SYNTHESIS AND APPLICATIONS OF 2-QUINOXALINOL SALENS AND

THEIR METAL COMPLEXES

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SYNTHESIS AND APPLICATIONS OF 2-QUINOXALINOL SALENS AND THEIR METAL COMPLEXES

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DISSERTATION ABSTRACT

SYNTHESIS AND APPLICATIONS OF 2-QUINOXALINOL SALENS AND THEIR METAL COMPLEXES

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Salen ligands have been of interest to a wide variety of chemists for several reasons. They have been investigated in large part due to their ease of preparation and their ability to form stable metal complexes. Derivatives of 2-quinoxalinol are key intermediates as bioactive agents in agriculture, dyes, and have been key pharmaceutical intermediates. The combination of salen and 2-quinioxalinol, 2-quinioxalinol salens (salqu) are expected to be of use in the development of new catalysts, sensor and pharmaceutical agents. In the first portion of this work, a solution-phase parallel method for the synthesis of salqu ligands was designed and optimized. Simple laboratory techniques with low sensitivity to moisture and air for solution-phase parallel reactions were coupled with convenient workup and purification procedures to give high-purity and good yields for a small

salqu ligands library of 20 compounds. During preparation of this library, it was found that upon reaction with salicylaldehydes, 2-quinoxalinol imines were obtained as byproducts. Diamino-2-quinoxalinols produce 2-quinoxalinol imines regioselectively as the only isomer in good yield. The regioselectivity of this reaction was determined by use of isotopic ^{15}N labeling experiments. The 2-quinoxalinol imines may then be reacted to yield unsymmetrical substituted salqu ligands. Salqu ligands can be further reacted with different metal salts to form salqu metal complexes. Salqu metal complexes were usually applied as pharmaceutical agents and catalysts for many asymmetric reactions. They can be prepared with simple workup process and are usually stable to both air and moisture condition. These complexes present one option for the extraction of metal ions from wastes or waste streams. To take further advantage of these properties, solid phase catalysts have become popular in organic synthetic methods because of increased ease of workup after reactions. Recently, SPE (solid phase extraction) technology has been well developed for use in many purposes. Based on these, salqu ligands and salqu metal complexes, solid phase salqu ligands and their complexes demonstrate promise in new research fields for their catalytic application. Finally, salqu copper complexes have been found to be a kind of high efficient catalysts for the oxidization of C-H bond of aryl methylene compounds.

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Reference format follows the format of The Journal of Organic Chemistry.

Structures are drawn by using *Chem. Window 6th Version.*

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Format of figures or tables follows the format of The Journal of Organic Chemistry.

Portions of this dissertation are from my published articles (Journal of combinatorial chemistry; The Journal of Organic Chemistry; Tetrahedron Letters and Inorganic Chemistry Acta articles.)

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CHAPTER 1

INTRODUCTION

Hugo Schiff, a German chemist (1834-1915), first described Schiff bases and other imines, and was responsible for research into the synthesis and characterization of imines. For this work, the C=N bond named a Schiff base after him. One common type of Schiff base currently of interest is a group called the salen ligands. Salen is the abbreviation for a popular chelating ligand used in coordination chemistry and homogeneous catalysis. The name salen is a contraction for salicylic aldehyde and ethylene diamine, which are the precursors to the ligand. A salen ligand, (**Figure 1**. **1)** in fact, is dianionic with two Schiff bases and two oxo- units forming tetradentate chelating ligand in a coordination complex of the type [O, N, N, O] (**Figure 1**. **3**). The ligand salenH_2 (**Figure 1**. **2**) is a derivative of salen ligand and first was prepared by Pfeiffer.[1] Dr. Eric Jacobsen (Harvard University) and coworkers developed and widened the application of these kinds of ligands and their complexes as organic catalysts and are most famous for using these catalysts for asymmetrically catalyzing reactions with high stereoselectivity.[2] Numerous variations of the simple salen ligand are known with various substituents. For example, ligands abbreviated "Salph" or “Salqu are derived from the condensation of 1, 2-phenylenediamine or 2-quinoxalinol and salicyaldehyde.

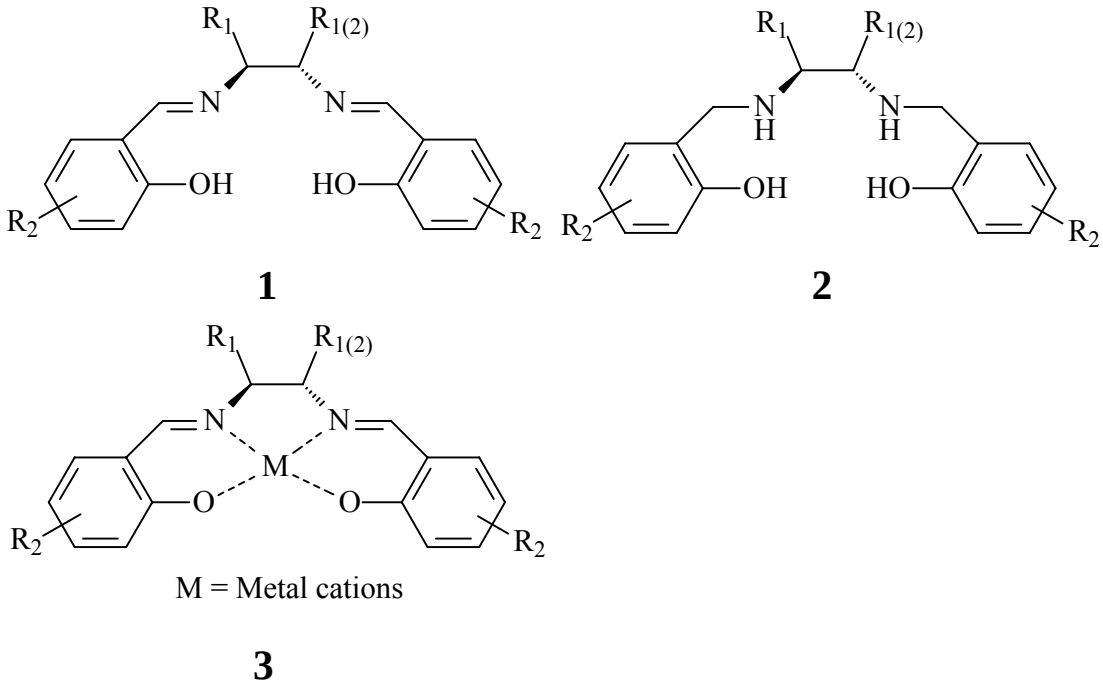


Figure 1. Salen Salen structure, salenH_2 structure (**1**, **2**) and structures of metal complexs (**3**)

Salen and the related salophen (abbreviated "salph") ligands have been investigated in a variety of applications, because of their ease of preparation and ability to form stable metal complexes.[3] Numerous applications have been proposed in bioinorganic chemistry and medicine. For example, copper (I) complexes have been investigated as anti-tumor agents and have been found to be more bioactive than the currently available metal-based anti-tumor drug cisplatin.[4] Ruthenium salen complexes have been studied as protein kinase inhibitors mimicking organic indolocarbazoles.[5] Salen and salph Mn complexes have also been applied as catalytic scavengers of hydrogen peroxide for cytoprotective agents.[6]

Another application investigated with using salen or salph ligands is as metal catalyst supports. Their transition metal complexes (Cr, Al, Ti, Co, Cu, Ni, Fe, Mn, Ru

and Zr), have been found to be of great utility in the development of such catalysts and some of these have been used to increase the stereoselectivity of products in a variety of reactions as chiral catalysts. When salen or salph Cr complexes act as catalysts, they can promote the coupling of CO_2 into aziridine to form 5-substituted asymmetric oxazolidinones.[7] Such 5-substituted oxazolidinones act as high potential antibacterial agents and are widely used in the pharmaceutical industry, they also have demonstrated utility in organic synthesis as chiral synthons.[8,9] Many Lewis acid catalysts including Cr salen complexes have been applied for this reactions with high enantioselectivity.[10] Allylation of aldehydes,[11] asymmetric ring opening,[12] and enantioselective aminolytic kinetic resolution (AKR) of epoxides[13] are also catalyzed with high enantioselectivity by Cr salen or salph complexes. Salen or salph Al complexes have been found to catalyze enantioselective Michael addition reactions, an important method for C-C bond construction in organic synthesis.[14] The enantioselective formal hydration of α, β-unsaturated imides which was once a challenging problem in organic synthesis has also been successfully accomplished with the aid of salen and salph Al catalysts.[15] Ti salen complexes have been used to catalyze the asymmetric ring opening of epoxides[16] and asymmetric addition of KCN and Ac_2O to aldehydes to form cyanohydrin esters in good yields and with excellent enantioselectivity.[17] Enantiomerically enriched cyanohydrins are versatile intermediates in organic synthesis and many synthetic approaches towards their synthesis are being pursued based on this research.[18] Ti salen complexes may also efficiently catalyze oxidation of cyclic dithioacetals with high enantioselectivity in the system of urea hydrogen peroxide (UHP).[19] Diol analogs are usually synthesized by dihydroxylation of olefins;[20] however, enantioselective synthesis through carbon-carbon bond formation has not been very successful until the development of

enantioselective pinacol coupling of aryl aldehydes catalyzed by Ti salen complexes. This offers an excellent alterative way to synthesize diol analogs.[21]

Asymmetric ring opening of epoxides can also be done by using Co salen or salph complexes.[22] In fact, the asymmetric ring opening of epoxides is the most commonly reported reaction catalyzed with various salen or salph metal systems. Different metal salen or salph systems have shown good catalytic effect with high enantioselectivity.[12,16,22] Co salen complexes can also catalyze asymmetric intramolecular cyclopropanation[23] and enantioselective Baeyer-Villiger oxidization reactions, which may convert carbonyl groups into ester groups.[24]

The oxidation of alcohols into compounds containing carbonyl functional group is one of the most important fundamental reactions in organic chemistry both in the laboratory and the industrial level. Numerous methods have been developed using a variety of reagents for this purpose,[25] but all of these oxidation methods involve environmental hazardous or expensive oxidants and catalysts. Oxidation of alcohols into carboxylic acids and ketones with hydrogen peroxide and Co salen complexes offers a cleaner and more economical method for use in the pharmaceutical industry.[26] In another example, heteroarenes represent structural units frequently found in a broad range of organic compounds including natural products, pharmaceuticals, dyes. An important modification of these, the arylation of azole heteroarenes, can also be fulfilled with Co salen complexes and iodobenzene as catalysts through C-C forming reactions.[27] The hydrolytic kinetic resolution (HKR) of terminal epoxides[28] and enantioselective cyclopropanation to form asymmetric lactone[29] can be catalyzed by Co salen catalysts as well. Methods for the asymmetric synthesis of α-amino acids have been actively pursued for a long time, because of applications for not only

natural α-amino acids, but alsoartificial α-amino acid analogs for use in biochemistry, pharmacy, and organic synthesis.[30,31]

Recently, salen and salph Cu complexes have been found to be efficient catalysts for asymmetric syntheses of α-amino acid and α,α-disubstituted amino acids.[32] In the C-H oxidation of alkylbenzenes and cyclohexane with hydrogen peroxide, salen Cu complexes were also tested as catalysts.[33] Asymmetric addition of trimethylsilyl cyanide (TMSCN) to carbonyl compounds can be performed using chiral Mn salen catalysts. In this way, chiral cyanohydrins that are useful intermediates for the synthesis of numerous pharmaceuticals intermediates[34] including α-hydroxy acids, [35] α-hydroxy aldehydes,[36] α-hydroxy ketones, [36] and α-amino acid derivatives[37] and β-hydroxy amines can be produced. [35, 36]

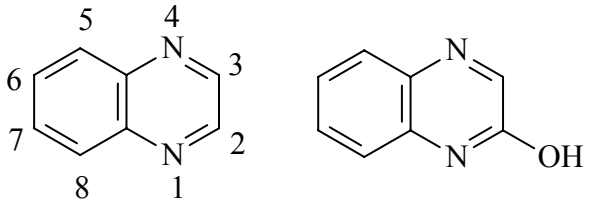
Chiral Mn salen complexes are excellent catalysts for the asymmetric epoxidation of unfunctionalized conjugated cis-olefins.[37,38] Catalytic enantioselective epoxidation is one of the most important processes for the synthesis of chiral epoxides, which can be further converted into many important chiral building blocks via stereoselective ring-opening or functional group transformations.[39] This same reaction may also be catalyzed by Mn salen axially immobilized onto insoluble polymers with high enantioselectivity and yields.[40]

Ru salen or salph complexes can selectively catalyze the reaction of aerobic oxidation of alcohols to prepare carbonyls.[41] Asymmetric sulfimidation to form sulfoxide and sulfone which are always key pharmacophores may also be catalyzed using Ru salen complexes.[42] The application of these can overcome the key drawbacks of the Witting reaction, which are lower yields and the requirement of strongly basic conditions, in the olefination of aldehydes. [43,44,45]

Ni salen complexes have been demonstrated to act as redox catalysts in the reaction of indirect electroreductive cyclization (ERC) to form cycloalkane analogs by the redox of C=N of Ni salen complexes.[46] Fe salen or salph complexes can catalyze the aerobic oxidation of hydrocarbons[48] and cleavage of olefins.[49] Zr salen complexes were used for increasing the enantioselectivity in Baeyer–Villiger oxidations.[50] Because of this, these salen or salph metal catalysts have proven very useful in many different chemistry fields, in particular once incorporated into solid supports, because they can more easily be recovered using simple filtration methods.[40, 51]

A new possible application of salen or salph ligands is as scavengers to selectively extract excess metal ions either to increase the ease of using or recycling metal catalysts in combinatorial chemistry or for the recovery or identification of toxic or radioactive environmental contaminants.[52-55] Combining these with solid-phase extraction (SPE) technologies would further provide additional advantages.[56,57] To do this, and to develop new applications with salens, we thought to prepare new ligands with additional modifications to the basic salen system

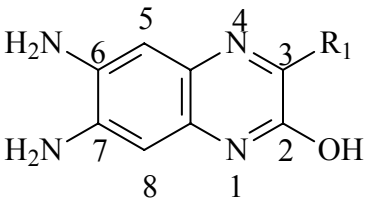
Quinoxaline was first discovered by German chemist Hinsberg in 1880 (**Figure 2**. **4**). Quinoxaline derivatives have been found to have anti-tumor, antibiotic, antifungal bioactivies and have been investigated as receptor inhibitors for N-methyl-D-aspartic acid (NMDA) and as HIV-1 inhibitors. [58] An important derivative, 2-quinoxalinol (**Figure 2**. **5**), is a key intermediate for bioactive agents in agriculture,[59] and have been used in dyes[60] and other pharmaceutical applications.[61] Synthetic methods for both parallel solid phase and solution phase methods of synthesis for 2-quinoxalinol derivatives have been previously reported.[62, 63, 64]



4 **5**

Figure 2. Structure of quinoxaline (**4**) and 2-quinoxalinol (**5**).

Other compounds containing imine functional groups also have broad applications in organic chemistry. One application of interest is in the preparation of amino acids *via* a Strecker reaction in bioorganic field.[31] When catalyzed by chiral catalysts, nucleophilic addition to imines is also used for the preparation of compounds possessing secondary amine groups with high stereoselectivity.[65] In medicinal chemistry, imines have been found to have broad bioactivities from anti-tumor to antibacterial bioactivity[66] and to serve as protein synthesis inhibitors.[67] In recent reports, imine coordination ligands supporting copper metal complexes have been demonstrated to trap toxic gases.[68] In addition, imines are useful as protecting groups for amines.[69] Imines can also play a crucial role as coordination ligands in catalyst supports.[70]



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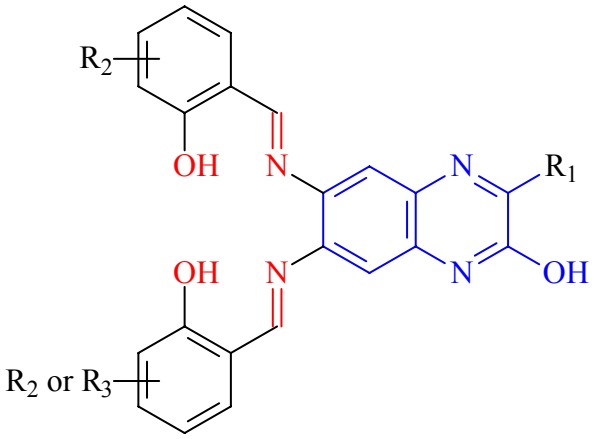
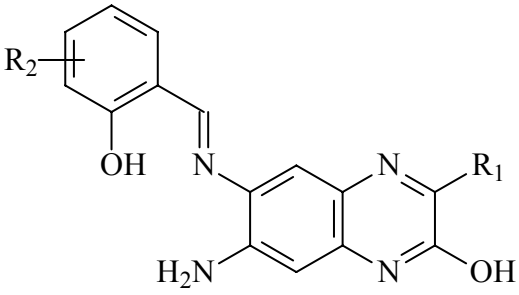
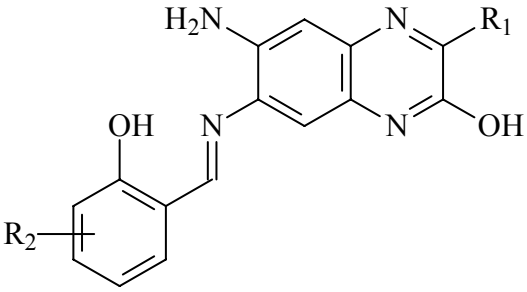


7, 8 (7: R_1, R_2, R_2; 8: R_1, R_2, R_3)



9a



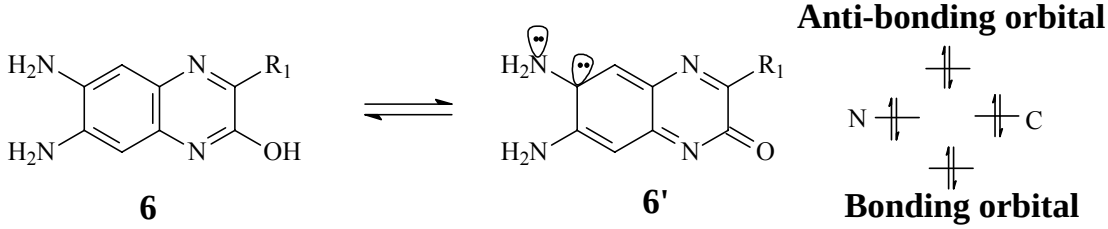
9b

Figure 3. Structures of diamino-2-quinoxalinols (**6**), salqu ligands (**7, 8**) and 2-quinoxalinol imines (**9**).

All of these factors have served to peak our interest in combining these two systems (salen and 2-quinoxalinol) for the preparation of a new series of symmetric and unsymmetric salqu framework ligands based on a Schiff base synthesis. (**Figure 3**. **7** and **8**) **[Chapter 2]** Previously, no salqu ligands have been reported, perhaps because of the difficulty in preparing the required diamino 2-quinoxalinol intermediate (**Figure 3**. **6**), and the typical Schiff base methods of preparation vary widely or require additional catalysts because of steric constraints.[71, 72] Both problems restrict the development of a synthetic library. In addition, in order to allow for the preparation of unsymmetric salqu ligands, the most challenging thing is the synthesis of 2-quinoxalinol imines (**Figure 3**. **9**), because they are often unstable with side

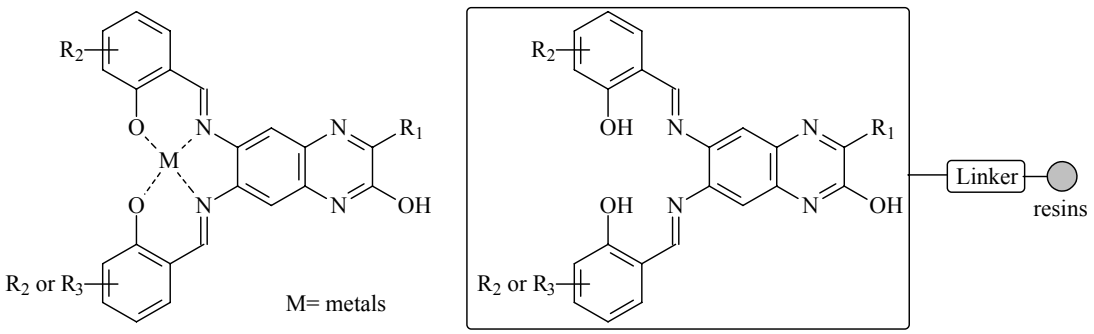
reactions that occur during imine formation.[73] It can be especially difficult to obtain a single isomer as the final product.[74,75] If the reaction can be controlled such that only one amine is reacted with an aldehyde, this would provide a method to prepare unsymmetric salqu ligands (**8**) **[Chapter 3]**. A second challenge was in the identification of the exact structure of 2-quinoxalinol imines, because two isomers are possible. (**Figure 3**. **9a** or **9b**) **[Chapter 3]**

From the structure of the diamino-2-quinoxalinol (**6**), it is possible that there is a difference in the reactivity of the amino groups at the 6 position and the 7 position, because of the 2-hydroxy group of diamino-2-quinoxalinol. Therefore, these two amino groups could be reacted with different salicylaldehydes to produce unsymmetric salqu ligands; however, to do this, it is crucial to consider which amino group is more reactive or reacts first with salicylaldehyde. In theory, the 6-amino group should be more reactive than 7-amino group since α- nucleophile effect caused by both the electron donor 2-hydroxy group and the aromatic 2-quinoxalinol ring system.[76] (**Scheme 1**) This must be first proven by experiment. It could be proved by both calculation methods[77] and by isotopic labeling such as in a ^{15}N label method which can differentiate the 6 and 7 amino group **[Chapter 3]**. From these asymmetrically substituted salqu ligands, SPOS methods could be used to prepare salqu ligands on resins to form solid phase salqu ligands (**12**).

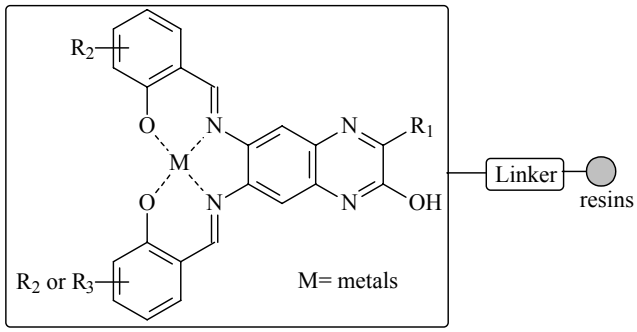


Scheme 1. α- nucleophilic effect seen in diamino-2-quinoxalinol (**6**)

Once the conditions for ligand synthesis are optimized, salqu ligands can be reacted with different metal salts to prepare salqu metal complexes using literature methods.[3] (**Figure 4**. **10** and **11**). For the purpose of recognizing their structural character, it is necessary to develop crystal growing methods for the salqu metal complexes. Accurate structures of salqu metal complexes could also be obtained using small molecule X-ray diffraction (XRD) **[Chapter 4]**. Solid phase salqu ligands could be further designed and synthesized. (**Figure 4**. **12**) With the solid phase salqu ligands in hand, we could develop applications of solid phase salqu ligands for SPE (solid phase extraction) technology **[Chapter 5]**. Complexes will be investigated for the application of catalysts and their catalytic mechanism **[Chapter 6]**. Methods for immobilizing salqu ligands or their complexes onto polymers could then be developed and then their application as catalysts or in SPE technology could be further investigated. Solid phase salqu metal complexes (**Figure 4**. **13**) would be of interest for new solid phase catalysts if salqu metal complexes could be found to possess useful catalytic character. The preparation of these kinds of catalysts will require ligand design, metal complex syntheses, catalyst identification, reaction screenings for a given catalyst and catalyst optimization. All of these need to be considered along with a synthetic application for the new methods described.



10 (10: R_1,R_2,R_2; 11: R_1,R_2,R_3.) **12**

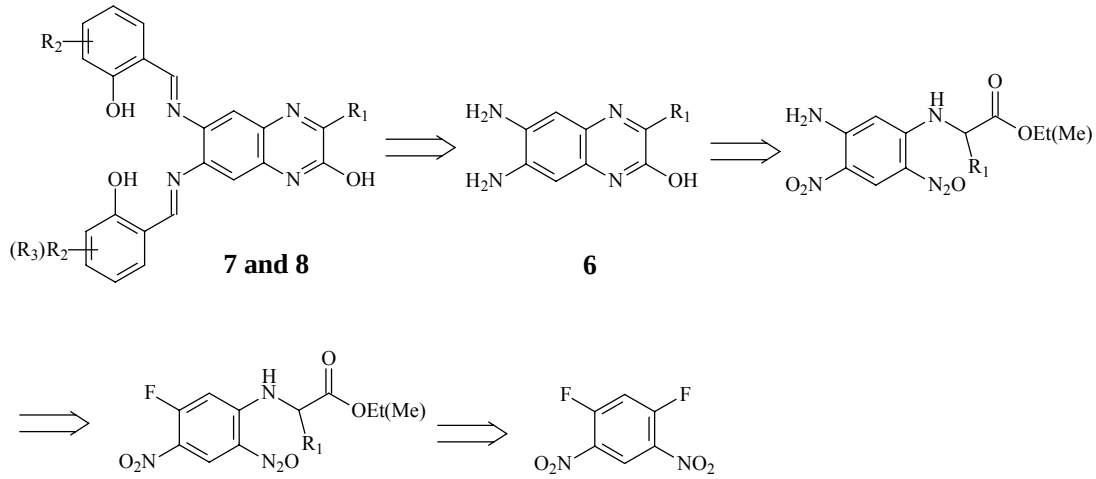


13

Figure 4. Structures of 2-quinoxalinol salen complexes (**10**, **11**) and solid phase 2-quinoxalinol salen and complexes (**12**, **13**)

CHAPTER 2

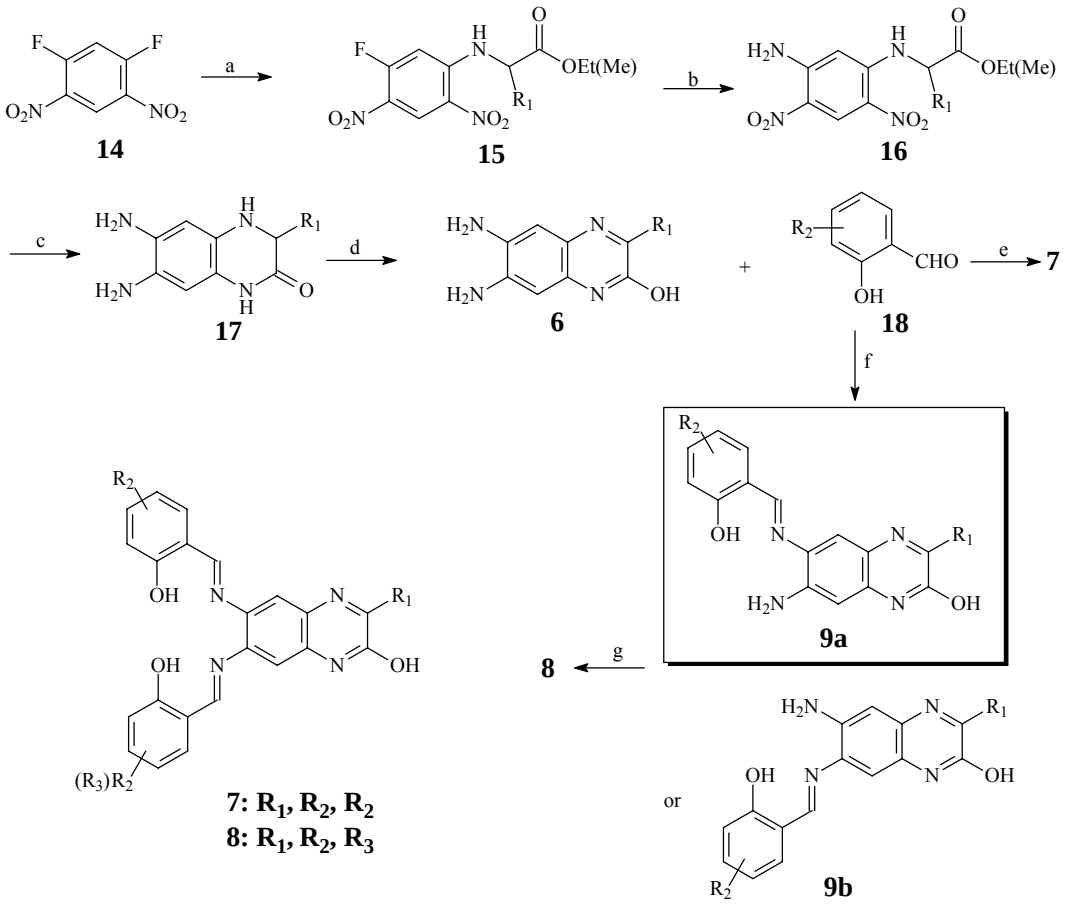
SYNTHESIS OF A SYMMETRIC SALQU LIGANDS LIBRARY



Scheme 2. Retrosynthetic analysis of salqu (**7** or **8**).

For the synthesis of a library of functionalized salqu ligands, the ability to incorporate molecular diversity is a key factor during the method design. The method of introduction of diversity sites decides the size of library.[78] From the retrosynthetic route, we determined that we might introduce three sites for diversity one with the amino acid (R_1) and two more by using different salicylaldehydes (R_2 and R_3) (**Scheme 2**). There are many different kinds of amino acids available commercially including the 20 most common naturally occurring amino acids and numerous unnatural amino acids. For the salicylaldehydes, there are many different kinds commercially available in addition to the simple salicylaldehyde including multi

hydroxy salicylaldehyde or 3, 5-di*tert*butyl salicylaldehyde. Therefore, in theory, we can synthesize this three diversity sites salen library in a combinatorial way. Therefore, in theory, we can synthesize this three diversity site salen library using combinatorial methods. There are two ways to do combinatorial synthesis, solution phase parallel synthesis, and solid phase organic synthesis (SPOS). Both methods are potentially useful to us. In this case, solution phase parallel synthesis could be readily used to obtain a library of salqu ligands.



a. THF, amino acid 1eq, DIEPA, b. $NH_3.H_2O$ 3eq, THF, c. Pd-C, $HCOONH_4$, EtOH(95%), N_2, d. Air or O_2. e. MeOH, refluxing, ratio of 6 to 18 is 1:10, 48hr. f. MeOH, refluxing, ratio of 6 to 18 is 1:1.2, 4-14hr. g. MeOH, refluxing, aldehyde 18', 14hr.

Scheme 3. Reaction route for the prepatation of salqu ligands (**7** and **8**).

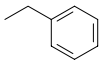
Previously, Liu and coworkers reported the solution-phase parallel synthesis of a series of diamino-2-quinoxalinol derivatives (e.g., **6**).[61-64] Our synthetic route to a combinatorial library of symmetric substituted salqu ligands is shown in **Scheme 3.** Based on Liu's previous work,[61-64] our synthesis employs a sequence of four straight forward and high-yielding reaction steps beginning from the commercially available 1,5-

difluoro-2,4-dinitrobenzene (DFDNB) and to obtain diamino-2-qnioxalinols (**6**). We have further simplified and optimized the synthetic methodology for the synthesis of the diamino-2-quinoxalinols (**6**), a kind of key intermediates. Here, the scavenger resins used in the previous investigations have been replaced by the use of two equivalents of DIPEA (diisopropylethylamine) to remove the acid of HF and HCl on the amino acid methyl group produced in the first step of the reaction sequence. Ammonium hydroxide in water (3 equivalents) was used in the substitution of the second fluorine (Step b, **Scheme 3**.). In this way, the preparation of the intermediate (**16**) does not require additional purification after the substitution of the two fluorine atoms, because any water or any remaining unreacted ammonium hydroxide can be removed using high vacuum. This serves to make it easier to prepare these compounds using parallel solution methods as well as reduce the costs of materials.

After reduction using 2.5 equivalents 5% wet Pd on carbon and 20 equivalents of ammonium formate, the target intermediates, diamino-2-quinoxalinols (**6**), are easily recrystallized from 95% ethanol. For the development of a diverse library of these intermediate diamino 2-quinoxalinols (**6**), different kinds of methyl ester amino acids to be used as the building blocks were selected for the initial library: phenylalanine with an aromatic group, methionine containing a hetero atom (sulfur), alanine, valine and leucine with simple alkyl groups, glycine with neutral hydrogen and the unnatural trifluoromethyl amino acid with a trifluoromethyl electron withdrawing group at R_1. The purity of each intermediate (**6**) is over 99.0% and the yields of them are over 90.0% (**Table 1**.). The sulfur atom in intermediate **6d** (made from the methionine starting material) leads to a poisoning of the catalytic palladium on carbon, so the yield of this product is lower than

others. When R_1 is hydrogen or the strong electron withdrawing group CF_3, their diamino 2-quinoxalinols (**6e** and **6f**) are very unstable and decompose quickly.

Table 1. Results of diamino-2-quinoxalinol synthesis (**6**).

No.	Compound	R_1	Purity (%)‡	R_t (min)	Yield (%)*
1	6a		99	3.46	97
2	6b		99	3.53	90
3	6c		99	3.18	99
4	6d		99	3.47	68
5	6e	CF_3	-	-	-
6	6f	H	-	-	-

‡ Identified by HPLC; R_t is retention time. *One step yield of the Pd-C reduction.

The available commercial salicylaldehydes chosen to prepare the salqu ligands from intermediates (**6**) included hydrophilic salicylaldehydes (dihydroxide, **18a** and **18b, Figure 5**.) and hydrophobic salicylaldehydes (mono- and di*tert*butyl, **18c** and **18d, Figure 5**.) to build our library or salqu ligands (**Table 2**.). These selections will also later provide a variety of compounds of varying solubility and coordination properties for the continuation of this project in the development of applications.

Four different reactions were used in order to optimize the solution phase parallel conditions (**Figure 6.**). The reaction conditions were optimized by evaluating the effects of varying the reaction times, temperatures, solvents, and reaction ratios of diamino-2-quinoxalinols (**6)** to substituted salicylaldehyde derivatives (**18**) on the formation of products. According to previously published preparations of Schiff base compounds in the literature,[71,72] we began using methanol as solvent, with a ratio of 1:2.5 of diamino-2-quinoxalinol (**6)** to salicylaldehyde derivatives (**18**) at room temperature. The reaction mixture was allowed to react and stir under nitrogen for 48 hours. Under these conditions, the desired products are not obtained. With heating from room temperature to reflux temperature for 48 hours, the major product is the half-unit ligand **9** which has two possible structures (**9a** or **9b**) and a small amount of the full unit target compound **7cd** (20.0%), 43.0% **7ad** and 60.0% **7ae**. Increasing the reaction time from 48 hours to 72 hours did not result in additional full unit products nor did increasing the reaction temperature benefit the reaction progress. Changing the solvent from methanol to higher boiling point solvents (e.g., toluene, DMF and benzene) allowed for increasing the reflux temperature, but did not produce the desired product.

Initially, we resisted increasing the ratio of salicylaldehyde derivatives to diamino-2-quinoxalinol derivatives (**6)** without efficient scavenging resins to remove the excess salicylaldehyde. Because of this, microwave methods were tried; however, this resulted in the decomposition of the starting materials within a short time demonstrated (**6**). Sonication was used in another intensive energy method, but again the expected salqu ligands were not generated.

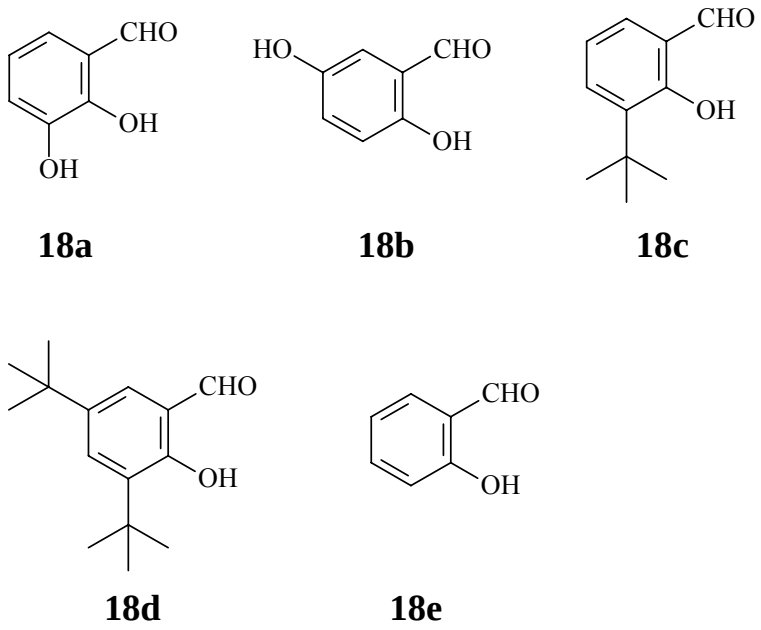


Figure 5. Selected salicylaldehyde derivatives (**18a**-**18e**).

On increasing the ratio of intermediates **6** to salicylaldehyde derivatives **18** from 1:2.5 to 1:5 (**Figure 6**), the yield of full unit target product went up from 20% to 31% for **7cd**. The yields of **7ad** and **7ae** do not change dramatically. On increasing the ratio of to 1:7.5, the yields of target products increased to 52% for **7ad**, 44% for **7cd** and 60% for **7ae**. Fortunately, the final products precipitate from methanol solution. This is a very beneficial phenomenon for solution phase parallel synthesis allowing the use of parallel filtration.[61-64]

When the ratio was increased from 1:7.5 to 1:10, the yields of **7cd** and **7ae** increased to 57% and 77%, but the yields for **7ad** did not change significantly. Continuing to increase the ratio to 1:15 does not lead to better results. Target products were filtered directly, resulting in yellow solids. These were washed with 95% ethanol and ice cold acetone five times each. It was determined that there was no final product in

the filtered solution using TLC, and the yellow solids are very pure symmetric substituted salqu ligands. These were characterized by ^{1}H-NMR, ^{13}C-NMR, MS and HRMS. The purity of **7ad**, **7cd** and **7ae** identified by ^{1}H-NMR is no less than 99%. For **7da**, at the ratio of 1:10 of **6d** to **18a**, we can not obtain any of the target product **7da**, but when we increased the reaction concentration by reducing the volume of solvent of methanol, using a ratio of 1:10, we can obtain **7da** in good yield (65%).

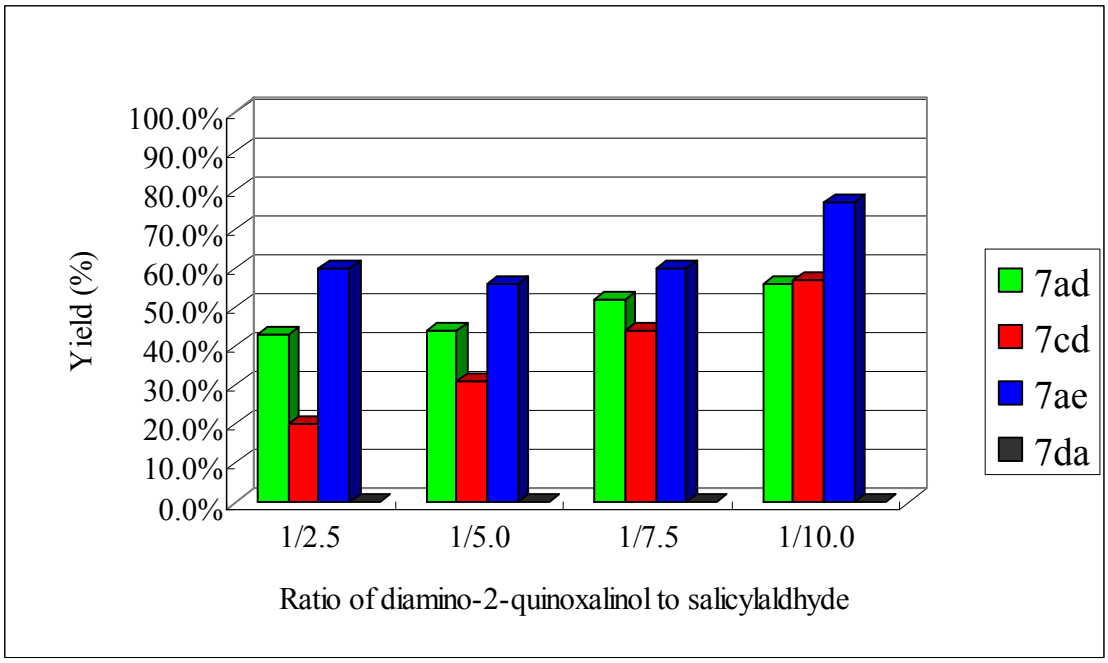


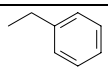
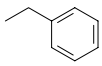
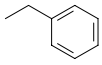
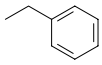
Figure 6. Optimized ratios of diamino-2quinoxalinol (**6**) to salicylaldhyde (**18**) in the preparation of four symmetric salqu ligands.

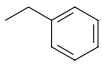
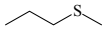
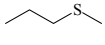
The final optimized conditions for the synthesis of the symmetric salqu ligands include the ratio of 1:10 of diamino-2-quinoxalinol derivatives (**6**) to salicylaldehyde

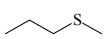
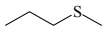
derivatives (**18**) heated to reflux temperature in methanol and allowed to react for 48 hours. When we synthesized this as a 4×5 library, we found that this procedure is very suitable for the solution phase parallel synthesis of symmetric salqu ligands. Results are shown on **Table 2**. All of these twenty targeted products are synthesized by parallel methods. The yields and purities of the products are very high. Purity of the final products was determined by the proportion of typical peak areas of ^{1}H-NMR, assuming the half unit Schiff base ligand (**9**) is the only major byproduct. HPLC can not identify the exact percentage of this major impurity because the large difference of absorbance of their UV (254 or 214nm).

Table 2. Library of symmetric salqu ligands.

¶ One-step yield from diamino 2-qunioxalinol **6** to final salqu ligands **7**.

No.	Product	R_1	R_2	Purity (%)	Yield (%)¶
1	7aa		3-OH	>90	50
2	7ab		5-OH	>95	41
3	7ac		3-*tert*-butyl	>95	55
4	7ad		3,5-Di-*tert*-butyl	>99	56

5	7ae		H	>99	77
6	7ba		3-OH	>90	64
7	7bb		5-OH	>95	44
8	7bc		3-*tert*-butyl	>99	56
9	7bd		3,5-Di-*tert*-butyl	>99	55
10	7be		H	>90	70
11	7ca		3-OH	>95	50
12	7cb		5-OH	>90	67
13	7cc		3-*tert*-butyl	>95	52
14	7cd		3,5-Di-*tert*-butyl	>99	57
15	7ce		H	>99	86
16	7da		3-OH	>90	65
17	7db		5-OH	>90	57

18	7dc		3-*tert*-butyl	>95	46
19	7dd		3,5-Di-*tert*-butyl	>99	56
20	7de		H	>95	81

From these results and optimized conditions, some trends are clear. With each diamino-2-quinoxalinol (**6**), the yield of the product with aldehyde **18e** was significantly higher most likely due to limited steric hindrance, but yields were quite good with using aldehyde **18d** or **18c**, which should be the most sterically hindered aldehyde. This is also the aldehyde with the best solubility and products from this aldehyde are soluble in chlorinated solvents, whereas some of compounds synthesized from aldehyde **18a** and **18b** are soluble only in DMF or DMSO. The most likely causes of the inhibition of product formation in reactions with aldehyde **18a** and **18b**, are hydrogen bonding or an unfavorable electronic effect caused by electron donor 3 or 5 position hydroxyl group on salicylaldehyde **18a** and **18b**. More positive charge on the carbon of aldehyde group will favor the formation of C=N bond.

In summary, an optimized solution phase parallel synthetic method for symmetric substituted salqu library (**7**) has been developed and by this method a library of 20 symmetric substituted salqu ligands has been obtained with good yields and high purities. Some byproducts, the 2-quinoxalinol imines (**9**), were obtained at the same time. These byproducts have two possible structures (**9a** or **9b**). In theory, **9a** should be the preferred product based on α - nucleophilic effect, but this requires support with by experiments

and/or accurate calculations. Once the structures of 2-quinoxalinol imines (**9a**) have been identified, a series of unsymmetric substituted salqu ligands could then be prepared. In the next chapter, the methods of confirming the accurate structure of the 2-quinoxalinol imines (**9a**) will be illustrated, and a developed method for synthesis of unsymmetric substituted salqu ligands will be introduced.

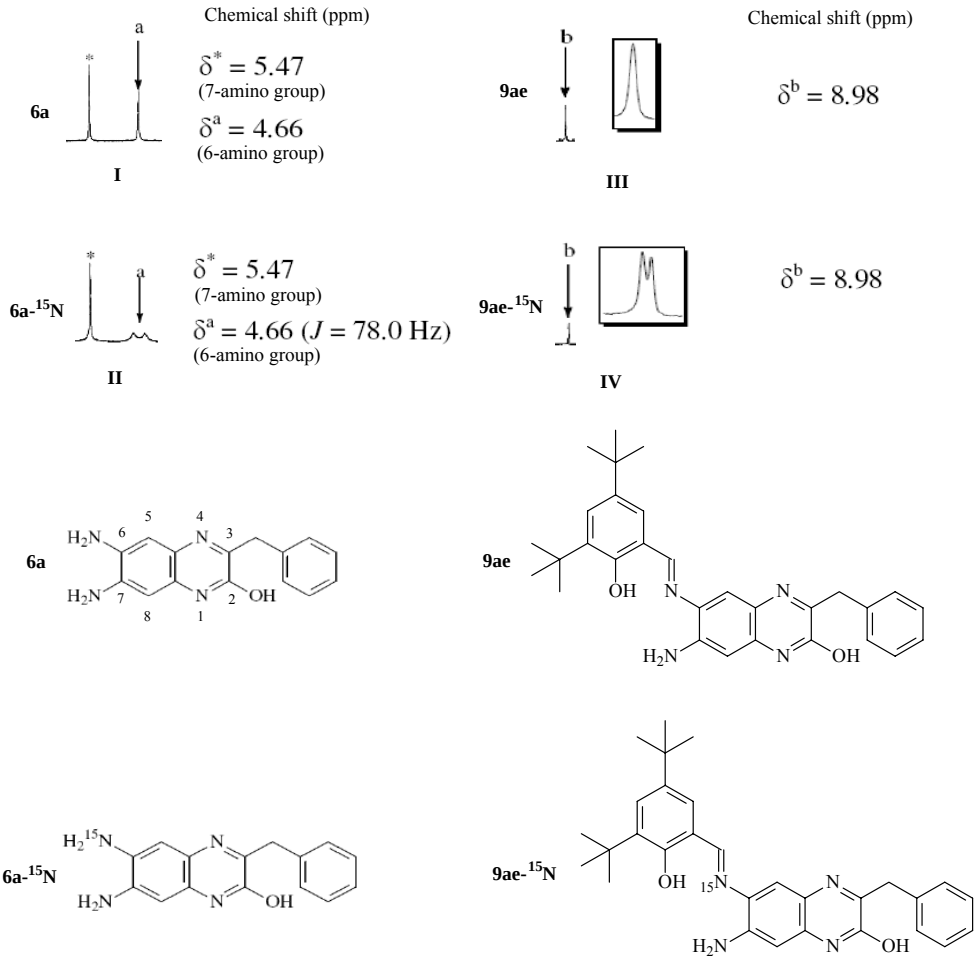
CHAPTER 3

IDENTIFICATION OF 2-QUINOXALINOL IMINE AND SYNTHESIS OF UNSYMMETRIC SALQU LIGANDS

We have synthesized a library of symmetric substituted salqu ligands.[79] In order to incorporate chiral character into salqu ligands to prepare unsymmetric substituted salqu ligands, the introduction of unsymmetric substitution is necessary. We identified that the ratio of intermediates used diamino 2-quinoxalinols (**6**) to salicylaldehyde derivatives (**18**) is crucial to results of the reaction. [79] When the ratio is 1:2.5, a 2-quinoxalinol imine (**9**) is the major byproduct with high regioselectivity. Continuing to decrease the ratio of intermediates (**6**) to salicylaldehyde derivatives (**18**) (1:1.2), 2-quinoxalinol imines (**9**) are the major products whereas yields of symmetric salqu ligands (**7**) are very low. The identification of 2-quinoxalinol imines (**9**) in the reaction is very important to determine the utility of these compounds in unsymmetric syntheses, because two configurations (**9a** or **9b**) are possible.

In order to identify the exact structure, we differentiated these two amino groups of diamino 2-quinoxalinol intermediate (**6**) by replacing ammonium hydroxide with ^{15}N labeled ammonium hydroxide during the secondary substitution of DFDNB. Because of the heteronuclear coupling of ^{15}N, ^{1}H-NMR can be used to demonstrate a difference

between the two amino groups of intermediate (**6**). Thus, in the 2-quinoxalinol imine intermediate (**9**), the position of the imine formation (whether on the ^{15}N or ^{14}N of intermediate **6**) can be identified. The simplified ^{1}H-NMR spectra with intermediate (**6a**), 2-quinoxalinol imine (**9ae**) and the ^{15}N labeled intermediate (**6a-^{15}N**), 2-quinoxalinol imine (**9ae-^{15}N**) are shown in **Figure 7**.



Note: For intermediate (**6a**), ^{1}H-NMR of hydrogen of two amino groups has been shown. For 2-quinoxalinol imine (**9ae**), just the hydrogen on the carbon of imine group has been shown.

Figure 7. ^{1}H-NMR results of intermediate (**6a**) and 2-quinoxalinol imines (**9ae**).

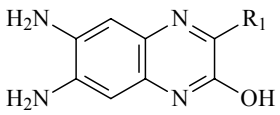
In **Figure 7**, for intermediate (**6a)**, the "a" labeled peaks corresponded to the two protons of the ^{14}N and ^{15}N amino groups are different in spectra **I** and **II**. In spectra **I**, it is a broad single peak, while in spectra **II**, with ^{15}N heteronulear coupling, the protons are split (J=78.0Hz). For the ^{15}N labeling 2-quinoxalinol imine (**9ae-^{15}N**), the peak marked "b" corresponded to the proton on the carbon of imine group are split by ^{15}N (J=3.0) (spectra **IV**), whereas it is still a single peak in spectra **III**. At the same time, in the spectra **III** and **IV**, the peak (δ=4.66ppm) disappear. Therefore, it is obvious to conclude that the final structure of 2-quinoxalinol imines is **9ae**.

The reason as to why the 6-amino group is higher reactivity than the 7-amino group can be explained based on either a kinetic or a thermodynamic argument. In the kinetic explanation, 2-quinoxalinol ring is an aromatic system, and 2-hydroxyl group is an electron-donor group which increases electron density of the carbon contacting 6-amino group and so making 6-amino group more reactive than the 7-amino group (an α-nucleophile effect). This effect is evident in the ^{1}H-NMR of intermediate **6** (**Figure 7**). There is a substantial difference between the chemical shift of hydrogen on 6 and 7 amino groups ($\Delta\delta$ = 0.81ppm, as identified in the labeling study). The two amino groups are in the same benzene ring, the up-field hydrogen of the 6-amino group must have more electron density and, therefore, the 6-amino group is more reactive than the 7-amino group downfield.

This can be further confirmed by computational results. The density functional theory method B3LYP/6-31G(d) was used to characterize some intermediates **(6)** and 2-quinoxalinol imines (**9a**) and ground states in vacuum using Gaussian 03.[77] Calculations

using B3LYP/6-31G(d) were used for geometry optimizations and the calculation of vibrational frequencies, which confirmed all stationary points as minima and provided thermodynamic corrections. The effect of methanol was approximated by subsequent single-point calculations using the conductor-like polarizable continuum model (CPCM).[77] The default Gaussian 03 dielectric constant of 32.63 was used for methanol. Partial charges for the intermediate **(6)** and 2-quinoxalinol imines (**9a**) were obtained using CHELPG method.[77] The calculation results show that the 6-nitrogen in each case has more negative charge than the 7-nitrogen. (**Table 3**) Therefore, 6-amino group of 2-qunioxalinol should be more reactive that 7-amino group.

Table 3. Calculation results of intermediate **6**.



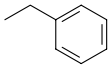
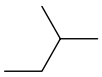
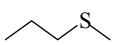
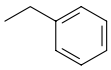
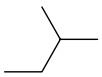
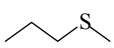
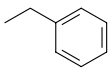
6

Intermediate	R_1	Charge of 6-N (δ_6)	Charge of 7-N (δ_7)	$\Delta\delta_{6-7}$
6a		-0.857	-0.831	0.026
6b		-0.856	-0.831	0.025
6c		-0.861	-0.839	0.022
6d		-0.848	-0.817	0.039
6e	H	-0.852	-0.823	0.029

Finally, for a justification based on thermodynamics, the minimized energy of three pair of 2-quinoxalinol imine's isomers (**9ad** and **9bd**, **9af** and **9bf** and **9ai** and **9bi**) has been calculated with the same method (*vida supra)* in the model of gas and methanol. Minimized energy **9ad**, **9af** and **9ai** are lower 0.869, 0.931 and 0.954 in gas model; 0.8, 0.889 and 0.106 Kcal/mol in MeOH model than their respective isomers (**9bd**, **9bf** and **9bi**). Therefore, from the thermodynamic view, **9ad, 9af** and **9ai** are much more stable than their isomers, in other words, the 6-amino group should be higher in reactivity (as measured by decreased potential energy of the isomer) than the 7-amino group isomers. Therefore, based on the identified 2-quinoxalinol imines (**9ae**), a series of 2-quinoxalinol imines have been prepared (**Table 4**).

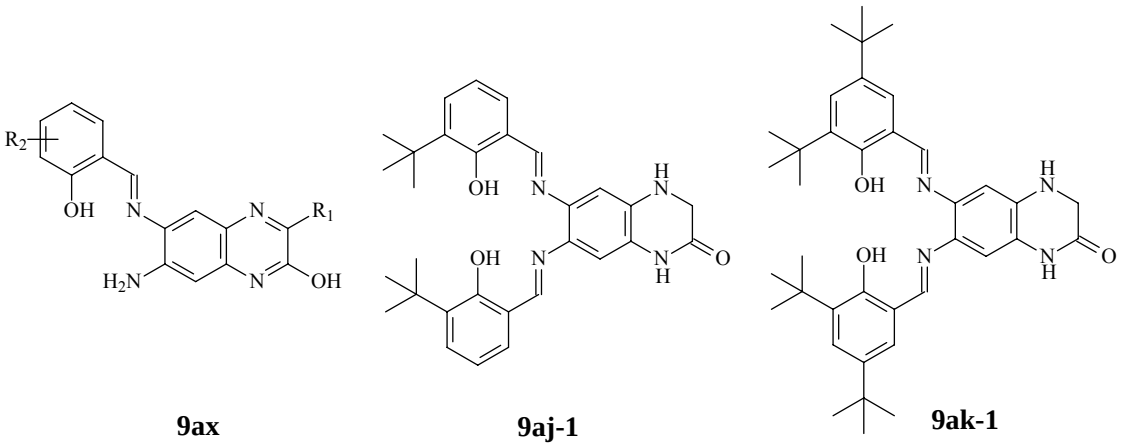
The synthetic method for the preparation of 2-quinoxalinol imines (**9ax**) begins with the addition of 1.0 equivalent of the intermediates (**6**) dissolved in methanol to a methanol solution of 1.2 equivalents substituted salicylaldehyde derivatives (**18**). The two are combined with stirring, and after heating at refluxing temperature for 1 hour, the reaction mixture becomes deep yellow or red. Stirring at reflux temperature was continued for 14 hours, and monitored by TLC. Once it is observed that the reaction mixture no longer contains intermediates (**6**), the reaction is stopped by allowing the mixture to cool to room temperature. Pure 2-quinoxalinol imines (**9ax**) are obtained by flash column chromatography using hexane : ethyl acetate, 3 : 1 as eluent. According to this method, eight different 2-quinoxalinol imines (**9aa-9ah**) were prepared. (**Table 4**) The yield of final products ranges from 65.0% to 94.0%.

Table 4. Preparation of 2-quinoxalinol imines (**9ax**).

Product	R_1	R_2	Yield (%)
9aa		3-*tert*-butyl	93.8*
9ab		3-*tert*-butyl	70.2*
9ac		3-*tert*-butyl	71.5*
9ad		3-*tert*-butyl	65.5*
9ae		3,5-Di-*tert*-butyl	76.7*
9af		3,5-Di-*tert*-butyl	66.0*
9ag		3,5-Di-*tert*-butyl	89.2*
9ah		3,5-Di-*tert*-butyl	80.0*
9ai		3-OH	68.5*
9aj	H	3-*tert*-butyl	-¶
9ak	H	3,5-Di-*tert*-butyl	-¶

* This is a one-step yield after purification by column chromatography.

¶ The major byproducts are **9aj-1** and **9ak-1**.



9ax **9aj-1** **9ak-1**

When R_1 is a hydrogen atom, this diamino-2-quinoxalinol (**6e**) is not stable and was found to decompose on exposure to air. Because of this, it was used directly for the following reaction with 1.2 equivalents salicylaldehyde derivative (**18c** and **18d**) under nitrogen gas protection without purification after the reduction reaction. In fact, it is the hydrogenating diamino 2-quinoxalinol (**17**) that directly reacts with salicylaldehyde derivatives without regioselectivity. The major byproducts are **9aj-1** (11.0%) and **9ak-1** (10.0%). The expected products **9aj** and **9ak** may not be obtained.

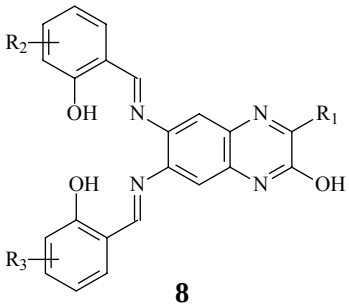
For sample **9ai**, a modified procedure was used. After heating to reflux temperature for 4 hours, a red precipitate (**9ai**) forms. The red solid was filtered off and washed with 95% ethanol followed by ice cold acetone resulting in the pure final 2-quinoxalinol imine (**9ai**). Unlike the previous reactions, prolonging the reaction time did not increase the yield of product (**9ai**). Other salicylaldehyde derivatives with different functional groups in the 3 position were tried, but the expected final 2-quinoxalinol imines (e.g., **9a**) were not obtained.

In contrast, in some cases, low yields of the symmetric substituted salqu ligands (**7)** were obtained. Presumably due to steric hindrance, we found that primarily when the 3 position has a bulky group such as the *tert*-butyl group, the 2-quinoxalinol imines (**9a**) were formed as the major products. The **9ai** is a special case, but when another intermediate (**6**) with different group R_1 is reacted with 2, 3-dihydroxy salicylaldehyde, the expected products are not formed. These results demonstrate that the 2-quinoxalinol aromatic system and 3 position bulky group of salicylaldehyde derivatives are necessary to the regioselective effect. All of the final products were identified and characterized by ^{1}H-NMR, ^{13}C-NMR, MS, HR-MS, and IR.

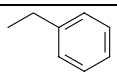
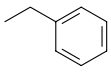
Based on these experiments, nine 2-quinoxalinol imines (**9aa-9ai**), and twelve unsymmetrically substituted salqus ligands (**8a-8l**) were obtained. (**Table 5**) The procedure for the synthesis of these unsymmetrical salqu ligands is unique and can be done in one pot. According to the general procedure of synthesis of 2-quinoxalinol imines **9a**, when the imines are formed, without additional purification, a second substituted salicylaldehyde derivative (**18'**) was directly added into the methanol reaction solution. The reaction mixture was allowed to heat to reflux temperature for another 14 hours, and in the end, a precipitate forms. The end product can be filtered and washed with 95% ethanol and ice cold acetone five times each. These precipitates were directly identified by NMR and MS. The purities of them are very high. All of unsymmetrical salqu ligands (**8a-8l**) are of low solubility in water, hexane, methanol, or ethanol. When R_3 is H, these ligands are very soluble in DMSO or DMF, but not in DCM or $CHCl_3$, whereas other unsymmetric salqu ligands are, in contrast, soluble in DCM or $CHCl_3$, but of low solubility in DMSO.

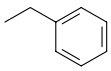
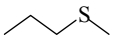
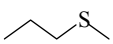
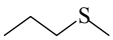
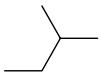
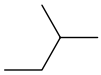
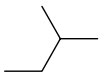
Combinations of different R_1, R_2 and R_3 groups were tested. Altering the R_1 group does not appear to affect the reactivity of 6, 7-amino group. When intermediate **6a** is reacted with the first salicylaldehyde **18** containing the R_2 group being 3-*tert*-butyl, R_3 of the second salicylaldehyde **18'** added could be H or 3,5-di-*tert*-butyl and the yield of these unsymmetrical salqu ligands (**8a, 8b, 8d, 8e, 8g, 8h, 8j and 8k**) are 50.0%~70.0%, whereas when R_2 is a hydroxyl group, there is no expected product; however, when R_2 is 3,5-di-*tert*-butyl, there is only one combination which has a good yield of these unsymmetrical salqu ligands, that is, R_3 is 3-*tert*-butyl, the yield is a bit lower (~45%). The reason why these combinations can form and other combinations can not form is not entirely clear yet, but presumably it is due to steric hindrance in the transition state.

Table 5. Preparation of unsymmetrically substituted salqu ligands (**8**).



8

Product	R_1	R_2	R_3	Yield (%)*
8a		3-*tert*-butyl	3,5-Di-*tert*-butyl	49.1
8b		3-*tert*-butyl	H	60.5

8c		3,5-Di-*tert*-butyl	3-*tert*-butyl	41.0
8d		3-*tert*-butyl	3,5-Di-*tert*-butyl	54.2
8e		3-*tert*-butyl	H	63.0
8f		3,5-Di-*tert*-butyl	3-*tert*-butyl	44.7
8g		3-*tert*-butyl	3,5-Di-*tert*-butyl	50.0
8h		3-*tert*-butyl	H	68.5
8i		3,5-Di-*tert*-butyl	3-*tert*-butyl	38.5
8j		3-*tert*-butyl	3,5-Di-*tert*-butyl	50.5
8k		3-*tert*-butyl	H	66.4
8l		3,5-Di-*tert*-butyl	3-*tert*-butyl	43.7

* The yield is a two step yield, that is, the yield from diamino-2-quinoxalinol **6** to final products **8.**

Previously, all of the final imine formation reactions described have been prepared in methanol.[79, 80] Other solvents such as toluene, acetonitrile, THF and DCM were tested in the process of optimization, but these resulted in lower yields or poor

results. The success of the 2-Quinoxolinol Salen (or Salqu) ligands synthesized in methanol with high yields could be explained to some extent through the use of calculations of the solute-solvent energy pair distributions in explicit methanol solvent. Monte Carlo (MC) simulations, as implemented in BOSS4.6,[77] was carried out using the OPLS-AA force field.[77] Solute-solvent energy pair distributions record the average number of solvent molecules interacting with the solute. The associated energies are shown in **Figure 8**. From these calculations, the numbers of solvent molecules (methanol) that contribute to the stabilized salqu ligands through hydrogen bonding interactions are quantified.

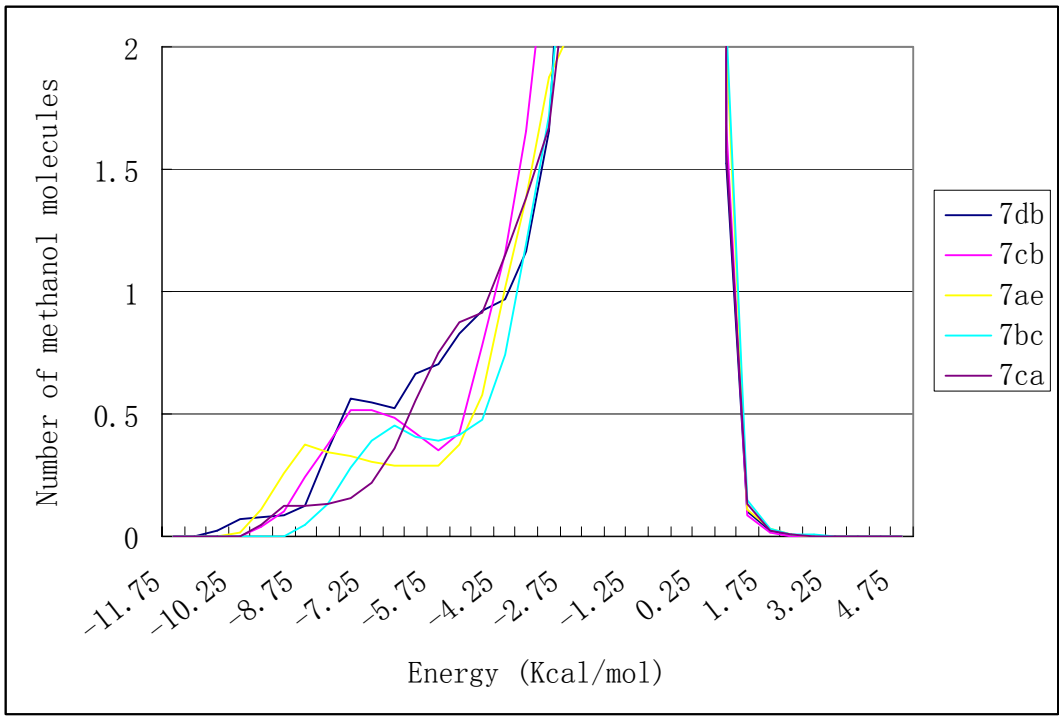


Figure 8. Solute-solvent energy pair distributions for **7ae**, **7bc**, **7ca**, **7cb** and **7db**.

Hydrogen bonding in methanol is reflected in the left-most region, with energies more attractive than -5 kcal/mol. The large bonds near 0 kcal/mol result from the many distant solvent molecules in outer shells. From **Figure 8**, there are strong H-bonding interactions occurring between salqu ligands and solvents. Integration of bands from -15 to -5 kcal/mol for **7ae**, **7bc**, **7ca**, **7cb**, and **7db**, result in three, three, four, four and five methanol molecules. From visual inspection of the solvent environment around salqu ligands, **7ae**, **7bc**, **7ca**, **7cb**, and **7db**, it appears that three, three, four, four and five methanol molecules are coordinated with the hydroxyl groups of solute, which is in agreement with calculated results.

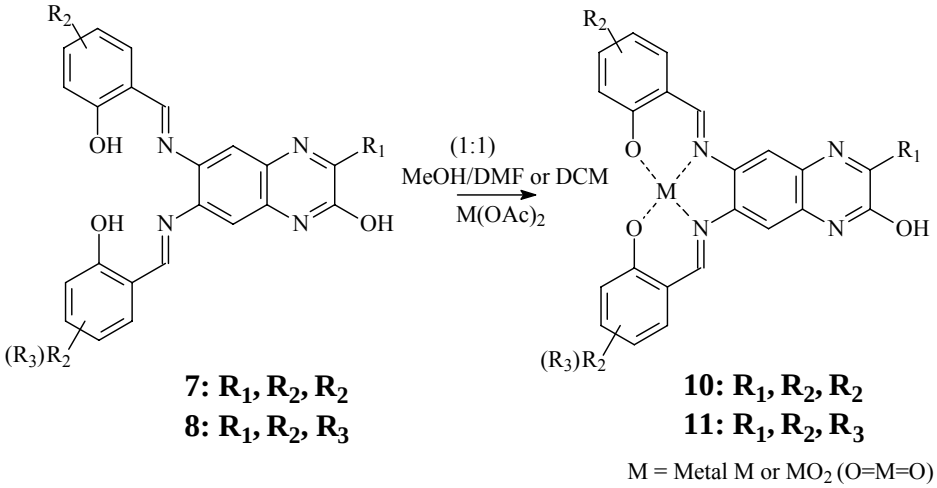
CHAPTER 4

2-QUINOXALINOL SALEN METAL COMPLEXES: SYNTHESIS AND CHARACTERIZATION

Once the syntheses of the symmetric and unsymmetric salqu ligands were optimized, we became interested in the preparation of metal complexes. These could have applications as metal complexes for pharmaceutical use, in catalysis or asymmetric reactions, or as colorimetric or fluorescent sensors. Since many different metal salen complexes have been developed for use in catalysis,[8-51] salqu ligands coordinated should also prove useful in this application. Salen ligands usually react easily with +2 metal salts to form salen metal complexes in good yields, +2 metal salts with acetate, sulfate, chloride or nitrate counter ions were selected to react with salqu ligands. Methanol was selected as solvent to dissolve metal salts. If there is a *tert*-butyl group in salqu ligands, DCM was selected as solvent to dissolve ligands. Otherwise, DMF was used to dissolve ligands. When the two solutions were allowed to mix and react at room temperature, the formation of metal complexes was noted by a change of the reaction solution from bright yellow. If metal salts can not dissolve into methanol, the reactions are usually very slow

with very low yields. Most metal acetates have good solubility in methanol whereas metal sulfate and nitrate salts have poor solubility. Therefore, a series of transition metal acetate salts were selected for investigation, including $Ni(AcO)_2$, $Cu(AcO)_2$, $Mn(AcO)_2$, $Co(AcO)_2$, $Pd(AcO)_2$, $Mg(AcO)_2$, $Zn(AcO)_2$ and the, radioactive actinide $UO_2(AcO)_2$. $FeCl_2$ which has good solubility in methanol was also selected to test for possible complexation with salqu ligands. The lanthanide salts, Ce (III) acetate and chloride salts and Gd (III) chloride were also tested for coordination with salqu ligands.

It was found that Ce, Ga, Mg and Zn cations did not coordinate with salqu ligands even if the temperature was increased to reflux temperature for 24 hours. The application of sonication was also tested with these unreacted metal cations, but salqu ligands were not found to form metal complexes. Other metal cations including uranyl acetate may completely coordinate with salqu ligands to generate corresponding complexes (**10** and **11**) in very good yields (>80.0%) in less than 2 hours at room temperature. The purities and yields of complexes are very high. (**Scheme 4** and **Table 6-9**)



7: R_1, R_2, R_2
8: R_1, R_2, R_3

10: R_1, R_2, R_2
11: R_1, R_2, R_3

M = Metal M or MO_2 (O=M=O)

Scheme 4. Synthetic route for the prepatation of salqu metal complexes (**10** and **11**).

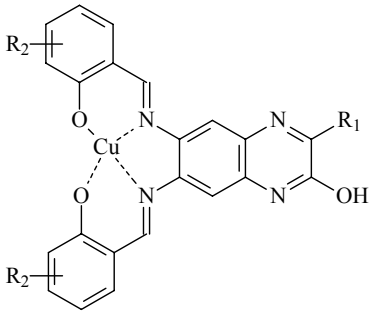
Preparation of the salqu metal complexes begins from a DMF or DCM solution of 1 equivalent salqu ligands (**7** and **8**) were mixed with 1.2 equivalent methanol metal salts solution and stirred at reflux temperature for two hours (with the exception that the uranyl acetate salts are reacted at room temperature). The reaction color changed from bright yellow. The solution was concentrated and washed with 95% EtOH, ether or hexane to obtain salqu metal complexes (**10** and **11**) with yields from 80.0-98.0% (See **table 6** and **table 7**). These complexes are found to be very stable to air or moisture.

Metal cations which can react with salqu ligands under reflux temperature may also coordinate with salqu ligands at room temperature; however, heating reactions with the transition metals to reflux temperature was used to prepare pure complexes by breaking coordination bonds between acetic acid and salqu metal complexes. On the other hand, uranyl metal salqu complexes were found to not coordinate with the acetate as strongly in this case. These also formed single crystals suitable for characterization by small molecular X-ray diffraction (XRD) easily, thus uranyl metal acetate still reacts with salqu ligands at room temperature.

From the results of the metal complex preparations presented in **tables 6-9**, six single crystals of salqu uranyl metal complexes were obtained (marked in the table by the symbol ζ). These were characterized using single crystal X-ray diffraction (XRD). None of the transition metal complexes resulted in crystals suitable for characterization by XRD. Uranyl salqu complexes which were marked by symbol ¶ were characterized using ^{1}H-NMR, but other metal complexes are paramagnetic, and so this effect limits the utility of NMR technology. MS and HR-MS were run for many of these complexes to confirm

their structures, which are marked by†. Complexes were run IR marked by ‡. All of complexes which are marked by star were tested as catalysts for different reactions. These will be described in **chapter 6**.

Table 6. Preparation of copper complexes with symmetric salqu ligands (**10xyCu**).



10xyCu

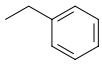
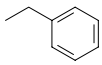
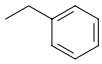
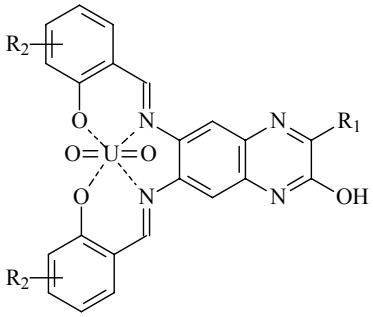
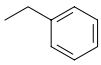
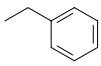
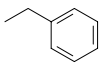
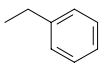
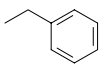
Entry	R_1	R_2	Yield (%)
10aaCu		3-OH	89.0
10adCu†‡		3,5-Di-*tert*-butyl	82.8
10aeCu†		H	88.0
10beCu*		H	87.8
10ceCu*		H	91.0

Table 7. Preparation of uranyl complexes with symmetric salqu ligands (**10xyU**).



10xyU

Entry	R_1	R_2	Yield (%)
10aaU [ζ¶††‡]		3-OH	85.9
10abU[†]		5-OH	94.0
10acU		3-*tert*-butyl	86.4
10adU [ζ¶††‡]		3,5-Di-*tert*-butyl	80.1
10aeU [ζ¶††‡]		H	80.7
10bdU [ζ¶††‡]		3,5-Di-*tert*-butyl	87.5
10beU [ζ¶††‡]		H	97.8
10caU		3-OH	91.0

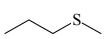
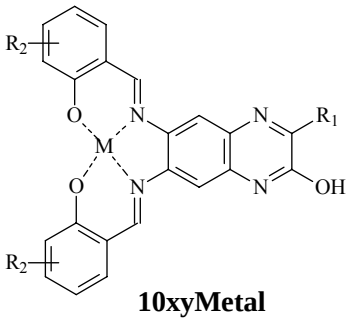
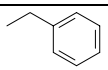
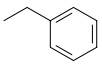
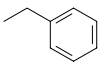
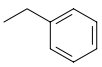
10cbU[†]		5-OH	90.5
10cdU		3,5-Di-*tert*-butyl	91.0
10ceU[ζ¶†‡]		H	88.0
10deU[¶†‡]		H	92.2

Table 8. Preparation of transition metal complexes with symmetric salqu ligands.



10xyMetal

Entry	R_1	R_2	M	Yield (%)
10aaFe		3-OH	Fe	95.0
10adMn[†*]		3,5-Di-*tert*-butyl	Mn	96.5
10adCo[†‡*]		3,5-Di-*tert*-butyl	Co	80.0
10adNi[†‡*]		3,5-Di-*tert*-butyl	Ni	92.7

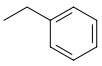
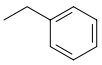
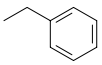
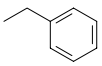
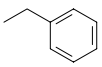
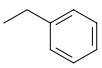
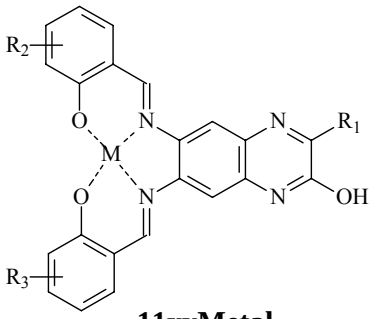
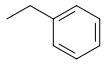
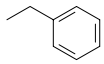
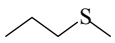
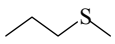
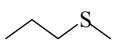
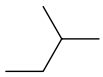
10adPd[†]		3,5-Di-*tert*-butyl	Pd	92.0
10aeMn[*]		H	Mn	91.0
10aeNi		H	Ni	90.7
10aeCo		H	Co	94.1
10aePd		H	Pd	86.0
10aeFe[*]		H	Fe	87.4
10bdMn[*]		3,5-Di-*tert*-butyl	Mn	79.8
10cbCo		5-OH	Co	89.7

Table 9. Preparation of metal complexes with unsymmetric salqu ligands (**11xyMetal**).



11xyMetal

Entry	R_1	R_2	R_3	M	Yield (%)
11bMn[†*]		3-tert-butyl	H	Mn	80.0
11bU[†]		3-tert-butyl	H	UO_2	82.0
11dCo[*]		3-tert-butyl	3,5-Di-tert-butyl	Co	89.7
11eNi[*]		3-*tert*-butyl	H	Ni	85.3
11eFe		3-tert-butyl	H	Fe	81.9
11fCu[*]		3,5-Di-tert-butyl	3-tert-butyl	Cu	90.0
11iMn[*]		3,5-Di-tert-butyl	3-tert-butyl	Mn	88.4
11jCu[*]		3-tert-butyl	3,5-Di-tert-butyl	Cu	86.2

In the ^{1}H-NMR spectra of the uranyl (UO_2^{2+}) complexes, a significant shift in the imine CH=N proton is observed in the uranyl metal complexes (9.6-9.8ppm for **10aaU**, **10aeU**, **10ceU**, **10beU** and **10deU**, 9.1 - 9.3ppm for **10adU** and **10bdU**) as compared to these free ligands (8.9 - 9.3ppm). (This difference in **10adU** and **10bdU** is presumably due to the difference in solvation.) This is indicative of the imine nitrogen lone pairs

coordinating to the metal center. In a similar fashion, there are three or five hydroxyl peaks in the ^{1}H-NMR spectra of the free ligands (12.1 – 13.3 ppm) while in the uranyl (UO_2^{2+}) complexes, two of them are not seen due to coordination of the phenolic oxygens with metal center.

In the IR spectra of uranyl complexes **10aeU**, **10aaU,** and **10adU** have strong peaks around 1620 cm^{-1} (free ligands 1654 - 1658 cm^{-1}) indicating coordinated imine nitrogens.[81] The uranyl complexes of ligands **10beU**, **10ceU** and **10deU** have a strong vibration around 1603 cm^{-1} (free ligand 1658 cm^{-1}) indicating coordinated imine nitrogens. This slight difference from **10aeU, 10aaU,** and **10adU** may be the result of the absence of the phenyl group in the quinoxolinol backbone. Coordination through the phenolic hydroxyl unit in the salicylaldehyde coordination site can also be shown by the shift in the C-O band for uranyl complexes of **10aeU**, **10aaU** and **10deU** (around 1200 cm^{-1}) as compared to these free ligands (around 1270 cm^{-1}, respectively).[82] This is also seen in **10beU** and **10adU** although it is shifted slightly from the other ligands with bands at 1263 cm^{-1} and 1229 cm^{-1} respectively compared to their free ligands (1278 and 1261 cm^{-1}). Bands around 900 cm^{-1} seen in these uranyl complexes are due to the asymmetric and symmetric UO_2 stretching characteristic of linear uranyl ion in the complex.[83] Broad peaks in free ligand**s** seen in the IR spectra around 3400 cm^{-1} are indicative of the presence of the hydroxyl groups. These are seen for uranyl complexes (around 3400 cm^{-1}) but prove to be absent in the transition metal complexes **10adCu**, **10adMn**, **10adCo** and **10adNi**, presumably indicating the formation of metal complex with oxygen of 2-hydroxyl of 2-quinoxalinol backbone. This coordination can be confirmed using the shift in the C-O band of the hydroxy unit in the salqu coordination site for the transition metal

complexes of **10adCo** (1256 cm^{-1}), **10adCu** (1260 cm^{-1}), **10adNi** (1260 cm^{-1}) and **10adMn** (1248 cm^{-1}), compared to their free ligand, **7ad** (1261 cm^{-1}). This is also seen in bands indicative of binding to the lone pairs of the imine nitrogens in the complexes of **10adCo** (1614 cm^{-1}) and **10adNi** (1616 cm^{-1}) compared to the free ligand **7ad** (1656 cm^{-1}).

In DMF, ligand **7ae** features two UV peaks at 305nm (ε=32000) and 390nm (ε=32000). The addition of an aqueous solution of HCl causes (2-fold excess, PH=4) a very slight shift from the peaks at 305nm and 390nm to 300nm and 390nm with no change seen in the extinction coefficients. Upon the addition of the uranyl ion (UO_2^{2+}), as a solution of uranyl acetate, the absorption maximum in the UV-*Vis* spectra demonstrates a shift to 290nm (ε=20000) and 370nm (ε=15000) and the formation of an additional peak at 440 nm (ε=15000), indicating the formation of uranyl complex. Similar bands have been reported for multidentate hydroxyl-containing uranyl complexes (390 and 450 nm).[84] A similar shift is seen in the spectra of uranyl complex **10beU** which features additional peaks with maxima at 287 nm ($\varepsilon = 1.7\times10^4$), 304 nm ($\varepsilon = 1.6\times10^4$), 360 nm ($\varepsilon = 1.3\times10^4$), 385 nm ($\varepsilon = 1.3\times10^4$), and 419 nm ($\varepsilon = 1.4\times10^4$). The **10adU** complex in DMF also demonstrated a shift due to the formation of metal complex with maximum absorption at 295 nm ($\varepsilon = 2.5\times10^4$), 375 nm ($\varepsilon = 1.6\times10^4$), and 440 nm ($\varepsilon = 1.5\times10^4$).

When the solvent was changed to acetone, the same ligand (**7ad**) was titrated with uranyl ion, and UV-*Vis* data was recorded after each addition of uranyl ion. As the titration proceeded, the absorbance maximum due to the free ligand **7ad** at wavelength 390 nm decreased as another maximum formed at 428 nm due to the formation of the uranyl complex, as shown in **Figure 9**, proceeding from the spectrum labeled A to the

one labeled E. It was found to be significantly different than the copper complex of the same ligand in DMF, **10adCu** 280 nm ($\varepsilon = 3.4\times10^4$), 325 nm ($\varepsilon = 2.8\times10^4$), and 454 nm ($\varepsilon = 1.5\times10^4$).

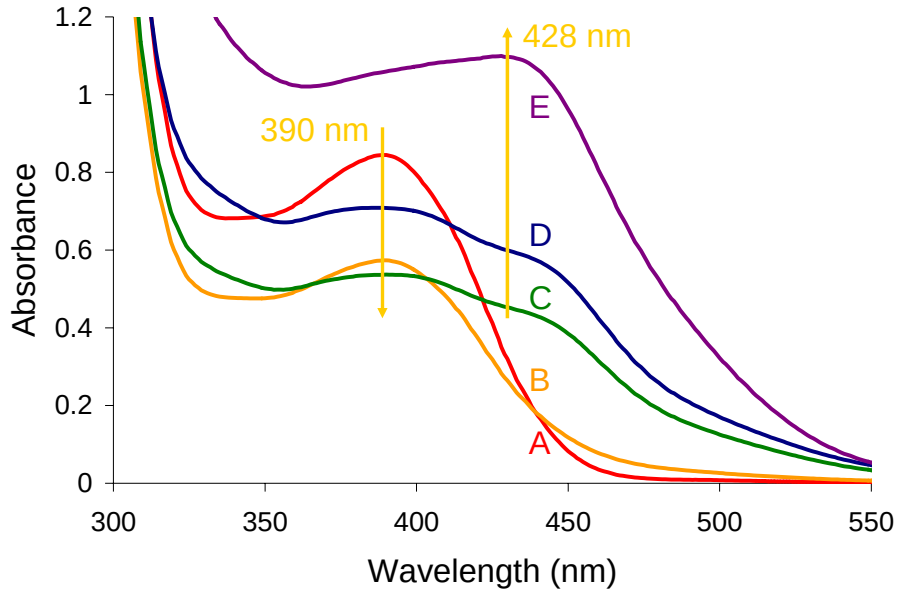


Figure 9. Titration curve of ligand **7ad** by uranyl ion in acetone. (A is the curve of free ligand **7ad**, E is the curve of **10adU** complex.).

Because of spectral changes due to the effects of solvent and from ligand to ligand, in order to have a better comparison between uranyl and other potentially competing metals, the transition metal complexes of ligand **7ad** were prepared along with the uranyl complex in dichloromethane for UV-*Vis* spectroscopy. The results are shown in **table 10**. The different metal complexes can be distinguished by their distinct spectra. The differences between the spectra seen in the coordinating solvent DMF and the non-coordinating DCM, are due to the fact that the fifth coordination site in the plane of the

uranyl is not filled by solvent, possibly leading to dimers. The cobalt complex has two intense peaks at 322 nm ($\varepsilon=6.0\times10^4$) and 437 nm ($\varepsilon=6.9\times10^4$). The copper complex demonstrated the most intense peaks with the highest extinction coefficients at 330nm ($\varepsilon=7.6\times10^4$) and 458nm ($\varepsilon=9.2\times10^4$) and an additional peak at 286 nm ($\varepsilon=6.2\times10^4$). The manganese complex demonstrated two intense peaks at 372 nm ($\varepsilon=4.0\times10^4$) and 510 nm ($\varepsilon=7.1\times10^4$), and so could be distinguished by the unique peak at 510 nm. The nickel complex had four peaks with one very close to the 458 nm of copper at 452 nm ($\varepsilon=9.1\times10^4$), but could be distinguished from copper by the additional peaks at 388 nm ($\varepsilon=5.7\times10^4$), 314 nm ($\varepsilon=4.8\times10^4$) and 268 nm ($\varepsilon=4.6\times10^4$). Finally, the uranyl in dichloromethane is unique with two shoulders at 379 nm ($\varepsilon=2.4\times10^4$) and 456 nm ($\varepsilon=1.7\times10^4$) resulting from the metal complex and peaks at 250 nm ($\varepsilon=3.4\times10^4$) and 300 nm ($\varepsilon=2.9\times10^4$) from the π-π * interactions.

When salqu ligands were reacted with different metals, it was found that Mg, Zn, Ga and Ce cations do not coordinate with salqu ligands under these conditions although these metal salts totally dissolve into solvent methanol. The configuration and geometry of ligands usually determines their coordination properties. Numerous preparations of transition metal complexes with some salqu ligands were prepared to try to grow for single crystals suitable for diffraction by several different conditions, but no of these resulted in quality single crystals. Therefore, calculation methods have been applied to investigate the configuration and geometry of the salqu ligands and their transition metal complexes for comparison.

Table 10. UV-Vis extinction coefficients of metal complexes of ligand **7ad** in dichloromethane.

Metal Ion (Max Wavelength)	Extinction Coefficient	Metal Ion (Max Wavelength)	Extinction Coefficient
Free ligand (301 nm)	44500	Cobalt (437 nm)	69000
Free ligand (391 nm)	44100	Cobalt (322 nm)	60000
Manganese (510 nm)	71000	Copper (458 nm)	92000
Manganese (372 nm)	40000	Copper (330 nm)	76000
Nickel (452 nm)	91000	Copper (286 nm)	62000
Nickel (388 nm)	57000	Uranyl (250 nm)	34000
Nickel (314 nm)	48000	Uranyl (300 nm)	29000
Nickel (268 nm)	46000	Uranyl (379 nm)	24000
		Uranyl (456 nm)	17000

To simulate the structure of salqu ligands (**7aa, 7cb** and **7db**) in MeOH, Monte Carlo (MC) simulations, as implemented in BOSS4.6,[77] was carried using the OPLS-AA force field method.[77] The results showed an enlarged coordination cavity caused by twisting structure from a planar configuration. (**Figure 11**) This can be explained by an electrostatic repulsion of the two phenolic oxygens on the interior of the ligand system, but hydrogen bonding of the lone pair of the imine nitrogen may also contribute. From these calculation results, the NO and NO dihedral angles – or coordination bite angles - of the salqu cavity coordination were computed. (**Figure 10**) Their respective dihedral angles (**7aa**, **7cb** and **7db)** were determined to be 25.0^{o}, 34.9 ^{o} and 30.3^{o}. The corresponding distance between the cooridation sites likely produce a cavity suitable for

binding transition metal Cu, Mn, Ni, and the larger actinide UO_2. The atomic radii and preferred coordination bite angle of Zn, and Mg will likely have smaller distance for the cavity of salqu ligands. The lanthanides Ce and Ga are bigger than that of transition metals, but they typically have shorter bond lengths and reduced flexible in term of geometry than that of uranyl. Thus the preferred geometry of uranyl might be described as closer to that of Cu but with longer bond lengths. The calculated results suggest that salqu ligands may be well sorted to bind Cu, Mn, Ni and UO_2 as opposed to the smaller Zn and Mg or bigger Ce and Gd metal cations.

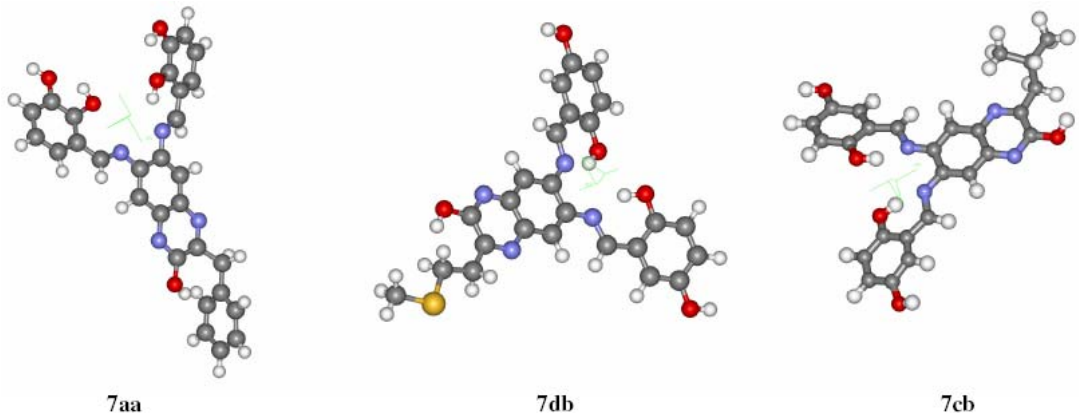


Figure 10. MC with OPLS-AA force field calculated structures of symmetric salqu ligands (**7aa**, **7db and 7cb**).

To support the calculation results, twist configuration and geometry of salqu ligands, single crystals of salqu uranyl complexes can be easily grown for understanding their real configurations although single crystals of their ligands can not be obtained. Methods for growing crystals of their uranyl complexes have been obtained by solution diffusion and vapor diffusion methods (**Figure 11, 12**). Crystals of **10aeU•DMF,**

10aaU•DMF, **10beU•DMF** and **10ceU•DMF** were grown by solvent diffusion of the uranyl complex in dimethyl formamide with ether. (**Figure 11**) Uranyl complexes **10adU•H_2O** and **10bdU•H_2O** were prepared to demonstrate a second crystallization method, solution diffusion method, grown from a saturated solution of salqu ligand in acetone layered with a saturated aqueous solution of uranyl acetate. (**Figure 12**)

X-ray diffraction data was collected at -80 °C on a Bruker SMART APEX CCD X-ray diffractometer unit using Mo Kα radiation from crystals mounted in Paratone-N oil on glass fibers. SMART (v 5.624) was used for preliminary determination of cell constants and data collection control. Determination of integrated intensities and global cell refinement were performed with the Bruker SAINT Software package using a narrow-frame integration algorithm. The program suite SHELXTL (v 5.1) was used for space group determination, structure solution, and refinement.[85] Refinement was performed against F^2 by weighted full-matrix least square, and empirical absorption correction (SADABS[86]) were applied. H atoms were placed at calculated positions using suitable riding models with isotropic displacement parameters derived from their carrier atoms.

Crystals of **10aeU•DMF, 10aaU•DMF**, **10beU•DMF** and **10ceU•DMF** formed as dark red acicular prisms, conforming to space group C2/c with Z = 4 or 8. The general coordination motif of uranyl-Schiff base complexes is similar to that seen in the uranyl (UO_2^{2+}) salophen (*N,N'*-disalicylidene-o-phenylenediaminate) complexes having a pentagonal-bipyramidal geometry with the equatorial plane of the uranyl ion coordinated by the two oxo- and two aza- coordination sites of the ligand and the fifth position in that plane occupied by a DMF solvent molecule.[87] (**Figure 13**) This was typical with what

was seen in this series of ligands. These salqu metal complexes demonstrate a significant twist upon coordination of a metal, which is in accordance with calculation results. This can be seen in the side view of the salqu uranyl complex **10aeU**. (**Figure 14**) This is more pronounced than the 35° seen in the salqu uranyl complex, close to 45° from the coordination plane of the metal ion indicating a strongly bonded complex. The average U-N bond distance in the coordination core is 2.55(3) Å, and the average U-O bond distance is 2.25(5) Å. These bond distances are comparable to the salophen uranyl complexes reported previously.[87] (**Figure 13**)

Single crystals of the uranyl complexes **10adU•H_2O** and **10bdU•H_2O** were prepared using a solution diffusion method. Such a method might be more suitable for modelling or demonstrating possible uses in extraction applications. This serves to demonstrate the strong coordination capability of the ligand specific to the uranyl ion. Crystals formed as red needles at the interface of the two layers, conforming to space group $P2_{1/}n$ with Z=4 for **10adU•H_2O** and space group C2/c with Z=8 for **10bdU•H_2O**. The asymmetric unit cell contains two independent, seven-coordinate uranyl complexes that differ in the conformation of the ligand substituents. This results in a noticeable difference in the bond distances despite similar environment around uranium center. (**Table 12**) Each complex has one ligand coordinating the metal ion and the fifth coordination site occupied by a water or DMF molecule. The U-O bond distances in the "yl" oxygens are typical for uranyl complexes, averaging 1.78(2) Å. The angles of the O-U-O of the uranyl metal ions are near linear at 177.6(10) for U1 and 178.51(11) for U2. The average bite angle of the N-U-O angle is 68.9(3). The average U-N and U-O bond

distances in the coordination core of the two molecules are very similar to that seen before, 2.56(4) Å and 2.25(2) Å, respectively.

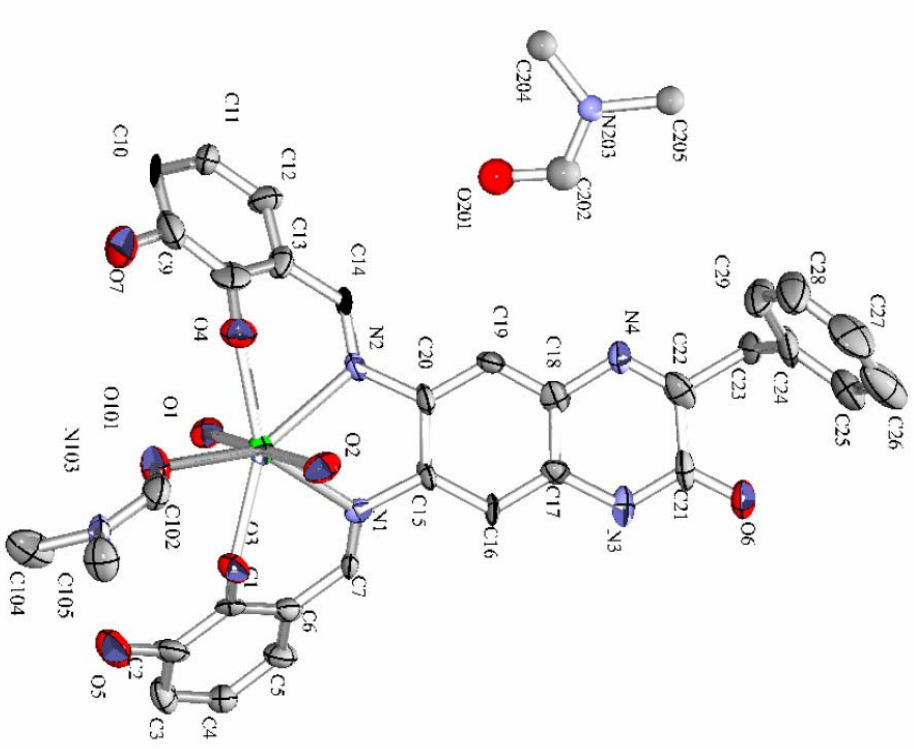
Crystals of **10aeU•DMF, 10aaU•DMF**, **10beU•DMF** and **10ceU•DMF** (vapor diffusion)

Figure 11. Crystals grown by the method of vapor phase diffusion.

Crystals of **10adU•H_2O** and **10bdU•H_2O** (solution diffusion)

Figure 12. Crystals grown by the method of solution phase diffusion.

In summary, a method for preparing salqu metal complexes has been developed. By analysis of their NMR, IR, MS (HRMS) and UV-*vis* data, strong coordination between the salqu cavity (C=N, O, O, C=N) of salqu ligands and metals has been disclosed. For some small radii transition metals and lanthanide metals Ce and Gd metals, they can not coordinate with salqu ligands, which can be explained by calculation results of configuration and geometry of salqu ligands. These calculation results can be further supported by the interpretation of uranyl salqu complexes single crystal structures. In addition, competing experiments indicate that salqu ligands are more selective to copper cation than nickel and manganese cations, which indicate that if salqu ligands were immobilized onto insoluble polymers, SPE technology can be further developed.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O7
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C102
O3
N1
C15
C16
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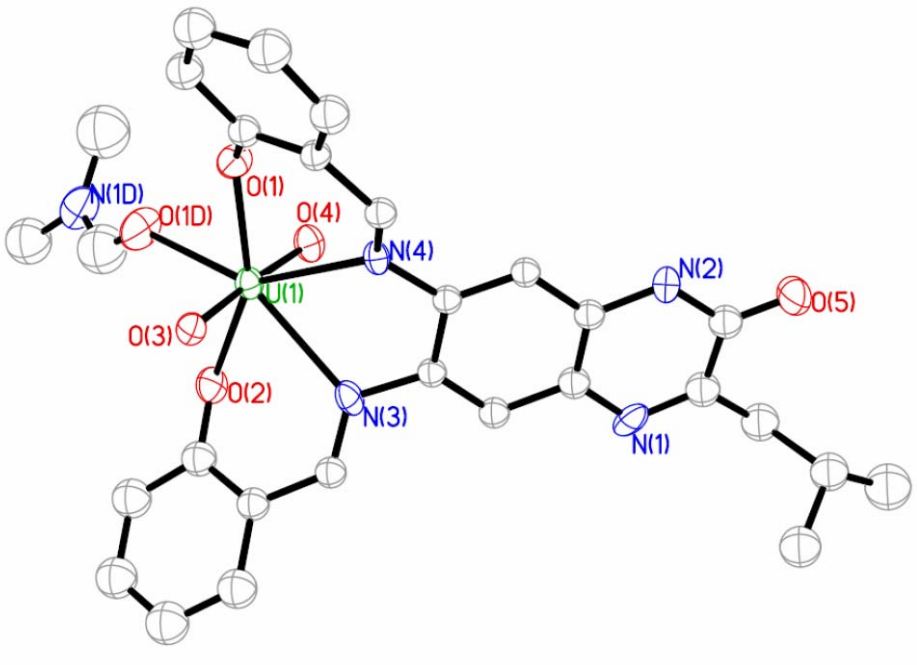
C6
C2
O5
C5
C3
C4

10aaU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O(1D)
O(1)
O(4)
N(4)
U(1)
O(3)
O(2)
N(3)
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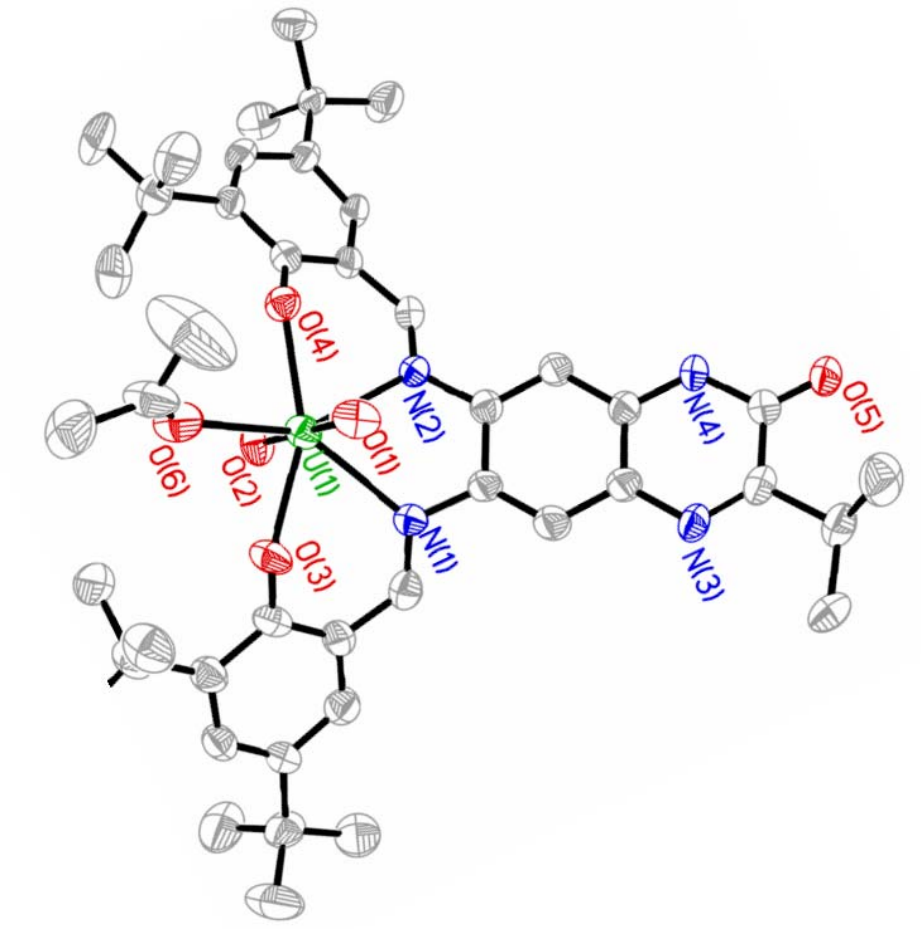
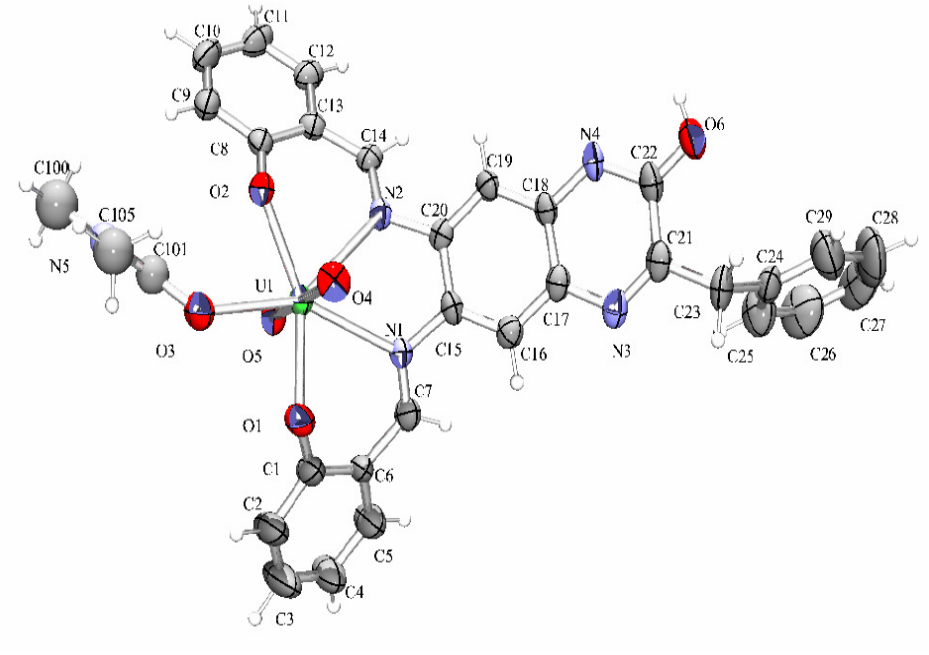
O(5)
N(1)

10ceU



10bdU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C28
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C21
C24
N5
C101
U1
O4
C23
C17
C27
O3
O5
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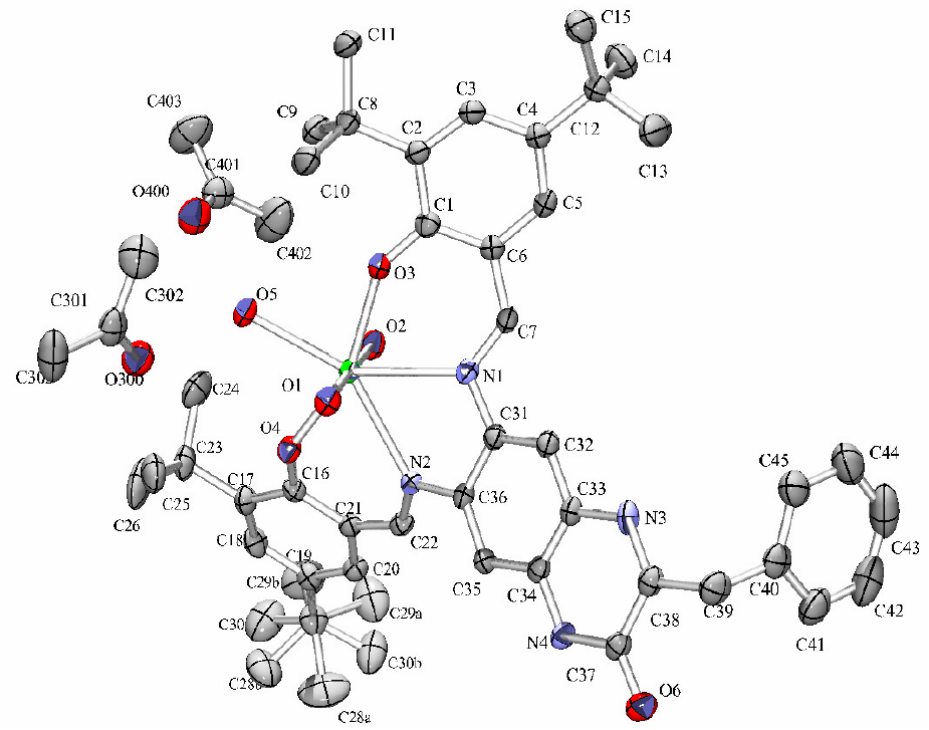
C1
C6
C2
C5
C4
C3

10aeU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O2
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O1
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C31
O4
C32
C23
C45
C44
C16
N2
C33
C17
C36
C25
C21
N3
C26
C22
C43
C18
C19
C20
C40
C29b
C35
C34
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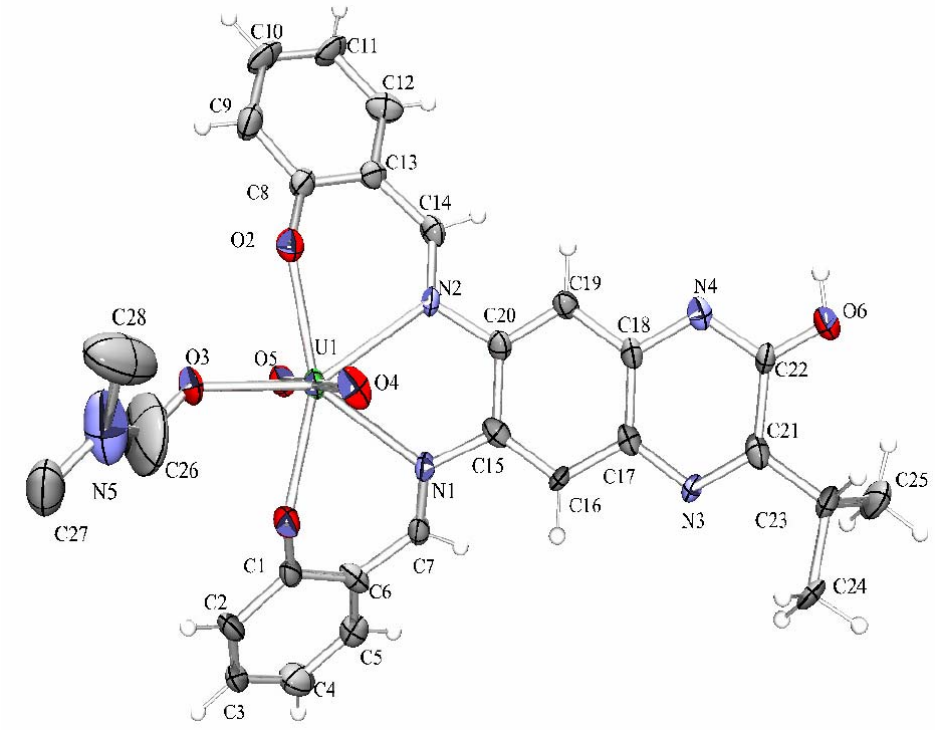
C38
C39
C30
N4
C41
C30b
C37
C28b
O6
C28a

10adU



10beU

Figure 13. Crystal structures of **10aaU**, **10adU**, **10aeU**, **10bdU**, **10beU** and **10ceU**.

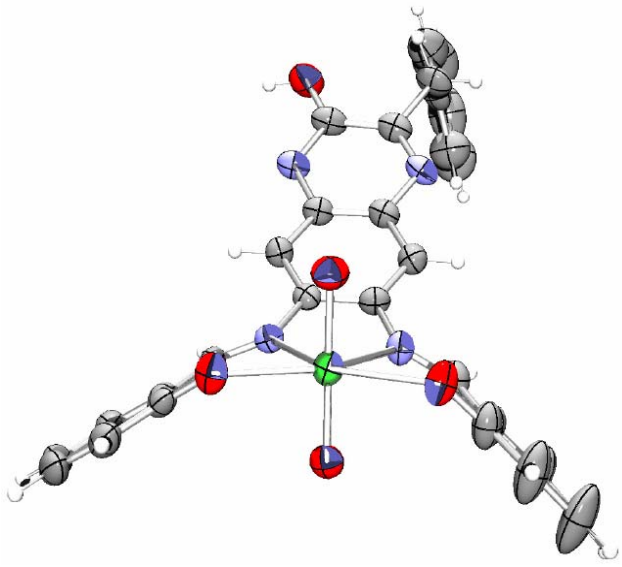


Figure 14. Crystal structures of **10aeU.** (Side view)

Table 11. Crystallographic data for salqu uranyl complexes **10aeU**, **10aaU**, **10beU**, **10adU**, **10bdU**, **10ceU**.

Compounds	**10aeU**	**10aaU**	**10beU**
Empirical formula	$C_{32}H_{27}N_5O_6U$	$C_{32.75}H_{28.75}N_{5.25}O_{8.25}U$	$C_{28}H_{26}N_5O_6U$
Fw (g/mol)	815.62	865.89	767.58
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	*C*2/*c*	*C*2/*c*	*C*2/*c*
Z	8	4	8
a (Å)	33.449(2)	16.403(2)	26.074(2) Å
b (Å)	7.404(4)	7.196(4)	7.291(5) Å
c (Å)	28.564(1)	28.974(3)	28.868(2) Å
a (deg)	90	90	90
β (deg)	124.200(1)	93.968(3)	99.572(1)
g (deg)	90	90	90
V ($Å^3$)	5851.0(5)	3412.0(6)	5411.7(6)
Density calc'd (g/cm^3)	1.852	1.686	1.882
Abs coeff (mm^{-1})	5.603	4.814	6.051
F(000)	3152	1680	2952
Cryst size (mm^3)	0.03x0.1x0.02	0.02x0.1x0.02	0.02x0.1x0.02
Reflns collected	28742	10978	17281
Indep reflns	7246 [$R_{(int)}$ = 0.0603]	7362 [$R_{(int)}$ = 0.0608]	6501 [$R_{(int)}$ = 0.0496]
Refinements method	Full-matrix Least Squares on F^2	Full-matrix Least Squares on F^2	Full-matrix Least Squares on F^2
GOF of F^2	1.025	1.030	0.950
Final R indices [I>2σ(I)]	R_1 = 0.0435 $_wR^2$ = 0.0968	R_1 = 0.0746 $_wR^2$ = 0.1967	R_1 = 0.0388 $_wR^2$ = 0.0863
R indices (all data)	R_1 = 0.0668 $_wR^2$ = 0.1051	R_1 = 0.0746 $_wR^2$ = 0.1967	R_1 = 0.0684 $_wR^2$ = 0.1036
Largest diff peak and hole (e/ $Å^3$)	2.561 and -0.561	2.845 and -2.384	2.074 and -1.089

Compounds	**10adU**	**10bdU**	**10ceU**
Empirical formula	$C_{108}H_{146}N_8O_{19}U_2$	$C_{95.50}H_{113}N_8O_{16.5}$	$C_{29}H_{28}N_5O_6U$
Fw (g/mol)	2336.39	$_0U_{22336.39}$	780.59
Wavelength (Å)	0.71073	2099.06	0.71073
Crystal system	Monoclinic	0.71073	Monoclinic
Space group	$P2_1/n$	Monoclinic	C2/c
Z	4	C2/c	8
a (Å)	21.084(2)	8	27.907(4)
b (Å)	23.115(2)	56.825(5)	7.2573(10)
c (Å)	23.334(2)	14.2963(13)	28.949(4)
a (deg)	90	33.170(3)	90
β (deg)	107.461(1).	90	107.420(3).
g (deg)	90	107.461(1).	90
V (Å^3)	10848(1)	90	5594.2(13)
Density calc'd (g/cm^3)	1.431	23188(4)	1.854
Abs coeff (mm^{-1})	3.050	1.211	5.855
F(000)	4744	2.845	3061
Cryst size (mm^3)	0.4 x 0.02 x 0.25	8464	0.25 x 0.07 x 0.07
Reflns collected	94464	0.3 x 0.3 x 0.1	12158
Indep reflns	26956	64823	4005
	$[R_{(int)} = 0.0513]$	16800	$[R_{(int)} = 0.0775]$
Refinements method	Full-matrix Least	$[R_{(int)} = 0.0567]$	Full-matrix Least
GOF of F^2	Squares on F^2	Full-matrixLeast	Squares on F^2
Final R indices	0.950	Squares on F^2	1.005
$[I>2\sigma(I)]$	$R_1 = 0.0333$	1.026	$R_1 = 0.0469$
R indices (all data)	$_wR^2 = 0.0789$	$R_1 = 0.0407$	$_wR^2 = 0.1031$
	$R_1 = 0.0517$	$_wR^2 = 0.1246$	$R_1 = 0.0743$
	$_wR^2 = 0.0848$	$R_1 = 0.0565$	$_wR^2 = 0.1295$
Largest diff peak	1.766 and -0.876	$_wR^2 = 0.1339$	1.559 and -1.186
and hole (e/ Å^3)		1.448 and -0.572	

Table 12. Selected interatomic distances (Å) and angles (°) for uranyl complexes **10aeU**, **10aaU**, **10beU**, **10cdU**, **10bdU** and **10adU**.

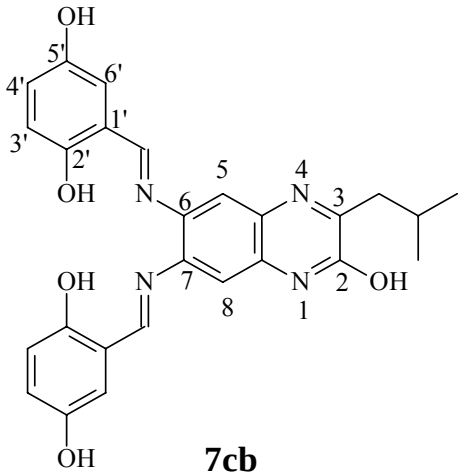
10aeU			
U1-O1	2.241(4)	O1-U1-N1	70.57(2)
U1-O2	2.250(4)	O2-U1-N2	69.38(1)
U1-O3	2.400(4)	O4-U1-O5	176.71(2)
U1-N1	2.521(4)	N1-U1-N2	62.83(1)
U1-N2	2.582(4)	O1-U1-O4	93.03(2)
U1-O4	1.782(4)	O2-U1-O4	92.37(2)
U1-O5	1.796(4)		
10aaU			
U1-O3	2.233(8)	O3-U1-N1	70.1(3)
U1-O4	2.239(9)	O4-U1-N2	71.3(3)
U1-O101	2.415(9)	O1-U1-O2	176.71(2)
U1-N1	2.571(10)	N1-U1-N2	63.6(3)
U1-N2	2.528(9)	O2-U1-O3	93.0(4)
U1-O1	1.800(9)	O2-U1-O4	92.9(4)
U1-O2	1.786(8)		
10beU			
U1-O1	2.252(4)	O1-U1-N1	69.96(2)
U1-O2	2.259(4)	O2-U1-N2	69.75(2)
U1-O5	2.375(5)	O4-U1-O3	176.15(2)
U1-N1	2.549(5)	N1-U1-N2	63.28(2)
U1-N2	2.571(4)	O1-U1-O3	87.57(2)
U1-O3	1.805(4)	O2-U1-O3	86.76(2)

U1-O4	1.782(4)		
10adU			
U1-O3	2.254(2)	O3-U1-N1	69.23(9)
U1-O4	2.255(2)	O4-U1-N2	68.71(8)
U1-O5	2.456(2)	O1-U1-O2	177.62(10)
U1-N1	2.551(3)	N1-U1-N2	63.54(8)
U1-N2	2.577(3)	O1-U1-O4	91.67(9)
U1-O1	1.774(2)	O2-U1-O4	87.38(10)
U1-O2	1.779(2)		
10bdU			
U1-O3	2.241(5)	O3-U1-N1	69.77(18)
U1-O4	2.455(5)	O4-U1-N2	70.06(17)
U1-O6	2.510(6)	O1-U1-O2	177.20(2)
U1-N1	2.504(6)	N1-U1-N2	63.71(17)
U1-N2	2.524(6)	O1-U1-O4	92.00(2)
U1-O1	1.779(5)	O2-U1-O4	88.10(2)
U1-O2	1.780(5)		
10ceU			
U1-O1	2.277(7)	O2-U1-N3	70.20(3)
U1-O2	2.262(8)	O1-U1-N4	69.30(3)
U1-O(1D)	2.386(8)	O4-U1-O(1D)	175.80(3)
U1-N3	2.539(9)	N3-U1-N4	63.10(3)
U1-N4	2.631(8)	O2-U1-O(1D)	78.40(3)
U1-O3	1.794(7)	O1-U1-O(1D)	80.30(3)
U1-O4	1.779(7)		

CHAPTER 5

APPLICATION 1: METAL EXTRACTIONS WITH SALQU RESINS (SALQU LIGANDS INCORPORATED INTO FUNCTIONALIZED RESINS FOR SELECTIVE SOLID-PHASE EXTRACTION OF COPPER (II))

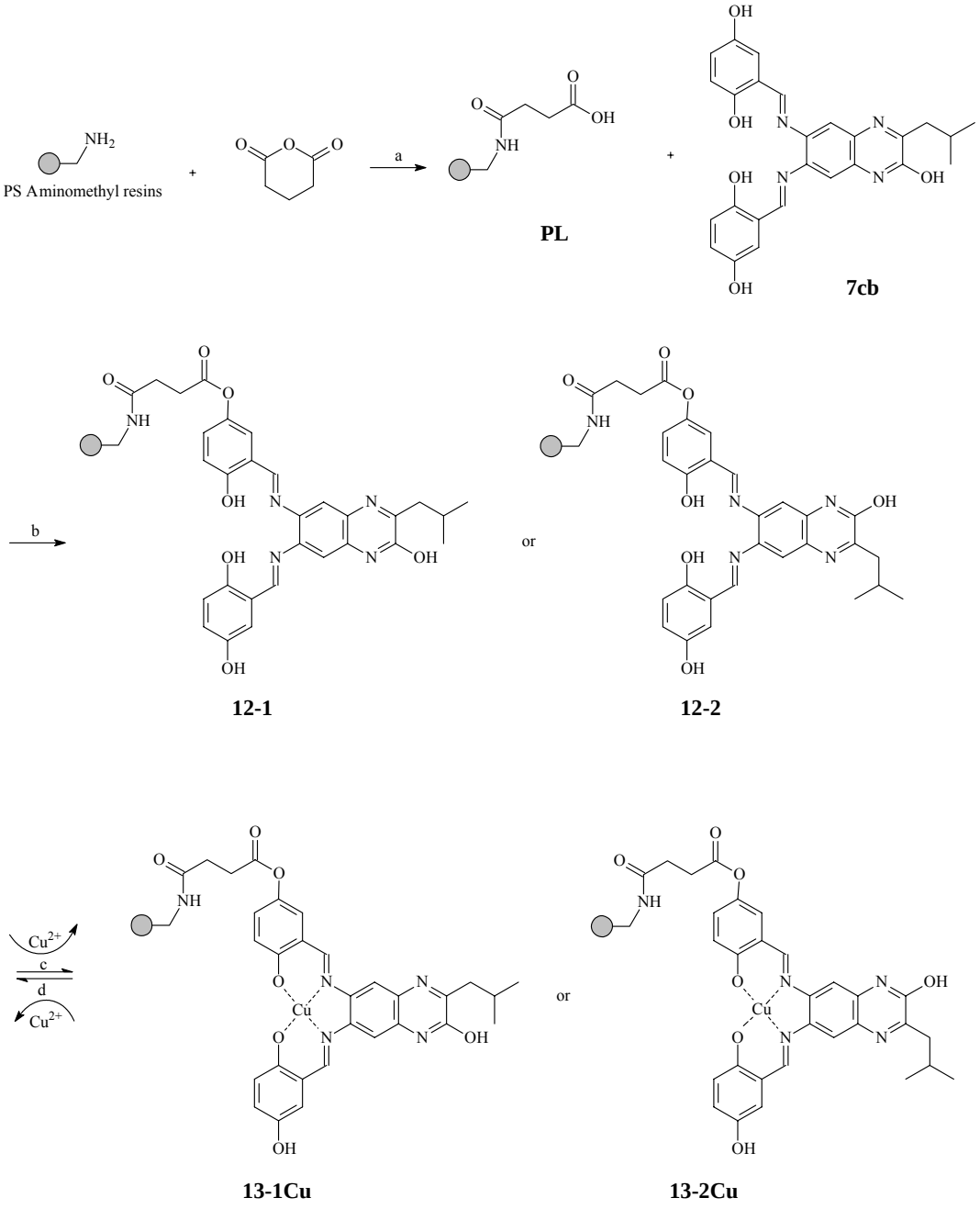
In our previous research, both symmetric and unsymmetric 2-quinoxalinol salen ligands have been prepared (See structure **7cb** as an example).[79, 80] It has been found that these ligands can strongly coordinate +2 metal cations.[88] This made us consider the possibilities of incorporating these salqu ligands into solid phase resins (**12**) for use in applications. In this chapter, we will detail the methods of preparing solid phase reagents (e.g., **12**), and their application in the selective extraction and recovery of copper cations.



7cb

Polystyrene (PS) aminomethyl resin was selected as solid carrier, because this resin can swell in many organic solvents. Glutaric anhydride was selected as linker between solid carrier and salqu ligands. Isopropyl-salqu ligand (**7cb**) was selected as the coordination ligand, both because the 5'-hydroxyl group on the outer portion of the salqu is a convenient site for incorporating the resin, and because its yield is the highest of the symmetric salqu ligand library.[79]

Presented in **Scheme 5** is the optimized method for the synthesis of solid reagents **12-1** and **12-2**. Different molar ratios and various solvents were investigated to optimize the acylation of the amino group onto the (PS) aminomethyl resin. Finally, a molar ratio of glutaric anhydride to (PS) aminomethyl resin 5:1 using dichloromethane (DCM) as solvent at room temperature for 24 hours was found to be the optimum conditions for acylation of the amino group. After acylation was completed, the resin was washed with DCM, DMF and MeOH, three times each. The loaded resin **PL** can be further acylated with 1.5 equivalent of ligand **7cb** by using 2.2 equivalents 4-dimethyl-aminopyridine (DMAP) and 2.2 equivalents *N,N'*-diisopropyl-carbodiimide (DIC) in distilled, dry *N,N'*-dimethylformamide (DMF) at room temperature for three days. Extending the reaction time does not increase loading. Without DMAP, the loading is very low. If wet DMF was used, the loading capability is decreased, because DIC can be decomposed easily by moisture.



Reaction conditions: a. 5equiv Glutaric anhydride, DCM, r.t., 24hr. b. 2.2equiv DMAP, 2.2equiv DIC, 1-2equiv 7cd, DMF, r.t., 72hr. c. Cu^{2+}, DCM, MeOH, r.t., 30min. d. $NaBH(OAc)_3$, DCM, AcOH, r.t., 4hr.

Scheme 5. Reaction route for the prepatation solid phase salqu (**12-1** and **12-2**).

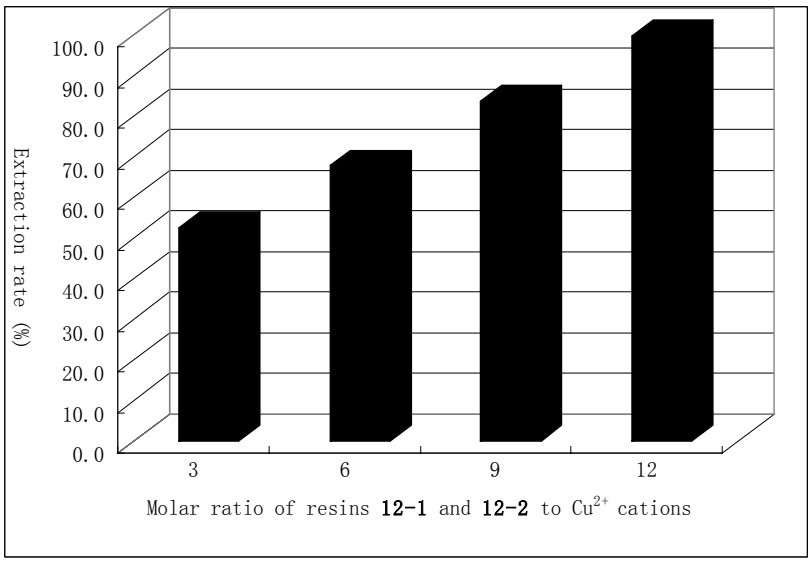
There are three potential binding sites (2, 2' and 5' positions) for the carboxylic acid linker to attach to ligand **7cb**. Positions 2 and 2'cannot react with the carboxylic acid moiety due to reactive inertia of 2 position and steric hindrance of the 2' position. Hydrogen bonding also limits the reactivity of the hydroxyl group on the 2' position.[74] Reaction with hydroxyl groups in the two 5' positions, results in two possible products (i.e., **12-1** and **12-2**). They have the same coordination capability to bind +2 valence metal cations because the salen coordination cavity is not affected by their position. By this procedure, **PL** was obtained with 100.0% loading by ninhydrin test and solid phase salqu ligands **12-1** and **12-2** were obtained with 60.0-65.0% loading, as determined by mass. Identification of solid phase salqu ligands **12-1** and **12-2** was made by comparing the major peaks of an IR spectra of ligand **7cb** (3381.2, 1658.8, 1622.3, 1577.8, 1489.1, 1278.8 cm^{-1}.).

With these solid ligand functionalized reagents (**12-1** and **12-2**) in hand, extraction studies were run in several different solvent combinations: DMF, DMF/MeOH, MeOH, THF/MeOH, DCM/MeOH and DCM/EtOH. Finally, we found DCM/MeOH is the best combination for our extraction experiments, because the DCM can best swell the PS resins while MeOH still readily dissolves the metal salts. Metal salts of Cu^{2+}, Mn^{2+}, and Ni^{2+} were used in extraction studies. Solutions containing these metal cations were prepared using copper acetate, manganese acetate, and nickel nitrate salts in a 50:50 solution of DCM/MeOH.

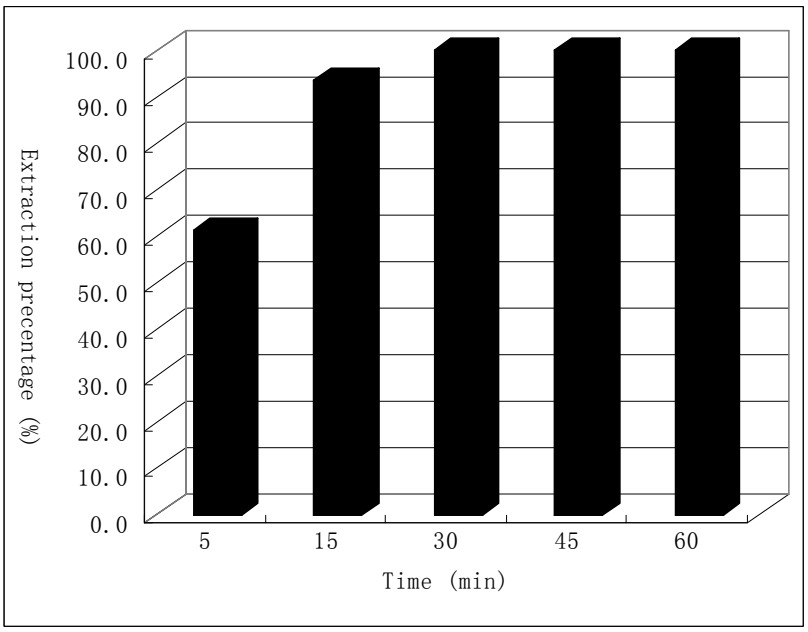
To determine extraction capability, 3ml of a prepared solution of 2×10^{-4} mol/L Cu^{2+} was mixed with 5mg, 10mg, 15mg, 20mg prepared **12-1** and **12-2** (The molar ratios of Cu^{2+} to **12-1** and **12-2** are 1:3, 1:6, 1:9, 1:12) respectively at room temperature for

stirring 40min. The extraction results for Cu^{2+} metal solution are shown in (**Figure 15**. **I**). It was found that 20mg **12-1** and **12-2** resins may completely extract 3ml Cu^{2+} 2×10^{-4} mol/L solution at 40min. Further optimization of extraction time using 20mg **12-1** and **12-2** resins with 3 ml 2×10^{-4} mol/L concentration copper (II) cations solution at room temperature (**Figure 15**. **II**) indicated that the shortest time for 100% extraction is 30 minutes. Complexed Cu resin (**13-1Cu** and **13-2Cu**) can be directly filtered off to separate from the organic solvent.

For nickel, 20mg of prepared **12-1** and **12-2** was mixed with 3ml of the nickel (II) (2×10^{-4} mol/L) salt solution at room temperature. After 24 hours, only 30% of nickel cations was extracted, and after 72 hours, only 45.7% of the nickel cations was extracted. (The final metal ion concentrations were determined using atomic absorption.) For Mn, the Mn (II) salt solution must be prepared as a 1×10^{-4} mol/L solution, because the detection limit for Mn cations by atomic absorption using a hollow cathode lamp is limited. A 3ml 1×10^{-4} mol/L manganese salt solution was extracted at room temperature by 10mg **12-1** and **12-2** resins for 24 hours. It was found that 63.0% of the manganese cations was removed by the resin.



I



II

Figure 15. I: Cu^{2+} extraction bar graphs indicating the different molar ratios of **12-1** and **12-2** resin to Cu^{2+} extracted. **II:** Cu^{2+} extraction with **12-1** and **12-2** resin with respect to agitation time. (Quantified using atomic absorption.)

This leads us to a surprising conclusion. **12-1** and **12-2** resins might selectively extract Cu^{2+} within a short time (30min). To confirm this, we combined 3ml 2×10^{-4} mol/L Cu^{2+} and 3ml 2×10^{-4} mol/L Ni^{2+} solution to prepare a 6 ml 1×10^{-4} mol/L Cu^{2+} and Ni^{2+} mixed solution; 3ml 2×10^{-4} mol/L Cu^{2+} solution and 3ml 1×10^{-4} mol/L Mn^{2+} solution were combined to obtain a 6ml 1×10^{-4} mol/L Cu^{2+} and 5×10^{-5} mol/L Mn^{2+} solution. To these mixed solutions, 20mg of the prepared **12-1** and **12-2** resins was added at room temperature and allowed to extract for 45min. After filtering off the **12-1** and **12-2** resins, the extraction solution were analyzed by atomic absorption. It was found that 80.0% of the Cu^{2+} was removed, but only 7.8% Ni^{2+} in the Cu^{2+}/Ni^{2+} solution, and only 22.0% Mn^{2+} was extracted in the Cu^{2+}/Mn^{2+} mixed solutions.

For the recovery of copper from the **13-1Cu** and **13-2Cu** resins, several different conditions were tried (**Scheme 5**). Routine cleavage or recovery conditions, DCM with different organic acids including trifluoroacetic acid were not found to release copper ions, nor were strong bases.

Because sodium triacetoxyborohydride can efficiently reduce the imine group (C=N) to amino group (C-N) which coordinates only weakly with the metal, the 20mg **12-1** and **12-2** resins were mixed with 3ml DCM/CH_3COOH (2:1). To this, 10mg sodium triacetoxyborohydride was added, and the reaction progress was measured over time (**Figure 16**).[89] The results show that after 4 hours the maximum amount of Cu^{2+} can be recovered (70.0%). Extending the reaction time or increasing the amount of sodium triacetoxyborohydride does not increase this recovery rate.

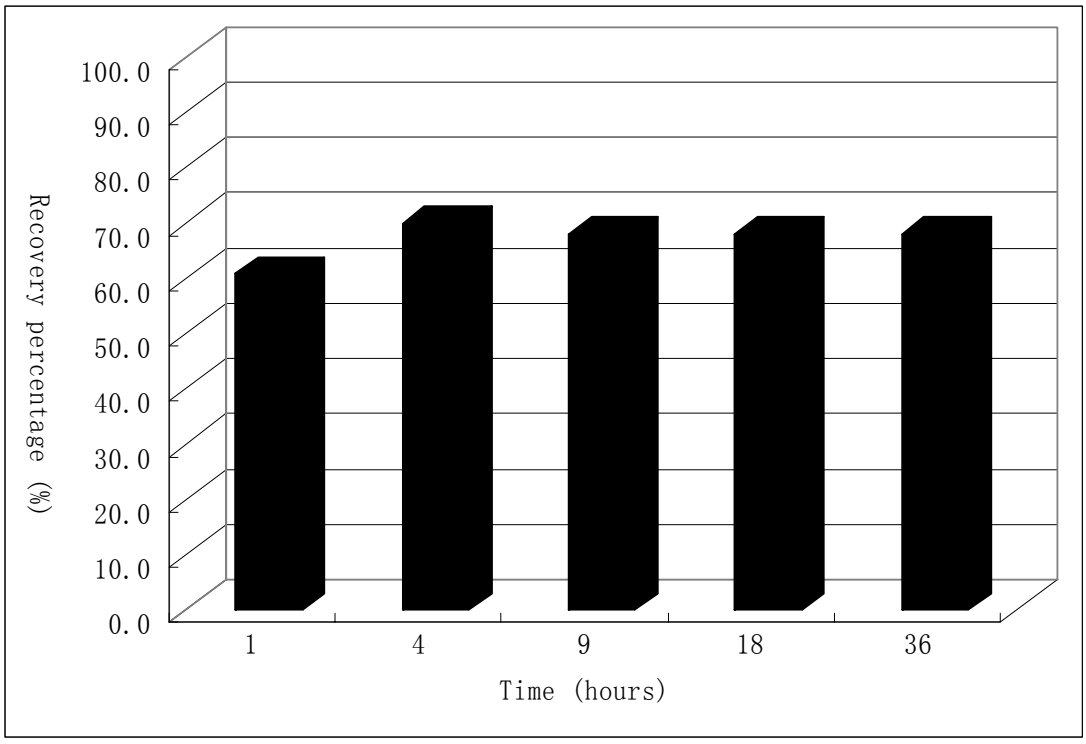


Figure 16. Cu^{2+} recovery with time. (Quantified using atomic absorption.)

Thus, an optimized synthetic route for resins **PLG1** and **PLG2** has been obtained. It has been found that this kind of resin can selectively extract copper (II) cations in a short amount of time. The copper can then be recovered using simple reducing conditions from the resin. This has the potential to enable the selective extraction of copper even from a mixture containing other metals. **PLG1** and **PLG2** resins could also be applied in environmental or materials chemistry to remove copper or in combinatorial chemistry as a metal scavenging agent to remove excess copper. In the future, we will design new solid reagents to selectively extract other metals and to continue to improve on the selectivity or application of this system.

CHAPTER 6

APPLICATION 2: COPPER SALQU COMPLEXES FOR USE IN CATALYSIS

The development of new metal catalysts has long been investigated for specialized synthetic applications; [90] however, the application of these in the pharmaceutical industry has been limited for many reasons. Commonly used laboratory catalysts can be difficult or costly to synthesize on a large scale, they are often sensitive to moisture or oxygen, and they often use potentially environmentally hazardous metals such as palladium or ruthenium. Developing less-expensive, easier to use, or more environmentally friendly catalysts is a promising trend for new synthetic methods.[91] Because salen metal complexes can catalyze many reactions, most notably used in chiral reactions, some of these reactions were tested by our salqu metal complexes.

The easy to prepare salen metal (Mn, Ru, Co, Cu, etc.) complexes have been used in the development of catalysts for numerous reactions,[92] among these the oxidation of activated C-H bonds; however, this reaction has some limitations because of the low solubility of salen ligands and low yields.[33] Converting C-H bonds of organic molecules directly into the desired organic functional group can potentially offer benefits for organic synthesis because of increased resource efficiency, energy efficiency, and

operational simplicity, while at the same time reducing the environmental impacts of wastes.[93] For these reasons, we were interested in developing our salqu metal complexes to be used in catalytic oxidation of activated C-H bonds.

Oxidation of C-H of an aryl methylene to form an aryl carbonyl group or aryl α-hydroxyl group has been well studied in recent years, because of the numerous potential applications.[94] To date, many methods have been developed depending on the application and the required selectivity. In the 1970's, for this kind of oxidation, the oxidant researchers most commonly uwas sed Se_2O; however, the mechanism of selenium dioxide oxidation involved the formation of β-ketoseleninic acids as intermediates, and this lead to the numerous potential side products and low yields.[95] Manganese salts or nitropyridinium salts as oxidants were found to use a hydrogen transfer and radical mechanism, and usually results in yields of no more than 60%.[96] Singlet oxygen has also been used as an oxidant. This process also involves a radical mechanism, and so a mixture of α-keto and α-hydroxyl group products is often obtained.[97] More recently, oxidations with hypervalent iodine,[98] *tert*-butylhydroperoxide,[99] Jones reagent, DDQ and peroxyacid[100] have been explored. Yields all of these methods are less than 80%, and they require rigorous conditions which can limit their use in industrial applications.

For this kind of oxidation, catalysts are required for acceleration of the reaction or improvement of yields. Catalysts used in this way have been copper, cobalt, [101] or ruthenium salts. [102] Salen ligands used as manganese or copper catalyst supports have also been used.[103] One recent technique developed is the *Gif system*, in which an iron catalyst is combined with a suitable carboxylic acid, pyridine, and zinc dust (as a reductant) with oxygen as the oxidant, for the oxidation to acylate methylene.[104] In this

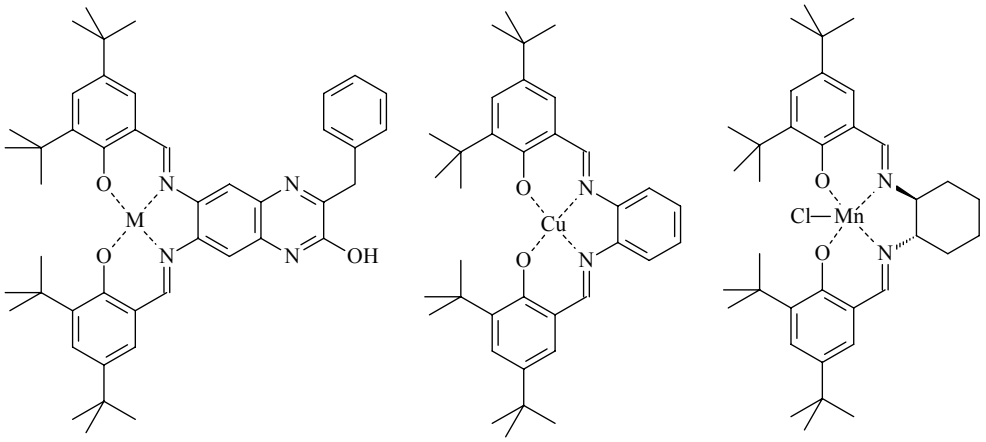
reaction, less than 40% yields limit industrial development of the *Gif system*.[104,105] Many articles reported high conversion rates of this oxidation which were determined by GC or HPLC technology. It is important to note, that this is not a good reflection of their isolable yields, because of different absorptions between starting materials and products, especially for this oxidation which converts an aryl methylene group into aryl carbonyl group would inherently exhibit a stronger UV absorption.

Until now, for this particular oxidation, it has been difficult to identify a metal catalyst which has both good solubility in organic polar aprotic solvents (e.g., CH_3CN) and non polar solvents (e.g., hexane), which could be another bottleneck to the oxidation of non polar compounds like steroids. Based on our library of 2-quinoxalinol salen ligands (salqu), we have developed a new copper catalyst, **10adCu** which has good solubility in most organic solvents (**Figure 17**). Catalyst **10adCu** can be easily prepared and can convert aryl methylene groups into aryl carbonyl groups with very high yields under mild conditions. In this chapter, we introduce the optimized process, describe selectivity, and proposed potential applications of salquCu catalyst **10adCu**.

The conversion of diphenylmethane (**19**) into benzophenone (**20**) was selected to test salquCu catalyst **10adCu** and optimize conditions. Based on previous reports with salphCu,[33] we began using the addition of 3 equivalents H_2O_2, in CH_3CN as solvent with 1% by molar of the salquCu catalyst **10adCu,** heated to reflux temperature for 18 hours. Under this condition, the isolated yield of benzophenone is only 27.0%. Six experimental factors were considered to optimizing this reaction: oxidant (**Figure 18**), catalyst ratio (**Figure 19**), time (**Figure 20**), oxidant ratio (**Figure 21**), solvents (**Figure 22)** and types of catalyst (**Figure 23** and **Table 13**). Four oxidants, first, were tested with CH_3CN as

solvent, 1% catalyst **10adCu** at reflux temperature for 18 hours. (**Figure 18**) It was found that *tert*-butylhydroperoxide in decane was the best oxidant, quantitatively converting diphenylmethane into benzophenone. If *tert*-butylhydroperoxide in water was used as oxidant, the yield of the desired product, benzophenone, is around 80%. (**Figure 18**) The reason why *tert*-butylhydroperoxide in decane is better than in water is that a uniform solvent system is used during this oxidation. Using *tert*-butylhydroperoxide in decane as oxidant, the catalyst ratio was increased from 0.1% to 3%. (Their turnover numbers are 736, 176, 99 and 32 respectively.)

It was found that 1% of catalyst **10adCu** is best for this oxidation. (**Figure 19**) Although 0.1% catalyst **10adCu** leads to highest turnover number which is most suitable to industrial use, 1% catalyst **10adCu** results in quantitatively conversion which is best for further optimization and reduces the need for separations. The addition of more catalyst does not decrease the amount of time that it takes to achieve the optimal yield and using less catalyst resulted in reduced yields. (**Figure 19**) Reducing the reaction time or decreasing the oxidant ratio also results in lower yields. (**Figure 20** and **21**) The addition of more of the *tert*-butylhydroperoxide oxidant also does not serve to decrease the reaction time required to achieve the optimal yield.



M = Cu (**10adCu**), Mn (**10adMn**), Ni (**10adNi**), Co (**10adCo**), UO_2 (**10adU**).

Regular Salph Cu Complex (**3Cu**)

Regular Salen Mn Complex (**3Mn**)

Figure 17. Structures of salen, salph and salqu copper complex catalysts.

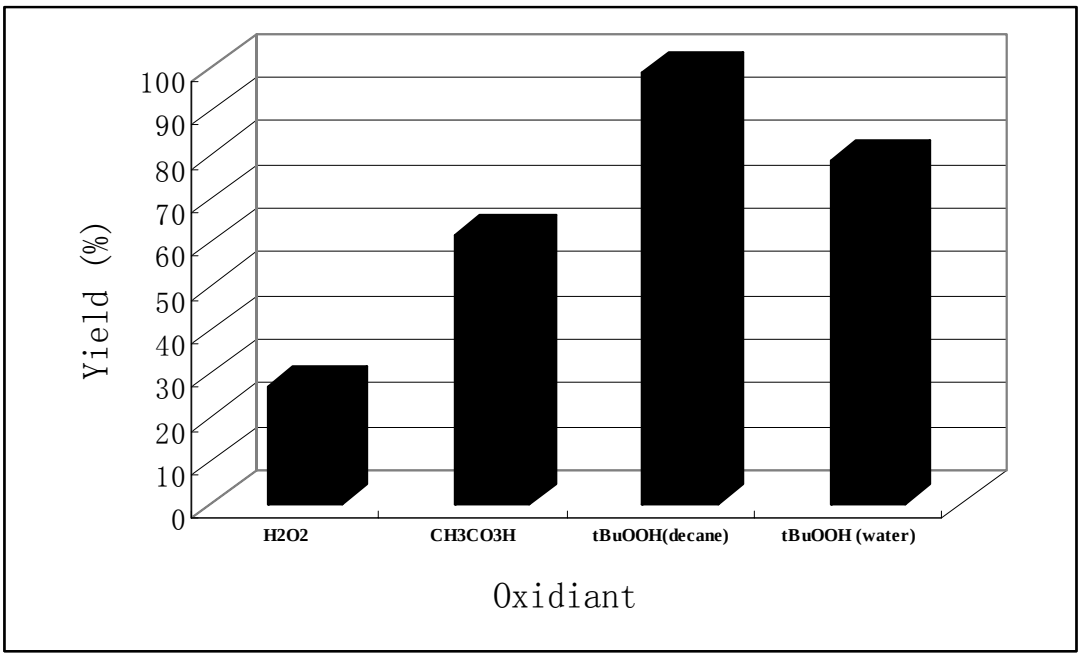


Figure 18. Oxidant optimized for conversion of diphenylmethane into benzophenone. Yields are based on purification by flash column chromatography and mass calculation.

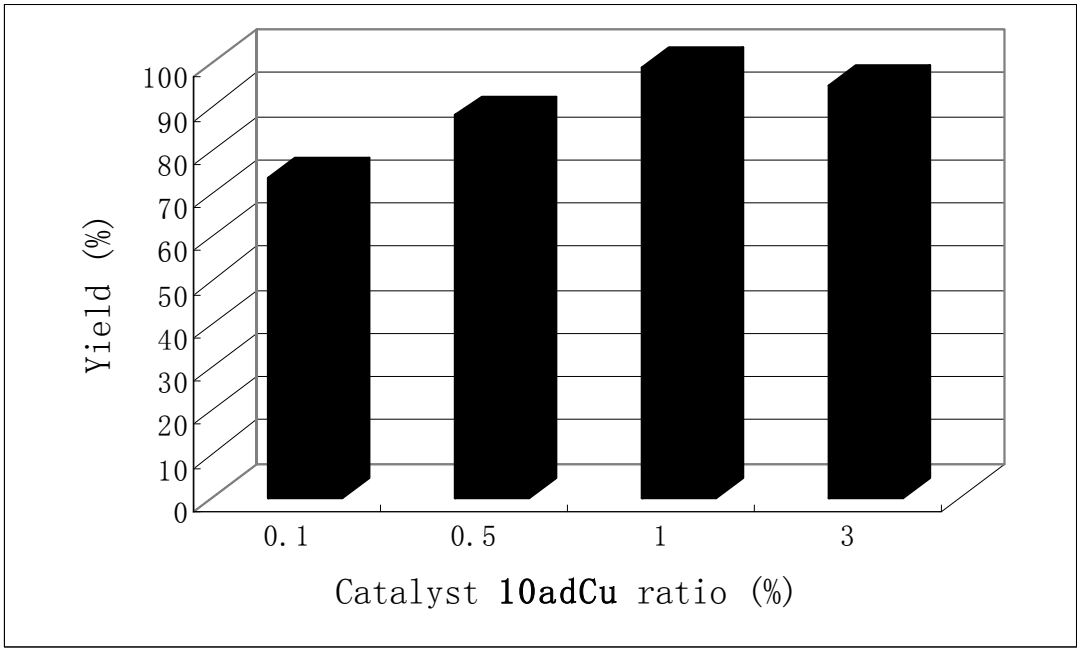


Figure 19. Catalyst **10adCu** ratios optimized for conversion of diphenylmethane into benzophenone. Yields are based on purification by flash column chromatography and mass calculation.

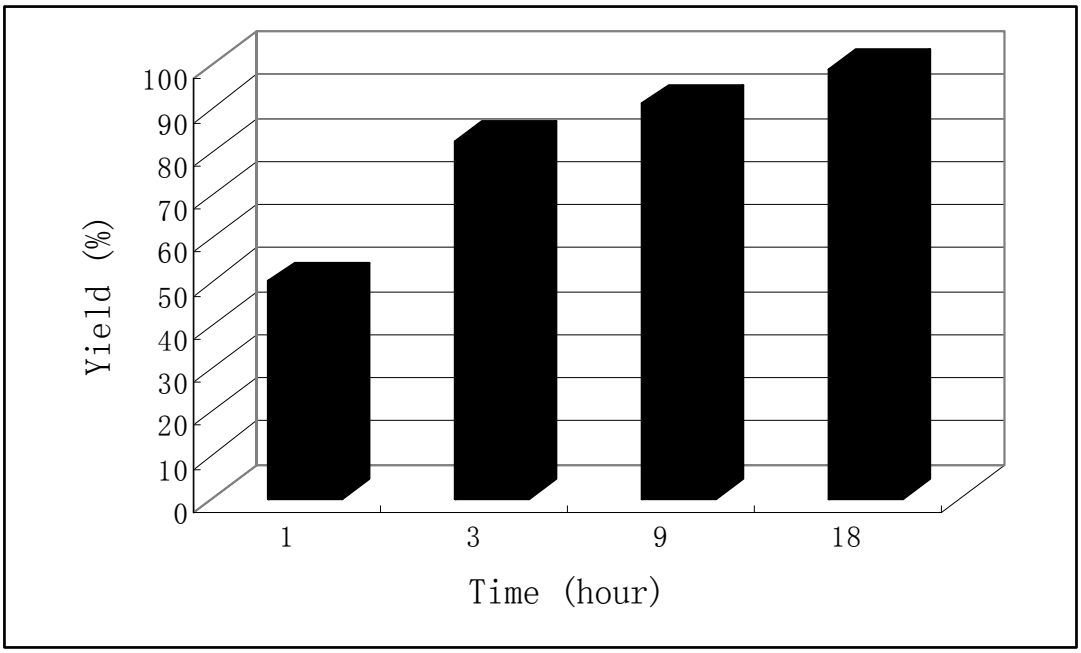


Figure 20. The effects of time on conversion of diphenylmethane into benzophenone.

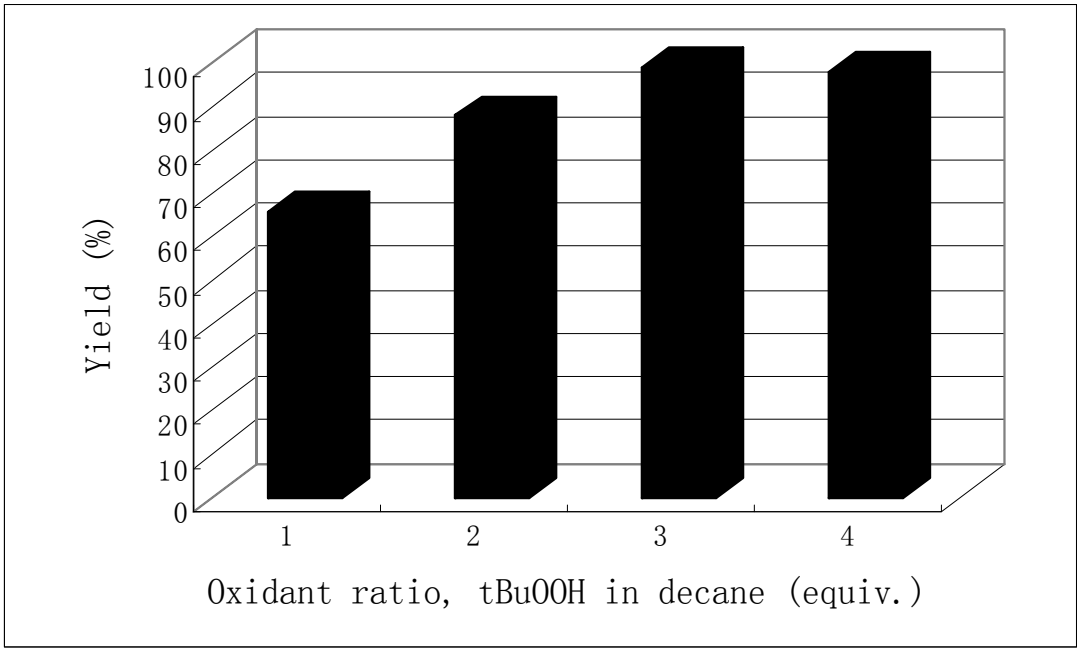


Figure 21. Oxidant ratios optimized for conversion of diphenylmethane into benzophenone. Yields are based on purification by flash column chromatography and mass calculation.

Finally, several polar and non polar solvents were tested. With acetonitrile, chloroform, toluene and hexane as solvents, the yields of the desired product, benzophenone, are very high (over 95%), but using THF as solvent, the yields are very low, because of the degradation of THF under oxidative conditions (**Figure 22**).[106] It is worth mentioning that when toluene was used as the solvent, there were not any byproducts generated by reaction of the toluene obtained. (This makes sense if we assume that the catalyst procedes through a radical reaction, because a reaction with toluene with produce a primary radical.) Therefore, the optimal reaction conditions are to use acetonitrile as the solvent, (although toluene, hexane or chloroform are also suitable

solvents) and include 3 equivalents of *tert*-butylhydroperoxide in decane as oxidant, with 1% of the catalyst **10adCu** heated to reflux temperature for 18 hours.

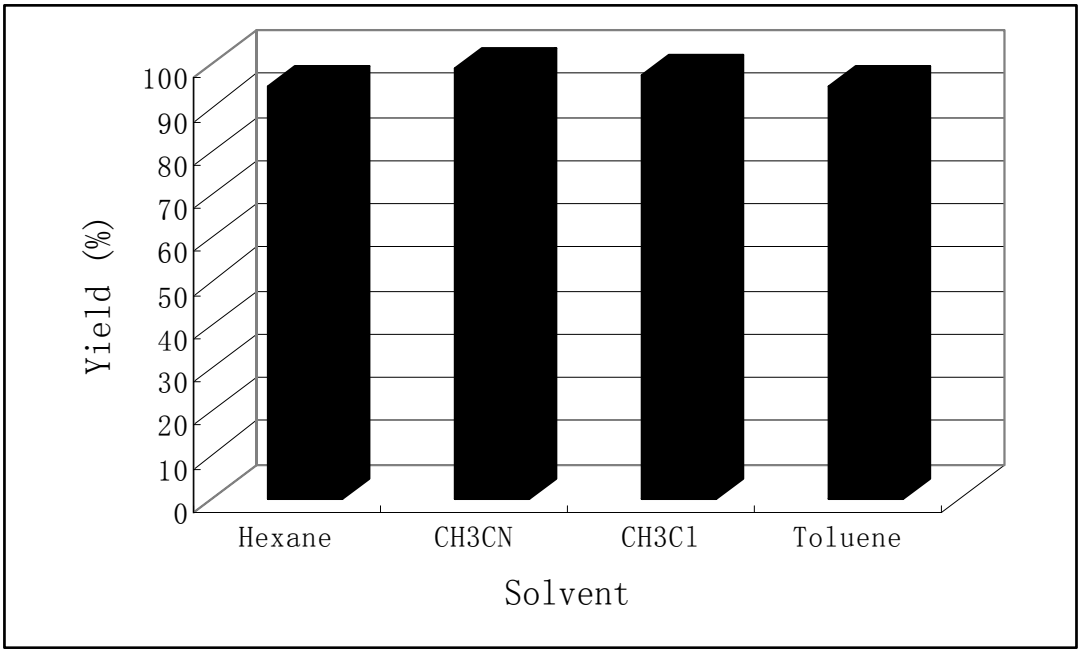
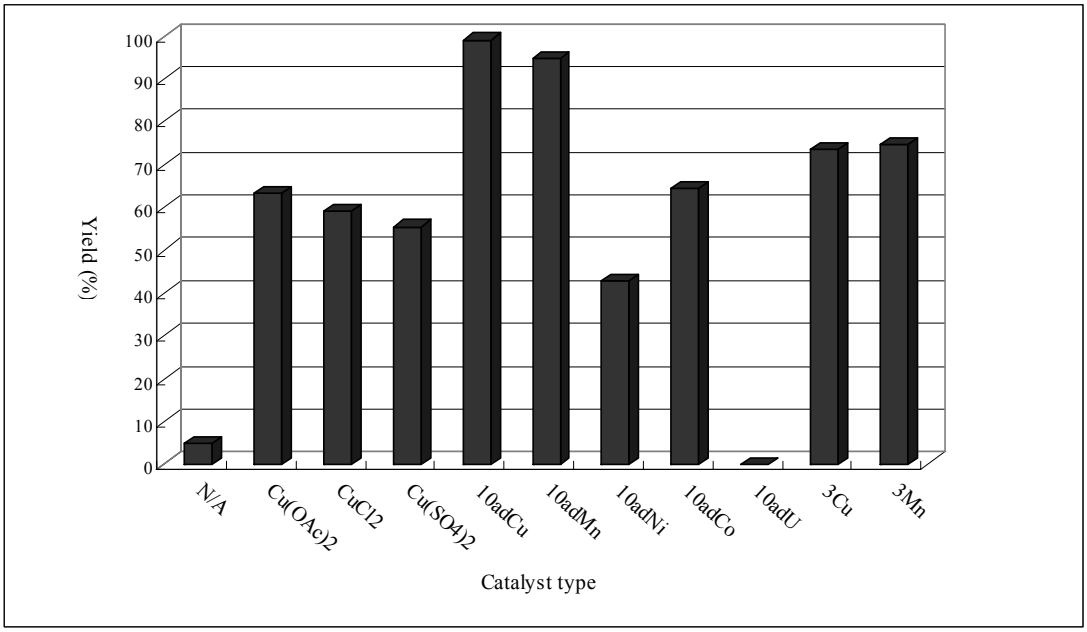


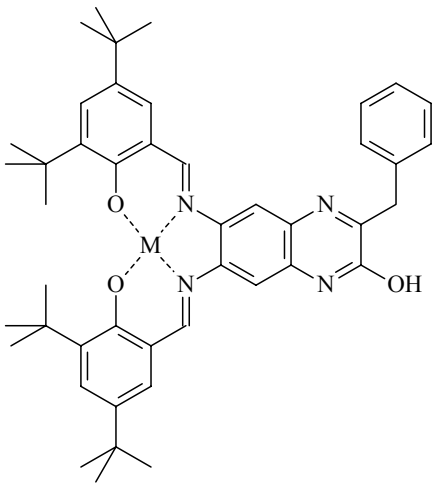
Figure 22. Solvent effect for conversion of diphenylmethane into benzophenone. Yields are based on purification by flash column chromatography and mass calculation.

In chapters 2 and 3, we described the preparation of a library of salqu ligands.[79, 80] These have been demonstrated to form stable complexes of broad solubility with many metal salts (Ni^{2+}, Co^{2+}, Cu^{2+}, Mn^{2+} or UO_2^{2+}).[88] Different metal complexes were tested as catalysts. (**Figure 23**) Without the addition of catalyst, the oxidation using 3 equivalents of *tert*-butylhydroperoxide in decane as oxidant in acetonitrile heated to reflux temperature for 18 hours, resulted in only a very modest yield, 5-10% of the desired product, benzophenone, was obtained. With the addition of copper salts such as copper sulfate or copper chloride, 50-60% benzophenone was obtained. Using a regular salph Cu

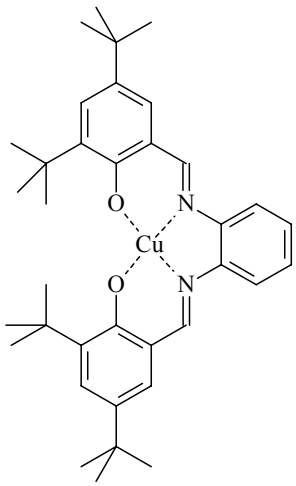
complex **3Cu** as catalyst further enhances yields to 73.6%, still less than that of catalyst **10adCu**, whereas salen Mn complex **3Mn** gave almost same yield (74.7%) as that of regular salph Cu complex **3Cu**.

The reason why catalysts **3Cu** and **3Mn** give lower yields than catalyst **10adCu** remains unclear, but two possibilities come to mind. First, the salqu metal complexes (**10adMetal**) have different configuration from complexes **3Cu** and **3Mn,** and they have good solubility in numerous organic solvents.[88] Either possibility might affect the mechanism, which would lead to improved yields. This improved solubility of catalyst **10adCu** also allows for the ability to eliminate the need for a biphasic system which would be very useful in increasing the ease of use in larger scale applications.

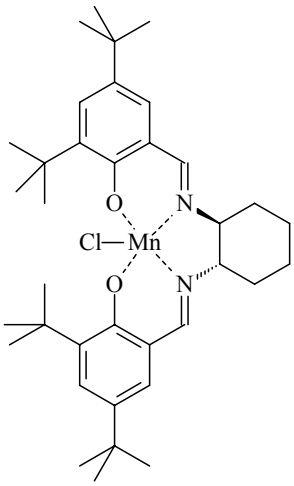




M = Cu (**10adCu**), Mn (**10adMn**), Ni (**10adNi**), Co (**10adCo**), UO_2 (**10adU**).



Regular Salph Cu Complex (**3Cu**)

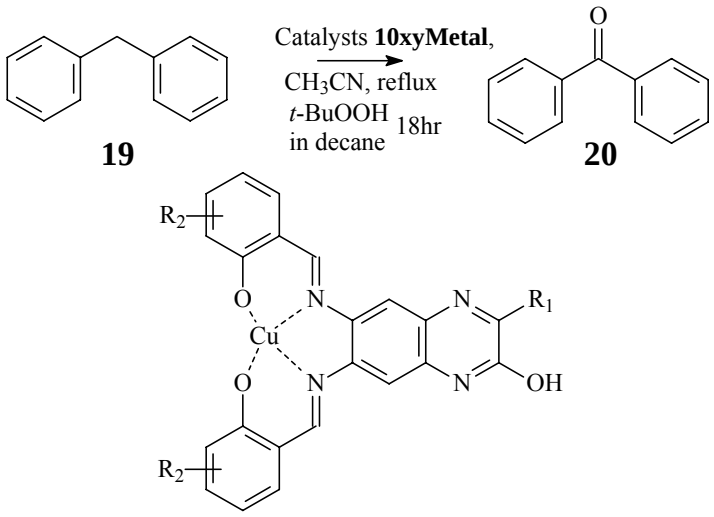


Regular Salen Mn Complex (**3Mn**)

Figure 23. Optimized conditions for catalyzed conversion of diphenylmethane into benzophenone.with copper salt and different salen, salph, or salqu metal complexes.

As a demonstration of the importance of solubility toward the efficacy of this reaction, different salqu copper complexes from our library were selected for catalytic studies. These results are depicted in **Table 13**. Besides catalyst **10adCu,** *tert*-butyl functionalized copper complexes **10acCu** and **10cdCu** show good catalytic effect, whereas hydroxyl functionalized complexes **10bbCu, 10daCu** and **10cbCu** lead to similar yields as regular manganese salen and copper salph complexes **3Cu** and **3Mn**. It is also possible that the extra hydroxyl group impairs the catalytic function of Cu or Mn, leading to the lower yields. Complexes **10ceCu** and **10beCu** gave lower yields than catalysts **10adCu**, **10acCu** and **10cdCu,** because of the reduced solubility.

Table 13. Optimized conditions for different salquCu catalysts (**10xyMetal**).



Catalyst 10xyMetal

No.	R_1	R_2	Yield (%)*
10adCu	CH_2Ph	3,5-di*tert*butyl	99.0
10acCu	CH_2Ph	3-*tert*-butyl	92.8
10cdCu	$CH_2CH(CH_3)_2$	3,5-di*tert*butyl	99.0
10ceCu	$CH_2CH(CH_3)_2$	H	90.4
10cbCu	$CH_2CH(CH_3)_2$	5-OH	80.4
10becu	$CH(CH_3)_2$	H	90.3
10bbCu	$CH(CH_3)_2$	5-OH	65.0
10daCu	$CH_2CH_2SCH_3$	3-OH	77.0

*Yields are based on separation by flash column chromatography and mass calculation.

Stability is also an important character of the salqu copper catalysts. Catalysts that are found to be stable both to air and moisture are much more convenient for us in applications. Our catalyst (**10adCu**) is stable to air and moisture and can be reactivated at least twice. The potential capability for recycling of our catalysts was tested using the optimized reaction condition to oxidize diphenylmethane. Diphenylmethane was reacted with 1% catalyst **10adCu** and 3 equivalents *tert*-butylhydroperoxide in acetonitrile heated to reflux temperature for 18 hours. After 18 hours, another equivalent of starting material, diphenylmethane and an additional 3 equivalents of the oxidant, *tert*-butylhydroperoxide in decane, were added into reaction system. This was allowed to continue heating at reflux temperature for another 18 hours. This addition was repeated for a third addition the same as the second.. Finally, pure benzophenone was obtained by flash column separation and the total yield for all three additions is over 98.0%. This indicated that the catalyst **10adCu** can be recycled or reused at least twice, as there was no loss in yield between additions. This suggests that the catalyst can be reused several times, and the ability to continue this without the addition of catalyst, can be used to reduce the cost of the reaction as dependent on the amount of copper catalyst as well as the volumes of volatile organic solvents required in large scale reactions.

Once the optimal conditions were determined, these were used in reactions with several compounds containing aryl methylene group to be oxidized. (**Table 14**) It was found that if there is an electron donor group neighboring to the methylene group to be oxidized, the yield is increased (**Entry 1**, **2** and **3**. **20**, **22** and **24**), whereas a neighboring electron withdrawing group will decrease the yield (**Entry 4**, **5**. **26** and **28**). An aryl

methylene with an electron withdrawing group neighboring can be oxidized a second time to enhance the final yields (**Table 2**, **Method 2**). Aryl methylene groups can be selectively oxidized, whereas other methylene groups are not affected (**Entry 6**. **30**). If an amino or hydroxyl group is present neighboring the methylene group, the final product produced is an aldehyde (**Entry 2** and **Entry 9**. **22** and **36**). By this method, not only may the aryl methylene be oxidized to carbonyl group, but an ether group can be converted to an ester in good yield (**Entry 3**. **24**).

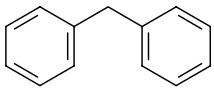
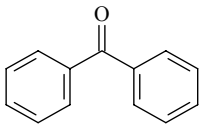
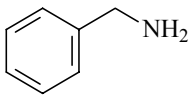
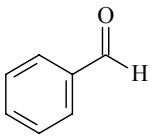
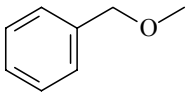
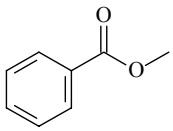
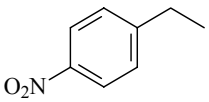
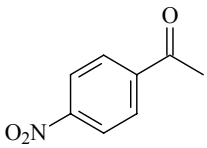
If there is no aryl group neighboring the methylene group, the expected product is not found (**Entry 16**). This could also be due to a limitation of configurational geometry of the mechanism as when there is a bulky group *tert*-butyl group on the methylene, there is also none of the expected product (**Entry 13**). If a halogen is directly neighboring to the aryl methylene, there is also none of the expected product (**Entry 14**). Compounds containing a hydroxyl group were found to have no reaction (**Entry 15**) or lower yields (**Entry 9**. **36**), presumably because the oxygen atom could coordinate with the catalyst metal center, (in this case copper), and thus block the catalyst mechanism. Remarkably, *tetra*-hydroisoquinoline and *tetra*-hydroquinoline were special cases. Oxidation of these using this method leads to isoquinoline and quinoline (**Entry 17** and **18**. **53** and **55**), but not the α-ketoisoquinoline or α-ketoquinoline analogs. For some of the oxidation reactions found to have poor yields, the final yields can be improved using a modified reaction scheme, **method 2**. (**Entry 4**, **5**, **10** and **11**)

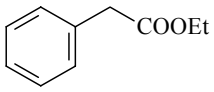
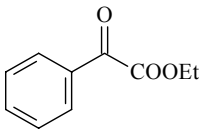
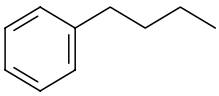
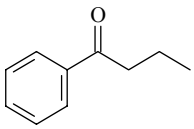
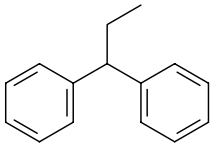
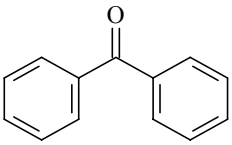
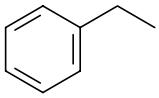
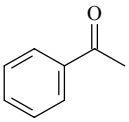
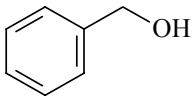
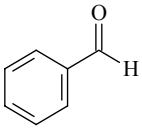
Also of interest, the oxidation of benzylamine directly into benzaldehyde by the salqu copper catalyst **10adCu** mimics the important biological processes of oxidation of amine substrates to aldehydes as catalyzed by the naturally occurring copper containing

amyl and lysyl oxidases (**Entry 2**).[107] Because of the benzaldehyde generated, the benzaldehyde may directly react with unreacted benzylamine to form *N*-benzylidenebenzylamine, which is an unexplored method to prepare *N*-benzylidenebenzylamine solely from just cheap benzylamine as compared to established methods.[108] *N*-benzylidenebenzylamine is a useful, costly but commercially available, indicator reagent used for organolithium assays and as an intermediate of amino acid syntheses.[109]

In another example of the potential utility of this catalyst, 1, 4-naphthoquinone is typically prepared from naphthalene using oxygen gas with a vanadium catalyst at high temperature and pressure with yield no more than 40%.[110] This is a key intermediate of several natural products including phylloquinone and menaquinone (vitamin K_1 and K_2),[111] the derivatives of which have been found to have broad bioactivity ranging from anticancer to antifungal bioactivity.[112] Several new methods for preparing 1, 4-naphthoquinone derivatives have been developed, but all of them involve more expensive and environmentally hazardous metal catalysts.[113] Here, we set up a new method for preparing 1, 4-naphthoquinone by using inexpensive commercial available starting material 1, 2, 3, 4-tetrahydronaphthalene and easily prepared salquCu catalysts **10adCu** with 62.5% yield. (**Entry 10**. **39**) This conversion also mimics another crucial biological oxidized process catalyzed by galactose oxidase.[114]

Table 14. The aryl methylene compounds tested with salquCu catalysts **10adCu.**

Entry	Starting material	Final product	Yield (%)*
1	 **19**	 **20**	99.0[1]
2	 **21**	 **22**	88.8[1Д]
3	 **23**	 **24**	93.0[1]
4	 **25**	 **26**	50.0[1]; 89.9[2]

5	 **27**	 **28**	14.0[1]; 82.0[2]
6	 **29**	 **30**	80.0[1]
7	 **31**	 **32**	81.1[1]
8	 **33**	 **34**	80.2[1]
9	 **35**	 **36**	47.1[1]

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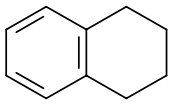

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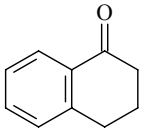

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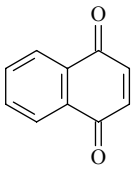
25.7[2]



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65.5[2]

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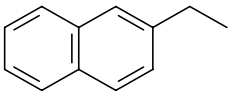

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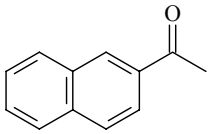
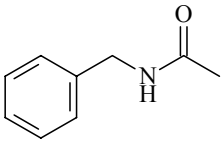


41

60.0[1]; 91.1[2]

12



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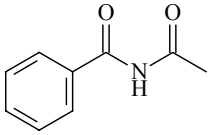

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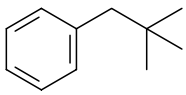

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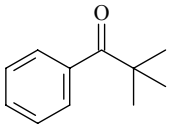

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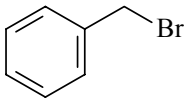
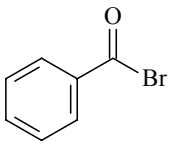
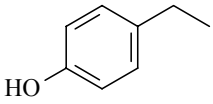
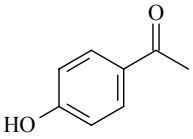
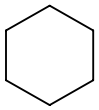
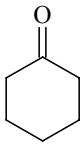
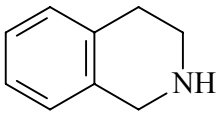
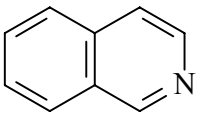
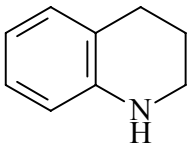
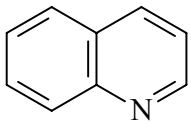
14	 **46**	 **47**	-[¶]
15	 **48**	 **49**	-[¶]
16	 **50**	 **51**	-[¶]
17	 **52**	 **53**	55.5[1]
18	 **54**	 **55**	66.0[1]

* Yields are based on separation by flash column chromatography.

[¶] There is no expected final product obtained.

[1] **Method 1:** 1% catalyst **10adCu**, CH_3CN, 3 equivalents *t*-BuOOH (in decane), reflux for 18 hours.

[2] **Method 2:** (1) 1% catalyst **10adCu**, CH_3CN, 3 equivalents *t*-BuOOH (in decane), reflux for 18 hours. (2) 3 equivalents *t*-BuOOH (in decane), CH_3CN, reflux for 18 hours.

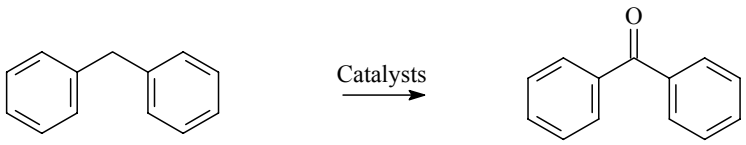
[Д] After 40 minutes the Schiff base product, N-benzylidenebenzylamine is formed. 88.8% of benzaldehyde was determined by adding the reacted benzaldehyde with pure isolated benzaldehyde.

It remains to determine the specific oxidation mechanism. This is difficult, because if the mechanism involves a carbon cation or anion and leaving group mechanism, the methoxyl group should be a better leaving group than hydrogen (**Entry 3**) in the conversion of the phenyl methyl ether to methyl benzoate. In contrast, we find that in this case, the hydrogen is a "leaving group". Secondly, in the conversion of 1,1-diphenylproane to benzophenone and *tetra*-hydroquinoline to quinoline, the expected products 1, 1-diphenylproanol and α-ketoquinoline have not been obtained, which indicate an unexpected mechanism occur. (**Entry 7** and **53** or **55**) Another case which is intricate to this mechanism is benzylamine. (**Entry 2**) The expected product should be benzoic amide, but benzaldehyde in very good yield is found to be the major product.

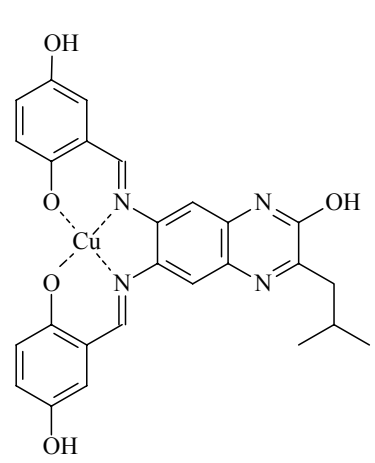
According to the procedure mentioned in the chapter 5, the solid phase resins functionalized with the copper salqu complexes (**13-1Cu** and **13-2Cu**) were prepared and tested as solid phase catalysts to catalyze the inserted oxidization of aryl C-H bond of

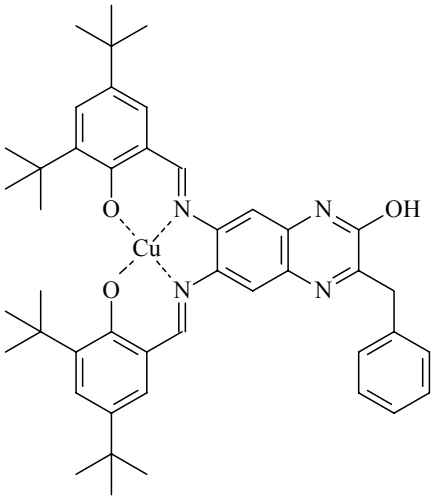
diphenylmethane to benzophenone. (**Scheme 6**) Compared to solution phase salqu copper catalysts (**10adCu**), solid phase salqu copper catalyst (**13-1Cu** and **13-2Cu**) show lower catalytic effect (their yield is 77.7%); however, when compared to its corresponding solution phase salqu copper catalyst (**10cbCu**), they show almost same catalytic effect (**10cbCu's** yield is 80.4%). Until now, no solid phase catalysts to oxidize this kind of reaction with good yields have been developed. Solid phase catalysts have the potential to simplify work up of reactions to a large extent, although its catalytic yield is a little lower than that of solution phase catalyst **10adCu**.

In conclusion, a new kind of solution phase salqu copper catalyst **10adCu** and solid phase salqu copper catalysts **13-1Cu** and **13-2Cu** have been developed for selective oxidization of aryl C-H to aryl carbonyl group with high yields. The optimized process indicates that the configuration and solubility of salqu copper complex catalyst (e.g., **10adCu)** are key factors during the process of oxidization. Besides salqu copper complex **10adCu**, the salqu manganese complex **10adMn** also shows catalytic ability.

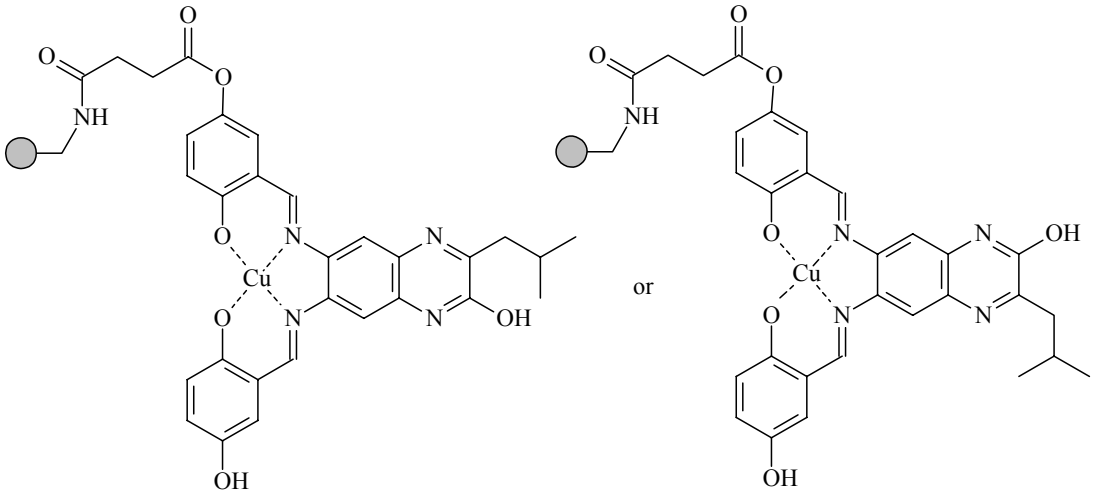


19 **20**





10cbCu (Yield: 80.4%) **10adCu (Yield: 99.0%)**



13-1Cu **13-2Cu**

13-1Cu and 13-2Cu (Yield: 77.7%)

Solution phase salqu copper catalysts 10cbCu, 10adCu.
Soild phase salqu copper catalysts: 13-1Cu and 13-2Cu.

Scheme 6. Regular and solid phase catalysts for the conversion of diphenylmethane into benzophenone.

Using the copper catalyst **10adCu**, an important fragment of natural compound, 1, 4-naphthoquinone, can be easily obtained in high yields and two kinds of oxidases, the oxidations of amine oxidase and galactose oxidase, can be mimicked. These types of catalysts present a new option for use in industry or organic synthesis because of their relative ease of preparation, low sensitivity to moisture and air, their use of more environmentally friendly metals, and their solubility in most solvents. They possess high catalytic efficiency and can be recycled at least twice. In future, the mechanism of this oxidization and new reactions catalyzed by our salqu metal complexes will be further investigated. New solid phase salqu copper catalyst will be designed to improve the catalytic yield by immobilizing salqu copper complex **10adCu** onto insoluble polymers.

CHAPTER 7

CONCLUSIONS AND FUTURE WORK

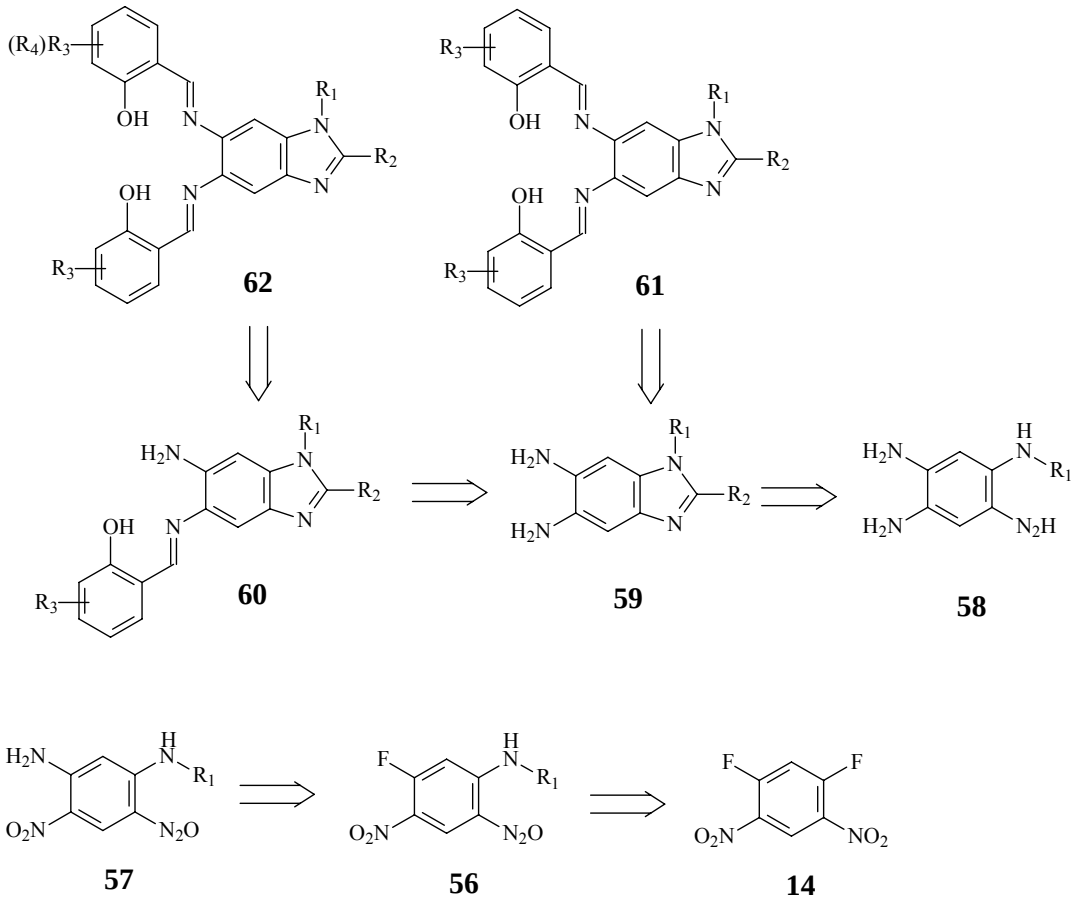
A symmetric salqu library (**7**) has been prepared and optimized using a simple and efficient solution phase parallel method. It was found that these organic salqu ligands are stable at high temperature (<200^{o}C) and not sensitive to oxygen, water, alkaline conditions or most solvents. In this optimized process, the synthetic method for the key intermediate diamino-2-quinoxalinol (**6**) has been further optimized and simplified from methods used in previous reports. Further investigations are ongoing with computational analyses to identify and characterize the transition states in the final step of the Schiff base formation and the limits to the product formation in the ligand systems that result in decreased final yields. Also included in later work will be investigations to determine bioactivity of these compounds.

During the synthesis of the symmetric salqu library, some 2-quinoxalinol imines (**9a**) were obtained as byproducts. We have identified the exact structure of 2-quinoxalinol imines (**9a**) using isotope ^{15}N labeled compounds and NMR technology. Based on this, we have successfully developed a series of new compounds, 2-quinoxalinol imines (**9a**), and we have used these to generate a series of unsymmetrical salqu ligands (**8**). With the imine functional group in these compounds, we will continue with the development of artificial amino acids and labeled peptides, as well as secondary

amine products for screening for bioactivity. With the unsymmetrical salqu ligands in hand, many different metal salqu complexes have been obtained for application as catalysts or bioactivity screening. We have begun to explore ways to develop complexes as potential new chiral catalysts.

Based on the optimized method for synthesis of salqu ligands, a benzimidazole salen library (salbi) could also be developed by the similar way using the same starting material (DFDNB) and steps. Benzimidazole analogs not only have broad bioactivity,[115] but also have found applications in pesticides,[116] as a neurotropic reagents,[117] and in agricultural science.[118] (**Scheme 7**. **59-62**) Starting from DFDNB, it could be first substituted by primary amine and then secondary substituted by ammonium hydroxide to obtain the diamino dinitro benzene analog (**57**). After reduction of diamino dinitro benzene analog (**57**), an unstable intermediates (**58**) will be obtained.[64] Because the secondary amino group of intermediates **58** should be more reactive than other three primary amino groups, it could first form benzimidazole ring to obtain key intermediate diamino benzimidazole (**59**) if equivalent ratio of aldehyde and intermediate **58** would be allowed to react.

Because the secondary amino group of the diamino benzimidazole **59** is a strong electron donor group whereas the imine group is the electron withdrawing group, the two amino groups of **59** should have different reactivity. Therefore, an symmetric and an unsymmetric benzimidazole salen (salbi) library (**61**, **62**) could be developed. Overall, there are four diversity sites in the salbi library (R_1 to R_4). By adjusting different R groups, the properties of salbi ligands could be controlled for different purposes.

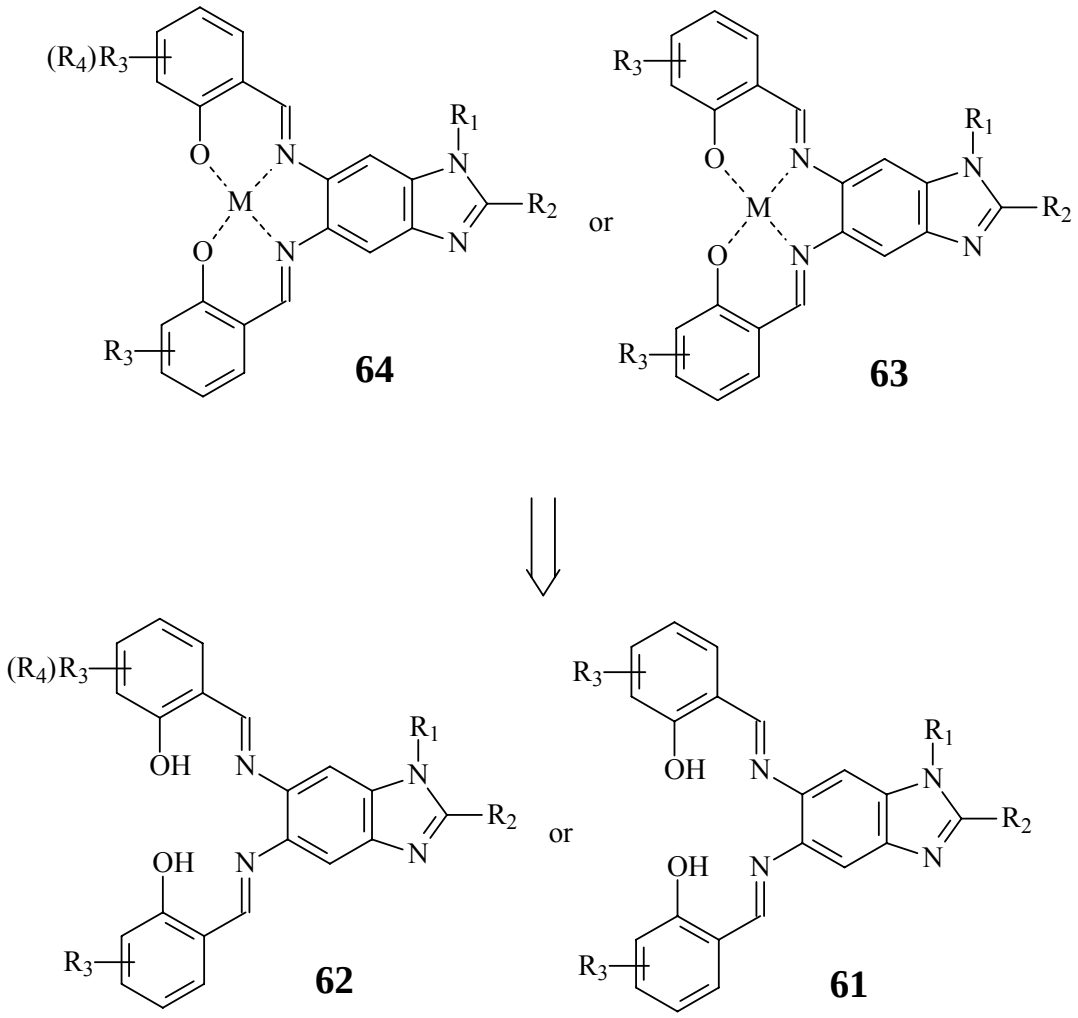


Scheme 7. Retrosynthetic analysis of salbi ligands (**61**, **62**).

Salqu uranyl-complexes have been synthesized and characterized. Crystal structures demonstrate a typical pentagonal bipyramidal geometry around the uranium center with the 2 aza and 2 oxo coordinating sites of the ligand perpendicular to the "-yl" oxygens. The remaining coordination site of the metal is occupied by a solvent molecule. A significant twist of salqu from planar is seen to occur upon coordination of a metal. This results in a change in the orbital overlap of the ligand backbone and makes contribution to a dramatic change in the ultraviolet-visible spectrum.

The presence of different substitutes on the salicylaldehyde moiety incorporated into the ligand backbone affects the solubility of the ligand greatly and also affects the response seen through spectroscopy. Combining oxo- and imine aza-coordination sites as used here, has been demonstrated to impart a degree of selectivity for uranyl in particular over lanthanides. The ligands have also been found to form stable complexes with Cu, Ni, Co, Fe, Pd and Mn cations with the addition of heat or base. The change in the UV-*Vis* spectra of the uranyl complex as compared to transition metal complexes, and a preference for uranyl cations, may be exploited in the development of sensors for actinides on surfaces or in contaminated areas.

Additional experiments to develop these ligands as selective metal coordination systems for use in sensors or extraction applications will continue with experiments to quantify selectivity for uranium or actinides over lanthanides and with experiments probing fluorimetric methods to increase sensitivity. The use of fluorimetry would be another way to rule out competition from transition metals in sensing of actinides. These investigations will broaden our understanding of the chemical behavior of the actinides and enable the development of new sensors and sensing materials for improved detection and isolation of actinides from fuel wastes or contaminated environmental sites. Based on the proposed synthetic route for salbi (**Scheme 8**. **61**, **62**), a new series of salbi metal complexes (**63**, **64**) could be developed for many purposes including new sensors, bioactivity, agriculture and catalysts. (**Scheme 8**)



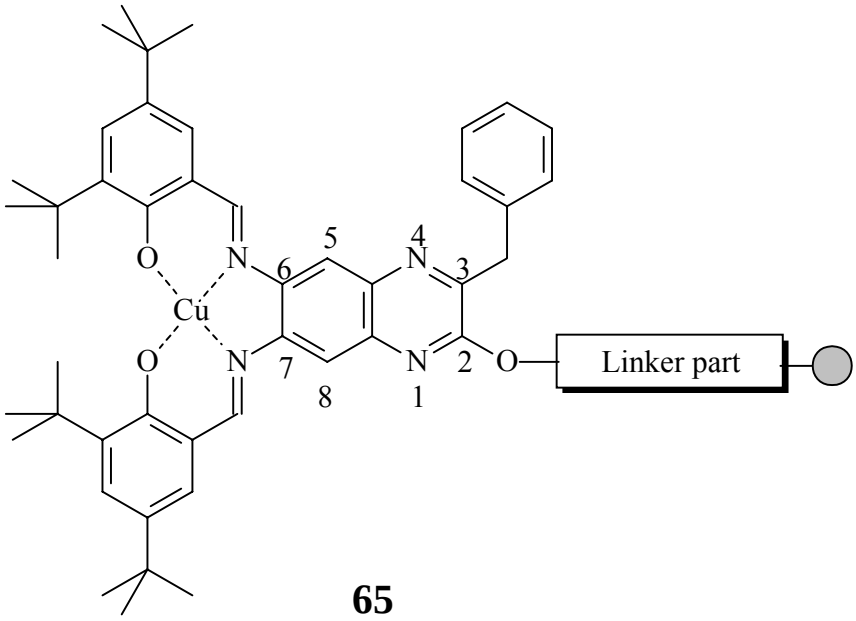
Scheme 8. Retrosynthetic analysis of salbi metal complexes (**63**, **64**).

An optimized synthetic route for solid phase salqu ligands (**12-1** and **12-2) w**as obtained. This kind of resin can selectively extract copper (II) cations within 30 minutes. The copper cations can then be recovered using simple reducing conditions from the resin. This has the potential to enable the selective extraction of copper even from a mixture containing other metals. Resins (**12-1** and **12-2)** could also be applied in environmental or materials chemistry to remove copper cations or in combinatorial chemistry as a metal

scavenging agent to remove excess copper cations. In the future, designing new solid reagents to selectively extract other metals or improvement on the selectivity of (**12-1** and **12-2)** will be investigated.

A new kind of catalyst, **10adCu** and its analogs, which are quite efficient for insertion oxygen into C-H bond of aryl methylene group were developed. The optimized process indicates that solubility and configuration of catalysts **10adCu** are key factors during the process of oxidization of aryl C-H bond and salqu manganese complex **10adMn** also shows excellent catalytic ability for this oxidization.

Using the catalyst **10adCu**, an important fragment of natural compound, 1, 4-naphthoquinone, can be easily obtained with high yield and two kinds of oxidases, the oxidations of amine oxidase and galactose oxidase, can be mimicked. The solid phase catalysts **13-1Cu** and **13-2Cu** have been proved to be efficient for insertion oxygen into aryl C-H bond; however, the solid phase versions, catalysts **13-1Cu** and **13-2Cu,** result in lower yields than the solution phase catalyst **10adCu**. In the future, preparing the immobilized **10adCu** incorporated into insoluble polymers (**Figure 24. 65**) is major step toward improving the catalytic ability of solid phase catalysts, but finding a suitable anchor point is difficult, because the 2-hydroxyl in the of 2-quinoxalinol ring is very unreactive. In addition, the mechanism of this oxidization and new reactions catalyzed by our salqu metal complexes will be investigated.



65

Figure 24. The ideal solid phase catalyst structure.

To sum up, symmetric and unsymmetric salqu ligands have been successfully developed. Their many metal complexes have been synthesized and their uranyl crystals have been obtained and characterized using X-ray diffraction. Two applications of salqu ligands have been explored. The first is the incorporation into SPE technology. Based on the successful immobilization of the salqu ligand, solid phase salqu ligands were found to selectively extract copper (II) within very short time. In a second application, the copper complexes of the salqu were tested as C-H activation catalysts for the oxidization of aryl C-H bond. An important fragment of natural compound, 1, 4-naphthoquinone, can be easily obtained by using our salqu copper catalyst. In addition, solid phase salqu copper catalysts have been developed with appealing catalytic characteristics.

CHAPTER 8

EXPERIMENTAL SECTION

Synthesis

All amino acid methyl esters, DFDNB, HCl (37%), aldehydes, and starting materials for catalytic oxidization were purchased from Acros. Ammonium hydroxide (5.0 N), *tert*-butylhydroperoxide in decane, palladium on carbon (wet, 5%) were purchased from Aldrich. Starting materials were used as received. Polystyrene (PS) aminomethyl resins (1%DVB, 0.59mol/g loading and 100-200 mesh.) were from ChemPep Inc. The ^{15}N labeled ammonium hydroxide was purchased from Cambridge Isotope laboratories, Inc. The parallel synthesis was carried out on a Corning parallel synthesizer. All organic solvents were purchased from Fisher Scientific and were directly used for synthesis.

HPLC analysis was performed on a Shimadzu apparatus equipped with a SPD-10A VP detector. Solutions for HPLC were eluted as 50/50 acetonitrile/H_2O with a buffer consisting of 0.05% TFA over 10 min at 1 mL/min with detection by UV at 254 nm. The column employed was a water C^{18} column (w33471F, 3.9×300 mm) from DIKMA. All melting points were recorded on a Mel-temp II melting point apparatus, and the values were uncorrected. The known ^{1}H and ^{13}CNMR data of commercial available compounds

are available from spectral database for organic compounds (SDBS), National Institute of Advanced Industrial Science and Technology (AIST), Japan.

Spectroscopy

^{1}H and ^{13}C NMR spectra were recorded on Bruker AC 250 spectrometer (operated at 250 and 62.5 MHz, respectively) or a Bruker AV 400 spectrometer (operated at 400 and 100 MHz, respectively). Chemical shifts are reported as δ values (ppm). Some ^{1}H-NMR data were collected using DMSO-d^6 and $CDCl_3$ to dissolve samples because they were not completely soluble only in DMSO-d^6; however, if just $CDCl_3$ is used, the active protons do not appear in D_2O/water exchange experiments. Reaction progress was monitored by thin-layer chromatography (TLC) using 0.25 mm Whatman Aluminum silica gel 60-F254 precoated plates with visualization by irradiation with a Mineralight UVGL-25 lamp. Electrospray ionization mass spectrometry was performed on a Micromass QTOF mass spectrometer (Waters Corp, Milford MA). Direct probe samples were on a VG-70S mass spectrometer (Waters Corp, Milford MA).

All UV data was collected using a Cary 50 UV-*Vis* spectrophotometer with a xenon lamp and an equipment range from 200 to 1250nm. Atomic absorption spectrum (VarianAA240), its software (AA240FS) and hollow cathode lamp (HLC; Ni 232.0nm, optimum working range: 0.1-20 mg/L; Mn 279.5nm, optimum working range: 0.02-5mg/L; Cu 324.8nm, optimum working range: 0.03-10mg/L) are from Varian Inc. IR spectroscopic data was collected using a SHIMSDZU Inc. IR, Prestige-21 Fourier Transform Infrared Spectrophotometer and KBr solid samples. Circular Dichroism (CD) spectra were collected using a Jasco J-810 spectropolarimeter.

Crystallography

X-ray diffraction data for **10aeU**, **10aaU**, **10beU**, **10adU**, **10bdU** and **10ceU** were collected at -80 °C on a Bruker SMART APEX CCD X-ray diffractometer unit using Mo Kα radiation from crystals mounted in Paratone-N oil on glass fibers. SMART (v 5.624) was used for preliminary determination of cell constants and data collection control. Determination of integrated intensities and global cell refinement were performed with the Bruker SAINT Software package using a narrow-frame integration algorithm. The program suite SHELXTL (v 5.1) was used for space group determination, structure solution, and refinement. Refinement was performed against F2 by weighted full-matrix least square, and empirical absorption correction (SADABS43) were applied. H atoms were placed at calculated positions using suitable riding models with isotropic displacement parameters derived from their carrier atoms. Crystal data, selected bond distances and angles, are provided in **Tables 7** and **8**. Crystallography data for structural analysis of uranyl complexes of compounds **10aeU**, **10aaU**, **10beU** and **10adU** have been deposited with the Cambridge Crystallographic Data Center as CCDC nos. 650168, 673941, 673940 and 650169, respectively.

General Procedure

Synthesis of intermediates (6), diamino-2-quinoxalinols. (Scheme 2, Chapter 2)

To a stirring solution of 150 mL of THF, 1.0 equivalent (10.0 mmol, 2.041g) of 1, 5-difluoro-2, 4-dinitrobenzene (DFDNB), 2.2 equivalents (22 mmol, 2.838g) of

diisopropylethylamine (DIPEA), and 1.0 equivalent methyl amino acid (10 mmol) were added. The reaction mixture was stirred continuously for 12 hours at room temperature. After it was confirmed by TLC that the starting materials (DFDNB) had been consumed, 3 equivalents (30 mmol, 6ml) of ammonium hydroxide in water was added as 5.0N in aqueous solution to the reaction mixture. The reaction solution is stirred at room temperature for an additional 5 hours until the reaction was determined to be complete, and this was confirmed by TLC. The reaction solution was concentrated to dryness using a rotary evaporator. The resulting product is a yellow oil or oily solid. The resultant yellow oil was dissolved in 100 mL of ethanol (95%) with stirring.

To this, $HCOONH_4$, 20 equivalents (0.2 mol, 12.620g) and 5% wet Pd-C (3.1 g, 7.0g for ligands prepared from amino acids containing sulfur) were added under a protective N_2 atmosphere. The reaction mixture was heated to reflux temperature for 15-30 minutes. During this time, the reaction mixture changed from the initial yellow to red and, finally, to fluorescent yellow. After this time, the catalyst Pd-C and unreacted $HCOONH_4$ were filtered from the solution. The filtrate was put into the freezer (0^oC) for 48-72 hours. Yellow crystals were found to form. If there are no solids that precipitate from the solution, using an ultrasonic bath for sonication of the sample can help precipitate the diamino 2-quinoxalinols (**6**) as a solid. Filtration of the solid from the reaction solution results in highly pure intermediate (**6**). The totally synthetic yields of **6a-d** are 97%, 90%, 99% and 68% respectively. (**Table 1**, **Chapter 2**) After drying on high vacuum, HPLC, ^{1}H-NMR and ^{13}C-NMR show the purity of each of these are not less than 98%.

^{15}N labeled diamino-2-quinoxalinol (6a-^{15}N)

^{15}N labeled diamino-2-quinoxalinol (**6a-^{15}N**) was synthesized in the same fashion as **6a** but secondary substituted by ^{15}N labeled ammonium hydroxide.

6a ^{1}H-NMR (400 MHz DMSO-d^6): δ 3.99 (s, 2H), 4.66 (bs, 2H), 5.47 (bs, 2H), 6.37 (s, 1H), 6.80 (s, 1H), 7.16-7.31 (m, 5H), 11.86 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 155.1, 152.2, 140.5, 139.4, 133.0, 129.4, 128.6, 126.4, 125.8, 111.0, 96.8, 38.8. Formula: $C_{15}H_{14}N_4O$. MS (M+H): 267.0. HRMS: found (267.1256), calc (267.1246). IR: 3172.9 cm^{-1} (bs), 3381.2 cm^{-1} (bs), 3182.6 cm^{-1} (bs), 3005.2 cm^{-1},1645.3 cm^{-1}, 1510.3 cm^{-1}, 1402.3 cm^{-1}, 1278.8 cm^{-1}. UV: 402.9nm (bs). mp: 261.4-263.5^{o}C.

6a-^{15}N ^{1}H-NMR (400 MHz DMSO-d^6): δ 3.99 (s, 2H), 4.57 (bs, 1H), 4.76 (bs, 1H), 5.47 (bs, 2H), 6.37 (s, 1H), 6.80 (s, 1H), 7.16-7.31 (m, 5H), 11.86 (bs, 1H).

6b ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.13 (d, J=6.8, 6H), 3.33 (sept, 1H), 4.66 (bs, 2H), 5.36 (bs, 2H), 6.33 (s, 1H), 6.78 (s, 1H), 11.73 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 157.7, 154.7, 140.1, 132.8, 125.9, 125.5, 111.3, 96.9, 29.7, 21.0. Formula: $C_{11}H_{14}N_4O$. MS (M+H): 219.0. HRMS: found (219.1248), calc (219.1246). IR: 3381.2 cm^{-1} (bs), 3365.1 cm^{-1} (bs), 2962.7 cm^{-1}, 2929.9 cm^{-1},1656.9 cm^{-1}, 1512.2 cm^{-1}, 1406.1 cm^{-1}, 1273.0 cm^{-1}. UV: 394.0nm (bs). mp: 234.5-236.5 ^{o}C.

6c ^{1}H-NMR (250 MHz DMSO-d^6): δ 0.90 (d, J=6.7, 6H), 2.15 (m, 1H), 2.50 (d, 2H), 4.62 (bs, 2H), 5.39 (bs, 2H), 6.35 (s, 1H), 6.79(s, 1H), 11.98 (bs, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d^6): δ 155.4, 153.2, 140.1, 132.8, 126.0, 125.8, 111.2, 96.9, 41.7, 26.9, 23.0. Formula: $C_{12}H_{16}N_4O$. MS (M+H): 233.0. HRMS: found (233.1410), calc (233.1402). IR: 3352.3 cm^{-1}(bs), 3277.1 cm^{-1} (bs), 2949.2 cm^{-1}, 2868.2 cm^{-1}, 2818.0 cm^{-1}, 1653.0 cm^{-1}, 1512.2 cm^{-1}, 1419.6 cm^{-1}, 1402.3 cm^{-1}, 1271.1 cm^{-1}. UV: 410.6nm (bs), 299.1 (wbs). mp: 249.5-250.3 ^{o}C.

6d ^{1}H-NMR (400 MHz DMSO-d^6): δ 2.09 (s, 3H), 2.83 (t, 2H), 2.95 (t, 2H), 5.19 (bs, 2H), 5.65 (bs, 2H), 6.39 (s, 1H), 6.82 (s, 1H), 11.99 (bs, 1H). ^{13}C-NMR (100MHz, DMSO-d^6): δ 155.2, 151.8, 140.4, 132.9, 126.2, 125.8, 111.1, 96.9, 32.9, 31.1, 15.1. Formula: $C_{11}H_{14}N_4OS$. MS (M+H): 251.0. HRMS: found (251.0966), calc (251.0963). IR: 3321.4 cm^{-1}(bs), 3219.2 cm^{-1}(bs), 2920.2 cm^{-1}, 2879.7 cm^{-1}, 1643.4 cm^{-1}, 1510.3 cm^{-1}, 1402.3 cm^{-1}, 1273.0 cm^{-1}. UV: 391.0nm (bs). mp: >300 ^{o}C.

Preparation of symmetric salqu ligands (7). (Table 2, Chapter 2)

To 1.0 equivalent (0.1 mmol) of the diamino 2-quinoxalinol intermediate (**6**) dissolved in 4 mL methanol, a solution of 10.0 equivalents (1.0 mmol) salicylaldehyde derivatives (**18a-e**) in 6 mL methanol was added. These two were combined with stirring, and after heating to reflux temperature for 1 hour, the reaction mixture becomes deep yellow or dark. After continued heating at reflux temperature for 48 hours, the product forms and precipitates as either dark yellow or red solids. The precipitate is filtered directly and washed with 95% ethanol and ice cold acetone 5 times each to obtain

symmetric salqu ligands as final products. Yields of the final products range from 40.0% to 80.0% with the purity of them ranging from 90.0% to 99.0%. All of the final products (except **7aa**, **7ca** and **7db**) were identified and characterized by ^{1}H-NMR, ^{13}C-NMR, MS, HRMS, UV-*Vis* and IR.

For the synthesis of **7aa**, **7ca** and **7db**, 1.0 equivalent (0.1 mmol) of diamino 2-quinoxalinols (**6**) was dissolved into 4 mL methanol and 10.0 equivalents (1.0 mmol) salicylaldehyde derivates (**18**) were dissolved into 2 mL methanol. With stirring, the reaction solution becomes red after heating to reflux temperature for 40 minutes. After this, the solution was aloowed to continue to heat at reflux temperature for 48 hours. At this time, there were found to be a lot of red precipitates. Filter directly and wash with 95% ethanol and ice cold acetone 5 times each. Yields of these ranged from 50.0-60.0%.

7aa ^{1}H-NMR (400 MHz DMSO-d^6): δ 4.14 (s, 2H), 6.77-7.34 (m, 12H), 7.87 (s, 1H), 8.83 (s, 1H), 9.04 (s, 1H), 9.22 (bs, 1H, D_2O exchangeable), 9.41 (bs, 1H, D_2O exchangeable), 12.18 (bs, 1H, D_2O exchangeable), 12.53 (bs, 1H, D_2O exchangeable), 12.99 (bs, 1H, D_2O exchangeable). ^{13}C-NMR (100MHz, DMSO-d^6): δ 165.6, 164.8, 160.7, 154.9, 150.0, 149.7, 146.2, 146.1, 145.7, 138.2, 137.9, 132.1, 129.7, 128.8, 126.9, 123.4, 122.9, 120.3, 120.2, 119.8, 119.6, 118.4, 106.0, 40.0. Formula: $C_{29}H_{22}N_4O_5$. MS: 507.0**.** HRMS: found (507.1666), calc (507.1668)**.** IR: 3392.8 cm^{-1}(bs), 3005.2 cm^{-1}, 1656.8 cm^{-1}, 1616.3 cm^{-1}, 1467.8 cm^{-1}, 1271.1 cm^{-1}, 1234.4 cm^{-1}. UV: 383.0nm (bs). mp: 251.0 ^{o}C (Color changed).

7ab ^{1}H-NMR (400 MHz DMSO-d^6): δ 4.14 (s, 2H), 6.74-7.35 (m, 12H), 7.87 (s, 1H), 8.74 (s, 1H), 8.97 (s, 1H), 9.08 (bs, 1H, D_2O exchangeable), 9.12 (bs, 1H, D_2O exchangeable), 11.43 (bs, 1H, D_2O exchangeable), 12.31 (bs, 1H, D_2O exchangeable), 12.50 (bs, 1H, D_2O exchangeable). ^{13}C-NMR (100MHz, DMSO-d^6): δ 164.3, 163.8, 160.6, 155.0, 153.8, 153.5, 150.2, 150.0, 146.5, 138.0, 137.9, 132.1, 131.1, 129.7, 128.9, 126.9, 122.4, 121.7, 120.2, 119.9, 118.1, 117.9, 117.7, 117.5, 116.5, 105.9, 40.0. Formula: $C_{29}H_{22}N_4O_5$. MS (M+H): 507.0. HRMS: found (507.1667), calc (507.1668)**.** IR: 3387.0 cm^{-1}(bs), 3005.0 cm^{-1}, 1662.6 cm^{-1}, 1616.4 cm^{-1}, 1573.9 cm^{-1}, 1487.1 cm^{-1}, 1282.7 cm^{-1}, 1153.4 cm^{-1}. UV: 378.0nm (bs). mp: 246.0 ^{o}C (Color changed).

7ac ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.31 (s, 9H), 1.34 (s, 9H), 4.15 (s, 2H), 6.77-7.44 (m, 12H), 7.62 (s, 1H), 8.58 (s, 1H), 8.70 (s, 1H), 12.26 (bs, 1H), 13.42 (bs, 1H), 13.60 (bs, 1H). ^{13}C-NMR (100MHz, DMSO-d^6): δ 165.4, 163.7, 160.6, 160.4, 155.1, 144.6, 138.4, 137.7, 137.4, 137.0, 133.9, 131.9, 131.7, 130.7, 129.3, 128.2, 126.4, 126.1, 119.2, 118.9, 118.7, 118.2, 117.9, 105.5, 34.7, 29.2. Formula: $C_{37}H_{38}N_4O_3$. MS (M+H): 587.0. HRMS: found (587.3028), calc (587.3022). IR: 3437.2 cm^{-1}(bs), 3417.9 cm^{-1}(bs), 2953.0 cm^{-1}, 2912.5 cm^{-1}, 1672.3 cm^{-1}, 1606.7 cm^{-1}, 1500.6 cm^{-1}, 1431.2 cm^{-1}, 1394.5 cm^{-1}, 1197.8 cm^{-1}, 1143.8 cm^{-1}. UV: 285.7nm (bs), 387.9nm (bs). mp: 271.0-273.5^{o}C.

7ad ^{1}H-NMR (250 MHz DMSO-d^6 and $CDCl_3$): δ 1.23 (s, 18H), 1.32 (s, 9H), 1.34 (s, 9H), 4.14 (s, 2H), 7.01 (s, 1H), 7.12-7.41 (m, 9H), 7.59 (s, 1H), 8.58 (s,1H), 8.68 (s, 1H), 12.22 (bs, 1H), 13.25 (bs, 1H), 13.36 (bs, 1H). ^{13}C-NMR (62.5MHz, DMSO-d^6 and $CDCl_3$): δ 165.9, 164.3, 160.2, 158.6, 158.3, 155.3, 144.9, 140.6, 140.5, 138.9, 137.2,

137.1, 136.9, 131.7, 131.5, 129.5, 128.7, 128.4, 128.2, 127.2, 127.0, 126.5, 118.4, 118.1, 118.1, 105.6, 35.1, 34.1, 31.5, 29.4. Formula: $C_{45}H_{54}N_4O_3$. MS (M+H): 699.0. HRMS: found (699.4276), calc (699.4274)**.** IR: 3435.2 cm^{-1}(bs), 3415.9 cm^{-1}(bs), 2956.9 cm^{-1}, 2910.6 cm^{-1}, 2873.9 cm^{-1}, 1656.9 cm^{-1}, 1612.5 cm^{-1}, 1529.6 cm^{-1}, 1477.5 cm^{-1}, 1442.8 cm^{-1}, 1261.5 cm^{-1}, 1168.9 cm^{-1}. UV: 299.1nm (bs), 390.9nm (bs). mp: 279.1-280.1°C.

7ae ^{1}H-NMR (400 MHz DMSO-d^6): δ 4.17 (s, 2H), 6.95-7.03 (m, 2H), 7.11 (s, 1H), 7.25-7.49 (m, 7H), 7.66 (d, 1H), 7.79 (d, 1H), 7.94 (s, 1H), 8.90 (s, 1H), 9.13 (s, 1H), 12.28 (bs, 1H), 12.57 (bs, 1H), 13.13 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 164.6, 164.0, 160.9, 160.8, 160.6, 155.0, 146.0, 138.1,137.9, 134.5, 133.8, 133.1, 132.3, 132.2, 131.2, 129.8, 128.9, 126.9, 120.2, 120.0, 119.9, 119.6, 118.1, 117.2, 117.1, 105.8, 40.0. Formula: $C_{29}H_{22}N_4O_3$. MS (M+H): 475.0. HRMS: found (475.1762), calc (475.1770). IR: 3448.7 cm^{-1}(bs), 3427.5 cm^{-1}(bs), 3055.2 cm^{-1}, 3030.2 cm^{-1}, 1654.9 cm^{-1}, 1610.6 cm^{-1}, 1570.1 cm^{-1}, 1481.3 cm^{-1}, 1276.9 cm^{-1}, 1197.8 cm^{-1}. UV: 305.6nm (bs, $\varepsilon = 3.2\times10^4$), 335.9nm, 390.5nm (bs, $\varepsilon = 3.2\times10^4$). mp: 264.1-266.1°C.

7ba ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.26 (d, J=6.8Hz, 6H), 3.50 (sept, 1H), 6.80 (t, 1H), 6.84 (t, 1H), 6.94 (d,1H), 6.99 (d, 1H), 7.01 (s, 1H), 7.14 (d, 1H), 7.22 (d, 1H), 7.92 (s, 1H), 8.87 (s, 1H), 9.11 (s, 1H), 9.24 (bs, 1H), 9.43 (bs, 1H), 12.24 (bs, 1H), 12.48 (bs, 1H), 13.06 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 166.0, 165.6, 164.8, 154.6, 150.0, 149.7, 146.2, 146.1, 145.4, 138.1, 131.8, 131.1, 123.5, 122.9, 120.3, 120.2, 120.0, 119.6, 119.2, 118.3, 106.0, 30.4, 20.6. Formula: $C_{25}H_{22}N_4O_5$. MS (M+H): 459.0. HRMS: found (459.1675), calc (459.1668). IR: 3421.7 cm^{-1}(bs), 3059.1 cm^{-1}, 2966.5 cm^{-1}

[1], 2926.0 cm^{-1}, 1656.9 cm^{-1}, 1616.4 cm^{-1}, 1556.6 cm^{-1}, 1465.9 cm^{-1}, 1373.3 cm^{-1}, 1273.0 cm^{-1}, 1230.6 cm^{-1}. UV: 306.5nm (bs), 389.6nm (bs). mp: >300 ^{o}C.

7bb ^{1}H-NMR (400 MHz DMSO-d^{6}): δ 1.23 (d, J=6.8Hz, 6H), 3.48 (sept, 1H), 6.74-7.12 (m, 7H), 7.88 (s, 1H), 8.74 (s, 1H), 9.01 (s,1H), 9.08 (bs, 1H, D_2O exchangeable), 9.13 (bs, 1H, D_2O exchangeable), 11.46 (bs, 1H, D_2O exchangeable), 12.36 (bs, 1H, D_2O exchangeable), 12.42 (bs, 1H, D_2O exchangeable). ^{13}C-NMR (100 MHz, DMSO-d^{6}): δ 165.9, 164.3, 163.8, 154.6, 153.8, 153.5, 150.2, 150.0, 146.2, 138.2, 131.8, 130.9, 122.3, 121.7, 120.2, 120.0, 118.0, 117.9, 117.6, 116.5, 105.8, 30.4, 20.6. Formula: $C_{25}H_{22}N_4O_5$. MS (M+H): 458.0**.** HRMS: found (459.1665), calc (459.1668). IR: 3400.5 cm^{-1}(bs), 2962.7 cm^{-1}, 2926.0 cm^{-1}, 1656.9 cm^{-1}, 1627.9 cm^{-1}, 1579.7 cm^{-1}, 1490.8 cm^{-1}, 1400.0 cm^{-1}, 1273.0 cm^{-1}, 1219.0 cm^{-1}. UV: 299.1nm (bs), 387.0nm (bs). mp: 221.5^{o}C (Color changed).

7bc ^{1}H-NMR (400 MHz DMSO-d^{6}): δ 1.27 (d, J=6.8Hz, 6H), 1.37 (s, 9H), 1.42 (s, 9H), 3.52 (sept, 1H), 6.93 (t, 1H), 6.95 (t, 1H), 7.20 (s, 1H), 7.38 (d, 1H), 7.44 (d, 1H), 7.54-7.58 (t, 2H), 8.00 (s, 1H), 8.94 (s, 1H), 9.19 (s,1H), 12.51 (bs, 1H), 13.73 (bs, 1H), 14.04 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^{6}): δ 167.1, 166.3, 165.5, 160.5, 160.4, 154.6, 144.5, 137.9, 137.6, 137.1, 137.0, 132.2, 132.0, 131.4, 131.3, 130.8, 119.7, 119.4, 119.1, 118.9, 118.3, 105.9, 34.9, 30.4, 29.7, 20.6. Formula: $C_{33}H_{38}N_4O_3$. MS (M+H): 539.0**.** HRMS: found (539.3024), calc (539.3022). IR: 3429.4 cm^{-1}(bs), 2956.9 cm^{-1}, 2872.0 cm^{-1}, 1660.7 cm^{-1}, 1606.7 cm^{-1}, 1467.8 cm^{-1}, 1431.2 cm^{-1}, 1388.8 cm^{-1}, 1270.0 cm^{-1}, 1199.7 cm^{-1}. UV: 302.2nm (bs), 386.2nm (bs). mp: 285.1-286.1^{o}C.

7bd ^{1}H-NMR (400 MHz DMSO-d^6 and $CDCl_3$): δ 1.20 (s, 9H), 1.21 (s, 9H), 1.21 (d, J=6.8Hz, 6H), 1.29 (s, 9H), 1.32 (s, 9H), 3.52 (sept, 1H), 6.99 (s, 1H), 7.17 (s, 2H), 7.34 (s, 1H), 7.37 (s, 1H), 7.62 (s, 1H), 8.59 (s, 1H), 8.72 (s, 1H), 12.12 (bs, 1H), 13.28 (bs, 1H), 13.39 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6 and $CDCl_3$): 165.9, 165.7, 164.1, 158.5, 158.3, 155.1, 144.5, 140.5, 140.4, 138.8, 137.1, 136.9, 131.5, 131.2, 128.6, 128.1, 127.1, 126.8, 118.3, 118.1, 118.0, 105.4, 35.0, 34.1, 31.4, 30.3, 29.3, 20.1. Formula: $C_{41}H_{54}N_4O_3$. MS (M+H): 651.0. HRMS: found (651.4274), calc (651.4268). IR: 3423.7 cm^{-1}(bs), 2958.8 cm^{-1}, 2910.6 cm^{-1}, 2870.1 cm^{-1}, 1653.0 cm^{-1}, 1614.4 cm^{-1}, 1581.6 cm^{-1}, 1469.8 cm^{-1}, 1437.0 cm^{-1}, 1390.7 cm^{-1}, 1363.7 cm^{-1}, 1253.7 cm^{-1}, 1203.6 cm^{-1}. UV: 299.6nm (bs), 387.9nm (bs). mp: 280.0-281.0^{o}C.

7be ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.23 (d, J=6.8Hz, 6H), 3.47 (sept, 1H), 6.91-7.00 (m, 4H), 7.08 (s, 1H), 7.39 (t, 1H), 7.44 (t, 1H), 7.66 (d, 1H), 7.76 (d, 1H), 7.93 (s, 1H), 8.87 (s, 1H), 9.15 (s, 1H), 12.28 (bs, 1H), 12.46 (bs, 1H), 13.14 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 166.1, 164.6, 163.9, 160.9, 160.6, 154.6, 145.7, 137.9, 134.4, 133.8, 133.1, 132.4, 132.0, 131.1, 120.2, 119.8, 119.5, 118.1, 117.2, 117.1, 105.7, 30.4, 20.6. Formula: $C_{25}H_{22}N_4O_3$. MS (M+H): 427.0. HRMS: found (427.1764), calc (427.1770). IR: 3441.0 cm^{-1}(bs), 2964.6 cm^{-1}, 2924.1 cm^{-1}, 1658.8 cm^{-1}, 1616.4 cm^{-1}, 1570.1 cm^{-1}, 1479.4 cm^{-1}, 1452.0 cm^{-1}, 1278.8 cm^{-1}, 1203.6 cm^{-1}. UV: 335.9nm (bs), 387.9nm (bs). mp: 288.5-289.3^{o}C.

7ca ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.23 (d, J=6.6Hz, 6H), 2.27 (m, 1H), 2.71 (d, J=7.0, 2H), 6.80 (t, 1H), 6.83 (t, 1H), 6.95 (d, 1H), 7.00 (d, 1H), 7.09 (s, 1H), 7.14 (t, 2H), 7.22 (t, 2H), 7.92 (s, 1H), 8.87 (s, 1H), 9.08 (s, 1H), 9.24 (bs, 1H, D_2O exchangeable), 9.42 (bs, 1H, D_2O exchangeable), 12.25 (bs, 1H, D_2O exchangeable), 12.47 (bs, 1H, D_2O exchangeable), 13.04 (bs, 1H, D_2O exchangeable). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 165.6, 164.7,161.7, 155.2, 150.0, 149.7, 146.2, 146.1, 145.4, 138.1, 131.9, 131.2, 123.4, 122.9, 120.3, 120.2, 120.0, 119.6, 119.2, 118.3, 106.0, 42.1, 26.6, 23.1. Formula: $C_{26}H_{24}N_4O_5$. MS (M+H): 473.0. HRMS: found (473.1818), calc (473.1825). IR: 3419.8 cm^{-1}(bs), 2949.2 cm^{-1}, 2866.2 cm^{-1}, 1656.9 cm^{-1}, 1618.3 cm^{-1}, 1579.7 cm^{-1}, 1465.9 cm^{-1}, 1373.3 cm^{-1}, 1271.1 cm^{-1}, 1232.5 cm^{-1}. UV: 301.3nm (bs), 381.0nm (bs). mp: 260.0-261.5^{o}C.

7cb ^{1}H-NMR (400 MHz DMSO-d^6): δ 0.98 (d, J=6.6Hz, 6H), 2.27 (m, 1H), 2.71 (d, J=7.0, 2H), 6.77-6.91 (m, 4H), 7.06 (s, 2H), 7.14 (s, 1H), 7.92 (s, 1H), 8.77 (s, 1H), 9.01 (s, 1H), 9.12 (bs, 1H), 9.15 (bs, 1H), 11.49 (bs, 1H,), 12.36 (bs, 1H), 12.45 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 164.4, 163.7, 161.5, 155.2, 153.8, 153.5, 150.2, 150.0, 146.2, 138.2, 131.9, 131.1, 120.2, 119.9, 117.9, 117.6, 117.5, 116.5, 105.8, 42.1, 26.7, 23.1. Formula: $C_{26}H_{24}N_4O_5$. MS (M+H): 473.0**.** HRMS: found (473.1832), calc (473.1825). IR: 3427.5 cm^{-1}(bs), 3412.1 cm^{-1}(bs), 2956.9 cm^{-1}, 2924.1 cm^{-1}, 1658.8 cm^{-1}, 1618.3 cm^{-1}, 1577.8 cm^{-1}, 1483.3 cm^{-1}, 1379.1 cm^{-1}, 1286.5 cm^{-1}, 1213.2 cm^{-1}. UV: 303.9nm (bs), 395.7nm (bs). mp: 290.5^{o}C (Color changed).

7cc ^{1}H-NMR (400 MHz DMSO-d^6): δ 0.99 (d, J=6.6Hz, 6H), 13.7 (s, 9H), 1.42 (s, 9H), 2.29 (m, 1H), 2.72 (d, J=7.0, 2H), 6.93 (t, 1H), 6.95 (t, 1H), 7.20 (s, 1H), 7.38 (d, 1H), 7.44 (d, 1H), 7.53-7.58 (m, 2H), 8.01 (s, 1H), 8.93 (s, 1H), 9.16 (s, 1H), 12.51 (bs, 1H), 13.73 (bs, 1H), 14.03 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 167.1, 165.5, 161.9, 160.5, 160.4, 155.2, 144.5, 137.9, 137.2, 137.0, 132.2, 132.0, 131.9, 131.4, 130.8, 119.7, 119.4, 119.1, 118.9, 118.2, 105.9, 42.1, 34.9, 29.7, 26.6, 23.1. Formula: $C_{34}H_{40}N_4O_3$. MS (M+H): 553.0**.** HRMS: found (553.3177), calc (553.3178). IR: 3423.7 cm^{-1}(bs), 2955.0 cm^{-1}, 2918.3 cm^{-1}, 2870.1 cm^{-1}, 1662.6 cm^{-1}, 1604.8 cm^{-1}, 1573.9 cm^{-1}, 1496.8 cm^{-1}, 1469.8 cm^{-1}, 1431.2 cm^{-1}, 1396.5 cm^{-1}, 1273.0 cm^{-1}, 1199.7 cm^{-1}. UV: 299.6nm (bs), 382.7nm (bs). mp: 285.1-286.7^{o}C.

7cd ^{1}H-NMR (250 MHz DMSO-d^6 and $CDCl_3$): δ 0.82 (d, J=6.6Hz, 6H), 1.10 (s, 9H), 1.11 (s, 9H), 1.19 (s, 9H), 1.22 (s, 9H), 2.13 (m, 1H), 2.57 (d, J=7.1, 2H), 6.88 (s, 1H), 7.04-7.06 (dd, 2H), 7.21 (d, 2H), 7.23 (d, 2H), 7.47 (s, 1H), 8.47 (s, 1H), 8.58 (s, 1H), 12.08 (bs, 1H), 13.15 (bs, 1H), 13.25 (bs, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d^6 and $CDCl_3$): δ 166.6, 164.1, 161.4, 158.4, 158.1, 155.6, 144.4, 140.4, 138.7, 136.9, 136.8, 131.3, 128.5, 128.0, 127.0, 126.8, 118.2, 118.0, 117.8, 105.4, 42.0, 34.9, 34.0, 31.3, 29.3, 26.5, 22.6. Formula: $C_{42}H_{56}N_4O_3$. MS (M+H): 665.0. HRMS: found (665.4431), calc (665.4430). IR: 3423.7 cm^{-1}(bs), 2956.9 cm^{-1}, 2920.1 cm^{-1}, 2880.1 cm^{-1}, 1656.9 cm^{-1}, 1616.4 cm^{-1}, 1583.6 cm^{-1}, 1469.8 cm^{-1}, 1437.0 cm^{-1}, 1386.8 cm^{-1}, 1367.5 cm^{-1}, 1255.7 cm^{-1}, 1207.4 cm^{-1}. UV: 301.3nm (bs), 389.6nm (bs). mp: 287.8-288.8 ^{o}C.

7ce ^{1}H-NMR (250 MHz DMSO-d^6): δ 0.98 (d, J=6.5Hz, 6H), 2.27 (m, 1H), 2.70 (d, J=6.9, 2H), 6.94-7.11 (m, 4H), 7.38 (s, 1H), 7.41-7.46 (m, 2H), 7.68 (d, 1H), 7.79 (d, 1H), 7.96 (s, 1H), 8.89 (s, 1H), 9.14 (s, 1H), 12.34 (bs, 2H), 13.14 (bs, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d^6): δ 164.6, 163.9, 161.7, 160.9, 160.6, 155.2, 145.6, 138.0, 134.4, 133.8, 133.1, 132.4, 132.0, 131.2, 120.2, 120.0, 119.8, 119.5, 118.0, 117.2, 105.8, 42.1, 26.6, 23.1. Formula: $C_{26}H_{24}N_4O_3$. MS (M+H): 441.0. HRMS: found (441.1922), calc (441.1926). IR: 3441.0 cm^{-1}(bs), 3425.6 cm^{-1}(bs), 2955.0 cm^{-1}, 2922.2 cm^{-1}, 2864.3 cm^{-1}, 1658.8 cm^{-1}, 1616.4 cm^{-1}, 1572.0 cm^{-1}, 1485.2 cm^{-1}, 1384.9 cm^{-1}, 1278.8 cm^{-1}, 1203.6 cm^{-1}. UV: 383.6nm (bs). mp: 286.5-288.5^{o}C.

7da ^{1}H-NMR (400 MHz DMSO-d^6): δ 2.14 (s, 3H), 2.95 (t, 2H), 3.13 (t, 2H), 6.81 (t, 1H), 6.84 (t, 1H), 6.95 (d, 1H), 7.00 (d, 1H), 7.11 (s, 1H), 7.15 (d, 1H), 7.23 (d, 1H), 7.92 (s, 1H), 8.88 (s, 1H), 9.08 (s, 1H), 9.25 (bs, 1H, D_2O exchangeable), 9.43 (bs, 1H, D_2O exchangeable), 12.23 (bs, 1H, D_2O exchangeable), 12.53 (bs, 1H, D_2O exchangeable), 13.02 (bs, 1H, D_2O exchangeable). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 165.7, 164.8, 160.6, 155.0, 149.9, 149.7, 146.2, 146.1, 145.6, 138.2, 132.0, 131.1,123.4, 122.9, 120.3, 120.2, 120.0, 119.6, 119.2, 118.3, 106.1, 33.2, 30.5, 15.0. Formula: $C_{25}H_{22}N_4O_5S$. MS (M+H): 491.0. HRMS: found (491.1389), calc (491.1389). IR: 3415.9 cm^{-1}(bs), 2920.2 cm^{-1}, 2852.7 cm^{-1}, 1656.9 cm^{-1}, 1616.4 cm^{-1}, 1467.8 cm^{-1}, 1373.3 cm^{-1}, 1271.1 cm^{-1}, 1230.6 cm^{-1}. UV: 307.4nm (bs), 390.5nm (bs). mp: >300 ^{o}C.

7db ^{1}H-NMR (400 MHz DMSO-d^6): δ 2.14 (s, 3H), 2.94 (t, 2H), 3.12 (t, 2H), 6.77-6.93 (m, 4H), 7.06 (s, 2H), 7.14 (s, 1H), 7.92 (s, 1H), 8.78 (s, 1H), 8.80 (s, 1H), 9.12

(bs, 1H), 9.16 (bs, 1H), 11.48 (bs, 1H), 12.34 (bs, 1H), 12.49 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 164.4, 163.8, 153.8, 153.5, 150.2, 150.0, 132.0, 121.7, 120.2, 119.9, 118.1, 117.9, 117.7, 116.5, 105.9, 33.1, 30.1, 15.2. Formula: $C_{25}H_{22}N_4O_5S$. MS (M+H): 491.0. HRMS: found (491.1384), calc (491.1389). IR: 3439.1 cm^{-1}(bs), 2972.3 cm^{-1}, 2924.1 cm^{-1}, 1654.9 cm^{-1}, 1624.1 cm^{-1}, 1575.8 cm^{-1}, 1477.5 cm^{-1}, 1388.8 cm^{-1}, 1282.7 cm^{-1}, 1220.9 cm^{-1}. UV: 302.2nm (wbs), 391.4nm (bs). mp: >300 ^{o}C.

7dc ^{1}H-NMR (250 MHz DMSO-d^6): δ 1.36 (s, 9H), 1.40 (s, 9H), 2.14 (s, 3H), 2.94 (t, 2H), 3.11 (t, 2H), 6.93-6.98 (m, 2H), 7.20 (s, 1H), 7.39 (d, 1H), 7.41 (d, 1H), 7.54 (t, 2H), 8.00 (s, 1H), 8.93 (s, 1H), 9.14 (s, 1H), 12.56 (bs, 1H), 13.72 (bs, 1H), 14.01 (bs, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d^6): δ 166.9, 165.2, 160.6, 160.4, 154.9, 144.6, 138.1, 137.2, 137.0, 132.1, 131.8, 131.3, 130.6, 119.6, 119.3, 118.9, 118.7, 118.2, 105.9, 34.9, 33.2, 30.5, 29.6, 15.3. Formula: $C_{33}H_{38}N_4O_3S$. MS (M+H): 571.0. HRMS: found (571.2738), calc (571.2743). IR: 3433.3 cm^{-1}(bs), 3417.9 cm^{-1}(bs), 2953.0 cm^{-1}, 2920.2 cm^{-1}, 2872.0 cm^{-1}, 1666.5 cm^{-1}, 1654.9 cm^{-1}, 1606.7 cm^{-1}, 1489.1 cm^{-1}, 1427.3 cm^{-1}, 1388.8 cm^{-1}, 1311.6 cm^{-1}, 1267.2 cm^{-1}. UV: 305.6nm (bs), 389.6nm (bs). mp: 262.0^{o}C (Color changed).

7dd ^{1}H-NMR (400 MHz DMSO-d^6 and $CDCl_3$): δ 1.20 (s, 9H), 1.21 (s, 9H), 1.29 (s, 9H), 1.32 (s, 9H), 2.15 (s, 3H), 2.90 (t, 2H), 3.12 (t, 2H), 6.97 (s, 1H), 7.14 (s, 2H), 7.31 (d, 1H), 7.34 (d, 1H), 7.56 (s, 1H), 8.55 (s, 1H), 8.65 (s, 1H), 12.20 (bs, 1H), 13.21 (bs, 1H), 13.32 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6 and $CDCl_3$): δ 165.8, 164.3, 159.8, 158.6, 158.3, 155.4, 144.9, 140.5, 140.4, 139.0, 137.1, 137.0, 131.4, 131.3, 128.7,

128.2, 127.1, 126.9, 118.3, 118.1, 118.0, 105.6, 35.0, 34.1, 33.1, 31.4, 30.6, 29.3, 15.5. Formula: $C_{41}H_{54}N_4O_3S$. MS (M+H): 683.0. HRMS: found (683.4005), calc (683.3995). IR: 3441.0 cm^{-1}(bs), 3425.6 cm^{-1}(bs), 2956.9 cm^{-1}, 2914.4 cm^{-1}, 2870.1 cm^{-1}, 1656.9 cm^{-1}, 1616.4 cm^{-1}, 1583.6 cm^{-1}, 1469.8 cm^{-1}, 1433.1 cm^{-1}, 1386.8 cm^{-1}, 1269.2 cm^{-1}, 1259.5 cm^{-1}. UV: 302.2nm (bs), 391.4nm (bs). mp: 286.0-287.5^{o}C.

7de ^{1}H-NMR (400 MHz DMSO-d^6): δ 2.14 (s, 3H), 2.95 (t, 2H), 3.13 (t, 2H), 6.95- 7.04 (m, 4H), 7.12 (s, 1H), 7.42 (t, 1H), 7.47 (t, 1H), 7.70 (d, 1H), 7.79 (d, 1H), 7.96 (s, 1H), 8.91 (s, 1H), 9.14 (s, 1H), 12.30 (bs, 1H), 12.54 (bs, 1H), 13.12 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 164.7, 164.0, 160.9, 160.6, 155.0, 145.8, 138.1, 134.5, 133.8, 133.1, 120.2, 120.0, 119.9, 118.1, 117.2, 117.1, 105.8, 33.2, 30.5, 15.2. Formula: $C_{25}H_{22}N_4O_3S$. MS (M+H): 459.0. HRMS: found (459.1489), calc (459.1491). IR: 3441.0 cm^{-1}(bs), 3423.6 cm^{-1}(bs), 2916.4 cm^{-1}, 2841.2 cm^{-1}, 2796.8 cm^{-1}, 1660.7 cm^{-1}, 1614.4 cm^{-1}, 1570.1 cm^{-1}, 1479.4 cm^{-1}, 1398.4 cm^{-1}, 1276.9 cm^{-1}, 1201.6 cm^{-1}. UV: 335.9nm (bs), 387.0nm (bs). mp: 270.5 ^{o}C.

Synthesis of intermediate 9ax, 2-quinoxalinol imines. (Table 4, Chapter 3)

The synthesis of 2-quinoxalinol imine (**9ax**) begins with the addition of 1.0 equivalent of intermediates (**6**, 0.1mmol) dissolved in 4 mL methanol to a solution of 1.2 equivalents substituted salicylaldehyde derivatives (**18**, 0.12mmol) in 6 mL methanol. The two are combined with stirring for 14 hours. This is monitored by TLC. Once the diamino 2-quinoxalinol (**6**) starting material can no longer be seen by TLC, the reaction is considered complete. Pure 2-quinoxalinol imines (**9a**) are obtained by purification

using flash column chromatography with a solution of hexane : ethyl acetate, 3:1 as eluent. For sample (**9ai**), a modified procedure was used. The product begins to form as a red solid (**9ai**) after heating at reflux temperature for 4 hours. The red solid was filtered off and washed with 95% ethanol followed by ice cold acetone to obtain pure final 2-quinoxalinol imines (**9ai**). The one step yields of these range from 60.0-90.0%.

9aa ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.44 (s, 9H), 4.04 (s, 2H), 5.84 (bs, 2H), 6.59 (s, 1H), 6.80 (s, 1H), 6.59-7.74 (m, 9H), 8.98 (s, 1H), 12.15 (bs, 1H), 13.58 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 167.4, 164.0, 159.8, 155.5, 154.2 145.6, 138.8, 136.8, 133.4, 132.3, 132.2, 132.0, 131.8, 130.4, 129.5, 129.2, 128.7, 126.6, 125.0, 120.0, 119.0, 117.1, 97.7, 40.0, 35.0, 30.0. Formula: $C_{26}H_{26}N_4O_2$. MS (M+H): 426.0. HRMS: found (426.2051), calc (426.2056). IR: 3470.0 cm^{-1} (bs), 3375.4cm^{-1} (bs), 3182.6 cm^{-1}, 2956.9 cm^{-1}, 2927.9 cm^{-1}, 2870.1 cm^{-1}, 1728.2 cm^{-1}, 1656.9 cm^{-1}, 1624.1 cm^{-1}, 1271.1 cm^{-1}. mp: 196.0-199.0^{o}C.

9ab ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.20 (d, J=6.8, 6H), 1.44 (s, 9H), 3.61 (sept, 1H), 5.77 (bs, 2H), 6.60 (s, 1H), 6.94 (t, 1H), 7.38 (d, 1H), 7.53 (d, 1H), 7.55 (s, 1H), 9.03 (s, 1H), 12.07 (bs, 1H), 13.64 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 170.8, 163.8, 159.8, 159.6, 155.1, 145.3, 136.8, 133.1, 132.1, 131.8, 130.4, 124.8, 120.1, 119.0, 117.7, 97.8, 35.0, 29.9, 20.8, 14.6. Formula: $C_{22}H_{26}N_4O_2$. MS (M+H): 378.0. HRMS: found (378.2052), calc (378.2056). IR: 3442.9 cm^{-1} (bs), 3402.4 cm^{-1} (bs), 2958.8 cm^{-1}, 2872.0 cm^{-1}, 1710.9 cm^{-1}, 1651.1 cm^{-1}, 1626.0 cm^{-1}, 1502.6 cm^{-1}, 1234.4 cm^{-1}. mp: 250.0- 253.0^{o}C (Color changed).

9ac ^{1}H-NMR (250 MHz DMSO-d^6): δ 0.93 (d, J=6.6, 6H), 1.43 (s, 9H), 2.19 (m, 1H), 2.58 (d, 2H), 5.77 (bs, 2H), 6.59 (s, 1H), 6.93 (t, 1H), 7.37(d, 1H), 7.52 (d, 1H), 7.55 (s, 1H), 8.99 (s, 1H), 12.06 (bs, 1H), 13.62 (bs, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d^6): δ 163.8, 159.8, 155.8, 155.2, 145.3, 136.8, 133.2, 132.1, 131.7, 130.4, 125.0, 120.3, 119.0, 117.6, 97.8, 41.7, 34.9, 29.7, 26.8, 23.1. Formula: $C_{23}H_{28}N_4O_2$. MS (M+H): 392.0. HRMS: found (392.2206), calc (392.2212). IR: 3392.8 cm^{-1}(bs), 2954.9 cm^{-1}, 2924.1 cm^{-1}, 2866.2 cm^{-1}, 1710.0 cm^{-1}, 1626.0 cm^{-1}, 1600.9 cm^{-1}, 1371.4 cm^{-1}, 1232.5 cm^{-1}. mp: >300.0^{o}C.

9ad ^{1}H-NMR (250 MHz DMSO-d^6): δ 1.43 (s, 9H), 2.09 (s, 3H), 2.86 (t, 2H), 2.97 (t, 2H), 5.82 (bs, 2H), 6.59 (s, 1H), 6.93 (t, 1H), 7.37 (d, 1H) 7.51 (d, 1H), 7.53 (s, 1H), 12.11 (bs, 1H), 13.59 (bs, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d^6): δ 163.9, 159.8, 155.5, 153.9, 145.5, 136.8, 133.3, 132.3, 131.8, 130.4, 125.0, 120.0, 119.0, 117.6, 97.8, 34.9, 32.8, 30.9, 29.7, 15.2. Formula: $C_{22}H_{26}N_4O_2S$. MS (M+H): 410.0. HRMS: found (410.1767), calc (410.1776). IR: 3469.9 cm^{-1}(bs), 3334.9 cm^{-1}(bs), 2920.2 cm^{-1}, 2954.9 cm^{-1}, 2918.3 cm^{-1}, 2875.9 cm^{-1}, 1710.8 cm^{-1}, 1662.6 cm^{-1}, 1626.0 cm^{-1}, 1429.3 cm^{-1}, 1234.4 cm^{-1}. mp: 225.0-227.0^{o}C.

9ae ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.31 (s, 9H), 1.44 (s, 9H), 4.05 (s, 2H), 5.81 (bs, 2H, D_2O exchangeable), 6.58 (s, 1H), 7.20-7.55 (m, 8H), 8.99 (s, 1H), 12.15 (bs, 1H, D_2O exchangeable), 13.32 (bs, 1H, D_2O exchangeable). ^{13}C-NMR (100MHz, DMSO-d^6): δ 168.2, 162.4, 160.5, 159.5, 145.7, 142.7, 141.4, 137.7, 137.5, 134.1, 133.0,

132.8, 131.8, 131.0, 130.6, 123.4, 121.8, 102.9, 40.0, 39.8, 38.9, 36.2, 34.2. Formula: $C_{30}H_{34}N_4O_2$. MS: 482.0. HRMS: found (482.2681), calc (482.2682). IR: 3491.2 cm^{-1}(bs), 3375.4 cm^{-1}, 2955.08 cm^{-1}, 2870.18 cm^{-1}, 2821.98 cm^{-1}, 1718.68 cm^{-1}, 1653.0 cm^{-1}, 1626.0 cm^{-1}, 1502.6 cm^{-1}, 1238.0 cm^{-1}. mp: 248.0-250.0^oC. **9ae** **^{15}N**: ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.31 (s, 9H), 1.44 (s, 9H), 4.04 (s, 2H), 5.81 (bs, 2H, D_2O exchangeable), 6.58 (s, 1H), 7.21-7.55 (m, 8H), 8.98 (d, 1H), 12.14 (bs, 1H, D_2O exchangeable), 13.32 (bs, 1H, D_2O exchangeable).

9af ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.18 (d, 6H), 1.26 (s, 9H), 1.28 (s, 9H), 4.00 (sept, 1H), 5.67 (bs, 2H), 6.59 (s, 1H), 7.40 (s, 1H), 7.54 (s, 1H), 7.58 (s, 1H), 9.04 (s, 1H), 12.06 (bs, 1H), 13.36 (bs, 1H). ^{13}C-NMR (100MHz, DMSO-d^6): δ 164.3, 159.6, 157.5, 155.1, 145.2, 140.7, 136.0, 133.0, 132.3, 128.2, 127.4, 124.8, 119.4, 117.6, 97.7, 35.1, 34.4, 31.8, 29.8, 20.8, 14.6. Formula: $C_{26}H_{34}N_4O_2$. MS (M+H): 434. HRMS: found (434.2675), calc (434.2682). IR: 3489.2 cm^{-1}(bs), 3387.0 cm^{-1}, 2958.88 cm^{-1}, 2910.68 cm^{-1}, 2870.18 cm^{-1}, 2819.98 cm^{-1}, 1739.88 cm^{-1}, 1651.1 cm^{-1}, 1620.2 cm^{-1}, 1502.6 cm^{-1}, 1240.1 cm^{-1}. mp: 275.0-276.0^oC (Color changed).

9ag ^{1}H-NMR (400 MHz DMSO-d^6): δ 0.94 (d, 6H), 1.32 (s, 9H), 1.44 (s, 9H), 2.20 (m, 1H), 2.59 (d, 2H), 5.76 (bs, 2H), 6.59 (s, 1H), 7.40 (s, 1H), 7.54 (s, 1H), 7.57 (s, 1H), 9.01 (s, 1H), 12.06 (bs, 1H), 13.36 (bs, 1H). ^{13}C-NMR (100MHz, DMSO-d^6): δ 164.4, 157.5, 155.8, 155.0, 145.3, 140.7, 136.0, 133.0, 132.4, 128.2, 127.5, 125.0, 119.4, 117.6, 97.7, 41.7, 35.1, 34.4, 31.8, 29.8, 26.7, 23.1. Formula: $C_{27}H_{36}N_4O_2$. MS (M+H): 448.0. HRMS: found (448.2839), calc (448.2838). IR: 3489.2 cm^{-1}(bs), 3400.5 cm^{-1}(bs),

2955.0 cm^{-1}, 2866.2 cm^{-1}, 2818.0 cm^{-1}, 1653.0 cm^{-1}, 1626.0 cm^{-1}, 1500.6 cm^{-1}, 1234.4 cm^{-1}. mp: >300.0°C.

9ah ^{1}H-NMR (250 MHz DMSO-d^6): δ 1.31 (s, 9H), 1.44 (s, 9H), 2.11 (s, 2H), 2.83 (t, 2H), 2.96 (t, 2H), 5.80 (bs, 2H), 6.59 (s, 1H), 7.40 (s, 1H), 7.56 (s, 1H), 7.70 (s, 1H), 8.99 (s, 1H), 12.12 (bs, 1H), 13.33 (bs, 1H). ^{13}C-NMR (62.5MHz, DMSO-d^6): δ 164.5, 157.5, 155.5, 153.8, 145.4, 140.7, 136.1, 133.2, 132.5, 128.2, 127.5, 125.0, 119.4, 117.6, 97.6, 35.1, 34.4, 32.8, 31.8, 30.8, 29.8, 15.2. Formula: $C_{26}H_{34}N_4O_2S$. MS (M+H): 467. HRMS: found (467.2475), calc (467.2480). IR: 3473.8 cm^{-1}(bs), 3333.0 cm^{-1}(bs), 2956.8 cm^{-1}, 2912.5 cm^{-1}, 2870.1 cm^{-1}, 1711.08 cm^{-1}, 1662.6 cm^{-1}, 1626.0 cm^{-1}, 1500.6 cm^{-1}, 1234.5 cm^{-1}. mp: 239.5-240.5°C.

9ai ^{1}H-NMR (400 MHz DMSO-d^6): δ 4.04 (s, 2H), 5.87 (bs, 2H, D_2O exchangeable), 6.57 (s, 1H), 6.78-7.34 (m, 8H), 7.49 (s, 1H), 8.94 (s, 1H), 9.26 (bs, 1H, D_2O exchangeable), 12.13 (bs, 1H, D_2O exchangeable), 12.47 (bs, 1H, D_2O exchangeable). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 162.6, 155.5, 154.0, 149.0, 146.0, 145.8, 138.8, 133.4, 132.8, 129.5, 128.7, 126.6, 124.9, 122.9, 120.8, 119.3, 119.2, 117.4, 97.5, 39.0. Formula: $C_{22}H_{18}N_4O_3$. MS (M+H): 387.0. HRMS: found (387.1452), calc (387.1457). IR: 3489.2 cm^{-1}(bs), 3429.4 cm^{-1}(bs), 3394.7 cm^{-1}(bs), 2941.4 cm^{-1}, 2877.8 cm^{-1}, 2818.0 cm^{-1}, 1656.8 cm^{-1}, 1626.0 cm^{-1}, 1500.6 cm^{-1}, 1465.9 cm^{-1}, 1275.0 cm^{-1}, 1236.4 cm^{-1}. mp: 260.0-261.0 °C.

9aj-1 ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 1.40 (s, 9H), 1.41(s, 9H), 3.87(s, 2H), 4.04(t, 1H), 6.37-7.50 (m, 8H), 8.78 (s, 1H), 8.84 (s, 1H), 10.49 (bs, 1H), 14.09 (bs, 1H), 14.16 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 166.0, 163.8, 161.2, 160.3, 160.0, 137.9, 137.0, 136.9, 135.7, 132.6, 131.6, 131.2, 130.0, 126.7, 119.7, 118.8, 105.5, 103.7, 60.2, 34.9, 29.7. Formula: $C_{30}H_{34}N_4O_3$. MS (M): 498.3. HRMS: found (498.2628), calc (498.2631). IR: 3386.9 cm^{-1}(bs), 2955.8 cm^{-1}, 2877.8 cm^{-1}, 2818.0 cm^{-1}, 1680.2 cm^{-1}, 1609.6 cm^{-1}, 1519.4 cm^{-1}, 1430.6 cm^{-1}, 1303.4 cm^{-1}, 1143.5 cm^{-1}. mp: 255.0-256.0 ^{o}C (Color changed).

9ak-1 ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 1.35 (s, 18H), 1.47 (s, 18H), 4.10 (s, 2H), 4.11 (t, 3H), 6.60 (s, 1H), 6.79 (s, 1H), 7.20-7.47 (m, 4H), 8.63 (s, 1H), 8.67 (s, 1H), 9.38 (bs, 1H), 13.55 (bs, 1H), 13.64 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 169.7, 163.2, 146.4, 145.3, 141.7, 133.1, 132.0, 123.1, 39.8, 38.9, 36.3, 34.2. Formula: $C_{38}H_{50}N_4O_3$. MS (M): 610.4. HRMS: found (610.3883), calc (610.3891). IR: 3489.2 cm^{-1}(bs), 3379.4 cm^{-1}(bs), 3232.1 cm^{-1}(bs), 2957.0 cm^{-1}, 2871.0 cm^{-1}, 2869.0 cm^{-1}, 1709.1 cm^{-1}, 1686.0 cm^{-1}, 1614.6 cm^{-1}, 1515.0 cm^{-1}, 1297.5 cm^{-1}, 1250.5 cm^{-1}. mp: 250.0-251.0 ^{o}C (Color Changed).

Preparation of asymmetric salqu ligands (8). (Table 5, Chapter 3)

This procedure is the same as that for preparing the 2-quinoxalinol imine (**9ax**); however, when diamino 2-quinoxalinol (**6**) can no longer be observed using TLC, a second 5 equivalents of the salicylaldehyde derivative **18'** (0.5mmol) can be added directly to the reaction mixture. The mixture was then allowed to heat at reflux

temperature for an additional 14 hours. This was found to result in a large quantity of precipitates. These precipitates were isolated by filtering, and then washed with 95% ethanol and ice cold acetone 5 times each. The pure products, asymmetric salqu ligands (**8**), were identified and characterized by NMR, IR, MS and HRMS. Two step yields of these range from 40.0-70.0%.

8a ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.31 (s, 9H), 1.36 (s, 9H), 1.42 (s, 9H), 4.18 (s, 2H) 6.90-7.56 (m, 11H), 7.97 (s, 1H), 8.94 (s, 1H), 9.13 (s, 1H), 13.49 (bs, 1H, D_2O exchangeable), 14.01 (bs, 1H, D_2O exchangeable) ^{13}C-NMR (100 MHz, DMSO-d^6): δ 167.1, 164.9, 160.4, 158.4, 145.0, 140.7, 138.2, 137.8, 137.2, 136.7, 131.7, 130.6, 129.6, 128.6, 128.1, 126.7, 119.6, 118.6, 118.3, 35.1, 34.9, 34.3, 31.7, 29.7, 29.6, 25.7. Formula: $C_{41}H_{46}N_4O_3$. MS (M^+): 642.0. HRMS: found (642.3559), calc (642.3570). IR: 3437.2 cm^{-1}(bs), 3423.7 cm^{-1}(bs), 2955.4 cm^{-1}, 2910.6 cm^{-1}, 2870.1 cm^{-1}, 1658.8 cm^{-1}, 1610.6 cm^{-1}, 1577.8 cm^{-1}, 1431.2.9 cm^{-1}, 1392.6.0 cm^{-1}, 1195.9 cm^{-1}, 1168.9 cm^{-1}. mp: 251.0-253.0 ^{o}C.

8b ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.38 (s, 9H), 4.17 (s, 2H), 6.88-7.88 (m, 13H), 7.96 (s, 1H), 8.90 (s, 1H), 9.11 (s, 1H), 12.12 (bs, 2H), 14.46 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 164.7, 164.2, 160.8, 160.5, 155.0, 146.2, 137.9, 137.3, 137.1, 134.4, 132.2, 132.0, 131.7, 131.1, 130.6, 129.7, 128.9, 126.9, 120.5, 119.7, 119.6, 118.7, 118.0, 117.0, 105.7. Formula: $C_{33}H_{30}N_4O_3$. MS (M^+): 387.0. HRMS: found (530.2320), calc (530.2318). IR: 3425.6 cm^{-1}(bs), 3147.8 cm^{-1}(bs), 3394.7 cm^{-1}(bs), 2920.2 cm^{-1}, 2864.3 cm^{-1}, 2785.2 cm^{-1}, 1660.7 cm^{-1}, 1608.6 cm^{-1}, 1483.3 cm^{-1}, 1384.9 cm^{-1}, 1201.7 cm^{-1}, 1147.7 cm^{-1}. mp: 239.0-241.0 ^{o}C.

8c ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 1.30 (s, 9H), 1.37 (s, 9H), 1.40 (s, 9H) 4.17 (s, 2H), 6.89-7.89 (m, 11H), 7.91 (s, 1H), 8.86 (s, 1H), 9.07 (s, 1H), 12.53 (bs, 1H), 13.65 (bs, 1H), 13.68 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 166.8, 166.7, 165.7, 160.7, 160.6, 160.4, 158.1, 154.9, 151.7, 144.6, 140.5, 138.4, 137.7, 137.2, 137.0, 136.3, 132.1, 131.8, 131.5, 131.2, 129.6, 128.7, 128.1, 127.9, 126.7, 119.6, 119.3, 118.9, 118.3, 105.9, 35.0, 34.9, 34.3, 31.9, 31.7, 29.6. Formula: $C_{41}H_{46}N_4O_3$. MS (M^+): 642.0. HRMS: found (642.3583), calc (642.3570). IR: 3373.5 cm^{-1}(bs), 2956.9 cm^{-1}, 2924.1 cm^{-1}, 2866.2 cm^{-1}, 1654.9 cm^{-1}, 1602.9 cm^{-1}, 1275.0 cm^{-1}, 1488.8 cm^{-1}, 1203.9 cm^{-1}, 1174.7 cm^{-1}. mp: 260.0-262.0 ^{o}C.

8d ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 1.17 (s, 9H), 1.25 (s, 9H), 1.29 (s, 9H), 2.04 (s, 3H), 2.87 (t, 2H), 3.08 (t, 2H), 6.70-7.54 (m, 7H), 8.52 (s, 1H), 8.61 (s, 1H), 12.13 (bs, 1H), 13.15 (bs, 1H), 13.50 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 165.8, 165.5, 164.2, 160.7, 159.9, 159.8, 158.5, 158.2, 155.3, 144.9, 144.6, 140.5, 140.4, 138.9, 138.6, 137.7, 137.0, 136.9, 131.5, 131.4, 131.2, 130.8, 128.7, 128.1, 127.0, 126.8, 118.8, 118.2, 105.6, 35.0, 34.8, 34.1, 33.1, 30.6, 29.3, 29.2, 15.4. Formula: $C_{37}H_{46}N_4O_3S$. MS (M^+): 626.0. HRMS: found (626.3279), calc (626.3291). IR: 3421.7 cm^{-1}(bs), 2953.0 cm^{-1}(bs), 2914.4 cm^{-1}(bs), 2862.4 cm^{-1}, 1656.9 cm^{-1}, 1610.6 cm^{-1}, 1577.8 cm^{-1}, 1431.2 cm^{-1}, 1313.5 cm^{-1}, 1267.2 cm^{-1}. mp: 244.0-245.0 ^{o}C (Color changed).

8e ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.38 (s, 9H), 2.15 (s, 3H), 2.94 (t, 2H), 3.13 (t, 2H), 6.89-7.99 (m, 9H), 8.92 (s, 1H), 9.13 (s, 1H), 11.99 (bs, 1H), 12.49 (bs, 1H),

14.47 (bs, 1H). ^{13}C-NMR (100 MHz, DMSO-d^6): δ 164.6, 164.1, 160.8, 160.5, 154.8, 146.0, 137.3, 137.1, 134.4, 132.1, 132.0, 131.7, 131.0, 130.6, 120.5, 119.7, 119.6, 118.7, 118.0, 117.0, 105.7, 34.9, 33.2, 30.5, 29.6, 15.2. Formula: $C_{29}H_{30}N_4O_3S$. MS (M^+): 514.0. HRMS: found (514.2039), calc (514.2039). IR: 3419.8 cm^{-1}(bs), 2914.4 cm^{-1}, 2864.3 cm^{-1}, 2787.1 cm^{-1}, 1658.8 cm^{-1}, 1608.6 cm^{-1}, 1483.3 cm^{-1}, 1392.6 cm^{-1}, 1207.4 cm^{-1}, 1143.8 cm^{-1}. mp: 229.0-230.0 ^{o}C (Color changed).

8f ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 0.92 (s, 9H), 1.01 (s, 9H), 1.04 (s, 9H), 1.80 (s, 3H), 2.62 (t, 2H), 2.82 (t, 2H), 6.46-7.31 (m, 7H), 8.28 (s, 1H), 8.40 (s, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 170.4, 170.3, 169.1, 168.6, 165.5, 165.3, 164.9, 163.0, 149.4, 149.3, 145.3, 143.7, 143.4, 142.5, 141.7, 138.9, 136.9, 136.4, 136.2, 135.9, 135.5, 135.3, 133.0, 131.8, 123.9, 123.7, 123.1, 122.7, 39.6, 39.0, 38.0, 37.9, 36.2, 35.4, 34.1, 34.0, 20.2. Formula: $C_{37}H_{46}N_4O_3S$. MS (M^+): 626.0. HRMS: found (626.3277), calc (626.3291). IR: 3466.1 cm^{-1}(bs), 3329.1 cm^{-1}(bs), 2955.0 cm^{-1}, 2899.0 cm^{-1}, 2873.9 cm^{-1}, 1662.6 cm^{-1}, 1618.3 cm^{-1}, 1492.9.6 cm^{-1}, 1427.3 cm^{-1}, 1236.4 cm^{-1}, 1205.5 cm^{-1}, 1172.7 cm^{-1}. mp: 240.0-241.0olor changed).

8g ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 0.92 (d, 6H), 1.22 (s, 9H), 1.30 (s, 9H), 1.32 (s, 9H), 2.24 (m, 1H), 2.69 (d, 2H), 6.74-7.58 (m, 7H), 8.58 (s, 1H), 8.66 (s, 1H). 13.23 (bs, 1H), 13.41(bs, 1H), 13.56 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 165.0, 164.0, 163.0, 160.5, 158.6, 155.7, 144.7, 144.5, 140.5, 138.6, 137.7, 137.6, 137.1, 131.4, 131.1, 130.9, 130.7, 130.5, 128.7, 127.1, 119.1, 118.9, 118.3, 118.1, 117.8, 105.6, 42.1, 35.0, 34.8, 34.1, 31.4, 29.4, 29.3, 26.7, 22.7. Formula: $C_{38}H_{48}N_4O_3$.

MS (M^+): 608.0. HRMS: found (608.3730), calc (608.3726). IR: 3421.7 cm^{-1}(bs), 2955.0 cm^{-1}(bs), 2910.6 cm^{-1}(bs), 2872.0 cm^{-1}, 1662.6 cm^{-1}, 1606.7 cm^{-1}, 1492.9 cm^{-1}, 1425.4 cm^{-1}, 1317.4 cm^{-1}, 1276.9 cm^{-1}, 1134.1 cm^{-1}, 1089.8 cm^{-1}. mp: 260.0-261.0 ^oC (Color changed).

8h ^{1}H-NMR (250 MHz DMSO-d^6): δ 0.98 (d, 6H), 1.37 (s, 9H), 2.27 (m, 1H), 2.70 (d, 2H), 6.86-7.98 (m, 9H), 8.90 (s, 1H), 9.12 (s, 1H). 12.36 (bs, 1H), 14.01(bs, 1H), 14.48 (bs, 1H). ^{13}C-NMR (62.5 MHz, DMSO-d^6): δ 164.5, 164.1, 161.9, 161.6, 160.8, 160.5, 155.2, 145.8, 144.5, 137.9, 137.2, 137.1, 137.0, 134.3, 132.2, 132.0, 131.6, 131.4, 131.1, 130.7, 130.6, 120.5, 119.7, 119.6, 119.4, 119.1, 118.9, 118.6, 118.1, 117.9, 117.0, 105.8, 42.1, 34.9, 29.7, 26.6, 23.1. Formula: $C_{20}H_{32}N_4O_3$. MS (M^+): 496.0. HRMS: found (496.2472), calc (496.2474). IR: 3435.2 cm^{-1}(bs), 3423.7 cm^{-1}(bs), 2953.0 cm^{-1}, 2916.4 cm^{-1}, 2868.2 cm^{-1}, 1656.9 cm^{-1}, 1610.6 cm^{-1}, 1473.6 cm^{-1}, 1431.2 cm^{-1}, 1392.6 cm^{-1}, 1276.8 cm^{-1}, 1193.9 cm^{-1}, 1143.8 cm^{-1}. mp: 271.0-273.0 ^oC (Color changed).

8i ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 0.91 (d, 6H), 1.22 (s, 9H), 1.28 (s, 9H), 1.32 (s, 9H), 2.23 (m, 1H), 2.69 (d, 2H), 6.73-7.58 (m, 7H), 8.58 (s, 1H), 8.66 (s, 1H). 13.22 (bs, 1H), 13.41(bs, 1H), 13.56 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 165.9, 165.2, 163.7, 161.8, 161.6, 160.7, 158.6, 155.7, 144.7, 144.4, 140.5, 138.6, 137.7, 137.6, 137.1, 131.4, 131.1, 131.0, 130.9, 130.7, 130.5, 128.7, 127.1, 119.1, 118.9, 118.3, 118.1, 117.7, 105.5, 42.1, 35.0, 34.8, 34.7, 31.4, 29.3, 29.2, 26.8, 22.7. Formula: $C_{38}H_{48}N_4O_3$. MS (M^+): 608.0. HRMS: found (608.3721), calc (608.3726). IR:

3500.0 cm^{-1}(bs), 2955.0 cm^{-1}(bs), 2912.5 cm^{-1}(bs), 2872.0 cm^{-1}, 1662.6 cm^{-1}, 1604.8 cm^{-1}, 1492.9 cm^{-1}, 1431.2 cm^{-1}, 1356.6 cm^{-1}, 1207.4 cm^{-1}, 1138.0 cm^{-1}. mp: 264.0-266.0 °C.

8j ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 1.21 (d, 6H), 1.30 (s, 9H), 1.33 (s, 9H), 1.34 (s, 9H), 3.49 (m, 1H), 6.74-7.61 (m, 7H), 8.57 (s, 1H), 8.68 (s, 1H). 12.05 (bs, 1H), 13.22 (bs, 1H), 13.58 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 165.4, 163.5, 160.7, 160.5, 158.6, 158.1, 155.1, 144.7, 144.4, 140.5, 138.5, 137.8, 137.6, 137.1, 131.5, 131.3, 131.0, 130.9, 130.7, 130.4, 128.7, 127.1, 119.1, 118.9, 118.3, 118.2, 118.1, 117.9, 105.4, 35.0, 34.8, 34.1, 31.4, 30.3, 29.4, 29.3, 20.2. Formula: $C_{37}H_{46}N_4O_3$. MS (M^+): 594.0. HRMS: found (594.3566), calc (594.3570). IR: 3415.9 cm^{-1}(bs), 3138.2 cm^{-1}(bs), 2955.0 cm^{-1}, 2872.0 cm^{-1}, 2792.9 cm^{-1}, 1664.6 cm^{-1}, 1606.7 cm^{-1}, 1489.1 cm^{-1}, 1479.4 cm^{-1}, 1211.3 cm^{-1}, 1184.3 cm^{-1}. mp: 269.0-271.0 °C.

8k ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 1.27 (d, 6H), 1.38 (s, 9H), 3.51 (m, 1H), 6.89-7.99 (m, 9H), 8.91 (s, 1H), 9.16 (s, 1H). 12.06 (bs, 1H), 12.43 (bs, 1H), 14.52 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 164.6, 164.1, 161.0, 160.9, 160.6, 160.5, 154.6, 145.9, 137.2, 137.1, 134.4, 133.1, 132.0, 131.7, 131.0, 130.6, 120.6, 120.1, 119.7, 119.6, 119.5, 118.7, 118.1, 117.9, 117.2, 117.0, 105.6, 34.9, 30.4, 29.6, 20.6. Formula: $C_{29}H_{30}N_4O_3$. MS (M^+): 482.0. HRMS: found (482.2313), calc (482.2318). IR: 3448.7 cm^{-1}(bs), 3145.9 cm^{-1}(bs), 2958.8 cm^{-1}, 2870.1 cm^{-1}, 2794.9 cm^{-1}, 1658.8 cm^{-1}, 1610.6 cm^{-1}, 1481.3 cm^{-1}, 1384.9 cm^{-1}, 1207.4 cm^{-1}, 1147.7 cm^{-1}. mp: 265.0-267.0 °C.

8l ^{1}H-NMR (400 MHz $CDCl_3$ and DMSO-d^6): δ 1.19-1.30 (m, 33H), 3.47 (m, 1H), 6.72-7.59 (m, 7H), 8.57 (s, 1H), 8.67 (s, 1H). 12.02 (bs, 1H), 13.35 (bs, 1H), 13.43 (bs, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$ and DMSO-d^6): δ 166.0, 165.4, 164.2, 160.7, 158.3, 155.0, 144.3, 140.4, 138.8, 137.7, 136.9, 131.5, 131.1, 131.0, 130.8, 128.1, 126.9, 118.9, 118.3, 118.2, 117.9, 105.5, 34.9, 34.7, 34.1, 31.3, 30.3, 29.3, 29.2, 20.1. Formula: $C_{37}H_{46}N_4O_3$. MS (M^+): 594.0. HRMS: found (594.3572), calc (594.3570). IR: 3417.9 cm^{-1}(bs), 3142.0 cm^{-1}(bs), 2956.9 cm^{-1}, 2877.8 cm^{-1}, 2868.2 cm^{-1}, 1656.9 cm^{-1}, 1606.7 cm^{-1}, 1469.8 cm^{-1}, 1433.1 cm^{-1}, 1209.4 cm^{-1}, 1172.7 cm^{-1}. mp: 258.0-260.0 ^{o}C.

Preparation of symmetric salqus copper complexes 10xyCu. (Table 6, Chapter 4)

To a 5mL DCM or DMF solution of symmetric salqu ligands (**7**, 0.05 mmol) (if salqu ligands contain *tert*butyl group, DCM were used as solvent otherwise DMF as solvent), 5 mL MeOH and metal acetate ($Cu(OAc)_2 \bullet H_2O$, 0.06 mmol, 11.98mg) was added and stirred at reflux temperature for two hours. The reaction solution changes to deep dark from bright yellow. The solution was concentrated and washed with 95% EtOH or ether to obtain **10xyCu** with a yield of no less than 82.0%.

10adCu: IR: 3067, 2955, 1661, 1586, 1528, 1491, 1416, 1377, 1260, 1209, 1173, 1130 cm^{-1}. MS: 760.0 (M+H); HRMS: found (760.3413); calc (760.3422). UV-Vis (DCM): 286 nm ($\varepsilon = 6.13\times10^4$), 330.0 nm ($\varepsilon = 7.54\times10^4$), 458.0 nm ($\varepsilon = 9.14\times10^4$). DMSO: 280.0 nm ($\varepsilon = 3.4\times10^4$), 325.0 nm ($\varepsilon = 2.8\times10^4$), and 454.0 nm ($\varepsilon = 1.5\times10^4$).

10aeCu: MS: 536.1 (M+H); HRMS: found (536.0912); calc (536.0909).

Preparation of symmetric salqus uranyl complexes 10xyU. (Table 7, Chapter 4)

To a 5mL DCM or DMF solution of symmetric salqu ligands (**7**, 0.05 mmol), (if salqu ligands contain *tert*butyl group, DCM were used as solvent otherwise DMF as solvent), 5 mL MeOH and uranyl acetate ($UO_2(OAc)_2 \bullet 2H_2O$, 0.06 mmol, 25.5 mg) was added and stirred at room temperature for two hours. The reaction solution becomes deep red from bright yellow. The solution was concentrated and washed with 95% EtOH to obtain **10xyU** with yield no less than 80.0%.

10aaU: ^{1}H-NMR (400 MHz DMSO-d^6): δ 4.22 (s, 2H), 6.54-8.67 (m, 13H), 9.55 (s, 1H), 9.71 (s, 1H), 11.77 (bs, 1H), 11.82 (bs, 1H), 12.69 (bs, 1H). IR: 3397 cm^{-1}, 3337 cm^{-1}, 2965 cm^{-1}, 1657 cm^{-1}, 1620 cm^{-1}, 1582 cm^{-1}, 1545 cm^{-1}, 1491 cm^{-1}, 1445 cm^{-1}, 1204 cm^{-1}, 903 cm^{-1}. MS: 816.2 (M+H+CH_3CN); HRMS: found (816.2178); cal (816.2183). UV-Vis (DMF): 365.0 nm ($\varepsilon = 1.10\times10^4$), 450 nm.

10abU: MS: 816.0 (M+H); HRMS: found (816.2186); calc (816.218).

10adU: ^{1}H-NMR (400 MHz DMSO-d6): δ 1.19 (s, 18H), 1.64 (s, 18H), 4.11 (s, 2H), 7.09-7.63 (m, 10H), 7.70(s, 1H), 9.19 (s, 1H), 9.32 (s, 1H), 12.18 (bs, 1H). IR: 3433 cm^{-1}, 2957 cm^{-1}, 1655 cm^{-1}, 1620 cm^{-1}, 1383 cm^{-1}, 1283 cm^{-1}, 1229 cm^{-1}, 1153 cm^{-1}, 937

cm^{-1}, 760 cm^{-1}. MS: 967.4 (M+H); HRMS: found (967.4514); calc (967.4524). UV-Vis (DMSO): 295.0 nm ($\varepsilon = 2.5\times10^4$), 375.0 nm ($\varepsilon = 1.6\times10^4$), and 440.0 nm ($\varepsilon = 1.5\times10^4$).

10aeU: ^{1}H-NMR (400 MHz DMSO-d^6): δ 4.20 (s, 2H), 6.73-6.77 (t, 2H), 7.00-7.04 (t, 2H), 7.24-7.88 (m, 10H), 8.12(s, 1H), 9.60 (s, 1H), 9.76 (s, 1H), 12.67 (bs, 1H). IR: 3397 cm^{-1}, 3337 cm^{-1}, 2965 cm^{-1}, 1657 cm^{-1}, 1620 cm^{-1}, 1582 cm^{-1}, 1545 cm^{-1}, 1491 cm^{-1}, 1445 cm^{-1}, 1204 cm^{-1}, 1144 cm^{-1}, 1040 cm^{-1}. MS: 784.0 (M+H+CH3CN); HRMS: found (784.2280); calc (784.2285). UV-vis (DMSO): 290 nm ($\varepsilon = 2.0\times10^4$), 370 nm ($\varepsilon = 1.5\times10^4$), 440nm ($\varepsilon = 1.5\times10^4$).

10bdU: ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.22 (d, 6H), 1.26 (s, 18H), 1.69 (s, 18H), 3.50 (m, 1H), 7.26-7.80 (m, 6H), 9.30 (s, 1H), 9.46 (s, 1H), 12.28 (bs, 1H). IR: 3444 cm^{-1}, 2958 cm^{-1}, 1710 cm^{-1}, 1666 cm^{-1}, 1587 cm^{-1}, 1423 cm^{-1}, 1371 cm^{-1}, 1224 cm^{-1}, 898 cm^{-1}. MS: 919.2 (M+H); HRMS: found (919.4514); calc (919.4524).

10beU: ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.28 (d, 6H), 3.56 (m, 1H), 6.74-8.17 (m, 10H), 9.61 (s, 1H), 9.81 (s, 1H), 12.58 (bs, 1H). IR: 3406 cm^{-1}, 2966 cm^{-1}, 1654 cm^{-1}, 1602 cm^{-1}, 1539 cm^{-1}, 1463 cm^{-1}, 1400 cm^{-1}, 1384 cm^{-1}, 1145 cm^{-1}, 898 cm^{-1}. MS: 736.2 (M+H); HRMS: found (736.2280); calc (736.2285). UV-Vis (DMF): 287nm (ε = 1.7×104), 304nm (ε = 1.6×104), 360nm ($\varepsilon = 1.3\times10^4$), 385nm ($\varepsilon = 1.3\times10^4$), 419nm ($\varepsilon = 1.4\times10^4$).

10cbU: MS: 782.2 (M+H+CH3CN); HRMS: 782.2343 (obs); 782.2340 (cal).

10ceU: ^{1}H-NMR (400 MHz DMSO-d^6): δ 1.00 (d, 6H), 2.28 (m, 1H), 2.74 (d, 2H), 6.75 (t, 2H), 7.03 (t, 2H), 7.44 (s, 1H), 7.65 (m, 2H), 7.87 (t, 2H), 8.19 (s, 1H), 9.61 (s, 1H), 9.78 (s, 1H), 12.54 (bs, 1H). IR: 3395 cm^{-1}, 2927 cm^{-1}, 1637 cm^{-1}, 1606 cm^{-1}, 1539 cm^{-1}, 1463 cm^{-1}, 1435 cm^{-1}, 1383 cm^{-1}, 1282 cm^{-1}, 937 cm^{-1}. MS: 709.2 (M+H); HRMS: found (709.2167); calc (709.2176).

10deU: ^{1}H-NMR (400 MHz DMSO-d^6): δ 2.15 (s, 3H), 2.96 (t, 2H), 3.16 (t, 2H), 6.75 (t, 2H), 7.03 (t, 2H), 7.46 (s, 1H), 7.66 (m, 2H), 7.87 (t, 2H), 8.19 (s, 1H), 9.62 (s, 1H), 9.78 (s, 1H), 12.64 (bs, 1H). IR: 3408 cm^{-1}, 1655 cm^{-1}, 1637 cm^{-1}, 1601 cm^{-1}, 1583 cm^{-1}, 1537 cm^{-1}, 1464 cm^{-1}, 1440 cm^{-1}, 1382 cm^{-1}, 1300 cm^{-1}, 1199 cm^{-1}, 1150 cm^{-1}, 897 cm^{-1}, 760 cm^{-1} . MS: 768.2 (M+H); HRMS: found (768.2013); calc (768.2006).

11bU: MS: 799.0 (M+H); HRMS: 799.2645 (obs); 709.2646 (cal).

Preparation of symmetric salqus cobalt complexes (10xyCo). (Table 8, Chapter 4)

To a 5mL DCM or DMF solution of symmetric salqu ligands (**7**, 0.05 mmol), (if salqu ligands contain *tert*butyl group, DCM were used as solvent otherwise DMF as solvent), 5 mL MeOH and cobalt acetate ($Co(OAc)_2 \bullet 4H_2O$, 0.06 mmol, 14.95mg) was added and stirred at reflux temperature for two hours. The reaction solution becomes blood red from bright yellow. The solution was concentrated and washed with 95% EtOH or ether to obtain **10xyCo** with yield no less than 80.0%.

10adCo: IR: 3066, 2957, 1665, 1614, 1572, 1524, 1501, 1462, 1410, 1256, 1180, 1128 cm^{-1}. MS: 755.3 (M+H); HRMS: found (755.3369); calc (755.3372). UV-Vis (DCM): 322.0 nm ($\varepsilon = 6.15\times10^4$), 437.0 nm ($\varepsilon = 7.08\times10^4$).

Preparation of symmetric salqus manganese complexes (10xyMn). (Table 8, Chapter 4)

To a 5mL DCM or DMF solution of symmetric salqu ligands (**7**, 0.05 mmol), (if salqu ligands contain *tert*butyl group, DCM were used as solvent otherwise DMF as solvent), 5 mL MeOH and manganese acetate ($Mn(OAc)_2\bullet4H_2O$, 0.06 mmol, 14.71mg) was added and stirred at reflux temperature for two hours. The reaction solution becomes dark from bright yellow. The solution was concentrated and washed with 95% EtOH or ether to obtain **10xyMn** with yield no less than 80.0%.

10adMn: IR: 3385, 3248, 3208, 2955, 2911, 1670, 1582, 1532, 1462, 1416, 1317, 1248, 1177, 1130 cm^{-1}. MS: 751.3 (M+H); HRMS: found (751.3420); calc (751.3429). UV-Vis (DCM): 372.0 nm ($\varepsilon = 4.06\times10^4$), 510.0 nm, ($\varepsilon = 7.13\times10^4$).

11bMn: MS: 583.0 (M+H); HRMS: 583.1531 (obs); 583.1542 (cal).

Preparation of symmetric salqus nickel complexes (10xyNi). (Table 8, Chapter 4)

To a 5mL DCM or DMF solution of symmetric salqu ligands (**7**, 0.05 mmol), (if salqu ligands contain *tert*butyl group, DCM were used as solvent otherwise DMF as solvent), 5 mL MeOH and nickel acetate ($Ni(OAc)_2 \bullet 4H_2O$, 0.06 mmol, 14.93mg) was added and stirred at reflux temperature for two hours. The reaction solution becomes red from bright yellow. The solution was concentrated and washed with 95% EtOH or ether to obtain **10xyNi** with yield no less than 90.0%.

10adNi: IR: 3067, 2955, 2870, 1665, 1616, 1584, 1533, 1598, 1464, 1414, 1379, 1260, 1182, 1130 cm^{-1}. MS: 755.3 (M+H); HRMS: found (755.3461); calc 755.3471. UV-Vis (DCM): 268.0 nm ($\varepsilon = 4.66\times10^4$), 314.0 nm ($\varepsilon = 4.81\times10^4$), 388.0 nm ($\varepsilon = 5.78\times10^4$), 452.0 nm ($\varepsilon = 9.24\times10^4$).

Preparation of symmetric salqus palladium complexes (10adPd, 10aePd). (Table 8, Chapter 4)

To a 5mL DCM solution of symmetric salqu ligands (**7ad**, 0.05 mmol, 35.00mg), 5 mL MeOH and palladium acetate ($Pd(OAc)_2$, 0.06 mmol, 13.47mg) was added and stirred at reflux temperature for two hours. The reaction solution becomes orange from bright yellow. Finally, there are a lot of orange solids that precipitate out. The solution was filtered and washed with ether to obtain **10adPd** with 92.0% yield.

To a 5mL DMF solution of symmetric salqu ligands (**7ae**, 0.05 mmol), 5 mL MeOH and palladium acetate ($Pd(OAc)_2$, 0.06 mmol, 13.47mg) was added and stirred at

reflux temperature for two hours. The reaction solution becomes deep orange from bright yellow. Finally, there are a lot of orange solids that precipitate out. The solution was filtered and washed with 95% EtOH to obtain **10aePd** with 86.0% yield.

Preparation of symmetric salqus iron complexes (10aaFe, 10aeFe). (Table 8, Chapter 4)

To a 5mL DMF solution of symmetric salqu ligands (**7aa**, 0.05 mmol, 25.33mg), 5 mL MeOH and ferrous chloride ($FeCl_2 \bullet 4H_2O$, 0.06 mmol, 11.93mg) was added and stirred at reflux temperature for two hours. The reaction solution becomes black from bright yellow. The solution was concentrated and washed with 95% EtOH to obtain 10aaFe with 95.0%.

To a 5mL DMF solution of symmetric salqu ligands (**7ae**, 0.05 mmol, 23.73mg), 5 mL MeOH and ferrous chloride ($FeCl_2 \bullet 4H_2O$, 0.06 mmol, 11.93mg) was added and stirred at reflux temperature for two hours. The reaction solution becomes black from bright yellow. Finally, there are a lot of black solids that precipitate out. The solution was filtered and washed with 95% EtOH to obtain **10aeFe** with 87.4%.

Preparation of symmetric salqus magnesium complexes (10adMg, 10bdMg, 10ceMg).

To a 5mL DCM solution of symmetric salqu ligands (**7ad,** 0.05 mmol, 35.00mg), 5 mL MeOH and magnesium acetate ($Mg(OAc)_2 \bullet 4H_2O$, 0.06 mmol, 12.87mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not

change. TLC show that the starting materials, symmetric salqu ligands **7ad**, was still in the reaction solution. **7ad** finally were separated to be proved by ^{1}HNMR.

To a 5mL DCM solution of symmetric salqu ligands (**7bd,** 0.05 mmol, 32.55mg), 5 mL MeOH and magnesium acetate ($Mg(OAc)_2 \bullet 4H_2O$, 0.06 mmol, 12.87mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that the starting materials, symmetric salqu ligands **7bd**, was still in the reaction solution.

To a 5mL DMF solution of symmetric salqu ligands (**7ce,** 0.05 mmol, 22.03mg), 5 mL MeOH and magnesium acetate ($Mg(OAc)_2 \bullet 4H_2O$, 0.06 mmol, 12.87mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that the starting materials, symmetric salqu ligands **7ce**, was still in the reaction solution.

Preparation of symmetric salqus zinc complexes (10adZn, 10aeZn, 10daZn).

To a 5mL DCM of symmetric salqu ligands (**7ad**, 0.05 mmol, 35.00mg), 5 mL MeOH and zinc acetate ($Zn(OAc)_2 \bullet 2H_2O$, 0.06 mmol, 13.64mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that only starting materials, symmetric salqu ligands **7ad**, was still in the reaction solution. **7ad** finally were separated to be proved by ^{1}HNMR.

To a 5mL DMF solution of symmetric salqu ligands (**7ae**, 0.05 mmol, 23.73mg), 5 mL MeOH and zinc acetate ($Zn(OAc)_2 \bullet 2H_2O$, 0.06 mmol, 13.64mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change.

TLC show that only starting materials, symmetric salqu ligands **7ae**, was still in the reaction solution.

To a 5mL DMF solution of symmetric salqu ligands (**7da**, 0.05 mmol, 24.53mg), 5 mL MeOH and zinc acetate ($Zn(OAc)_2 \bullet 2H_2O$, 0.06 mmol, 13.64mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that only starting materials, symmetric salqu ligands **7da**, was still in the reaction solution.

Preparation of symmetric salqus zinc complexes (10adZn).

To a 5mL DCM solution of symmetric salqu ligands (**7ad**, 0.05 mmol, 35.00mg), 5 mL MeOH and zinc chloride ($ZnCl_2$, 0.06 mmol, 8.18mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that only starting materials, symmetric salqu ligands **7ad**, was still in the reaction solution. **7ad** finally were separated to be proved by ^{1}HNMR.

Preparation of symmetric salqus gadolinium (III) complexes (10adGa, 10cbGa).

To a 5mL DCM solution of symmetric salqu ligands (**7ad**, 0.05 mmol, 35.00mg), 5 mL MeOH and gadolinium (III) chloride hydrate (0.06 mmol, 15.82mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that only starting materials, symmetric salqu ligands **7ad**, was still in the reaction solution. **7ad** finally were separated to be proved by ^{1}HNMR.

To a 5mL DMF solution of symmetric salqu ligands (**7cb**, 0.05 mmol, 23.63mg), 5 mL MeOH and gadolinium (III) chloride hydrate (0.06 mmol, 15.82mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that only starting materials, symmetric salqu ligands **7cb**, was still in the reaction solution.

Preparation of symmetric salqus cerium complexes (10adCe, 10aeCe).

To a 5mL DCM solution of symmetric salqu ligands (**7ad**, 0.05 mmol, 35.00mg), 5 mL MeOH and cerium (III) acetate hydrate (0.06 mmol, 19.04mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that only starting materials, symmetric salqu ligands **7ad**, was still in the reaction solution. **7ad** finally were separated to be proved by ^{1}HNMR.

To a 5mL DMF solution of symmetric salqu ligands (**7ae**, 0.05 mmol, 23.73mg), 5 mL MeOH and cerium (III) acetate hydrate (0.06 mmol, 19.04mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change. TLC show that only starting materials, symmetric salqu ligands **7ae**, was still in the reaction solution.

Preparation of symmetric salqus cerium complexes (10adCe).

To a 5mL DCM solution of symmetric salqu ligands (**7ad**, 0.05 mmol, 35.00mg), 5 mL MeOH and cerium (III) chloride hydrate (0.06 mmol, 15.82mg) was added and stirred at reflux temperature for 24 hours. The reaction solution color does not change.

TLC show that only starting materials, symmetric salqu ligands **7ad**, still in the reaction solution.

Crystal growth of salqu uranyl complexes 10aeU, 10aaU, 10beU and 10ceU. (Figure 12, 13 Chapter 4)

Crystals of salqu uranyl complexes **10aeU**, **10aaU**, **10beU** and **10ceU** were obtained in good yield from slow diffusion of diethyl ether into a saturated dimethyl formamide solution of salqu uranyl complexes at room temperature for one or two weeks. (Crystallographic data for salqu uranyl complexes see **Table 11**, **12 Chapter 4**)

Crystal growth of salqu uranyl complexes 10adU and 10bdU. (Figure 12, 13 Chapter 4)

Crystals of **10adU** and **10bdU** were grown by layering a saturated aqueous solution of uranyl acetate salt with a saturated acetone solution of salqu lignads **7ad** and **7bd** at room temperature for one or two weeks. (Crystallographic data for salqu uranyl complexes see **Table 11**, **12 Chapter 4**)

Preparation of solid phase salqu lignads 12-1 and 12-2. (Scheme 4, Chapter 5)

To a DCM solution of (PS) aminomethyl resin (0.1mmol), add glutaric anhydride (0.5 mmol) at room temperature reacts for 24 hours. Beads were on ninhydrin test, negative result will indicate 100.0% loading. After acylation of amino of resins was completed, the resin was washed with DCM, DMF and MeOH three times each. These were dried under vacuum for 1 day. Resin PL can be further acylation with 0.15mol

ligand **7cd** using 0.22 mmol 4-dimethyl-aminopyridine (DMAP) and 0.22 mmol *N,N'*-diisopropyl-carbodiimide (DIC) in the anhydrous DMF at room temperature for three days. Resins were then washed by DCM, DMF and MeOH three times each. Vacuum drying 1 day is needed for extraction test. IR of **12-1** and **12-2**: 3381.2, 1658.8, 1622.3, 1577.8, 1489.1, 1278.8 cm^{-1}.

Recovery of salqu Cu complexes 13-1Cu and 13-2Cu. (Scheme 4, Chapter 5)

20mg **13-1Cu** and **13-2Cu** resins were mixed with DCM/CH_3COOH (2:1) 3ml, 10mg sodium triacetoxyborohydride was added to keep reacting for 4 hours. The maximum amount of Cu^{2+} can be recovered (70.0%, determined by Atomic Absorption spectroscopy).

Method 1: application of salqu complexes as catalysts. (Table 14, Chapter 6)

The synthesis of products in **table 14**, **chapter 6** begins with the mixture of catalyst **10adCu** (0.02 mmol, 15.2mg), 2 mmol of starting materials (aryl methylene compounds) dissolved in 2 mL acetonitrile and 1mL *tert*-butylhydroperoxide decane solution (6 mmol). This solution was allowed to stir for 18 hours heated to 70^{o}C and monitored by TLC. Once starting material can no longer be seen by TLC, the reaction is considered complete. Pure products are obtained using flash column chromatography with a solution of hexane:ethyl acetate, 10-20:1 as eluent. The yields of final pure products are from 45.0-99.0%.

Method 2: application of salqu complexes as catalysts. (Table 14, Chapter 6)

For lower yielding products, a somewhat modified procedure begins with of the addition of catalyst **10adCu** (0.02mmol, 15.2mg) and 2.0mmol of starting materials (aryl methylene compounds) dissolved in 2.0mL acetonitrile and 1.0mL *tert*-butylhydroperoxide decane solution (6.0mmol). This reaction mixture is allowed to stir for 18 hours at 70^{o}C. After 18 hours, an additional 1.0mL *tert*-butylhydroperoxide decane solution (6.0mmol) is added and the solution is heated at reflux temperature for another 18 hours and monitored by TLC. Once the starting material can no longer be seen by TLC, the reaction is considered complete. Pure products are obtained by purification using flash column chromatography with a solution of hexane : ethyl acetate, 10-20:1 as eluent. The yields of final pure products are from 65.0-92.0%.

20 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.49 (t, 4H), 7.62 (t, 2H), 7.84 (d, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 196.8, 137.6, 132.5, 130.1, 128.3.

22 N-benzylidenebenzylamine: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.87 (s, 2H), 7.28-7.93 (m, 10H), 8.43 (s, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 162.5, 139.0, 136.4, 134.5, 130.9, 130.6, 64.9.

Benzaldehyde: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.50 (t, 2H), 7.60 (t, 1H), 7.86 (d, 2H), 10.01 (s, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 191.9, 136.0, 134.0, 129.3, 128.6.

24 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.91 (s, 3H), 7.43 (t, 2H), 7.53 (t, 1H), 8.05 (d, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 167.1, 132.9, 130.2, 129.6, 128.4, 128.2, 126.9, 52.0.

26 ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.71 (s, 3H), 8.15 (d, 2H), 8.35 (d, 2H). ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 196.3, 141.4, 129.3, 123.9, 27.0.

28 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.43 (t, 3H), 4.60 (q, 2H), 7.53 (t, 2H), 7.67 (t, 1H), 8.01 (d, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 186.5, 163.9, 134.9, 132.4, 130.0, 128.9, 62.4, 14.1.

30 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.02 (t, 3H), 1.97 (m, 2H), 2.96 (t, 2H), 7.46 (t, 2H), 7.53 (t, 1H), 7.96 (d, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 200.4, 137.1, 132.9, 128.4, 128.2, 128.0, 40.5, 27.2, 13.9.

32 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.50 (t, 4H), 7.62 (t, 2H), 7.85 (d, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 196.8, 137.6, 132.4, 130.1, 128.3.

34 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.57 (s, 3H), 7.49 (t, 2H), 7.60 (t, 1H), 7.94 (d, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 198.4, 137.3, 133.6, 129.1, 128.6, 27.2.

36 ^{1}H-NMR (400 MHz $CDCl_3$): δ 7.50 (t, 2H), 7.60 (t, 1H), 7.86 (d, 2H), 10.01 (s, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 191.9, 136.0, 134.0, 129.3, 128.6.

39 ^{1}H-NMR (400 MHz, DMSO-d^{6}): δ 7.02 (s, 2H), 7.80 (dd, 2H), 8.13 (dd, 2H). ^{13}C-NMR (100 MHz, DMSO-d^{6}): δ 185.1, 138.7, 134.0, 131.9, 126.5.

41 ^{1}H-NMR (250 MHz, $CDCl_3$): δ 2.71 (s, 3H), 7.56 (m, 2H), 7.62 (m, 4H), 8.05 (s, 1H). ^{13}C-NMR (62.5 MHz, $CDCl_3$): δ 198.1, 135.6, 134.4, 132.5, 130.2, 129.6, 128.5, 128.4, 127.8, 126.8, 123.9.

53 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.57-7.96 (m, 5H), 8.54 (d, 1H), 9.27 (s, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 152.5, 142.9, 135.8, 130.4, 127.6, 127.3, 126.5, 120.5.

55 ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.29 (m, 1H), 7.47 (t, 1H), 7.63 (t, 1H), 7.73 (d, 1H), 8.06 (m, 2H), 8.60 (m, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 150.3, 148.2, 136.0, 129.4, 128.2, 127.8, 126.5, 121.0.

Calculation Section (Table 3, Chapter 3)

Calculations were run using Gaussian 03 at Alabama super computer system. The density functional theory method B3LYP/6-31G(d) was used to characterize intermediates **(6)** and 2-quinoxalinol imines (**9a**) and ground states in vacuum using Gaussian 03. Calculations using B3LYP/6-31G(d) were used for geometry optimizations and the calculation of vibrational frequencies, which confirmed all stationary points as minima and provided thermodynamic corrections. The effect of methanol was

approximated by subsequent single-point calculations using the conductor-like polarizable continuum model (CPCM). The default Gaussian 03 dielectric constant of 32.63 was used for methanol. Partial charges for the intermediate **(6)** and 2-quinoxalinol imines (**9a**) were obtained using CHELPG method.

Calculation data was shown onto the support information of The Journal of Organic Chemistry article.

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