increasing the partitioning of the pair into the organic phase. (3) The solubility and partitioning behavior of quaternary salts are markedly affected by even slight changes in the organic phase. (4) Increasing the concentration of inorganic salts in the aqueous phase tends to "salt out" organic salts, pushing them into the organic phase. Increasing the inorganic salt concentration also ties up additional waters of hydration, reducing the amount of water available for anion hydration. In some cases this provides an easier transfer of the anion into the organic phase [65].

HPAs have been transferred from the aqueous phase to non-polar solvents using phase transfer agents [20, 44, 66, 67]. The transferred HPA loses the coordinated water molecule(s) which leads to coordinately unsaturated sites on the surface of the polyanion. The anhydrous HPA can react with a variety of donors [20].

I-7 The Purpose of this Study

The purpose of this study was to develop methods of preparation and to prepare cholesterylamine and cholesterylaminecobalto(III)-11-tungstate in order to investigate the structure of any HPAs formed. To achieve this purpose, various possibilities for the preparations were investigated and the phase problem caused by two mutually insoluble reagents needed to be resolved. To accomplish the goals of this thesis, four sets of experiments were designed.

The first set of experiments was to prepare potassium aquocobalto(II)-11-tungstosilicate ($Co^{2+}Si$), potassium aquocobalto(III)-11-tungstosilicate ($Co^{3+}Si$), potassium aquocobalto(II)-11-tungstoborate ($Co^{2+}B$), and potassium aquocobalto(III)-11-tungstoborate ($Co^{3+}B$). The second set of experiments was to use organic ligands (such as pyridine, isoquinoline, quinoline, 8-methylquinoline, indole and 2-octylamine) to coordinate with HPAs to investigate their possible inductive and steric effects in both PTC and non-PTC systems and to establish the coordinating possibility of cholesterylamine with HPA. In the process new complexes would be prepared. The third set was to prepare 2-octylamine using the reported method [56, 57], to observe the reaction procedure, to check the reagents used in the Mitsunobu reaction, and then to develop a preparation method for cholesterylamine based on these experiments. The fourth set was to prepare the cholesterylaminecobalto(III)-11-tungstoborate, hopefully in a crystalline form.

CHAPTER II. EXPERIMENTAL

Characterization of the intermediates and products was performed using a Fourier Transform Infrared (FTIR) Bomen MB-100 interfaced with Spectra Calc Software, a Hitachi Perkin-Elmer R-24B High Resolution Proton NMR Spectrometer (60 MHz), a GCA-McPherson model EU-700 Series UV-visible Spectrometer, and a Thomas Hoover Capillary Melting Point Apparatus. All reagents were from Fisher Scientific and were used without further purification unless otherwise noted.

The concentrations of buffers used in this thesis research are reported as the total analytical concentration of the buffer species. For example, a 0.1 M potassium acetate/acetic acid buffer contains 0.1 mol of acetate in all forms.

II-1. The Preparation of Heteropoly Tungstate

The heteropoly tungstates were prepared following the methods used by Landis[19]. These methods are given in the following paragraphs.

A. Potassium Aquocobalto(II)-11-tungstosilicate

Into a 250 mL beaker with a magnetic stirrer were placed 0.01 mol sodium silicate (2.84 g), 75 mL H_2O, and 0.11 mol sodium tungstate dihydrate (36.28 g from Aldrich Chemical Company). Glacial acetic acid (about 9.5 mL) was added drop by drop to adjust the pH to 5-6. The solution was heated to boiling and a hot solution containing 0.01 mol cobalt chloride (or cobalt acetate) and 25 mL H_2O

was added slowly. The wine-red solution which was produced was boiled 3 minutes and then filtered hot using fine-porosity filter paper. The aqueous filtrate was reheated to boiling and a hot solution of 0.33 mol potassium acetate in 16 mL H_2O containing enough glacial acetic acid to adjust the pH to 6-7 was added. The solution was let stand to cool. Wine-red crystals precipitated and were separated using fine-porosity filter paper. The crystals were washed using a small amount of dilute acetic acid solution and then dried at room temperature. The yield was 26.89 g (82.5% based on cobalt).

The red crystals were recrystallized by dissolving them in a minimum amount of 1% (v/v) acetic acid solution. The solution was heated to boiling, filtered hot, and the resulting solid dried at room temperature. The potassium aquocobalto(II)-11-tungstosilicate ($Co^{2+}Si$) of formula $K_6[H_2OCoO_5SiO_4W_{11}O_{30}]\cdot 15.2H_2O$ was obtained [19].

The IR spectrum of $Co^{2+}Si$ was determined by using a KBr pellet (Figure 5). The bands in the spectrum were consistent with those reported in the literature [19].

B. Potassium Aquocobalto(III)-11-tungstosilicate

A 2.4 mmol sample of potassium aquocobalto(II)-11-tungstosilicate (7.73 g) was dissolved in 17 mL water in a 50-mL beaker with a magnetic stirrer. The solution was heated to 90°C and 3.9 mmol solid potassium peroxydisulfate $K_2S_2O_8$

(1.05 g) was gradually added. The solution was kept at 90°C for 35 minutes after the addition. After the solution cooled to room temperature, it was placed in a small plastic dish to allow evaporation. Dark green crystals precipitated and were filtered from the mother liquor. The crystals were washed using small amounts of 1% (v/v) acetic acid solution and then dried in air.

The octahedral crystals were recrystallized from a minimum volume of hot water to which a few drops of glacial acetic acid had been added. A mixture of dark green and white octahedra was obtained. The yield was 5.75 g (74.6% based on $Co^{2+}Si$).

C. Potassium Aquocobalto(II)-11-tungstoborate

This salt was prepared by placing 66 mmol sodium tungstate dihydrate (21.8 g) and 42 mL H_2O into a 100 mL, 3-necked round-bottomed flask which was fitted with a condenser, a thermometer, and a magnetic stirrer. The solution was heated to about 85-90°C and 6 mmol boric acid was added. Then glacial acetic acid was added dropwise to adjust the pH to 5-6. The temperature of the reaction solution was maintained at 85-90°C for an additional 30 minutes and then cooled to 70°C. A hot solution of 6 mmol cobalt(II) acetate tetrahydrate (1.5 g) in 12 mL H_2O was added. After maintaining the temperature at 80°C for an additional 10 minutes, a hot solution of 0.06 mol potassium nitrate (6.1 g) in 12 mL H_2O was added. The temperature was maintained for an additional 5 minutes before the

solution was cooled to 70°C and filtered while hot through fine-porosity filter paper. The filtrate was evaporated at 70°C (about 20 minutes) and then allowed to cool to room temperature overnight. A brownish, fine crystalline solid, aquacobalte(II)-11-tungstoborate ($Co^{2+}B$), was obtained by filtration of the cooled mixture. The formula of this hydrated salt is $K_7[H_2OCoO_5BO_4W_{11}O_{30}]\cdot 13.7\ H_2O$ [19]. The yield was 8.86 g (45.3% based on cobalt).

D. Potassium Aquocobalto(III)-11-tungstoborate

Into a 50 mL beaker with a magnetic stirrer was placed 1 mmol potassium aquocobalto(II)-11-tungstoborate (3.225 g) from the above preparation and 10 mL of 0.5 M, pH 6, potassium acetate/acetic acid buffer. The mixture was stirred and heated to 80°C. Enough water (8 mL) was added to the buffered mixture to dissolve the solid at 80°C. After increasing the temperature to 90°C, this hot solution was filtered through fine-porosity filter paper. The filtrate with some wine-red precipitate was reheated to 90°C and enough water was added to dissolve the solid. Next 1 mmol of solid potassium peroxydisulfate (0.27 g) was added over a 10-minute period and the temperature was maintained at 90°C for an additional 10 minutes. The solution was cooled and the white solids were filtered. The filtrate was placed in a refrigerator. A green crystalline solid of potassium aquacobalto(III)-11-tungstoborate ($Co^{3+}B$) was obtained. The yield was 2.05 g (63% based on $Co^{2+}B$).

II-2. The Preparation of Amines

The Mitsunobu reaction was used to produce alkyl phthalimide intermediate from alcohol and phthalimide. Then the Gabriel hydrolysis was used to prepare amines from the intermediate [51, 56-58].

A. Preparation of 2-Octylamine

In a 100-mL three-necked round-bottomed flask were placed 20 mmol 2-octanol (2.6 g), 20 mmol phthalimide (2.94 g), 20 mmol triphenylphosphine (5.24 g), and 20 mL tetrahydrofuran (THF). The flask was fitted with a condenser. The system was flushed with N_2 and during the reaction a positive pressure of N_2 was maintained. A solution of 20 mmol diethyl azidodecarboxylate (3.48 g) in 8 mL THF was added dropwise to the solution. The clear-orange solution which resulted was stirred overnight at room temperature (about 23°C). The solvent was removed under vacuum. Ether was added to the residue and the solids were removed by filtration. The filtrate was evaporated by gently warming in air. A brown-yellow residue (3.16 g) was obtained.

The purity of this sample was checked using thin layer chromatography (TLC) following the procedure outlined by Heftmann [68]. In two test tubes, 1% (w/w) benzene solutions of this brown-yellow residue and of 2-octanol were prepared. These samples were spotted on a TLC plate prepared with silica gel (60G). Benzene was used as the eluant. Iodine was used as the detection reagent.

The R_f value for 2-octanol was 0.11. After developing, a sample of residue consisted of two spots, one darker than the other. The R_f values were 0 for the dark spot and 0.11 for the light spot.

To 3.16 g of the brown-yellow residue in a 100 mL, three-necked round-bottomed flask were added 25 mL 95% ethanol and 0.45 mL 95% hydrazine. The yellow solution was refluxed for 3 hr. The solvent was removed in vacuo, leaving a yellow residue. To the yellow solid, about 2.5 mL of 10% aqueous hydrochloric acid were added slowly to adjust the pH to 2-3. The precipitate which formed was removed by filtration. Then 2M NaOH was added to adjust the pH to 8-9. A yellow oil, the desired amine, with an ammonia-like odor floated on the surface. The oil was separated using a separation funnel and collected in a test tube. The pure 2-octylamine was obtained by distillation (bp 70-72°C/31 mmHg).

The FTIR spectrum of the yellow oil was taken using a liquid cell with a KBr window. The spectrum is shown in Figure 6.

B. Preparation of Cholesterylamine

Into a 50-mL three-necked round-bottom flask were placed 12 mmol cholesterol (2.32 g), 12 mmol phthalimide (0.88 g), 12 mmol triphenylphosphine (1.57 g), and 14 mL THF. The flask was fitted with a condenser and a magnetic stirrer. The system was flushed with N_2 and during the reaction a positive pressure of N_2 was maintained. A solution of 12 mmol diethylazido-dicarboxylate in 3.5

mL THF was added dropwise to the solution to produce a clear yellow-orange solution. The solution was stirred for 70 hours at room temperature (22°-25°). The solvent was removed under vacuum. Ether was added to the residue and the solids were removed by filtration. The filtrate was evaporated by gently warming in air. Carbon tetrachloride was added to the residue and a small amount of white solid was removed by filtration. The filtrate solvent was removed by distillation under vacuum. The raw cholesteryl phthalimide intermediate, a yellow residue (4.19 g), was obtained. The NMR spectrum of this intermediate is shown in Figure 8.

To the 4.19 g of raw cholesteryl phthalimide in a 100 mL round-bottomed flask were added 18 mL 95% ethanol and 0.27 mL 95% hydrazine. The yellow solution that formed was refluxed for 3 hours and then allowed to cool to room temperature. To the cooled solution were added 8 mL H_2O and about 2.5 mL 5% NaOH to adjust the pH to 8-9. Ether was added to the slightly basic solution. The mixture was shaken and separated using a separation funnel. To the separated ether phase were added 5 mL H_2O and about 1.5 mL 5% hydrochloric acid to adjust the pH to 2. The mixture was centrifuged and 0.3 g white solid was obtained. To the white solid was added a small amount of 5% NaOH. The mixture was allowed to stand overnight. Next, ether was added and the ether layer was separated using a separation funnel. The collected ether phase was washed with small amounts of water and then evaporated in air. Light-yellow solids were

obtained after drying. The mp of the solid was 89°-112°C. NMR spectrum of the solids was taken and is shown in Figure 9.

II-3. Ligand Substitution

The preparation and observation of ligand substitution by heteropoly tungstate with some derivatives of organic amines were attempted in two ways. One used phase-transfer-catalysts (PTC) and the other did not use the PTC. In all cases a reference or control sample of heteropoly dissolved in water was used as a qualitative and quantitative comparison. The starting aquoheteropoly anion had an aqueous color which is a different shade of green from the known solutions of amine-heteropoly complexes. Hence, it was expected that the amines to be prepared in this work when coordinated to the cobalt in the heteropoly would also be a different shade of green. For those experiments in which a reaction occurred a distinct color change could be observed. The post-treatment method for preparing the complexes of heteropoly with organic amines followed the method of Landis [19].

A. Potassium Cobalto(III)-11-tungstoborate ($Co^{3+}B$) with 2-Octylamine

To a solution of 30 μmol $Co^{3+}B$ (0.1 g) in 2 mL water a mixture of 1 mL toluene, 3 mg tetraheptylammonium bromide (THAB from Aldrich), and 10 μL 2-octylamine (prepared as above) were added. The light-yellow toluene phase on the top of the mixture was "muddy" (i.e. not clear). The mixture was heated slowly to

55°C. A homogeneous, clear, yellow-green two-phase mixture was formed and small amounts of dark grey-green solid stuck on the stir-bar.

To this stirred mixture was added 0.5 mL cyclohexane. The volume of the top phase in the mixture increased. This layer was a yellow-green color and again became "muddy". The mixture was heated slowly to 30-40°C. The color of the grey-green solid on the stir-bar changed to emerald-green. When the mixture was heated to 50-60°C, the color of the solid on the stir-bar changed back to dark grey-green again. To the dark grey-green solid separated from the stir-bar, a small amount of cyclohexane was added. No obvious solubility of the solid was observed in cyclohexane.

B. Potassium Isoquinolinecobalto(III)-11-tungstoborate

A small amount of sample, 30 μmol $Co^{3+}B$ (0.1g), 2 mL H_2O, 0.5 mL toluene, 30 μmol isoquinoline (3.9 mg refined by distillation), and 7.5 μmol THAB (4 mg) were placed into a test tube with a magnetic stir-bar. The two phases of the phase transfer mixture were stirred and heated to 30-40°C. Initially, the lower aqueous phase was olive-green and the upper toluene phase was colorless. After stirring and heating at 30-40°C for 3 hours, an emerald-green aqueous phase formed (Figure 11) and was separated. About 1 mL of cold acetone was slowly added dropwise with mixing to the cold aqueous phase. A small amount of brown-purple solid was removed by filtration. More acetone, about 5

mL, was added to the filtrate to produce a white-green precipitate. This mixture was centrifuged and the top pale-green solution was decanted. The residual solids were dissolved in 0.5 mL water to form a light-green solution. This light-green solution was placed in a plastic dish and allowed to evaporate slowly. An emerald-green solid (0.038 g) was obtained.

In another experiment using the phase-transfer-catalyst (PTC), 2 mL of toluene was used instead of 0.5 mL toluene. The other conditions and procedures were the same as above. In this experiment 32 mg of emerald-green solid was obtained.

The ligand substitution reaction of isoquinoline with $Co^{3+}B$ was attempted without using the PTC. Much white precipitate formed when the emerald-green solution was produced.

C. Potassium Cobalto-(III)-11-tungstoborate ($Co^{3+}B$) with Cholesterylamine

Into a test tube were placed 60 μmol $Co^{3+}B$ (0.2 g) and 4 mL H_2O. The olive-green solution which formed was divided into two equal portions in test tubes. To both tubes were added 1.5 mL toluene and an equal amount of THAB. One of them was used as the control and the other was used to observe the reaction change of $Co^{3+}B$ with cholesterylamine. Both tubes were maintained at the same conditions during the reaction and the changes in both tubes were observed with different amounts of THAB in the PTC system.

To one of the test tubes containing $Co^{3+}B$, H_2O, toluene two-phase mixture, and a magnetic stir-bar was added 30 μmol raw cholesterylamine (12 mg prepared as above). The mixture was stirred and heated for a few minutes. An emulsion layer appeared between the aqueous phase and the toluene phase. Into the mixture was added 75.5 μmol THAB (3 × 3.7 mg) and the mixture was stirred for 3 hours at 30°-40°C. The emulsion layer disappeared and the toluene phase changed gradually to emerald-green after THAB was added. The mixture was allowed to stand overnight. Into the mixture was added more THAB (52 mg). The aqueous phase was almost colorless after setting at room temperature for 3 days. The organic phase was evaporated in air and an emerald-green sticky solid was obtained.

UV-visible spectra were taken at ratios of 1:2.5 and 1:6 between $Co^{3+}B$ and THAB. The spectra of the aqueous and the toluene phases of control and reaction samples are shown in Figure 12-15, respectively.

D. Potassium Cobalto(III)-11-tungstoborate ($Co^{3+}B$) with 8-Methylquinoline

In these procedure, 30 μmol of $Co^{3+}B$ (0.1 g) were dissolved in 2 mL water. Then 31 μmol of the liquid 8-methyl-quinoline (4.4 mg) were added to the yellow-green solution. Two liquid phases formed. The two-phase mixture was heated for 3 hours at 30-40°C and then allowed to set at room temperature for 2 days. The color of the aqueous layer was not changed and two phases remained.

Next 7.5 μmol THAB (4 mg) dissolved in 0.5 mL toluene were added to the above solution to form a phase-transfer-catalyst (PTC) system. Only two phases were observed. The solution was heated to 50-60°C for 5 hours and allowed to set overnight. No obvious color change was observed in the aqueous phase (Figure 16).

E. Potassium Cobalto(III)-11-tungstoborate ($Co^{3+}B$) with Quinoline and Indole

The same procedure and conditions as above (section D) were used except that either quinoline or indole was substituted for the 8-methyl-quinoline. The color was not observed to change in either the PTC system or in the non-PTC system when reacted with either of these potential ligands (Figure 17, 18).

CHAPTER III. RESULTS AND DISCUSSION

III-1. Ligand Substitution

A. Structure Activity Relationships

1. The Structures of Heteropoly Anions

Polyoxometalate anions can act as ligands that are unique in two respects: topology and electron-acceptor ability due to the reducibility of the metal center [5]. Two methods of complex formation with polyoxomatalate ligands can be distinguished: (1) "complete" (plenary) structures binding the metal cation via surface terminal and bridging oxygen atoms [69], and (2) "defect" (lacunary) structures binding the metal cation in the vacancy [1, 4, 5].

The heteropoly anion (HPA) in a Keggin structure consists of a large polyhedral closed basket formed by 12 MO_6 octahedra (where M = W or Mo) sharing corners with the tetrahedrally coordinated PO_4^{3-} hetero group in the center, and the PO_4^{3-} group sharing each of its oxygens with three MO_6 octahedra. The Keggin anion (see Figure 1) therefore comprises four sets of three MO_6 octahedra with edge sharing within each set and corner sharing between them [10, 27].

According to the Baker-Figgis model [5, 17, 19, 45, 46], a modified Keggin structure of HPA with a formulation of $[(Y^{y-})M'^{m'+}O_5X^{x+}O_4M_{11}O_{30}]^{[12-m'-x+y]-}$ has a Y:M′:X:M molar ratio of 1:1:1:11, where Y = H_2O, NH_3, pyridine, pyrazine, etc.; M′= Co^{3+}, Co^{2+}, Ni; X = P, Si, B, Ge, Zn, Fe, As, etc.; and M = W or Mo [1, 5, 17,

19, 21]. This model indicated that one of the MO_6 octahedra in a Keggin structure was replaced by a YMO_5 octahedra (Figure 2). Therefore, the anion in a modified Keggin structure consists of a large polyhedral closed basket formed by 11 MO_6 octahedra, and 1 $YM'O_5$ octahedra in which Y connects with the M′ atom and spreads out from the closed basket. When Y = H_2O, it can be easily substituted by some ligands, such as NH_3, pyridine, pyrazine, etc. which have a higher activity than H_2O has [17, 19, 20, 45].

2. The Structures of Organic Ligands

Organic ligands as used in this thesis refer to some derivatives of organic amines. They are divided into two groups [Figure 19]. One of the groups is aromatic heterocyclic amines which includes pyridine, isoquinoline, quinoline, 8-methylquinoline, or indole. The other group is primary amines with various R groups such as 2-octylamine and cholesterylamine.

a. The structure of pyridine

Pyridine is classified as aromatic on the basis of its properties. It is flat with bond angles of 120°; the four carbon-carbon bonds are of the same length, and so are the two carbon nitrogen bonds [53]. In describing the electronic configuration, the nitrogen atom in pyridine, like each of the carbon atoms, is bonded to other members of the ring using of sp^2 orbitals, and the nitrogen provides one electron for the π cloud. The third sp^2 orbital of nitrogen simply contains a pair of

electrons which are available for sharing with acids or coordinating with ligands. The basicity of pyridine is $K_b = 2.3 \times 10^{-9}$ [53].

b. The structures of isoquinoline, quinoline, and 8-methylquinoline

Isoquinoline, quinoline, and 8-methylquinoline are also classified as aromatic and have similar properties to pyridine (Figure 19). Each of them has a pyridine ring fused with a benzene ring to form a planar double-ring structure. The difference between isoquinoline and quinoline is in the position of the nitrogen on the double-ring. The nitrogen in isoquinoline is located in the 2 position of the ring with a $K_b = 1.1 \times 10^{-9}$ while the nitrogen in quinoline is in the 1 position of the ring with a $K_b = 3 \times 10^{-10}$ [53].

The structure of 8-methylquinoline is the same as that of quinoline except that the hydrogen at position eight in quinoline is replaced by a methyl group. The methyl group spreads out from the double ring plane of quinoline and is parallel with the ring plane. It is believed that the property of nitrogen in 8-methyl-quinoline is similar to that of quinoline and isoquinoline except for the steric environment (the inductive effect of the 8-methyl group on the ring is ignored).

c. The structure of indole

Indole, which is a combination of a pyrrole ring fused with a benzene ring, also is considered as aromatic (Figure 19). The nitrogen in the indole molecule has similar properties to the nitrogen in pyrrole. In a pyrrole ring each atom of the

ring, whether carbon or nitrogen, is held by a σ bond to three other atoms. In forming these bonds, the nitrogen atom uses three sp^2 orbitals which lie on a plane and are 120° apart [53]. After contributing one electron to each σ bond, each carbon atom of the ring has one electron left and the nitrogen atom has two electrons left. These electrons occupy *p* orbitals giving rise to π clouds, one above and one below the plane of the ring; the π clouds contain a total of six electrons.

Nitrogen's extra pair of electrons, which is responsible for the usual basicity of nitrogen-containing compounds, is involved in the π cloud of an indole molecule. It is thus not available for sharing with acids or coordinating with central metal ions.

d. The structures of 2-octylamine and cholesterylamine

The 2-octylamine and cholesterylamine are classified as primary amines (Figure 19). These can be considered as being formed when one of the hydrogens in an ammonia is replaced by a 2-octyl or a cholesteryl group. In primary amines nitrogen has sp^3 hybridization, but has only three unpaired electrons. These electrons occupy three of the sp^3 orbitals. Overlap of these orbitals with two *s* orbitals of two hydrogen atoms and one sp^3 orbital of a carbon atom result in the formation of a primary amine. The fourth sp^3 orbital of nitrogen contains a pair of electrons. The sp^3 orbital occupied by the lone pair of electrons is a region of high electron density. This region is a source of electrons for sharing with acids.

Hence these compounds are potential ligands.

The R group in cholesterylamine is different from that of 2-octylamine. The cholesteryl group is composed of three cyclohexane rings, one cyclopentane ring, a C_8H_{17} alkyl chain, and two methyl groups that are connected as shown in Figure 19. The $-NH_2$ group is located at the 3-position of the steroid. A large non-polar group in cholesterylamine, a hydrophobic group, ensures that cholesterylamine is a solid under normal conditions and has a very low solubility in polar inorganic solutions.

The 2-octylamine has a C_8H_{17} alkyl chain. The $-NH_2$ group is located at the 2- position on the alkyl chain. The smaller, by comparison with the cholesteryl group, hydrophobic R group in 2-octylamine causes this compound to be a liquid in room temperature and pressure. The amine is essentially insoluble in a neutral inorganic polar solution. The 2-octylamine is expected to have a higher basicity than cholesterylamine based on the positive inductive effect caused by the neighboring methyl group in the 1 position of octylamine.

3. Substitution Reactivities Between Organic Ligands and $Co^{3+}B$

Various experimental observations and UV-visible spectra indicate that the substitution reactivities in the organic ligands used with $Co^{3+}B$ have the following order under the experimental conditions: pyridine > isoquinoline > cholesterylamine > 2-octylamine >> quinoline, 8-methylquinoline, indole.

a. The reactivity of pyridine

Pyridine had the highest reactivity of those molecules considered in these experiments. The color was immediately changed from olive-green to emerald green after adding pyridine to the 0.015 M $Co^{3+}B$ water solution.

b. The reactivity of isoquinoline

Isoquinoline had less substitution reactivity in 0.015 M $Co^{3+}B$ water solution than pyridine had. As the isoquinoline was added to the solution, the color began to change from olive-green to emerald-green after about 20 minutes. The UV-visible spectrum of the aqueous phase showed that the absorbance peak near 685 nm in the control solution moved to 645 nm in the reaction solution (Figure 11). Note that isoquinoline did not dissolve in the $Co^{3+}B$ water solution. The PTC technique that was used aided in completing the substitution reaction and also helped to protect the amine from side reactions (see II-3 B section).

c. The reactivity of cholesterylamine

Cholesterylamine has a large organic non-polar group and is insoluble in water solution. No color change was observed when cholesterylamine solids were placed in 0.015 M $Co^{3+}B$ water solution for several hours at 30-40°C. Nor did the color change with THAB in the aqueous phase (Figures 12 and 14). The substitution reaction occurred in the toluene phase in the PTC system. The color in the toluene phase began to change to emerald-green 30 minutes after adding

THAB to the 0.015 M $Co^{3+}B$ water-toluene mixture. The UV-visible spectra indicated that the absorbance peak near 690 nm in the control solution shifted to 640 nm in the toluene phase at the ratios of 1:2.5 and 1:6 between $Co^{3+}B$ and THAB (Figures 13 and 15).

d. The reactivity of 2-octylamine

The 2-octylamine is a liquid at normal conditions and is also insoluble in the aqueous phase. No obvious change was observed even after several hours when this amine was added to 0.015 M $Co^{3+}B$ solution. In the PTC system, some emerald-green solids separated from the mixture of water and toluene after reacting for several hours at 30-40°C. The emerald-green solids did not dissolve in either the aqueous phase or the toluene phase. The solid did not dissolve in cyclohexane.

e. The activities of quinoline, 8-methylquinoline, and indole

These experiments showed that quinoline, 8-methyl-quinoline, and indole did not produce different green color shades either in PTC or in the non-PTC systems. The emerald-green color could not be observed in either aqueous or toluene phases even after increasing the reaction temperature to 30-60°C or after prolonging the reaction for several days. All UV-visible spectra of the three compounds in aqueous reaction phases showed that the absorbance peaks at 658 nm in the aqueous reaction solution were the same as the absorbance of the control

solution. These results confirmed that the coordinated reaction among HPA and the three compounds did not proceed under the experimental conditions.

In indole the nitrogen's extra pair of electrons is involved in the π cloud of the molecule (see section III-1. A. 2. C.). It is therefore not available to coordinate with HPA.

The nitrogens in quinoline and 8-methylquinoline have similar properties to the nitrogens in pyridine and isoquinoline. The unshared pair of electrons of nitrogen in quinoline and 8-methyl-quinoline is available for coordinating with HPA. The results showed that quinoline and 8-methylquinoline did not react with HPA under the experimental conditions. This suggests that a stereo selectivity exits between HPA and the ligands. The coordination ability of a HPA with the Keggin structure was determined by both electronic and steric effects.

f. The steric effects and geometric size

The data show that isoquinoline coordinates to the cobalt atom in the HPA whereas the quinoline and 8-methylquinoline do not coordinate to the cobalt. From these data and the structures of the compounds one can deduce that the cobalt is situated in a cone-like cavity. The minimum depth of this cavity and the maximum cone angle can be calculated using quinoline as a model when the radius of the coordinated ligand from the axis of the N-Co bond and the angle around the axis are considered as the main factors. The bond lengths of quinoline were

calculated using the bond distances of pyridine, benzene, and N-Co bonds [19, 70, 71]. These are shown in the Figure 20.

The Cosine Theorem,

$$a^2 = b^2 + c^2 - 2bc\cos(A) \qquad (1)$$

was used to calculate the radius, a = N-C_8; where the ∠A is equal to the ∠N$C_{10}C_8$ = 116.1°; the b is equal to the N-C_{10} = 1.340 Å; and the c is equal to the C_8-C_{10} = 1.380 Å:

$(N\text{-}C_8)^2 = 1.340^2 + 1.380^2 - (2)(1.340)(1.380)\cos(116.1) = 5.327$

N-C_8 = 2.308 Å.

The half inside cone angle ∠NCoH was calculated using the trigonometric tangent function:

Tangent(∠NCoH) = N-C_8 / (N-Co - C_8-H_8) = 2.308 / (1.92 - 1.101) = 2.818

∠NCoH = 70.5°

These calculations suggest that the cobalt atom is located at the bottom of this cone-like cavity. The depth of this cavity is 0.82 Å (1.92Å - 1.101Å). The radius of this cone is 2.308 Å. Thus the inside cone angle is 141°, that is 2 tangent(2.308Å/0.82Å). If the size and orientation of a coordinated ligand are equal to or larger than the size of the conical cavity, then steric hindrance occurs and the coordination reaction between HPA and ligands proceeds with difficulty. The cause of steric hindrance is considered as the repulsive van der Waals force

among the surface oxygen atoms of HPA and the atoms of a potential ligand. Hence the quinoline and 8-methylquinoline are sterically prevented from bonding to the cobalt of HPA.

B. The Application of Phase Transfer Catalysis (PTC)

1. The Choice of Phase Transfer Agent, Polar Phase, and Nonpolar Organic Phase

In order to coax most of the anions into the organic phase, as in phase transfer catalysis, it is necessary to allow them to associate with a cation having much "organic structure" so that organic-phase solvation of the cation is stronger than the aqueous-phase solvation of the anion. The organic structure of quaternary ammonium salts can be adjusted over a wide range, from very small structures to very large structures. The small structures, such as tetramethylammonium, are highly soluble in aqueous media but only slightly soluble in most organic media. The large structures, such as $(C_{12}H_{25})_4N^+$ salts, are highly soluble in almost all organic media but only slightly soluble in water. Tetraheptylammonium bromide (THAB) has a middle-sized organic group and is soluble in some organic media such as toluene. Therefore, it was chosen as the phase transfer agent in this research.

Most anions reside in the aqueous phase rather than the organic phase, even a highly polar one, because of the favorable thermodynamic effect afforded by

anion hydration [65]. This results from the electronic charge spreading over the greater volume of the hydrated species, and is therefore dependent on the charge-to-volume ratio of the anion. In these experiments, HPA species with a Keggin structure are very soluble in water, soluble in a water-methanol solution, and barely soluble in acetone. In addition, it is very difficult to find a totally soluble condition with a five-component system including heteropolyanion, water, methanol, acetone, and an organic ligand. Therefore, water was chosen as the polar solvent.

The choice of organic phase is based on the solubility of the ligand. The solubility characteristics of non-ionic compounds are determined chiefly by their polarity. Non-polar or weakly polar compounds dissolve in non-polar or weakly polar solvents; highly polar compounds dissolve in highly polar solvents. "Like dissolves like" is an extremely useful rule. All of the ligands used in this thesis research have a large hydrophobic portion and are weakly polar compounds. Furthermore, cholesterol dissolves in aromatic solvents such as benzene. Thus it was presumed that the cholesterylamine would be soluble in a benzene derivative. Toluene is one of the benzene derivatives and is a weakly polar solvent which has been used as the organic phase in previously reported work [20, 44, 66, 67]. In addition, THAB, the phase transfer agent used in this research, is soluble in toluene. Therefore, toluene was chosen as the organic phase.

2. The Phase Transfer Catalysis and Ligand Substitution with HPA

Observations of the isoquinoline-PTC system with HPA : isoquinoline : THAB = 1 : 1 : 0.25 showed that the color changed from olive-green to emerald-green in the aqueous phase and that the maximum absorbance of the visible spectra shifted from 685 nm to 645 nm (Figure 11). These results suggest that the PTC reaction can be accomplished with ligand substitution under the experimental conditions.

The solubility of the amine-HPA complex in both the aqueous phase and the organic phase are important factors for PTC reaction. These solubilities may influence the partition and behavior of the cation-anion pair. The yield in the isoquinoline-$Co^{3+}B$ complex was 0.38 g when the ratio of HPA : toluene was 30 μmol : 0.5 mL; the yield was 0.32 g when the ratio was 30 μmol : 2 mL. These results support the hypothesis that the amine-HPA complex dissolves in both the aqueous phase and the organic phase with different equilibrium distributions. The organic phase as the reaction media maintained some of the amine-HPA complexes in it and formed an equilibrium system with the aqueous phase. The smaller the amount of the organic phase, the less of the amine-HPA complex maintained in the organic phase, and thus the higher the yield of the amine-HPA.

The experimental results for the $Co^{3+}B$ with 2-octylamine and cholesterylamine also supported the hypothesis that the solubility of amine-HPA

complex influences the PTC reaction and the behavior of cation-anion pairs. The 2-octylamine coordinated with $Co^{3+}B$ under PTC conditions to form an emerald-green solid phase. The color in the aqueous phase did not change to emerald-green. Furthermore, the cholesterylamine-$Co^{3+}B$ anion could not be returned to the aqueous phase after coordinating in the toluene phase. For the experiment with the mixture of 30 μmol $Co^{3+}B$, 2 mL H_2O, 30 μmol cholesterylamine, and 1.5 mL toluene, the toluene phase changed to emerald-green and the aqueous phase became colorless when sufficient THAB was added. The amount of THAB added was equivalent to the amount of charge on the HPA. A possible cause was that this complex, with a large hydrophobic steroid group, has a higher solubility in the toluene phase which changed the behavior of cation-anion pairs. An alternative explanation is given in Figure 21.

A third emulsion layer was easily formed between the aqueous phase and the toluene phase when cholesterylamine was used as the coordinating ligand. The formation of the emulsion layer inhibited the coordination reaction between HPA and cholesterylamine. Usually emulsions can be destroyed by adding a high concentration of electrolytes or a surfactant or by increasing the system temperature. The emulsion can also be broken by centrifugation, filtration, or electrophoresis [72]. Our experiments showed that THAB with the surfactant properties could break the emulsion and transfer HPA into organic phase.

C. The Preparation of Complexes by HPA Tungstate with Organic Amines

The methods for preparation of HPA complexes of tungstate with some derivatives of organic amines have been described in the experimental section. The potassium isoquinolinecobalto(III)-11-tungstoborate (isoquinolineCo^{3+}B), a new complex, was prepared by using the PTC technique. This represents a novel attempt to prepare the complex by ligand substitution in PTC with two mutually insoluble reagents, HPA and organic amines. The emerald-green sample of isoquinolineCo^{3+}B was not a crystalline but rather a finely divided solid. More work is needed to characterize the complex and to obtain crystals.

The complex of cholesterylamine-Co^{3+}B, another new complex, was prepared by the phase transfer technique. In this case the phase transfer agent THAB in catalytic quantities could not bring the reaction to completion in the aqueous phase because of the large hydrophobic steroid group. The reaction was completed in the toluene phase by using THAB with 1:6 ratio of THAB:HPA. An emerald-green oil-like solid was obtained after evaporating the toluene. Since the amine group is attached to a chiral carbon in the cholesterylamine, two forms are possible. These possible structures are shown in Figure 22. Further work is needed to isolate, purify, and characterize the complex.

The octylamine-Co^{3+}B complex prepared in this research could not be obtained in a stable state. The experiments confirmed that it was possible to form

a HPA-octylamine complex in PTC. However, further study is needed to determine the best organic phase and reaction conditions.

Quinoline, 8-methylquinoline, and indole could not be coordinated with HPA because of the steric effect and the unavailability of the nitrogen lone-pair electrons (see discussion of "Structure Activity Relationships" in section III-1. A.).

III-2. The Synthesis of Amines

A. The Reaction Mechanism

The Mitsunobu reaction is a mild method to prepare amines from alcohols [56, 58]. This reaction proceeds stereospecifically with complete inversion of the configuration of the alkyl group [56]. The probable reaction mechanism is shown in Figure 23. The reaction proceeds through (a) addition of 2 to 1 giving a quaternary phosphonium salt 3, (b) protonation of 3 with phthalimide to form 4, (c) formation of an alkoxyphosphorium salt 5 with alcohol, (d) S_N2 type displacement of 5 to form 6, (e) two steps of S_N2 (tetrahedral mechanism) with hydrazine to yield the resulting amine species 8. Therefore, this diethyl azodicarboxylate / triphenylphosphine system falls into the category of a redox reaction in which triphenylphosphine is oxidized to triphenylphosphine oxide and diethyl azodicarboxylate is reduced to diethyl hydrozinedicarboxylate [58].

B. Chromatography and Spectral Analysis

1. 2-Octylamine Preparation

Thin layer chromatography (TLC) has been widely used in organic syntheses, chemical and biochemical analyses, and in preparative separations since 1958 [72]. The relatively rapid spread in the use of TLC is due mainly to the fact that it permits an efficient separation in a very short time and by simple and inexpensive means. It may be used for the control of other methods of separation (distillation, column chromatography, control of purification procedure, etc.) In this research TLC was used to observe the progress of the reaction and to determine the purity of the intermediates.

The raw intermediate sample in the preparation of 2-octylamine produced two spots on the TLC plate. The two R_f values were 0.11 for a light spot and 0 for a dark spot. The R_f value of 2-octanol used was 0.11. From analysis of the intermediate structure, the designed intermediate 2-octylphthalimide was a more polar sample than 2-octanol was. The sample with less polarity should migrate faster than that of the higher polarity sample when benzene is used as the eluent. The result suggested that the intermediate was a relatively pure sample. Therefore, it was used directly in the next hydrolysis reaction.

The FTIR spectrum of 2-octylamine showed a broad absorbance peak around 3400 cm^{-1}, two strong peaks near 2900 cm^{-1} and 1620 cm^{-1}, and some

smaller peaks around the fingerprint range of 1000 cm^{-1} (Figure 6). The broad peak around 3400 cm^{-1} indicated a strong association of polar groups, such as -OH, $-NH_2$, and some kind of impurity compared with the 2-octanol FTIR spectrum (Figure 7). The peak near 2900 cm^{-1} indicated the C-H stretching vibration of the 2-octyl group. The important difference between amine and alcohol was the peak near 1620 cm^{-1} caused by N-H bending vibration. This result combined with the physical and chemical analysis of the product confirmed that it was an amine.

2. Cholesterylamine Preparation

a. Preparation of intermediate

The TLC R_f values for cholesterol, triphenylphosphine, diethylazido-dicarboxylate with benzene as the eluent were 0.06, 0.92, and 0.34, respectively. Phthalimide was insoluble in benzene and no spot appeared on the TLC plate. Samples from the reaction solution were taken at reaction times of 0.1, 21, 44, and 68 hours. The TLC showed that the cholesterol in the reaction solution had a R_f value of 0.05. This spot spread and lightened after reacting for 68 hours. The results suggested that the 68-hour reaction time for the Mitsunobu reaction with cholesterol was a better choice for the reaction time under the experimental conditions. In addition, the raw intermediate produced two spots on a TLC plate. The R_f values were 0 for a dark spot and 0.05 for a light spot. This result also supported the hypothesis that most of the cholesterol molecules in the reaction

mixture had undergone the Mitsunobu reaction.

The proton NMR spectrum of cholesterylphthalimide intermediate in CCl_4 produced a broad multiplet around 1.0 ppm, two smaller peaks near 4.0 and 5.2 ppm, and another multiplet near 7.4 ppm (see Figure 8). By comparison with the cholesterol NMR spectrum (Figure 10), the multiplet around 1.0 ppm represented the steroid protons and the peak near 5.2 ppm was the double-bond proton at the C_5=C_6 position in both compounds. The peak near 7.4 ppm in Figure 8 indicated the protons of the phthalimide benzene ring. One of the important differences between the two spectra was that the proton neighboring the hydroxy group near 3.4 ppm in cholesterol had shifted to lower-field near 4.0 ppm in the intermediate. This confirmed that the cholesteryl group had combined with the nitrogen atom in phthalimide to form the cholesteryl-phthalimide intermediate.

b. Preparation of cholesterylamine

The NMR spectrum of the raw cholesterylamine consisted of a multiplet near 1.0 ppm, a very small peak near 5.2 ppm, and a multiplet near 7.4 ppm [Figure 9]. The peaks near 1.0, 5.2, and 7.4 ppm represented the same kind of protons as mentioned above. The peak produced by the proton next to the nitrogen atom near 4.0 ppm in the intermediate did not appear in the spectrum. It is assumed that this phenomenon was caused by the quadrupole effect of the nitrogen atom [73]. The nitrogen atom has a nuclear quadrupole since its spin quantum

number I > 1/2. A quadrupole on a neighboring atom weakens the H NMR signal. In comparison with Figure 10, the small -OH proton peak near 2.3 ppm in the cholesterol spectrum had disappeared in the cholesterylamine spectrum. This suggested that the -OH group had been replaced by the $-NH_2$ group to form cholesterylamine. In addition, the fact that the product reacted with HPA to produce an emerald-green solution also supported the conclusion that the amine had been formed.

The peak near 7.4 ppm indicated that the raw cholesterylamine contained some kind of impurity. These results are consistent with the observed melting point. A large melting range (89-122°C) indicated an impurity. This suggests that either the Gabriel hydrolysis under the experimental conditions was not complete or further purification procedure was needed, or both.

III-3. The Preparation of Heteropoly Tungstate

Four heteropoly tungstates were prepared following the methods used by Landis [19]. The methods were well described and confirmed in the literature [19]. In this research the yields are reported. The yields were 82.5% for potassium aquocobalto(II)-11-tungstosilicate ($Co^{2+}Si$), 74% for potassium aquocobalto(III)-11-tungstosilicate ($Co^{3+}Si$), 45.3% for potassium aquocobalto(II)-11-tungstoborate ($Co^{2+}B$), and 60% for potassium aquocobalto(III)-11-tungstoborate ($Co^{3+}B$). The products were qualitatively examined using an optical

microscope. The microscope observation indicated that $Co^{2+}Si$, $Co^{2+}B$, and $Co^{3+}B$ had clear crystals and uniform color. The bands in the IR spectrum of $Co^{2+}Si$ between 1200 cm^{-1} and 400 cm^{-1} were consistent with those in the literature [19]. The results supported the conclusion that the $Co^{2+}Si$ prepared in the research was the expected product. Furthermore, these products with water and Zn produced the blue color characteristics of tungsten (V) in heteropoly anions. These properties also suggest that the HPA had been prepared in the experiment.

The $Co^{3+}Si$ contained some white impurity with the green octahedra. The phenomenon observed in the post-treatment procedure was a little different from that previously reported [19]. The crystals of $Co^{3+}Si$ could not be obtained by refrigeration but had to be obtained by evaporating the solution in air. The crystals of $Co^{3+}B$ were microscopically pure after having been refrigerated and filtered from the reaction solution. The success of the purification of $Co^{3+}B$ using acetone as given in the literature [19] leads one to conclude that one should use a similar method for the $Co^{3+}Si$ purification.

III-4. Conclusions and Further Considerations

Several points have been discussed in the previous section. Based on the experimental results and the data analysis, some important conclusions and further considerations are summarized in this section.

1. The study of structural reactivities confirmed our hypothesis that ligand substitution among HPA and organic amines was determined by both electronic and steric effects. The mathematical calculation (based on quinoline) indicates that the coordinatively unsaturated site of HPA has a cone-like cavity with the cobalt atom at the cone's apex and the axis of rotation along the cobalt-nitrogen bond. The cone has a minimum depth 0.82 Å and a maximum radius of 2.31 Å. This yields a maximum inside angle 141°. If the size and orientation angle of a coordinated ligand are equal to or larger than the size of the cavity, steric hindrance occurs. The special requirements of the cholesterylamine are less than the calculated cavity dimensions. This amine also has proper electronic effects for coordination to the cobalt atom. Further experiments and bond data are needed to verify the geometric size that produces steric effects.

2. Ligand substitution with phase transfer catalysis (PTC) with HPA is a new synthesis method. This study showed the possibility of substitution using PTC with HPA and a procedure to be applied to the PTC technique in this area. Further experiments with different ratios of HPA:PTC reagents will be helpful to find the best preparation conditions. In addition, further analysis of the coordination complex products is necessary to confirm the conclusions of this research.

3. The experiments conducted showed that the Mitsunobu reaction can be

used for the preparation of cholesterylamine. This work describes a method to prepare cholesterylamine by the Mitsunobu reaction. The reaction conditions, the ratio of reactants, and the post-treatment procedures in the Gabriel hydrolysis need to be investigated in order to increase the yield.

4. Cholesterylaminecobalto(III)-11-tungstoborate was prepared in the organic phase with the phase transfer reagent, THAB. Catalytic amounts of THAB were insufficient to make the coordinating reaction between cholesterylamine and $Co^{3+}B$ go to completion in aqueous phase because of the large hydrophobic organic steroid group.

5. The solubility of amine-HPA complexes influence the PTC reaction and the behavior of cation-anion pairs of HPA and THAB. Only ligands with smaller organic groups can be coordinated with HPA and obtained from the aqueous phase in a PTC system. Experiments choosing different solvents as the organic phases would be helpful to prepare different HPA-amine complexes.

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APPENDIX A

FIGURES

Figure 1.

Keggin Structure (1:12 heteropoly anion)

The smaller black spheres represent the oxygen atoms. The 12 lighter bigger spheres represent the addenda atoms, M, such as W or Mo. An even bigger sphere in the center represents the hetero atom X, (such as P, Si, B etc.) [This model was made by Dr. Manli Zheng of CAChe Scientific and Dr. A. Landis utilizing CAChe Scientific computer software].

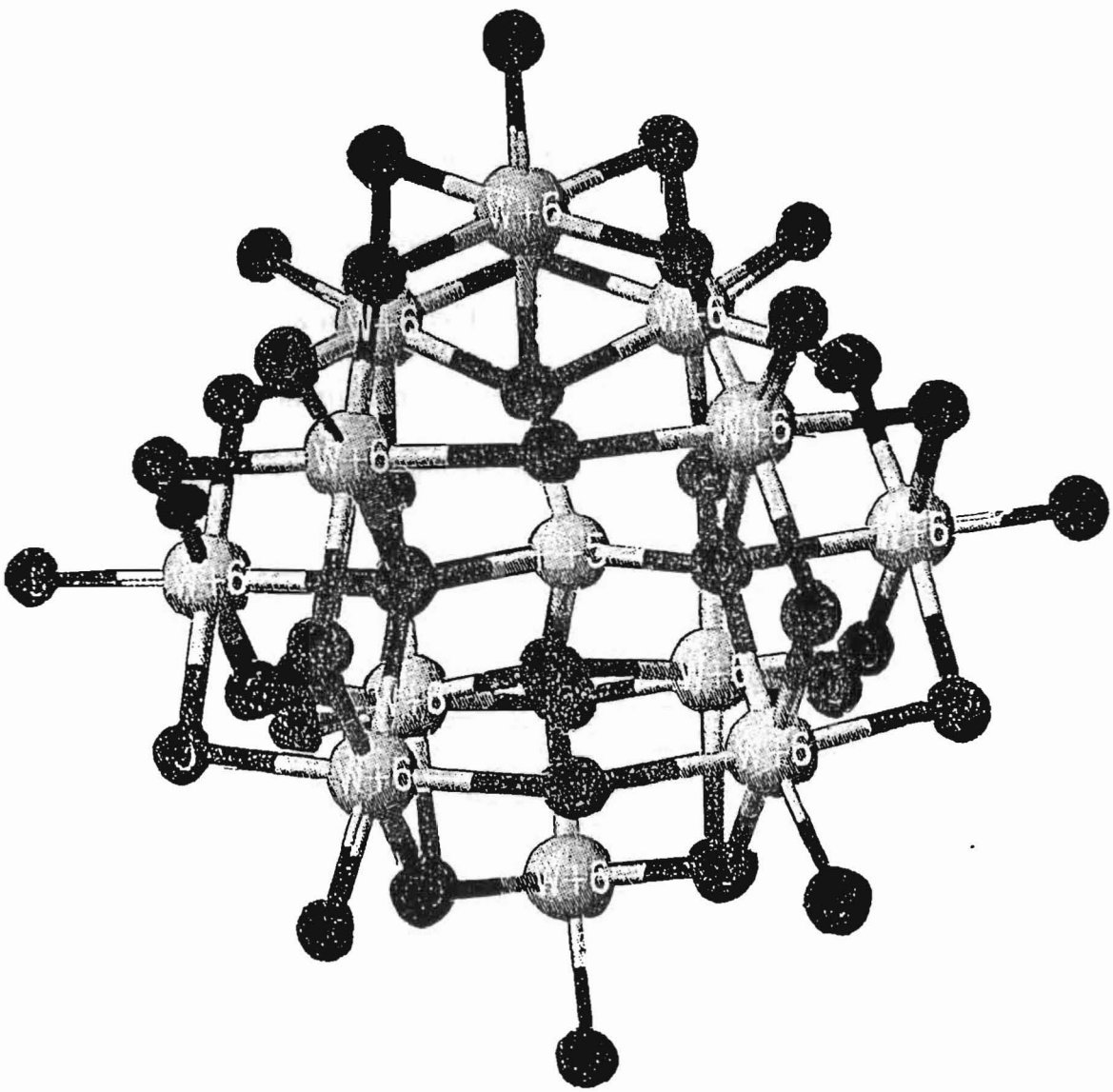


Figure 2.

Modified Keggin Structure

The modified Keggin structure is a 1:1:11 heteropoly anion. This is the Baker-Figgis model and is essentially the same as the Keggin structure. The difference between this model and the Keggin structure is that one of the addenda atoms M is replaced by a heteroatom X (such as Co^{2+}, Co^{3+}, etc.). An oxygen atom connected with the X is replaced by a H_2O molecule which connects with the X atom and spreads out the closed basket. [This model was made by Dr. Manli Zheng of CAChe Scientific and Dr. A. Landis utilizing CAChe Scientific computer software].

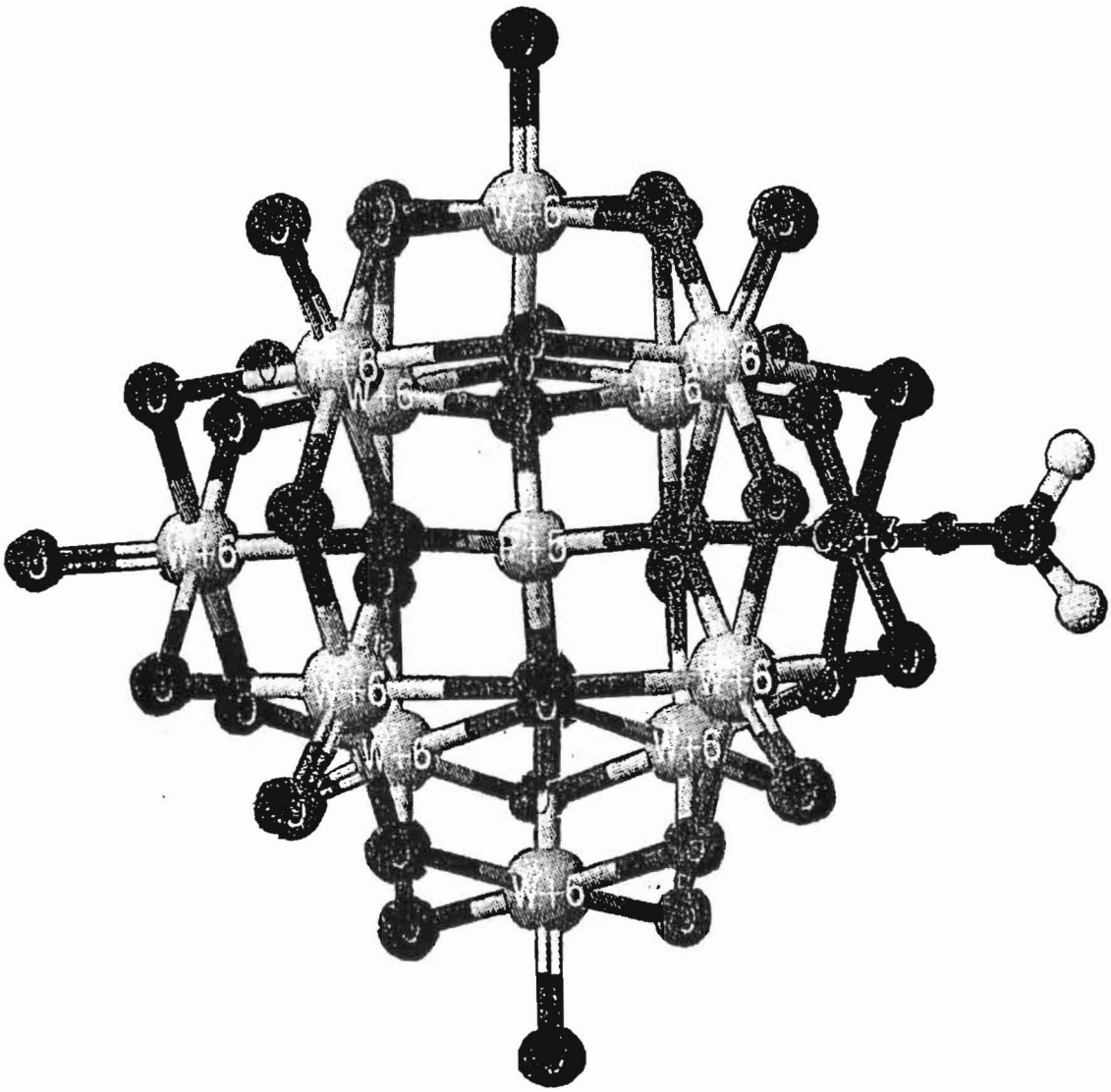

W+6
W+6
W+6
W+6
W+6
W+6
W+6
W+6
W+6
P+5
C+3

Figure 3.

Reaction Formula of

Modified Keggin Structure and Ligand Substitution

The probable reaction of the Baker-Figgis model including the ligand substitution is presented. A mixture of 1 mol heteroatom oxide, 11 mol addenda atom oxide, and 1 mol another heteroatom oxide are condensed at pH 6.0-6.5 to form the modified Keggin structure (I) with a higher negative charge. The more highly negative charged heteropoly is oxidized to form a lower negatively charged heteropoly (II) by using $K_2S_2O_8$ at pH 6.0. The species (II) coordinates with the organic amine ligands to form heteropoly-amine complexes in PTC or non-PTC system.

Fig. 3. The Reaction for The Modified Keggin Structure and Ligand Substitution

$$1X^{x+}O_r^{(2r-x+)-} + 11\ WO_4^{2-} + 1\ M'^{m'+} + H_2O \xrightarrow[\text{pH 6.0-6.5}]{H+}$$

$$[(H_2O)M'^{m'+}O_5X^{x+}O_4W_{11}O_{30}]^{[12-m'-x+]-} \xrightarrow[\text{pH 6.0}]{K_2S_2O_8}$$

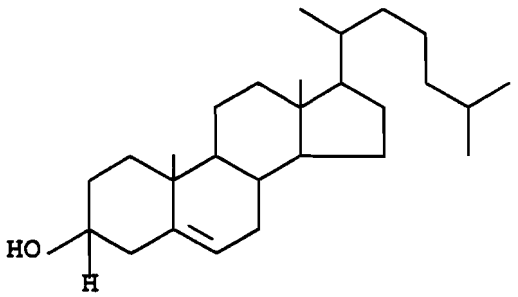
$$[(H_2O)M'^{(m'+1)}O_5X^{x+}O_4W_{11}O_{30}]^{[12-(m'+1)-x+]-} \xrightarrow[\text{PTC}]{\text{Ligand (Y)}}$$

$$[(Y^{y-})M'^{(m'+1)}O_5X^{x+}O_4W_{11}O_{30}]^{[12-(m'+1)-x+y]-} + H_2O$$

Figure 4.

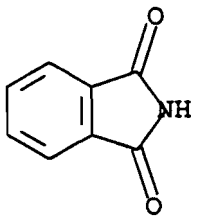
Mitsunobu Reaction and Gabriel Hydrolysis.

In this procedure the cholesterol is used as the initial material and reacts with phthalimide in the presence of triphenylphosphine (TPP), diethylazido-dicarboxylate (DEADC) in THF solvent. The cholesterol loses the -OH group to form the N-cholesteryl-phthalimide intermediate. This intermediate is changed to cholesterylamine and phthalazine-1,4-dione by refluxing in an ethanol solution with hydrazine.



Cholesterol

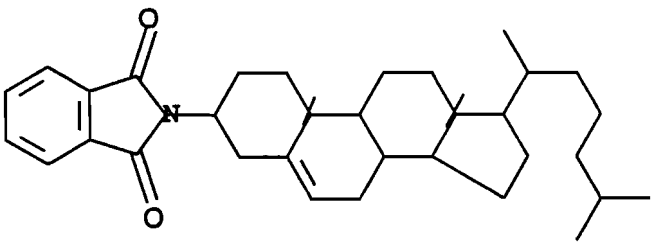
+



phthalimide

$- H_2O$

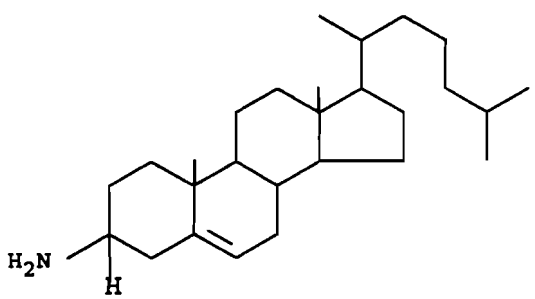
TPP, DEADC
THF



N-cholesterylphthalimide

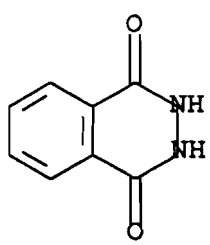
$+ H_2NNH_2$

ethanol reflux



cholesterylamine

+



phthalazine-1,4-dione

TPP : triphenylphosphine
DEADC : diehtylazido-dicarboxylate
THF : tetrahydrofuran

Figure 5.

FTIR Spectrum of Potassium Aquocobalto(II)-11-tungstosilicate ($Co^{2+}Si$)

The bands in the spectrum are consistent with those reported in the literature [1]. The spectrum was taken using 1:100 ($Co^{2+}Si$: KBr) KBr pellet with a resolution of 1 cm^{-1} and 8 scans.

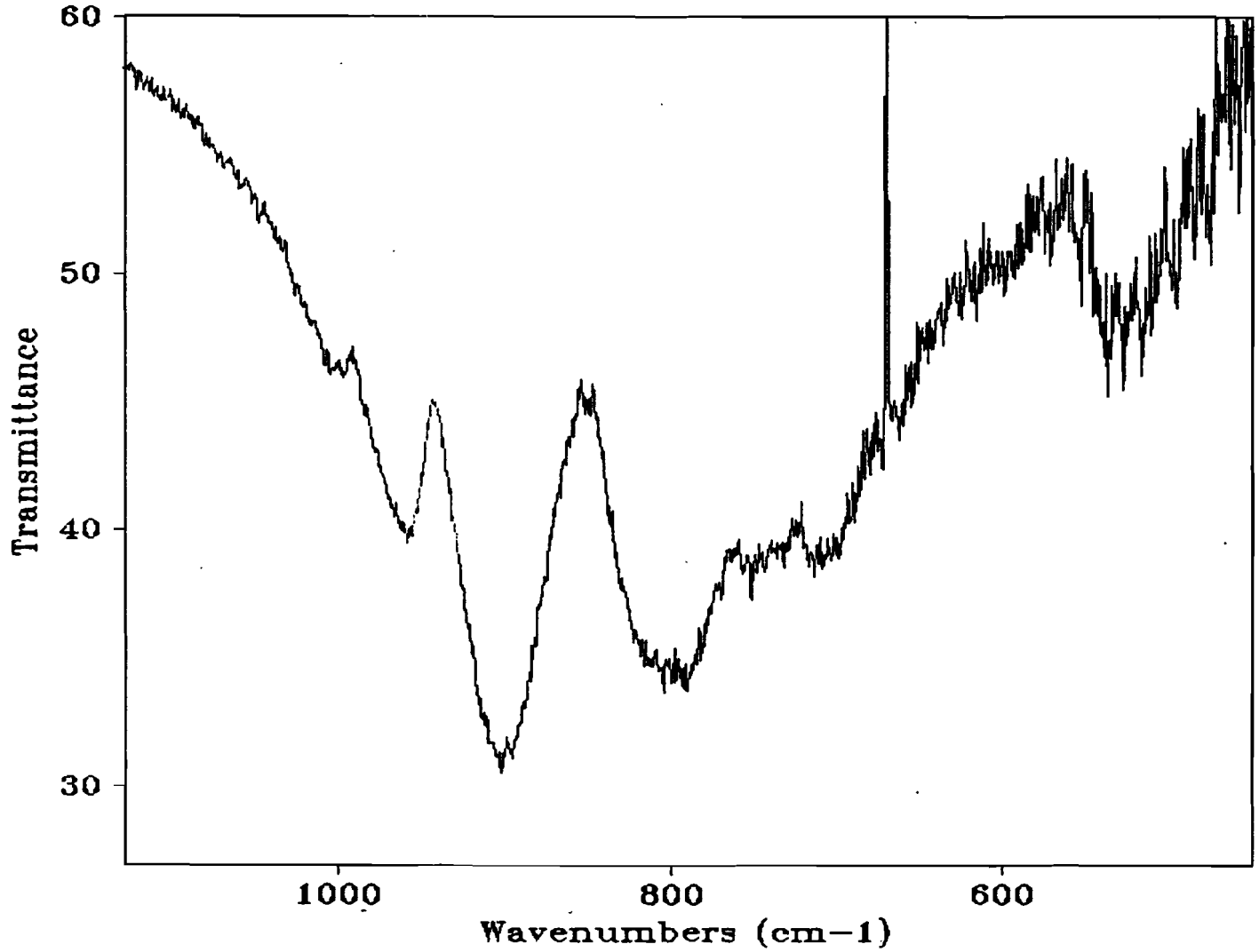

60
50
40
30
Transmittance
1000
800
600
Wavenumbers (cm−1)

Figure 6.

FTIR Spectrum of 2-Octylamine

The spectrum was taken using a liquid cell with KBr windows at a resolution of 4 cm^{-1} and 8 scans. The broad peak around 3400 cm^{-1} indicates a strong association of polar groups such as -OH, $-NH_2$, and some kind of impurity. The peak near 2900 cm^{-1} indicates C-H stretching vibration of the 2-octyl group. The peak near 1620 cm^{-1} is due to a N-H bending vibration.

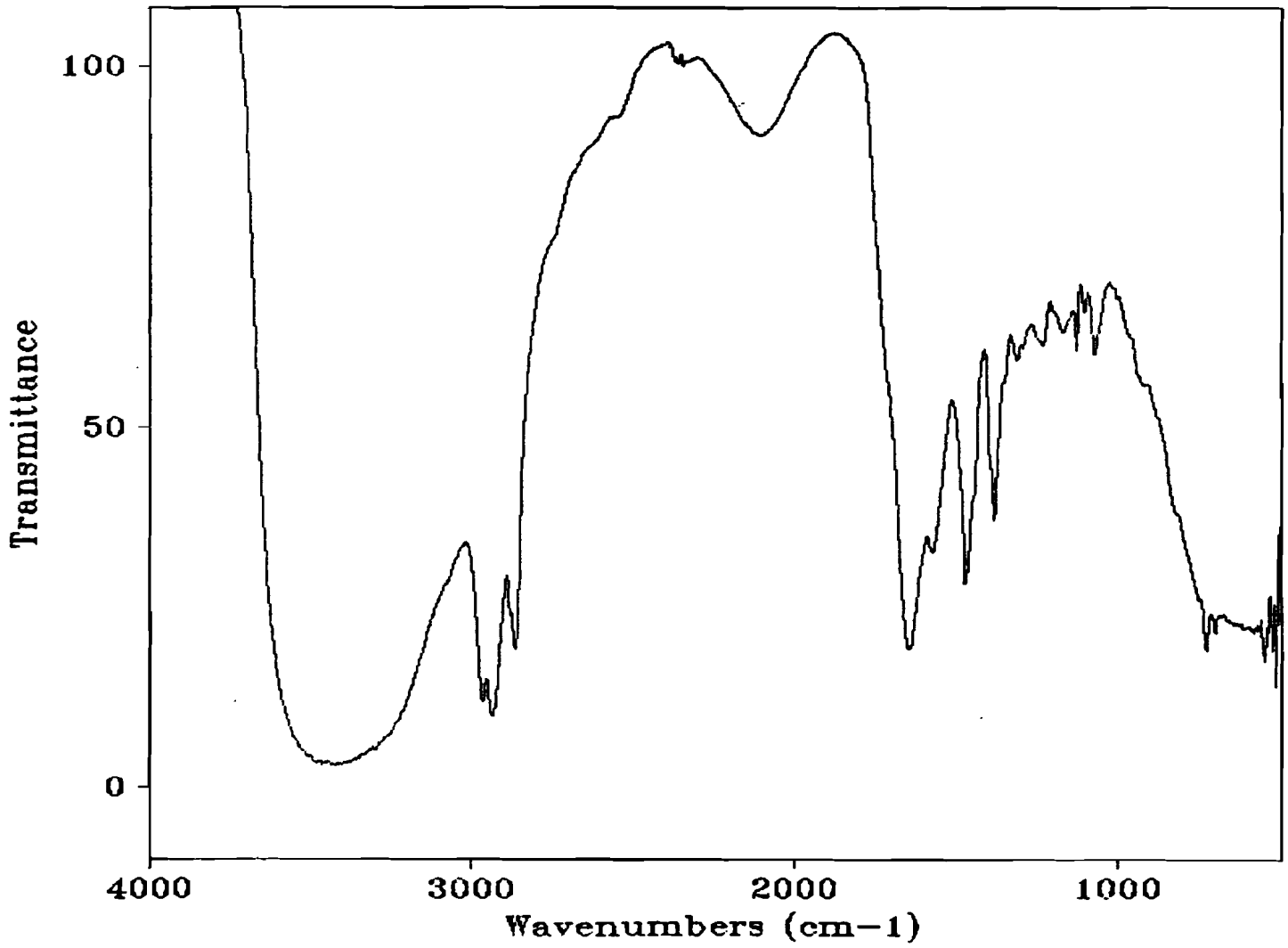

100
50
0
Transmittance
4000
3000
2000
1000
Wavenumbers (cm−1)

Figure 7.

FTIR Spectrum of 2-Octanol

The spectrum was taken using a liquid cell with KBr windows at a resolution of 4 cm^{-1} and 8 scans. The broad peak around 3400 cm^{-1} indicates a strong association of polar group such as -OH. The peak near 2900 cm^{-1} indicates the C-H stretching vibration of a 2-octyl group.

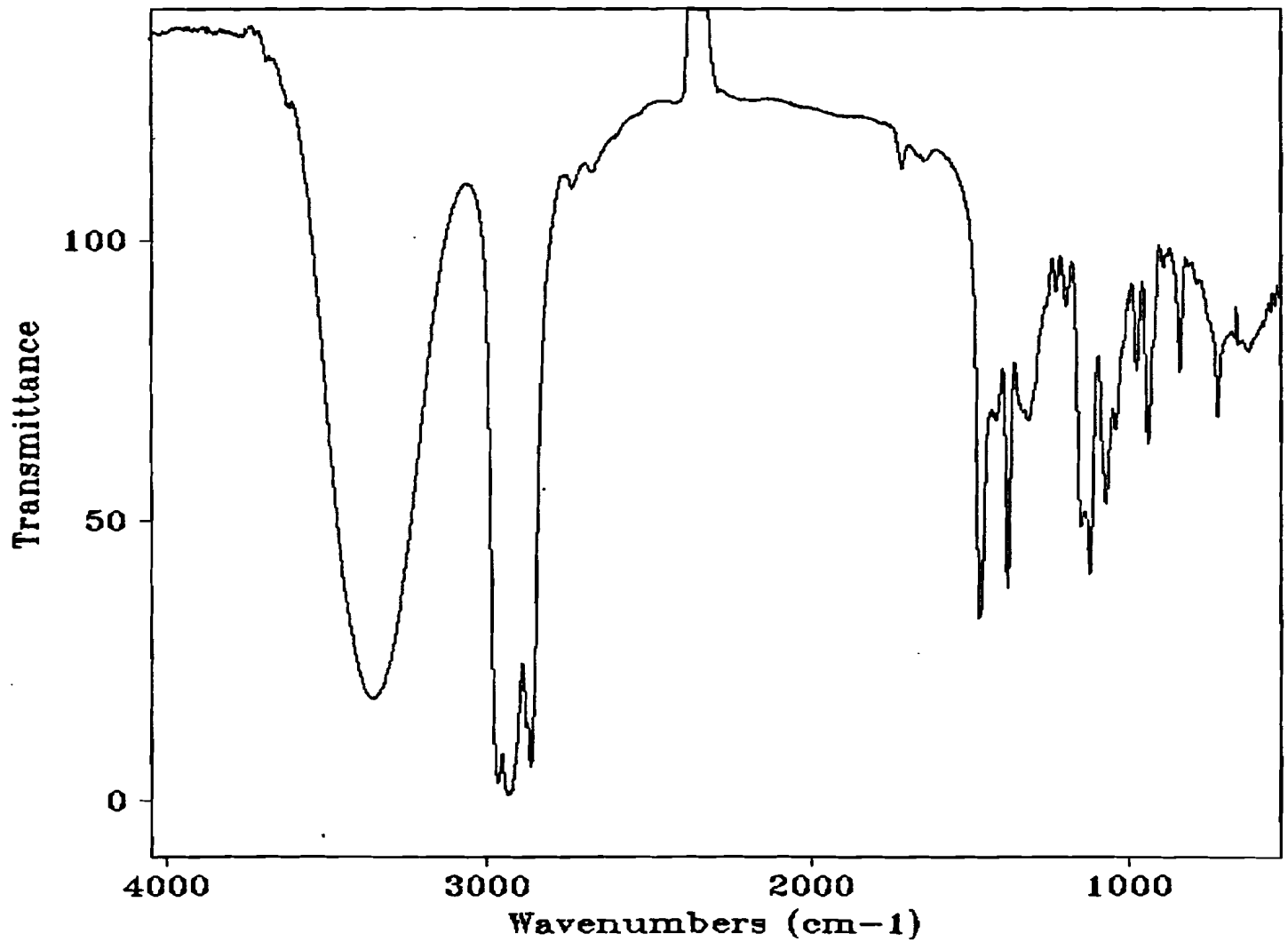

Transmittance
100
50
0
4000
3000
2000
1000
Wavenumbers (cm−1)

Figure 8.

Proton NMR Spectrum of N-Cholesterylphthalimide

The broad multiplet around 1.0 ppm is produced by steroid protons. The peak near 5.2 ppm represents the double-bond proton, and the peak near 7.4 ppm is from the protons of the phthalimide benzene ring. The peak at 4.0 ppm is the proton of the NCH between the N atom of phthalimide and the 3 position of the cholesteryl group. This confirms that the intermediate, N-cholesterylphthalimide, was formed by Mitsunobu reaction.

Reference	5% TMS
Solvent	CCl_4 + TMS (1%)
Concentration	1%
Amplitude	10
Integral	6

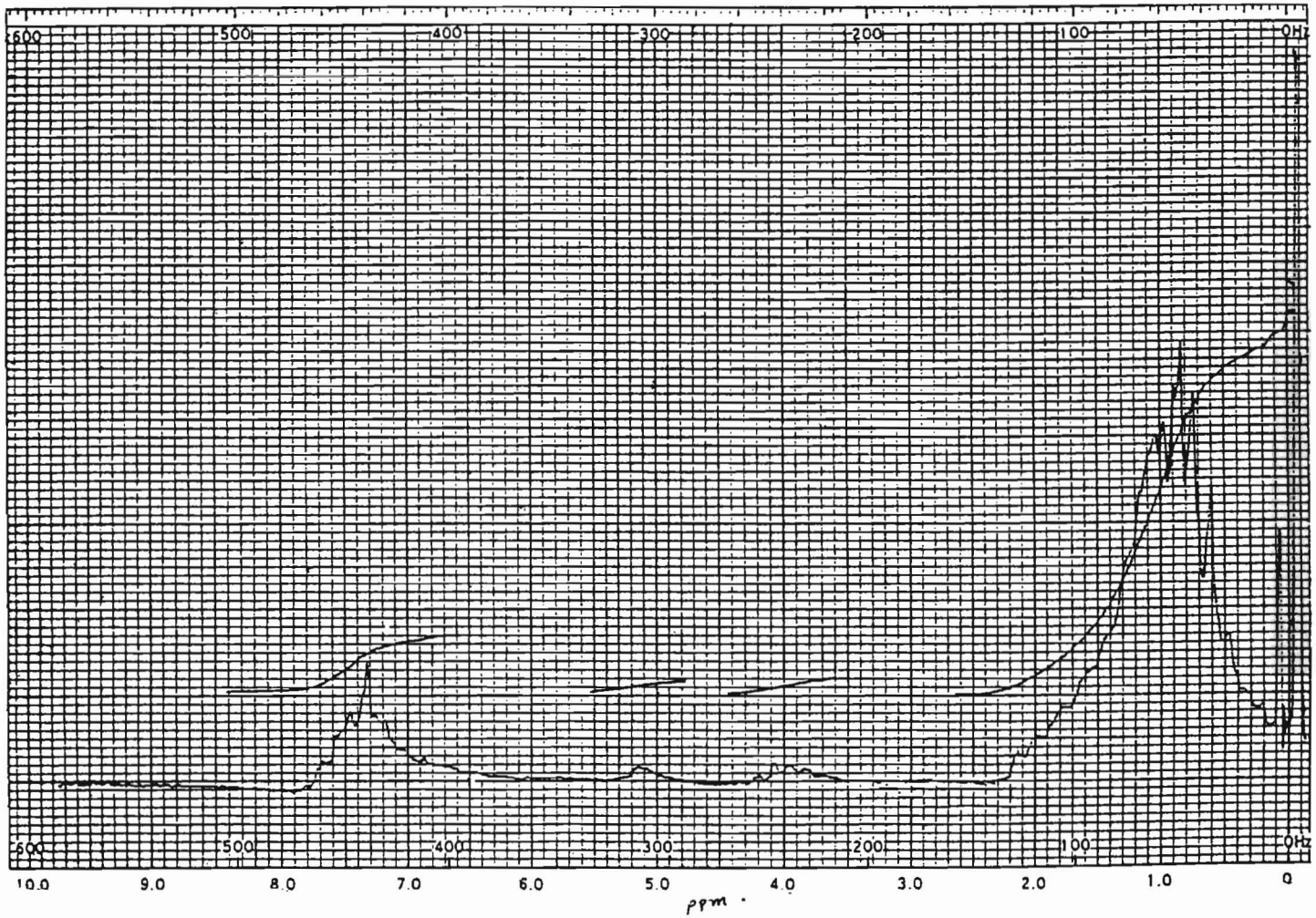

600
500
400
300
200
100
0Hz
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
ppm

Figure 9.

Proton NMR Spectrum of Cholesterylamine

The peaks near 1.0 ppm and 5.2 ppm are produced by the same kinds of protons mentioned in Figure 8. The peak near 7.4 ppm indicates some kind of impurity in this sample (probably phthalazine-1,4-dione). The NCH peak does not appear near 4.0 ppm due to the quadrupole effect.

Reference	5% TMS
Solvent	CCl_4 + TMS (1%)
Concentration	1%
Amplitude	12

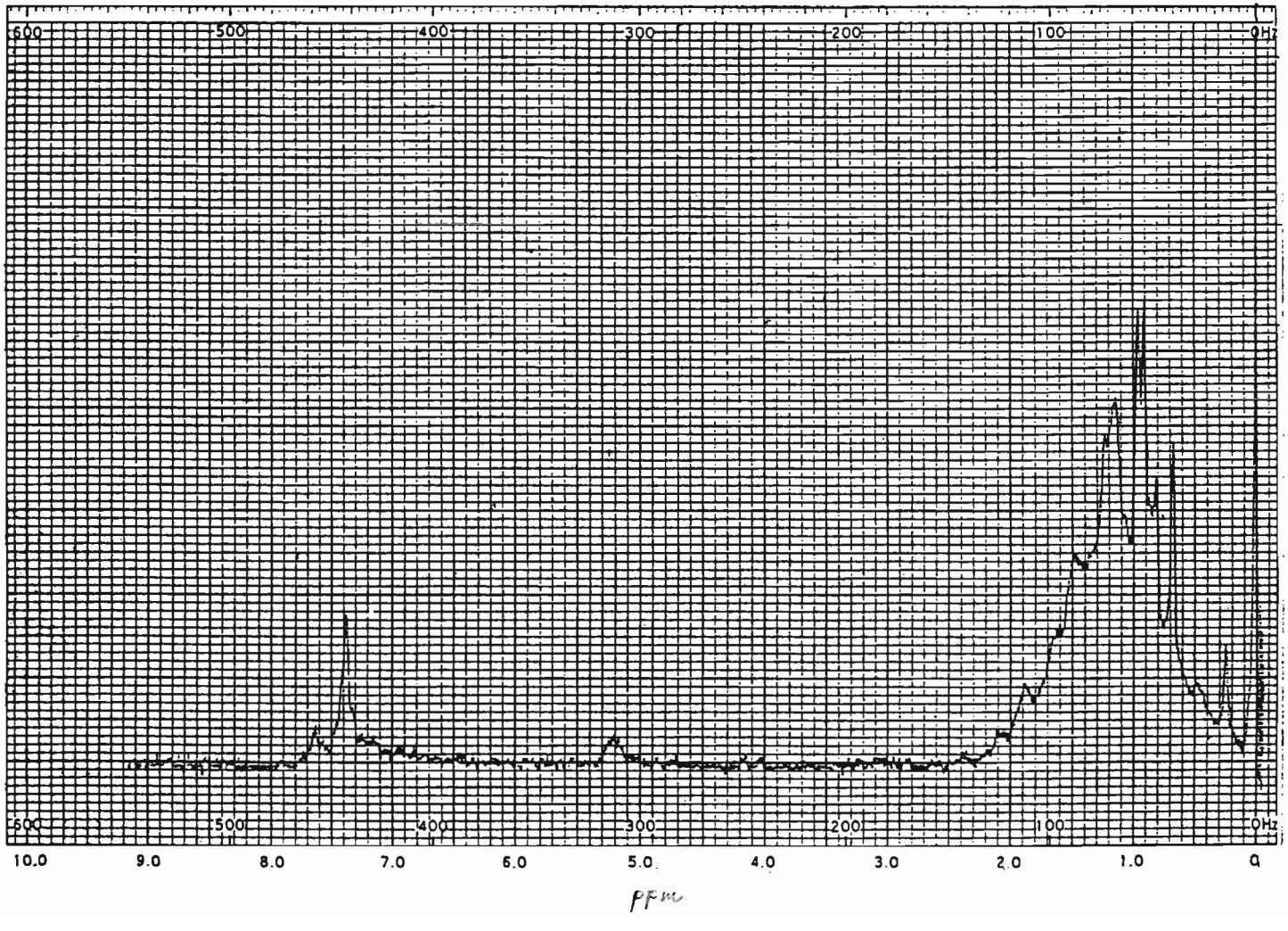

600
500
400
300
200
100
0Hz
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
ppm

Figure 10.

Proton NMR Spectrum of Cholesterol

The peaks near 1.0 ppm (broad peak) and 5.2 ppm are produced by the protons of steroid and the double-bond. The peak at 3.4 ppm is due to the proton of OCH at the 3 position of cholesterol. The small peak near 2.3 ppm is produced by the -OH proton.

Reference	5% TMS
Solvent	CCl_4 + TMS (1%)
Concentration	1%
Amplitude	11

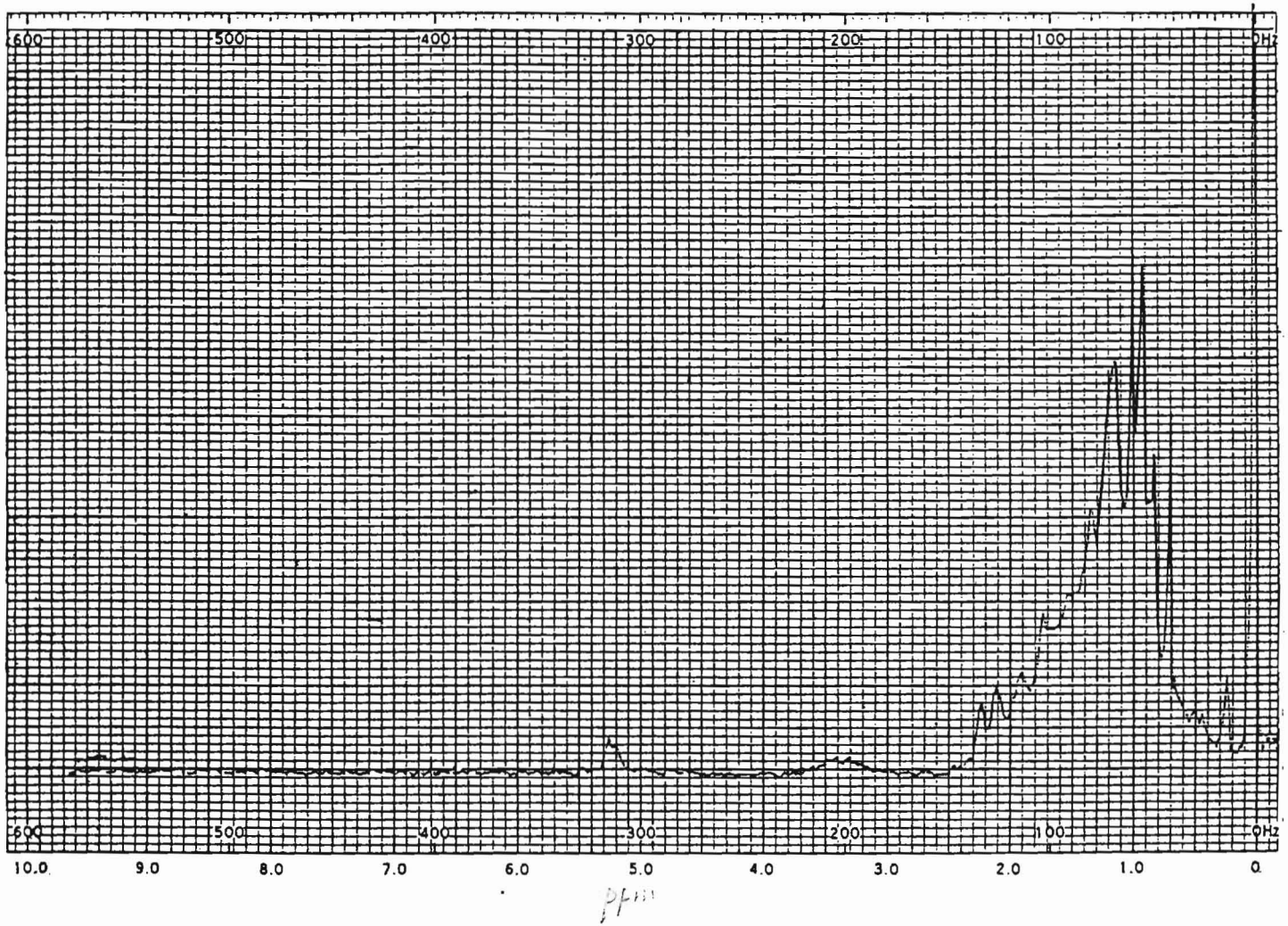

600
500
400
300
200
100
0Hz
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
ppm

Figure 11.

Visible Spectrum of Isoquinoline

The solid line represents the absorbance curve of isoquinoline with $Co^{3+}B$ in the aqueous phase of the PTC system. The dotted line represents the absorbance curve of the control sample. The maximum absorbance at 685 nm in the control curve shifts to 645 nm in the isoquinoline curve indicating that a coordination reaction has occurred with the isoquinoline in the aqueous phase.

Visible Spectrum 0f Isoquinoline

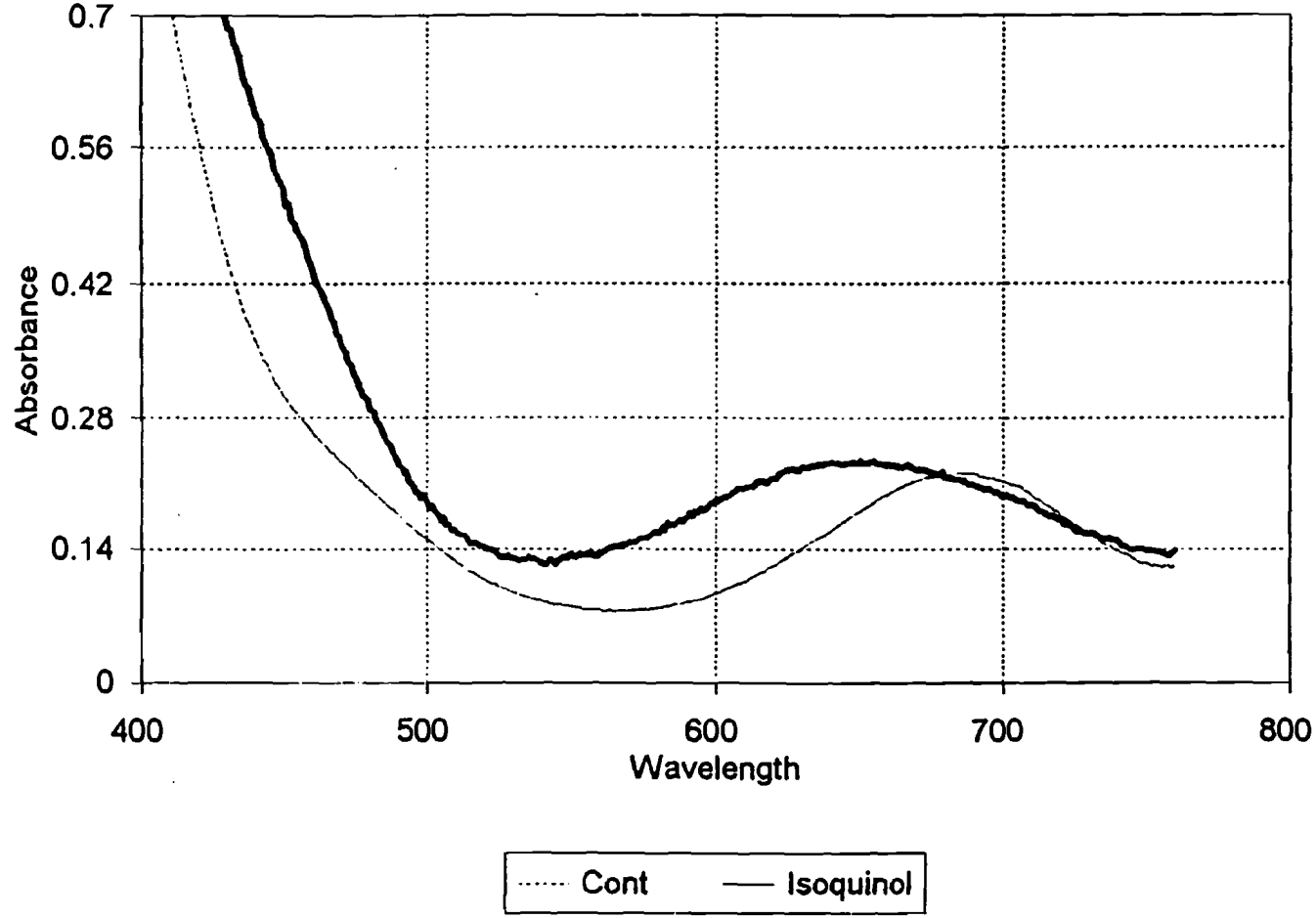


Figure 12.

Visible Spectrum of Cholesterylamine in the Aqueous Phase

(HPA:THAB = 1:2.5)

The solid line represents the absorbance curve of cholesterylamine (Cho.) with $Co^{3+}B$ in the aqueous phase with a mole ratio of HPA:THAB = 1:2.5. The dotted line represents the absorbance curve of the control sample. Both curves have the same maximum absorbance peak at 685 nm indicating that the coordination reaction between cholesterylamine and $Co^{3+}B$ did not proceed in the aqueous phase.

Visible Spectrum of Cho. in Aqueous

HPA:THAB = 1:2.5

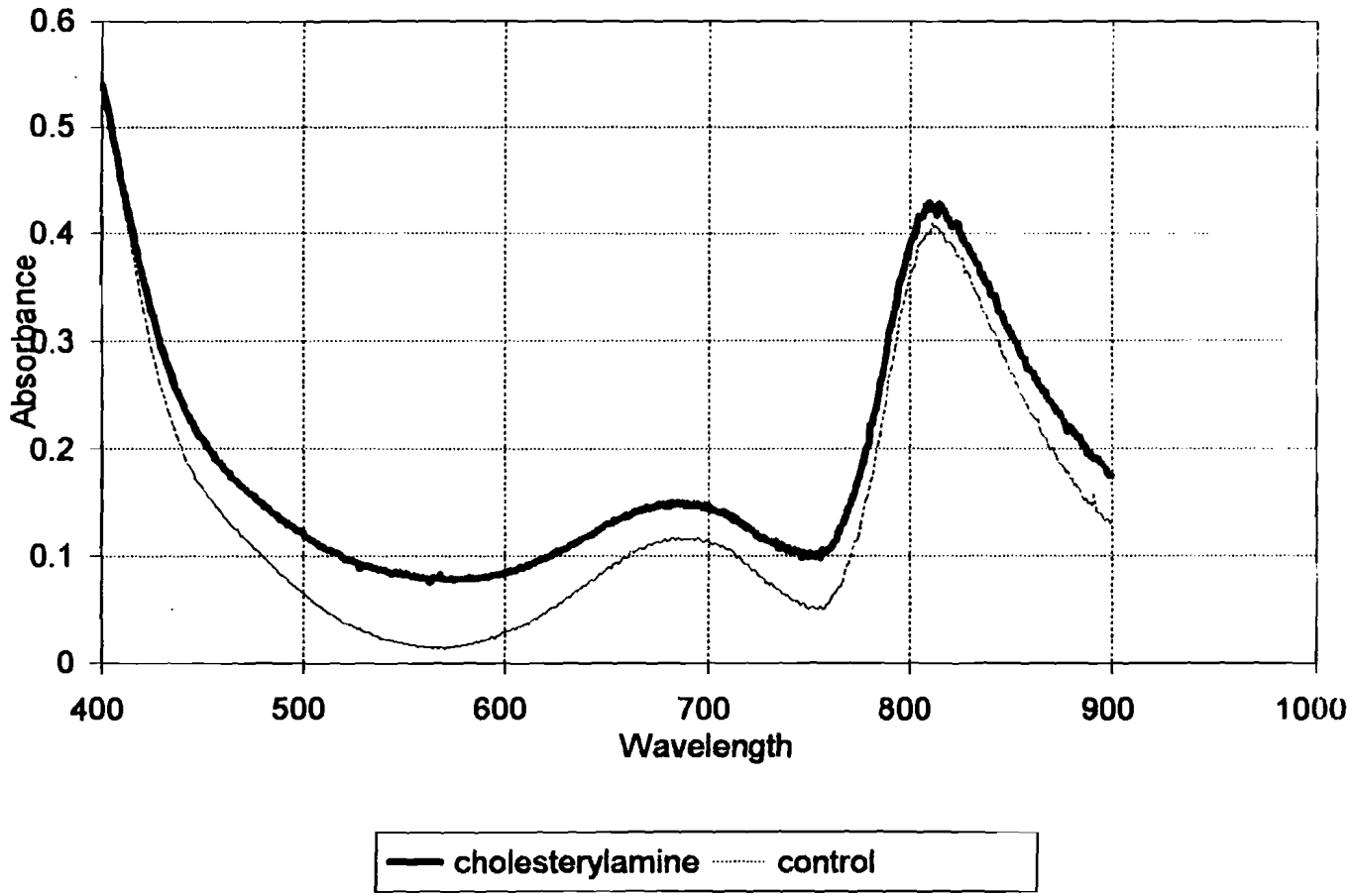


Figure 13.

Visible Spectrum of Cholesterylamine in the Toluene Phase

(HPA:THAB = 1:2.5)

The solid line represents the absorbance curve of cholesterylamine (Cho.) with $Co^{3+}B$ in the toluene phase with a mole ratio of HPA:THAB = 1:2.5. The dotted line represents the absorbance curve of the control solution. The maximum absorbance at 685 nm in the control solution shifts to 640 nm in the cholesterylamine solution, indicating that the coordination reaction between cholesterylamine and $Co^{3+}B$ had occurred in the toluene phase.

Visible Spectrum of Cho. in Toluene

HPA:THAB = 1:2.5

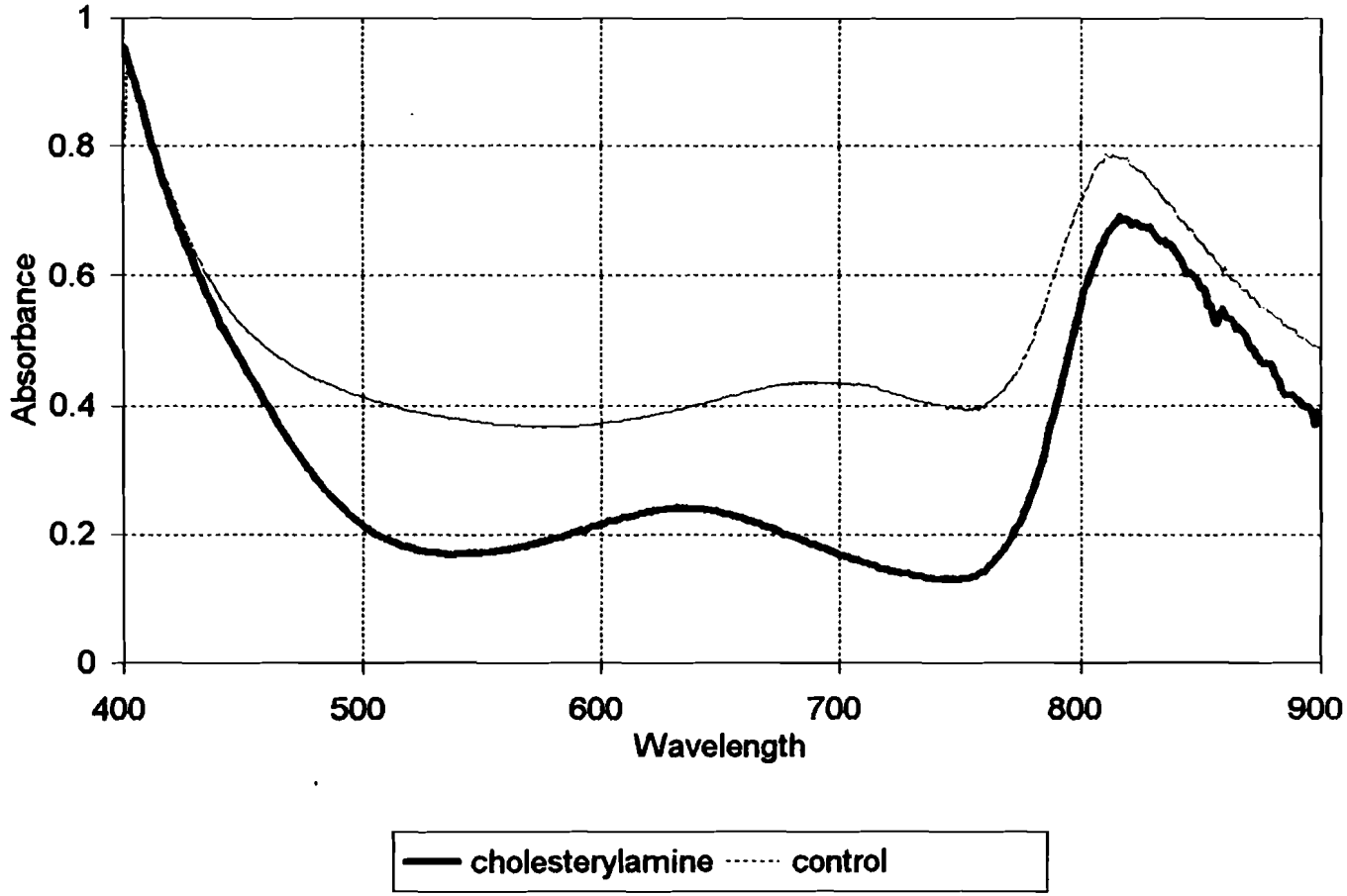


Figure 14.

Visible Spectrum of Cholesterylamine in the Aqueous Phase

(HPA:THAB = 1:6)

The solid line represents the absorbance curve of cholesterylamine (Cho.) with $Co^{3+}B$ in the aqueous phase with a mole ratio of HPA:THAB = 1:6. The dotted line represents the absorbance curve of the control solution. No obvious absorbencies around 650 nm occur in either curve. This spectrum shows that HPA in the aqueous phase had been almost totally transferred to the toluene phase when the amount of THAB added was equal to the amount of charge on the HPA.

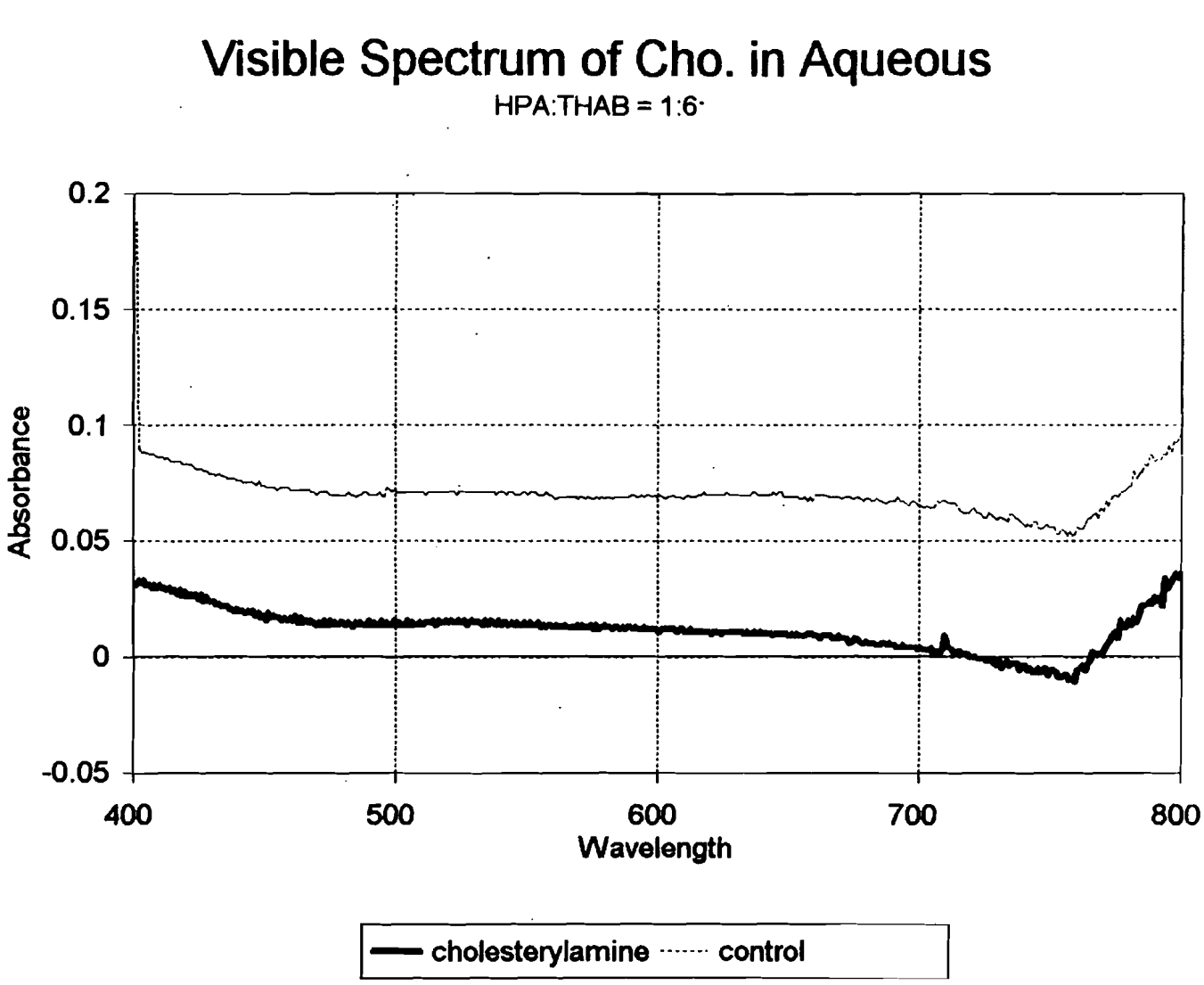

Visible Spectrum of Cho. in Aqueous
HPA:THAB = 1:6
0.2
0.15
0.1
0.05
0
-0.05
Absorbance
400
500
600
700
800
Wavelength
cholesterylamine
control

Figure 15.

Visible Spectrum of Cholesterylamine in the Toluene Phase

(HPA:THAB = 1:6)

The solid line represents the absorbance curve of cholesterylamine (Cho.) with $Co^{3+}B$ in the toluene phase with a mole ratio of HPA:THAB = 1:6. The dotted line represents the absorbance curve of the control solution. The maximum absorbance at 690 nm in the control solution shifts to 640 nm in the cholesterylamine solution indicating that the coordination reaction between cholesterylamine and $Co^{3+}B$ had occurred in the toluene phase.

Visible Spectrum of Cho. in Toluene

HPA:THAB = 1:6

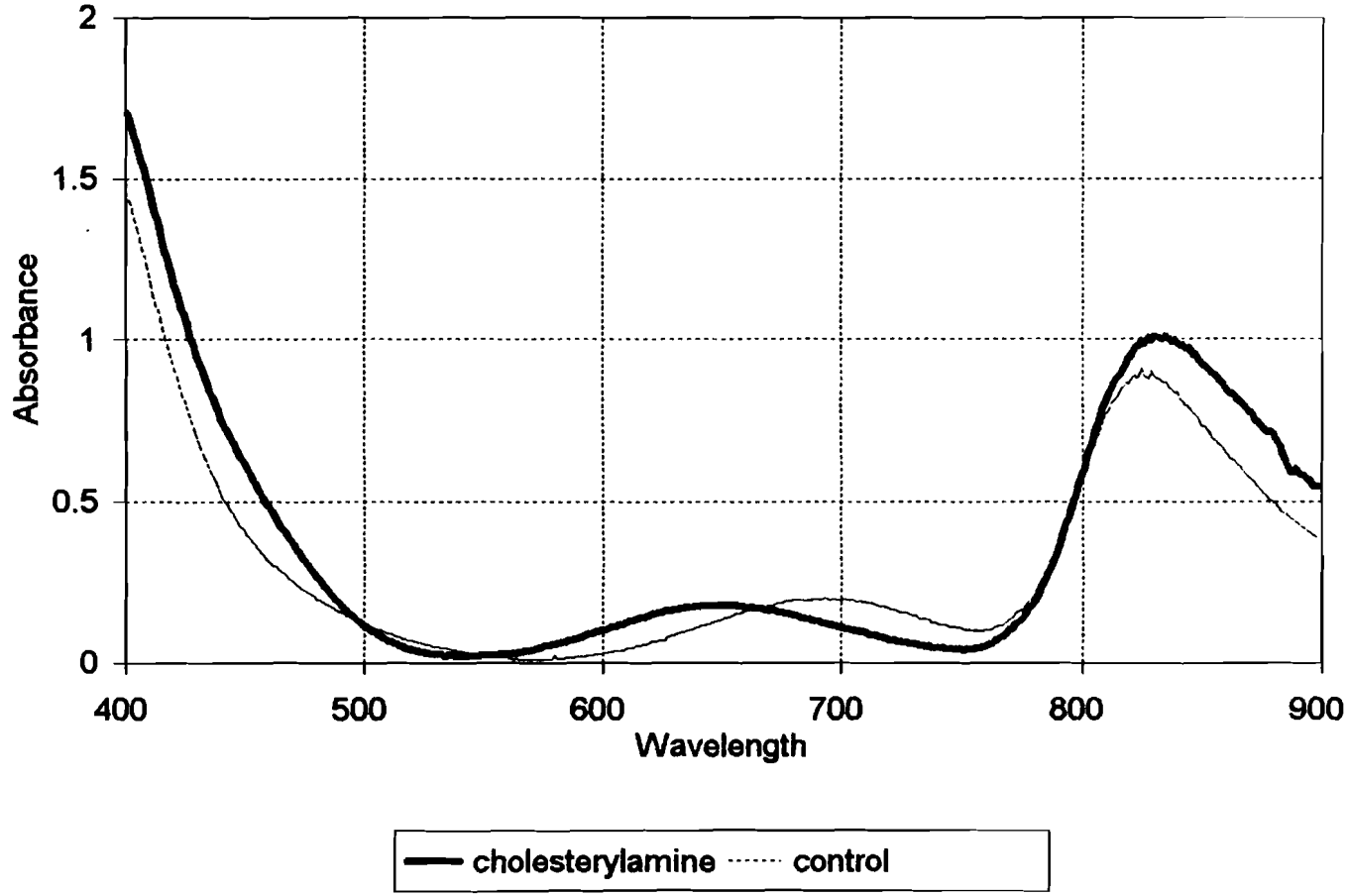


Figure 16.

Visible Spectrum of 8-Methylquinoline

The solid line represents the absorbance curve of 8-methylquinoline with $Co^{3+}B$ in the aqueous phase. The dotted line represents the absorbance curve of the control solution. Both solutions have the same maximum absorbance peak at 685 nm indicating that the coordination reaction between 8-methylquinoline and $Co^{3+}B$ did not proceed in the aqueous phase.

Visible Spectrum 0f 8-Mequinoline

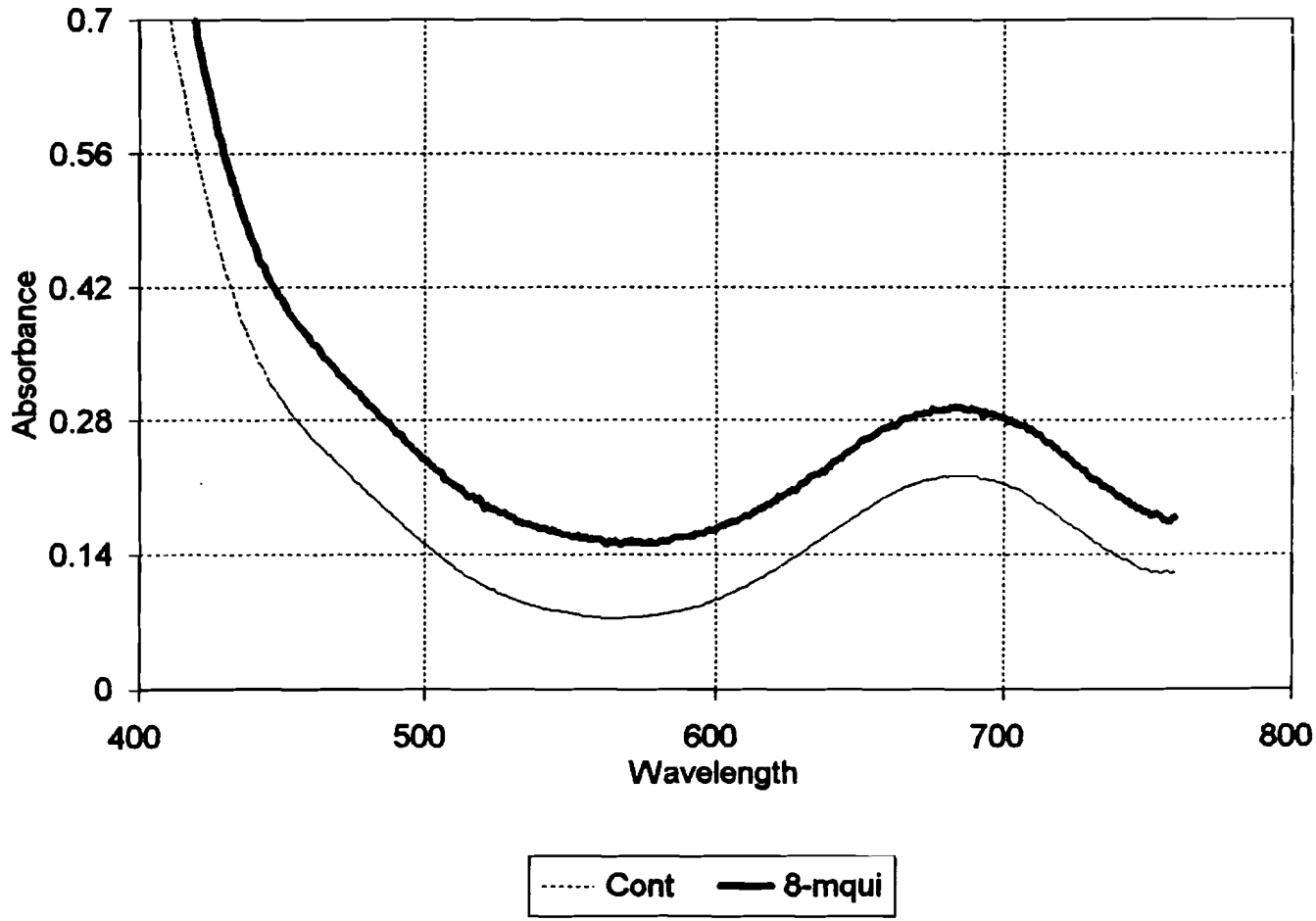


Figure 17.

Visible Spectrum of Quinoline

The solid line represents the absorbance curve of quinoline with $Co^{3+}B$ in the aqueous phase. The dotted line represents the absorbance curve of the control solution. The maximum absorbance for both solutions occur near 685 nm and almost overlap each other. The spectra indicate that the coordination reaction between quinoline and $Co^{3+}B$ did not proceed under the experimental conditions.

Visible Spectrum 0f Quinoline

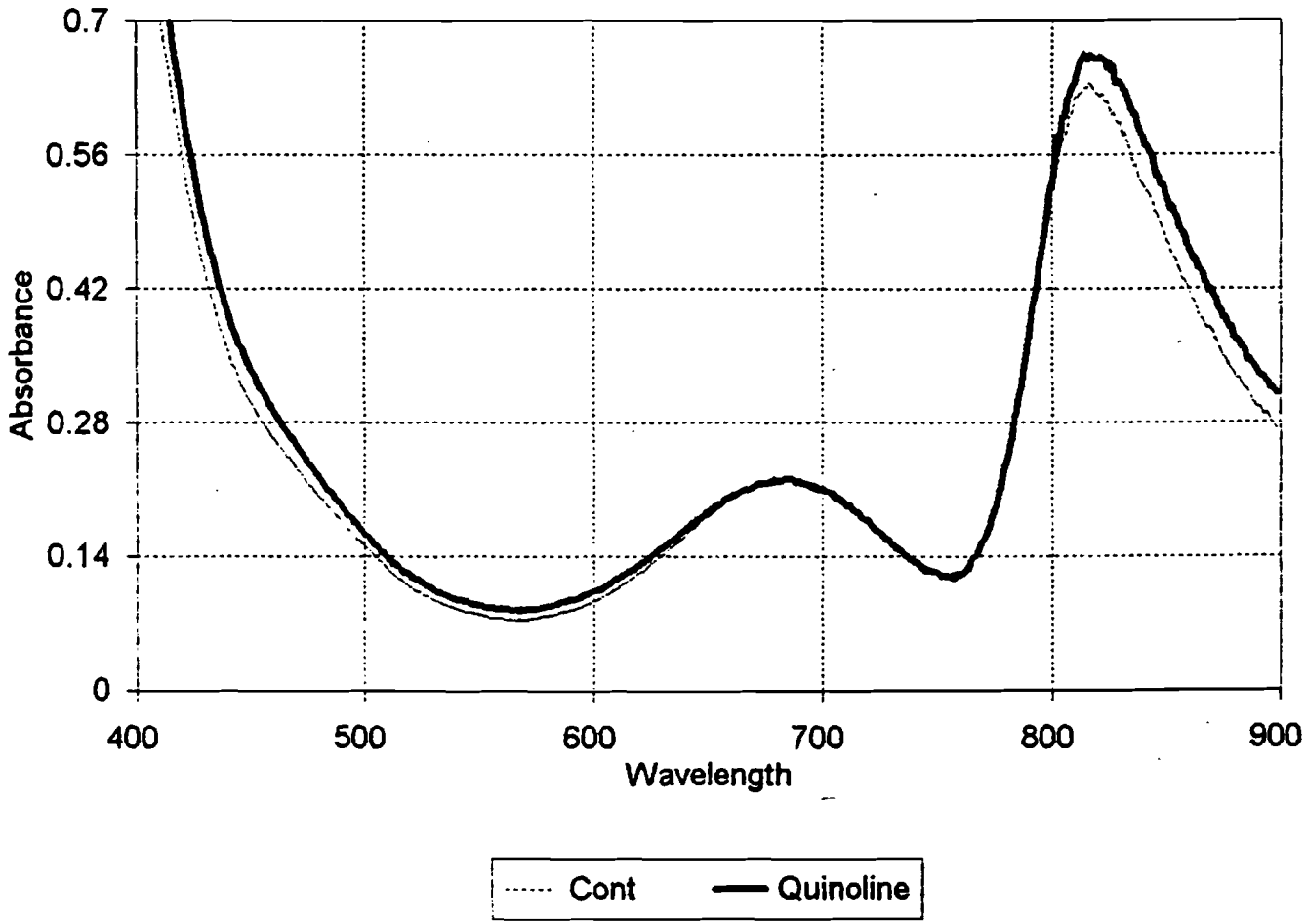


Figure 18.

Visible Spectrum of Indole

The solid line represents the absorbance curve of indole with $Co^{3+}B$ in the aqueous phase. The dotted line represents the absorbance curve of the control solution. The maximum absorbance for both solutions occurs near 685 nm and almost overlap each other. The spectra indicate that the coordination reaction between indole and $Co^{3+}B$ did not proceed under the experimental conditions.

Visible Spectrum 0f Indole

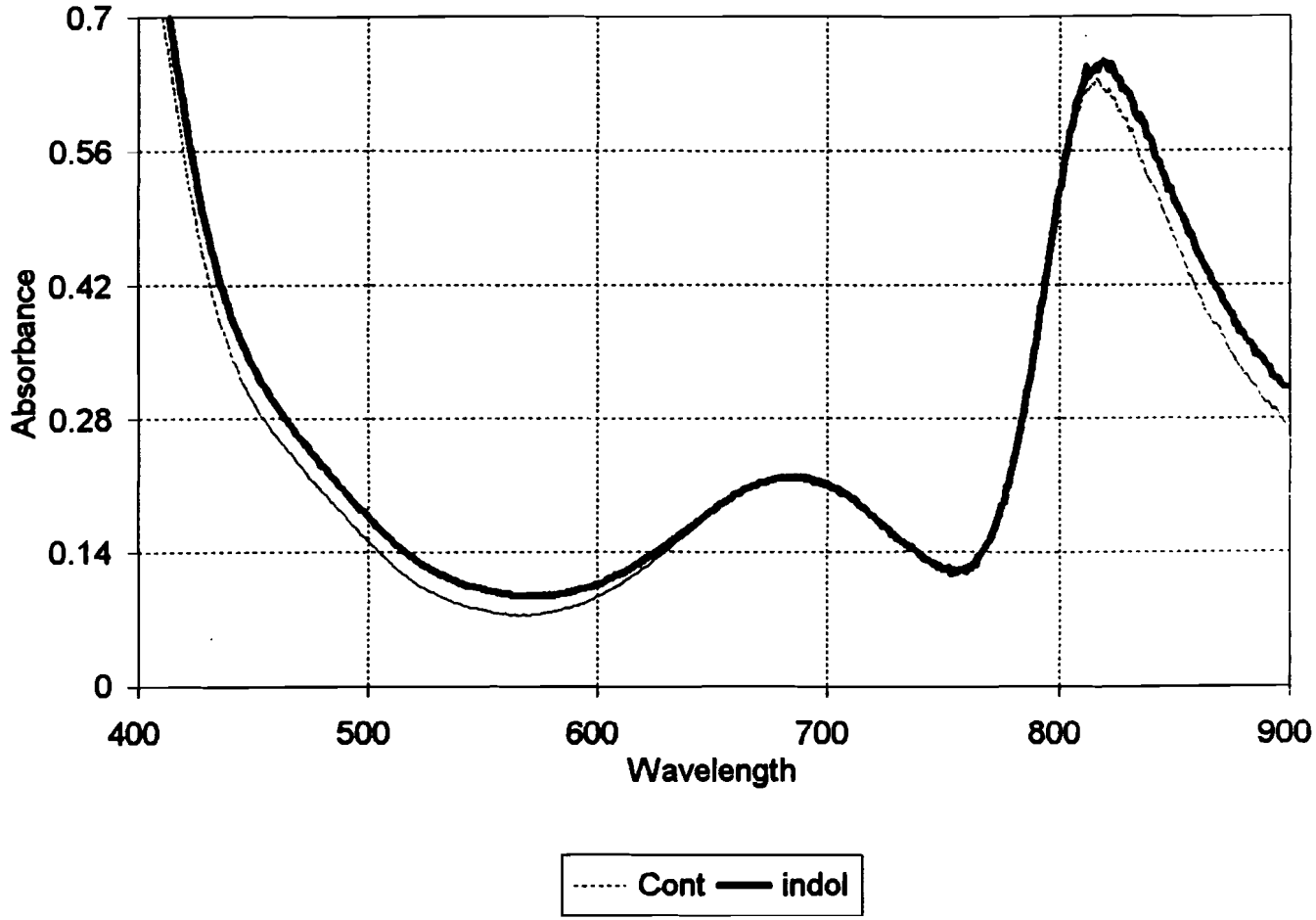
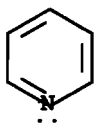


Figure 19.

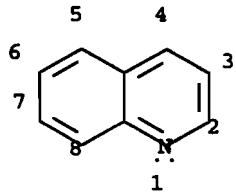
Organic Ligands Used in This Research

The organic ligands were used in attempts to form coordination complexes with heteropolyanion (such as $Co^{3+}B$). These derivatives of organic amines are divided into two groups. Group I consists of aromatic heterocyclic amines which include pyridine, isoquinoline, quinoline, 8-methylquinoline, and indole. Group II consists of primary amines which include 2-octylamine and cholesterylamine.

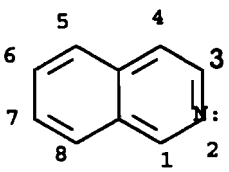
Group I: Aromatic Heterocyclic Amines



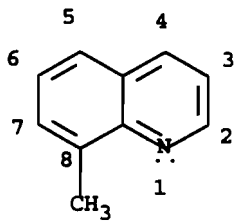
Pyridine



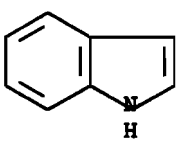
Quinoline



Isoquinoline



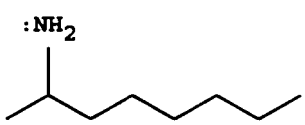
8-Methylquinoline



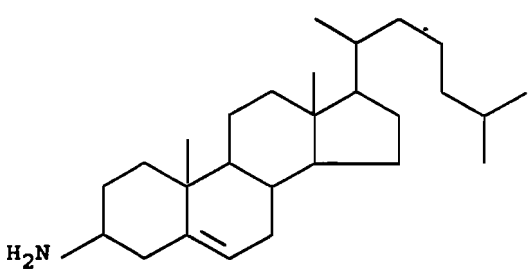
Indole

Pyrrole

Group II: Primary Amines



2-Octylamine



cholesterylamine

Figure 20.

The Geometric Size of the Conical Cavity of HPA

The coordinatively unsaturated site on the cobalt atom of the modified Keggin structure is a cone-like cavity in a Phase Transfer Catalysis system. The geometric size of the conical cavity for $Co^{3+}B$ is 2.308 Å radius, 0.82 Å depth, and 141° inside angle. The steric hindrance occurs if the size and orientation angle of a coordinated ligand is equal to or larger than the size of the conical cavity. (Note: The conical cavity should exist even though there is no coordinatively unsaturated site on the cobalt atom of the HPAs.)

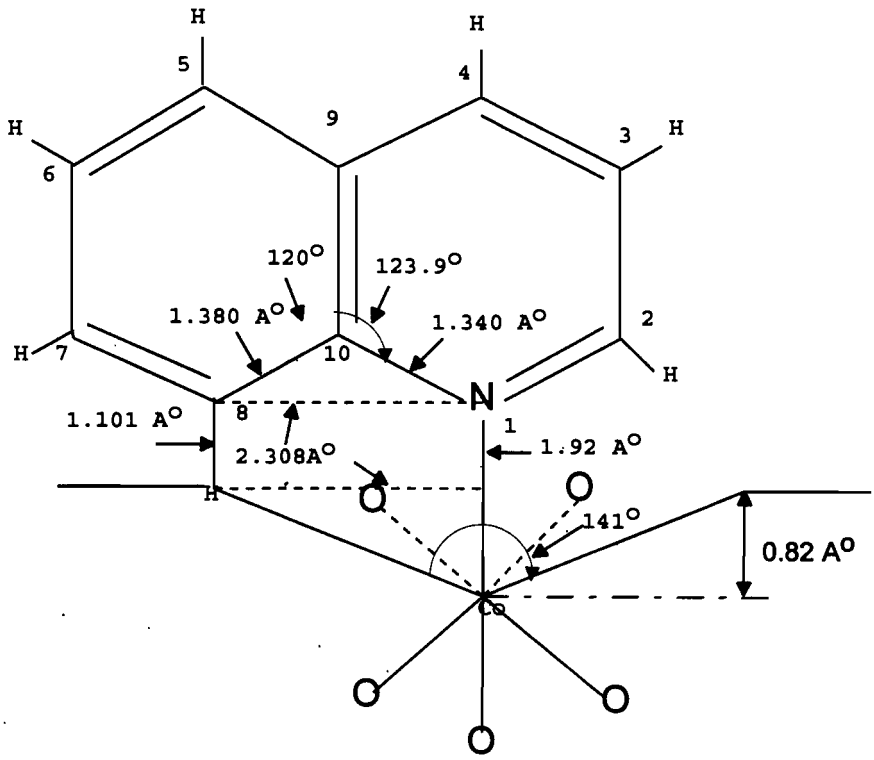
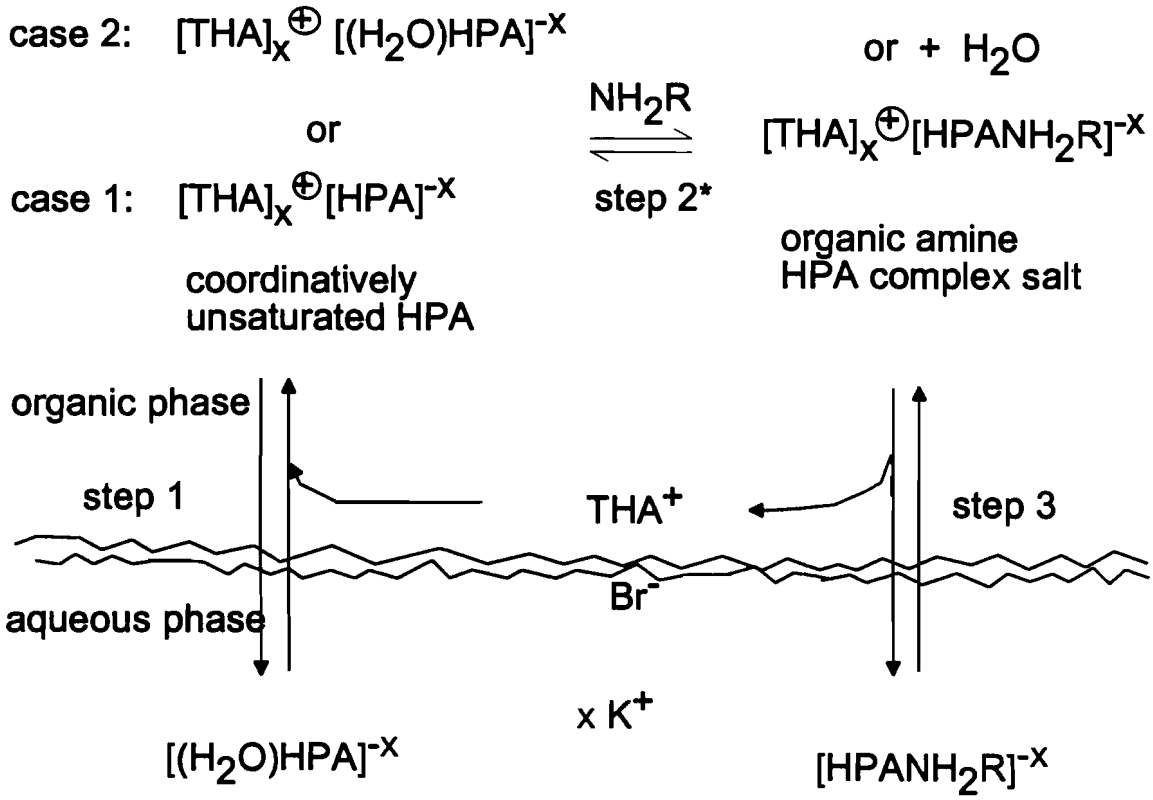

H
H
5
4
9
H
3
H
6
120°
123.9°
1.380 A°
1.340 A°
2
H
7
10
H
N
1.101 A°
8
1
2.308A°
1.92 A°
H
O
O
141°
0.82 A°
Co
O
O
O

Figure 21.

Phase Transfer Catalytic Cycle in Ligand Substitution of HPA

The tetraheptylammonium cation [THA^+] coaxes heteropolyanions from the aqueous phase to the organic phase in step 1 to form an anion-cation pair which is either a coordinatively unsaturated $[HPA]^{-x}$ (case 1) or a hydrated species $[(H_2O)HPA]^{-x}$ (case 2). The organic amine ligands coordinate with the anion-cation pair by addition or substitution to form the organic amine HPA complex salt in step 2. The complex salt decomposes to THA^+ and amine-HPA complex anions. The latter returns back to the aqueous phase while the former remains in the organic phase and is used in the next cycle of the PTC agent in step 3. The amine-HPA complex can not return back to the aqueous phase and the equilibrium shifts to the organic phase in step 3 when the R group is too big. Thus, larger amounts of PTC agent have to be used to transfer the HPAs in order to complete the ligand substitution reaction. The K^+ cation and Br^- anion are essentially spectator ions in the aqueous phase.



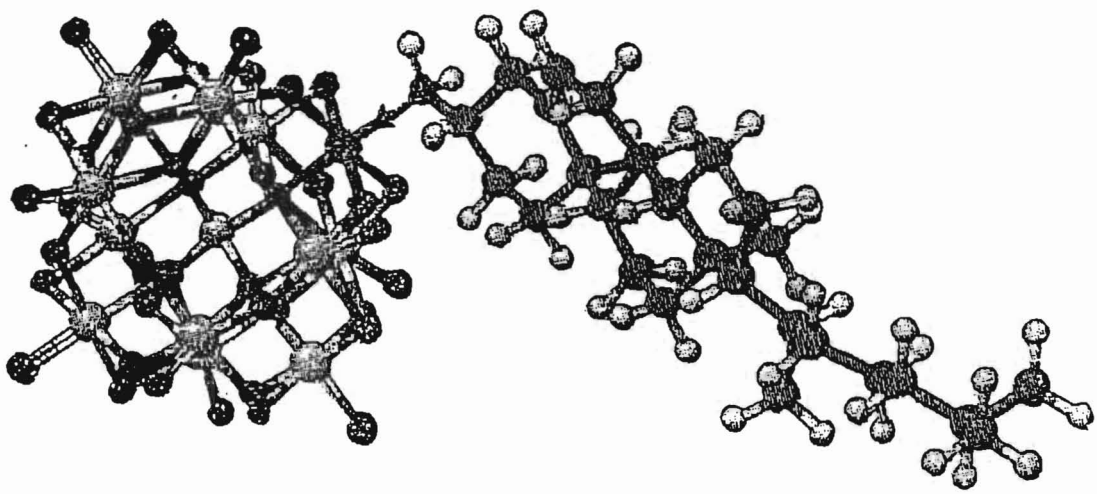
HPA: Heteropolyanion

THA^+: Tetraheptylammonium cation

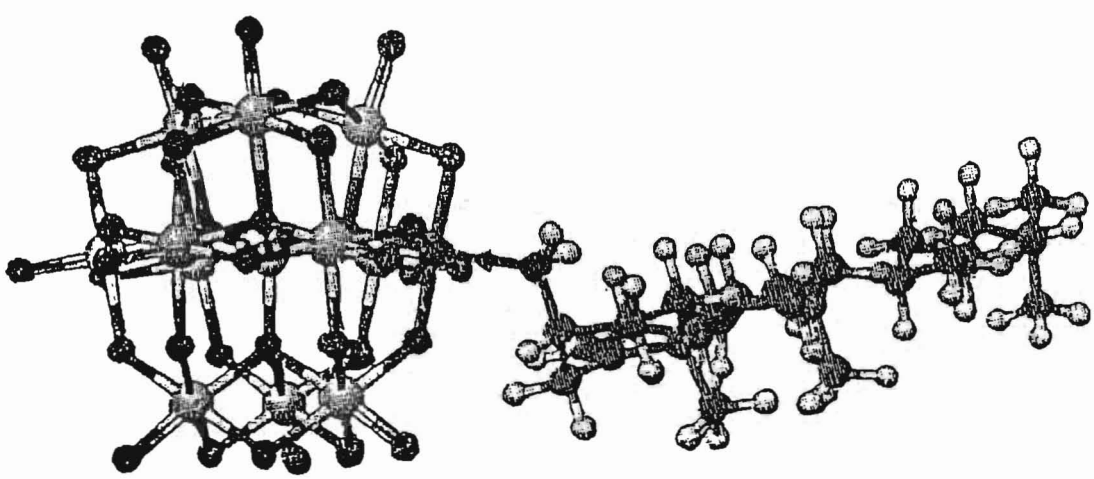
Figure 22.

Models of Cholesterylamine-HPA Complexes

The big basket-like portion of molecule on the left of the complex represents the Baker-Figgis model. The long tail on the right of the complex represents the cholesterylamine. The nitrogen on the 3-position of the cholesterylamine coordinates with the cobalt of HPA to form the cholesterylamine-HPA complex. Since the amine group is attached to a chiral carbon in the cholesterylamine, two forms are possible. Model A represents the S-cholesterylamine-HPA complex and model B represents the R-cholesterylamine-HPA complex. [The models were made by Dr. Manli Zheng of CAChe Scientific, Dr. A. Landis and J. Zhu utilizing CAChe Scientific computer software].



A



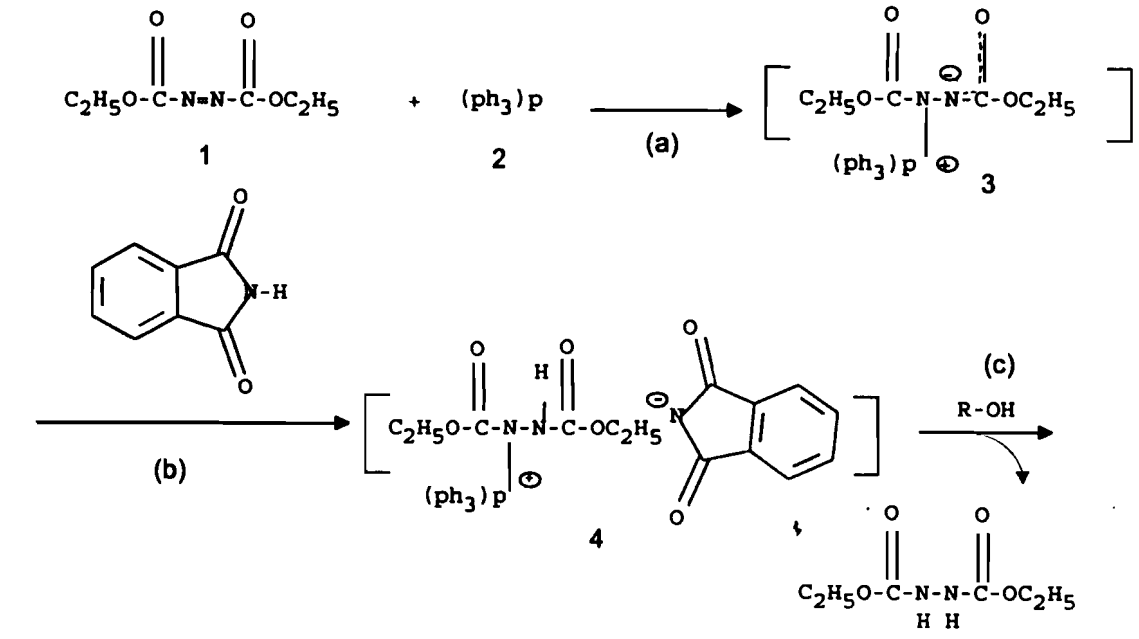
B

Figure 23.

The Probable Reaction Mechanism for the

Mitsunobu Reaction and the Gabriel Hydrolysis

The Mitsunobu reaction and Gabriel hydrolysis proceed through (a) the addition of 2 to 1 giving a quaternary phosphonium salt 3, (b) protonation of 3 with phthalimide to form 4, (c) formation of an alkoxyphosphorium salt 5 with alcohol, (d) S_N2 type displacement of 5 to form 6, (e) two steps of S_N2 (tetrahedral mechanism) with hydrazine to yield the resulting amine species 8.


1
2
(a)
3
(b)
4
(c)
R-OH
5
(d)
(ph3)p=O
6
(e)
H2N-NH2
7
(e)
R-NH2
8
R = CH3-CHC6H13
OH
or
HO

APPENDIX B

TABLE

Table I.

The Known Heteroatoms in Heteropolyanions

H																
Li[a]	**Be**											**B**	**C**			
Na	*Mg*											**Al**	**Si**	**P**	**S**	
K	*Ca*		**Ti**	**V**	**Cr**	**Mn**	**Fe**	**Co**	**Ni**	**Cu**	**Zn**	**Ga**	**Ge**	**As**	**Se**	
Rb	*Sr*	**Y**	**Zr**	**Nb**	**Mo**		*Ru*	**Rh**		*Ag*		**In**	**Sn**	**Sb**	**Te**	**I**
Cs	*Ba*	**La**	**Hf**	**Ta**	**W**	**Re**	Os		**Pt**			**Tl**	*Pb*	*Bi*		
			Ce	**Pr**	**Nd**		**Sm**	**Eu**	**Gd**	*Tb*		**Ho**	**Er**		**Yb**	
			Th		**U**	**Np**	**Pu**	**Am**	*Cm*		*Cf*					

Elements shown in italic type have been observed only as secondary heteroatoms.

Adapted from the literature [1].

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Zhu Jinjiang

Signature of Author

12-3-96

Date

Cholesterylaminecobalto(III)-11-tungstoborate and Other Organoheteropoly-tungstate Preparations: Organic Ligand Substrate and Heteropoly Anion Syntheses

Title of Thesis

Mary Cooper

Signature of Graduate Office Staff Member

12-4-96

Date Received