A NOVEL FLUOROUS BIPHASIC SYSTEM: WERNER-TYPE COMPLEXES IN FLUOROUS MEDIA

A Thesis

by

ANN R. SULLIVAN

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

December 2011

Major Subject: Chemistry

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Approved by:

Chair of Committee,	John A. Gladysz
Committee Members,	David E. Bergbreiter
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ABSTRACT

A Novel Fluorous Biphasic System: Werner-Type Complexes in Fluorous Media.
(December 2011)
Ann R. Sullivan, B.S., Lyon College
Chair of Advisory Committee: Dr. John A. Gladysz

Fluorous chemistry has seen a number of advances since its birth in the early 1990s. One of the most attractive characteristics of fluorous solvents is their unique solubility properties depending on temperature. This phenomenon has led to the development of a wide range of catalysts that are modified with fluorous tags and are used in biphasic catalysis and easily recovered.

Many fluorous phase transfer catalysts are confined to bringing small ions into fluorous media by using fluorous onium or crown ether vehicles. The most popular method to bring transition metal complexes into fluorous media is quite limited, usually resulting in ligand tuning and thus a change in reactivity at the metal center. This can be circumvented by pairing a cationic transition metal with a highly fluorous anion rendering the neutral species highly fluorophilic. To achieve this goal, we chose to use fluorous BAr_{f6}, $[B(3,5\text{-}C_6H_3(R_{f6})_2)_4]^-$, as the mode of transport and pair it with classic Werner-type complexes that recently have been shown act as organocatalysts in enantioselective Michael additions.

The literature synthesis of $Na[B(3,5\text{-}C_6H_3(R_{f6})_2)_4]$ (**3**) was improved and through salt metathesis two new fluorophilic salts were made. The Werner-type trication $[Co(en)_3]^{3+}$ was solubilized in PFMC (perfluoromethylcyclohexane) to generate $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ (**4**). This fluorophilic salt was found to be preferentially soluble in fluorous media with a partition coefficient in PFMC/H_2O of 99.0:1.0 and in PFMC/$CH_3C_6H_5$ of >99.3:<0.7. Another Werner-type trication, $[Co(R,R\text{-chxn})_3]^{3+}$, was also paired with $[B(3,5\text{-}C_6H_3(R_{f6})_2)_4]^-$ to afford $[Co(R,R\text{-chxn})_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ (**5**), whose partition coefficients in PFMC/H_2O and PFMC/$CH_3C_6H_5$ were the same as **4**.

Within the scope of Werner-type complexes, this work constitutes a significant stride toward developing a series of compounds that bring the concept of organocatalysis into fluorous media. The new compounds **3-5** show high preferences for the fluorous phase and provide a baseline for future Werner-type salt metathesis with fluorous BAr_{f6}.

ACKNOWLEDGEMENTS

I would like to thank my committee chair, Dr. Gladysz, and my committee members, Dr. Bergbreiter, Dr. Darensbourg, and Dr. Loving, for their guidance and support throughout the course of this research.

Thanks also go to my friends and colleagues within the department for their time and advice. Finally, thanks to my family for their encouragement and to Eric for his patience and love.

NOMENCLATURE

BAr_f	$[B(3,5\text{-}C_6H_3(CF_3)_2)_4]^-$
bipy	2,2'-bipyridine
br	broad (NMR)
chxn	trans-1,2-cyclohexanediamine
d	day
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
en	ethylene diamine
eq.	equivalents
FBS	fluorous biphasic system
FC-70	perfluorotripentylamine
FC-72	perfluorohexane (mixture of isomers)
FC-75	perfluoro(2-butyltetrahydrofuran)
fluorous BAr_{f6}	$[B(3,5\text{-}C_6H_3(R_{f6})_2)_4]^-$
h	hour
HPLC	High Performance Liquid Chromatography
Hz	hertz
IR	infrared spectroscopy
M	Molarity
m	multiplet (NMR)
min	minute
NBS	*N*-bromosuccinimide
NMR	Nuclear Magnetic Resonance

PFMC	perfluoromethycyclohexane
Ph	phenyl
ppm	parts per million
q	quartet (NMR)
R_{fn}	$(CF_2)_{n-1}CF_3$
R.T.	room temperature
s	singlet (NMR)
TFA	trifluoroacetic acid
TLC	Thin Layer Chromatography
UV	Ultraviolet
v/v	volume/volume
Vis	Visible

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CHAPTER I

GENERAL INTRODUCTION

1.1 Fluorous Chemistry

Fluorous biphasic systems (FBSs) have been an important area of interest for nearly two decades. The term "fluorous" was coined in 1994 by Horváth and Rábai to describe perfluorinated alkanes, aliphatic ethers, and tertiary aliphatic amines that showed phase separation when combined with organic materials.[1] Gladysz and Curran later expanded the definition to mean "of or relating to, or having the characteristics of highly fluorinated saturated organic materials, molecules, or molecular fragments."[2] These materials possess properties different from aqueous and organic materials and therefore need to be classified into a different genre. Much like aqueous and organic solvents, fluorous and organic solvents are not miscible under ambient conditions. However, at elevated temperatures these solvents become miscible allowing facile switching between heterogeneous and homogeneous systems. One challenge of such systems has been the necessity to design substrates that can be selectively retained in the fluorous phase of a biphasic system.

As a solution to this problem, Horváth also introduced the concept of "ponytails".[1] Fluorous ponytails are usually perfluoroalkyl moieties of the formula $(CH_2)_m(CF_2)_{n-1}CF_3$, abbreviated $(CH_2)_mR_{fn}$. The methylene groups are referred to as

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This thesis follows the style of *Journal of the American Chemical Society*.

"spacers" so the term "R_{f6} ponytail with two spacers" literally represents $CH_2CH_2CF_2CF_2CF_2CF_2CF_2CF_3$ or $(CH_2)_2R_{f6}$. The number of spacers and length of the perfluoroalkyl chain can be manipulated to tune the solubility of the fluorous moiety making it partially, preferentially, or exclusively soluble in fluorous solvents. The greatest advantage of such tuning can be seen in biphasic catalytic systems where the catalyst contains a fluorous tag. As shown in Figure 1.1, the biphasic system at a low temperature is transformed into a homogeneous system at a higher temperature, which allows the reaction to readily proceed. When the reaction mixture is cooled the phases separate. Then the products are isolated and the fluorous phase catalyst recycled.

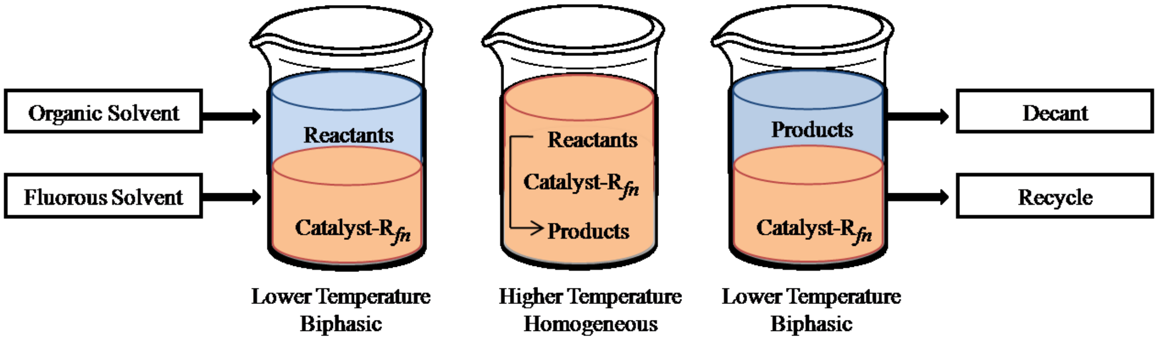
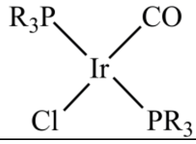


Figure 1.1. Fluorous biphasic system and catalyst recovery.

This type of catalyst recovery can be applied to a wide range of reaction types and substrates. The site of fluorination in the catalytic system is extremely flexible but often is localized in the ligand scaffold of a catalyst. The strong electron withdrawing effects of the perfluorinated chains typically induce changes in the overall steric structure and electronic properties of the ligand set. Rademacher, Nolan, and Gladysz analyzed a series of fluorous variants of Vaska's complex.[3] Phosphines of the formula $P(CH_2)_mR_{f8}$ (m = 2-5) showed IR ν_{CO} values decreasing from 1973.9 to 1946.1 cm^{-1} as the number of methylene spacers increased from two to five as illustrated in Table 1.1. With as many as five methylene spacers the fluorinated phosphines did not converge with the parent complex, showing there is still an electron withdrawing effect felt through even a long series of spacers.

Table 1.1. IR data ($C_6H_5CF_3$) of Vaska's-type complexes containing fluorous phosphines.



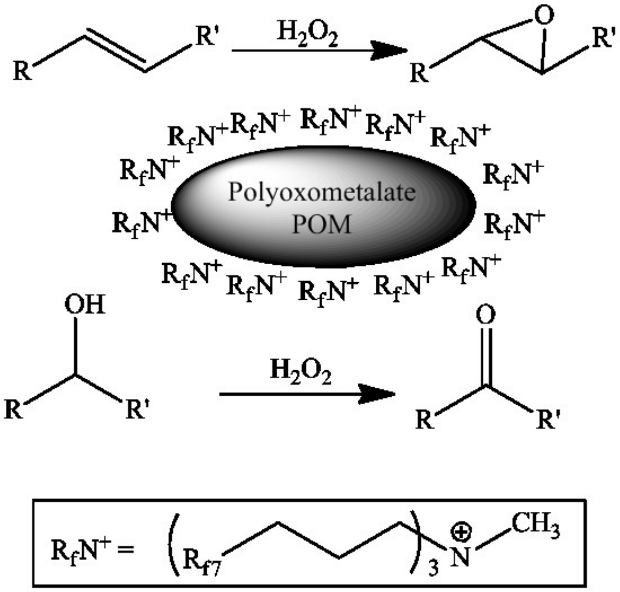
R	IR ν_{CO}
$(CH_2)_2R_{f8}$	1973.9
$(CH_2)_3R_{f8}$	1956.7
$(CH_2)_4R_{f8}$	1949.2
$(CH_2)_5R_{f8}$	1946.1
$(CH_2)_7CH_3$	1942.3

The authors conclude the effect can be virtually erased by eight or ten methylene groups based on computational data and gas-phase vertical ionization potentials (VIP). In order to avoid such electronic effects and tedious catalyst syntheses, the Gladysz group has focused on developing a highly fluorous, weakly coordinating anion to bring target cationic species into the fluorous phase. This is a concept that is gaining momentum but not without its share of challenges due to the non-polar and non-polarizable nature of fluorous solvents, which disfavor solvation of ionic species.

1.2 Phase Transfer Catalysis

Finding ways to bring ionic species into extremely non-polar fluorous solvents has been a hot topic resulting in several methods of transport between the organic/aqueous and fluorous phases.[4-13] Neumann first investigated the use of onium salts as phase transfer vehicles in 2003.[4] He used quaternary ammonium cations $(R_{f7}(CH_2)_3)_3)CH_3N^+$ to bring a large polyoxometalate anions (POMs) into perfluorodecalin for alcohol oxidation and alkene epoxidation shown in Scheme 1.1. The oxidation reactions were successful for a number of substrates, with and without using fluorous solvents for biphasic catalyst recovery.

Scheme 1.1. Neumann's phase transfer oxidation with fluorous ammonium cations.



In 2006, Gladysz demonstrated that the phosphonium salt $R_{f8}(CH_2)_2)_3R_{f6}(CH_2)_2)P^+ I^-$, shown in Figure 1.2 (top) induced ion displacement in a fluorous solvent.[5] Gladysz also found ammonium derivatives of the same type participated in phase transfer ion-displacement.[6] Fluorous alkyl halides $R_{f8}(CH_2)_mX$ (m = 2,3; X = Cl, I) were inert toward substitution with NaCl, KI, KCN, and NaOAc; however, in the presence of 10% of the fluorous ammonium salts $R_{f8}(CH_2)_2)R_{f8}(CH_2)_5)_3N^+ I^-$ or $(R_{f8}(CH_2)_3)_4)N^+ Br^-$ (Figure 1.2, middle and bottom), displacement occurred upon heating.

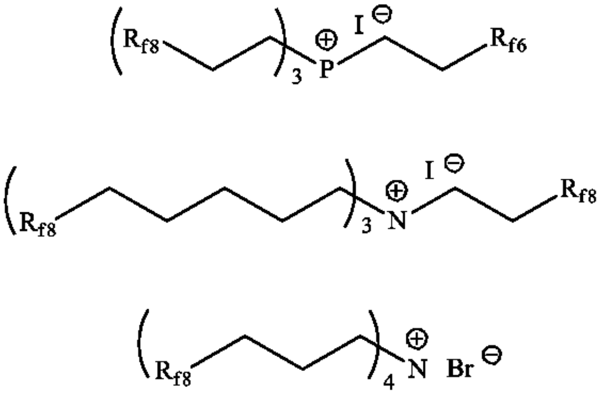


Figure 1.2. Gladysz's phosphonium (top) and ammonium (middle, bottom) fluorous salts.

Most reported salts were sparingly soluble in perfluoromethylcyclohexane (PFMC) at room temperature when combined with $CF_3SO_3^-$ or I^-, limiting their use as phase transfer catalysts.[4-6] However, Bülhmann's phosphonium salt (Figure 1.3) displayed solubility in PFMC, perfluorohexanes, and perfluoroperhydrophenanthrene as high as 0.014 M at room temperature.[7] Bühlmann did not employ this salt as a phase transfer catalyst but speculated that its viability was due to its unique high solubility in fluorous solvents. Each of these examples established significant progress toward classical phase transfer catalysis by expanding the solubility and range of fluorophilic cations.

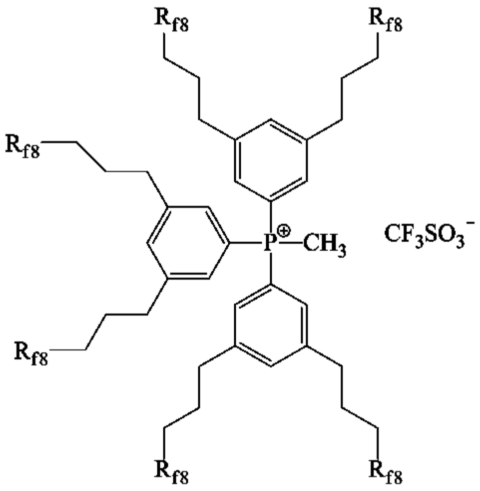
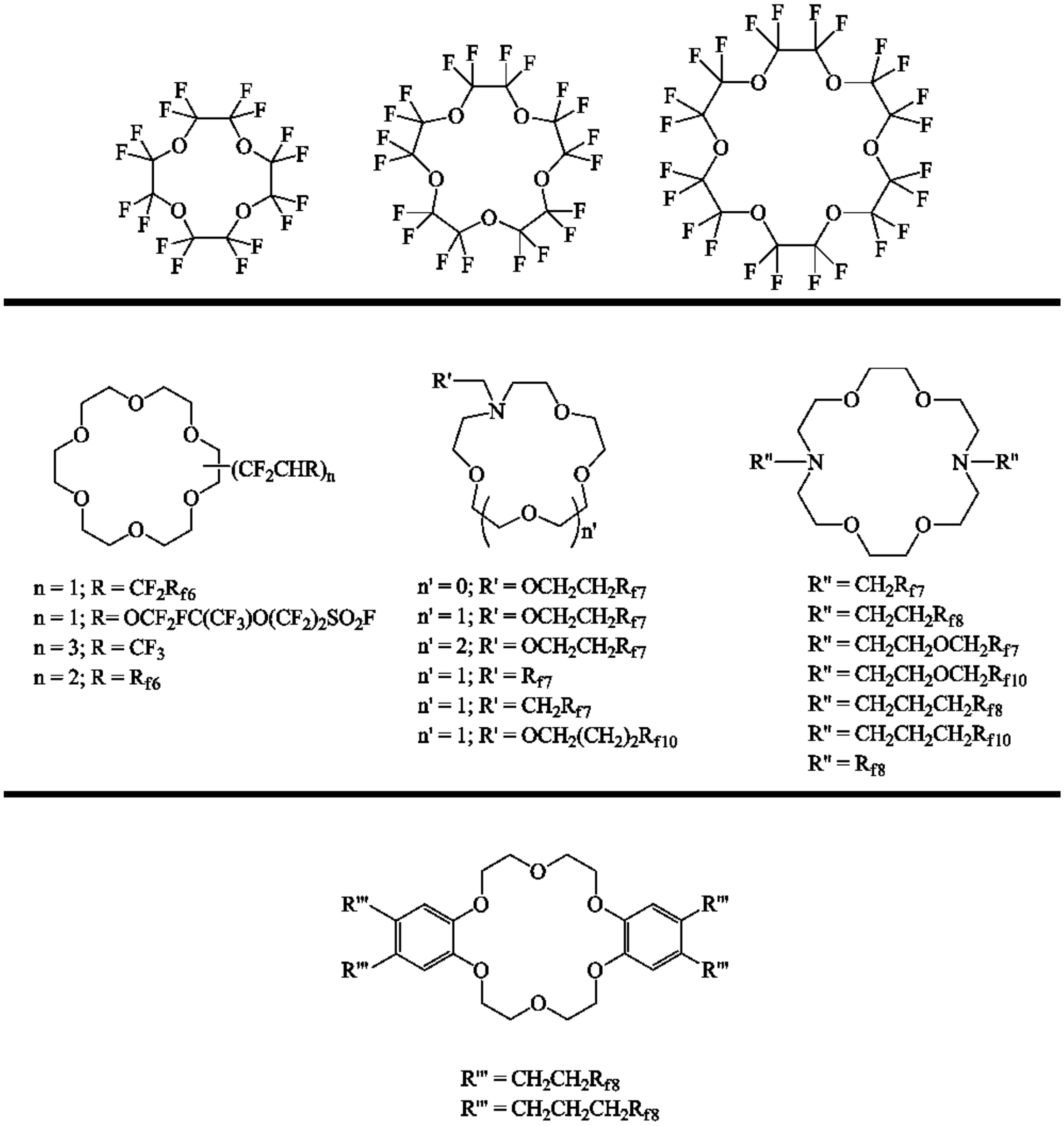


Figure 1.3. Bühlmann's fluorous phosphonium salt.

The same phase transfer possibility was probed with fluorinated crown ethers.[9-13] Even before the birth of fluorous chemistry, Lagow created perfluorinated analogs of several crown ethers (Figure 1.4, top).[10] Because of the CF_2 units, the basicities of the ether oxygen atoms were reduced significantly, rendering coordination of metallic cations infeasible. Researchers at DuPont avoided that problem by introducing the ponytail motif instead of direct fluorination shown in Figure 1.4, middle.[11a,b] Since then, many fluorophilic crown ethers have been explored in solid-liquid phase transfer catalyst.[11c-g] As an example, Pozzi created a fluorous 18-crown-6 derivative (Figure 1.4, bottom) that participated in the Finklestein reaction, nucleophilic displacements (S_NAr), and oxidation reactions.[12] Most of these examples use small ions that coordinate to the larger fluorous phase transport scaffold. What, then, are the options for large metal coordination compounds?

The most popular method to bring such cationic species into fluorous media is through ligand perfluoronation[14] which, as shown earlier, can lead to significant electronic changes to a metal center affecting its reactivity. The other option



$n = 1$; $R = CF_2R_{f6}$
$n = 1$; $R = OCF_2FC(CF_3)O(CF_2)_2SO_2F$
$n = 3$; $R = CF_3$
$n = 2$; $R = R_{f6}$

$n' = 0$; $R' = OCH_2CH_2R_{f7}$
$n' = 1$; $R' = OCH_2CH_2R_{f7}$
$n' = 2$; $R' = OCH_2CH_2R_{f7}$
$n' = 1$; $R' = R_{f7}$
$n' = 1$; $R' = CH_2R_{f7}$
$n' = 1$; $R' = OCH_2(CH_2)_2R_{f10}$

$R'' = CH_2R_{f7}$
$R'' = CH_2CH_2R_{f8}$
$R'' = CH_2CH_2OCH_2R_{f7}$
$R'' = CH_2CH_2OCH_2R_{f10}$
$R'' = CH_2CH_2CH_2R_{f8}$
$R'' = CH_2CH_2CH_2R_{f10}$
$R'' = R_{f8}$

$R''' = CH_2CH_2R_{f8}$
$R''' = CH_2CH_2CH_2R_{f8}$

Figure 1.4. Perfluorinated crown ethers: directly fluorinated (top), fluorous tagged (middle), Pozzi's phase transfer catalyst (bottom).

is to render the anion highly fluorophilic, creating a fluorous charge neutral salt without changing the transition metal reactivity. As an example, van Koten synthesized a series of fluorous borates to bring a rhodium diphosphine cation into the fluorous phase for hydrogenation reactions.[15]

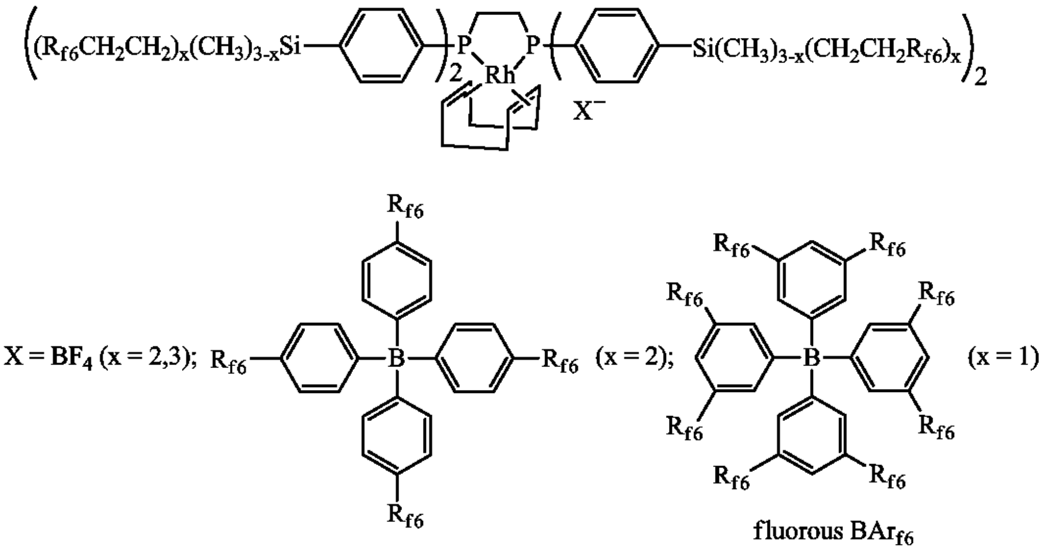


Figure 1.5. van Koten's fluorous rhodium complexes used in hydrogenation reactions.

van Koten found that introducing a highly fluorous anion alone did not induce a preference for the fluorous phase. However, when the phosphines were tagged with fluorous ponytails and the highly fluorous anion, tetrakis[3,5-bis(perfluorohexyl)phenyl]borate (fluorous BAr$_{f6}$, Figure 1.5 far right), was used the complex was soluble in fluorous media. FBS techniques resulted in the successful recycling of the catalyst. One aim of this study was to determine if fluorous BAr$_{f6}$ can bring "naked" cations (no ponytails) into the fluorous phase.

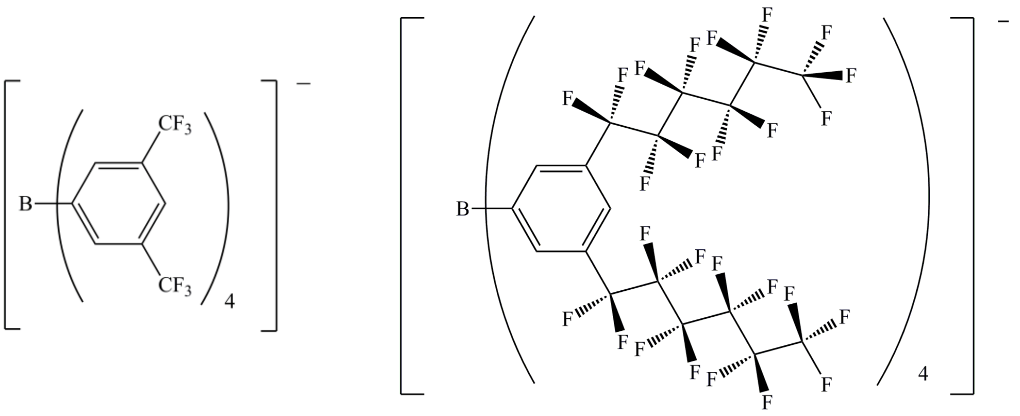


Figure 1.6. BAr$_f$ (left) and fluorous BAr$_{f6}$ (right).

Fluorous BAr$_{f6}$ is 69% weight fluorine compared to the traditional tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (traditional BAr$_f$) at 52% weight fluorine. The two BAr$_f$ derivatives are compared in Figure 1.6. An early paper by Horváth showed through partition coefficients that neutral compounds above 60% weight fluorine are preferentially soluble in fluorous solvents whereas a sizeable decrease in solubility arises at even 53% weight fluorine.[16] Horváth set 60% weight fluorine as a threshold to satisfy the "like dissolves like" effect which still stands as the rule of thumb. This cut-off renders fluorous BAr$_{f6}$ crucial in the development of a new FBS involving a cationic metallic complex. The proposed FBS we wish to create is a Werner-BAr$_f$ salt that can be retained in the fluorous phase as shown in Figure 1.7. For this purpose, the [Co(en)$_3$]$^{3+}$ trication was selected. The proposed [Co(en)$_3$](fluorous BAr$_{f6}$)$_3$ complex is 67% weight fluorine so, by Horváth's criterion, the complex would be preferentially soluble in fluorous media.

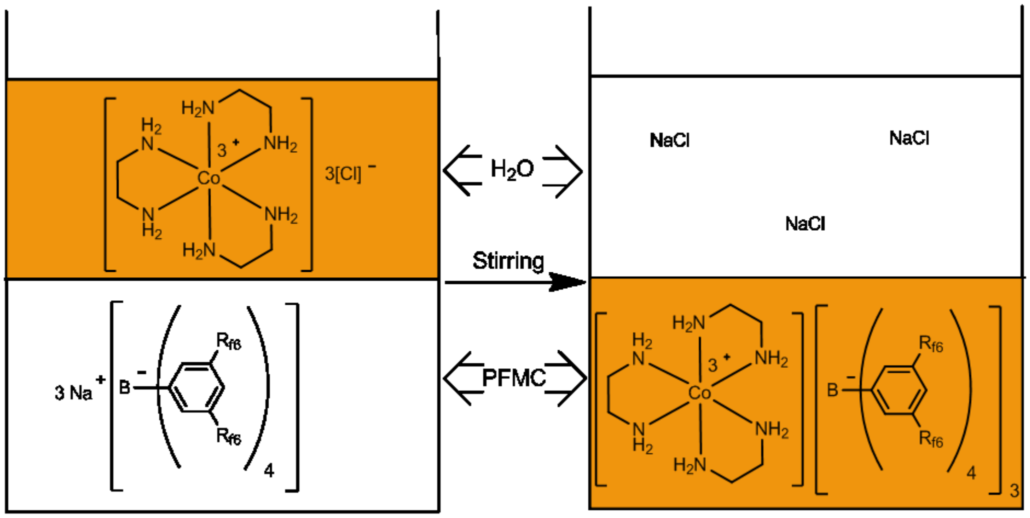


Figure 1.7. Proposed FBS with Werner complex $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$.

1.3 Werner-type Complexes

It has long been known that Werner complexes such as $[Co(en)_3]^{3+}$ can be separated into enantiopure salts *via* recrystalization of diastereomeric tartrate salts. Subsequent chromatography on an ion exchange resin gives the resolved enantiomers of $[Co(en)_3]Cl_3$.[17] Traditionally these salts are exclusively soluble in aqueous media causing the chemistry afforded by these compounds to be somewhat limited.[18-20] In 2008, the Gladysz group showed that $[Co(en)_3]^{3+}$ can be transferred into an organic phase by anion exchange with BAr_f.[21] Previously, the complex $[Co(en)_3](BPh_4)_3$ or similar species had been reported only soluble in methanol, acetone, THF, and 1:9 v/v methanol/CH_2Cl_2.[22-24]

Gladysz also showed that once soluble in CH_2Cl_2, the complex was capable of acting as a hydrogen bond donor in the enantioselective Michael addition of dimethyl malonate to 2-cyclopenten-1-one. The mechanism of catalysis was thought to mimic the chiral thiourea catalysts, which contain a similar platform for hydrogen bond donation.[25] The Werner-BAr_f complex gave a 78% yield of the addition product with 33% *ee*. After the reaction was completed, the cobalt-BAr_f salt was recovered in 81% yield. Because Werner cations are substitution inert, it follows to use them to induce asymmetric catalysis through a second coordination sphere. Current work in the Gladysz group is focused on expanding the scope and improving the selectivity of these organocatalysts.[26] A representation of the chiral scaffold used in Werner-type complexes is shown in Figure 1.8.

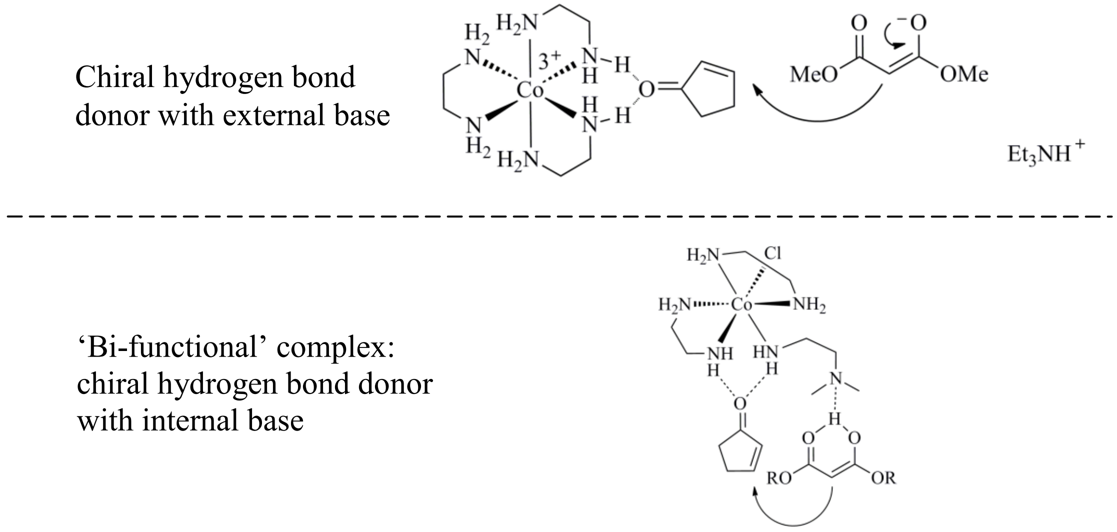


Figure 1.8. Proposed hydrogen bonding scaffold in the Michael addition of dimethyl malonate to 2-cyclopenten-1-one; Werner complex acting as a hydrogen bond donor (top) and a bifunctional Werner-type complex containing an internal base (bottom).

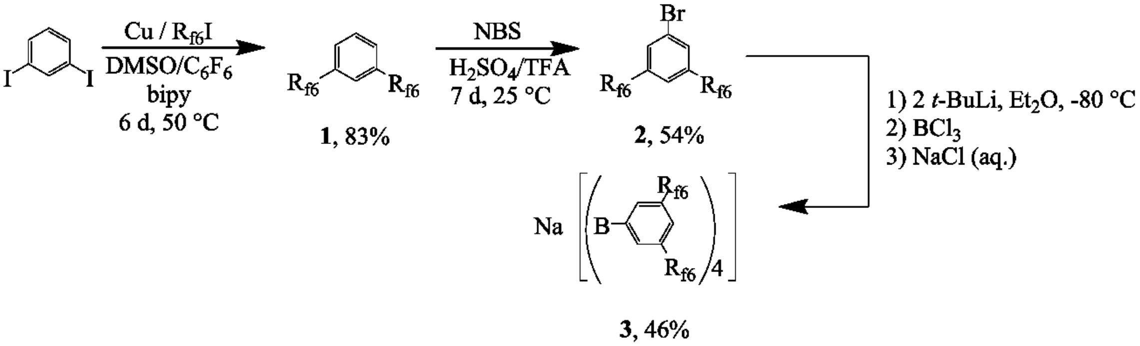
CHAPTER II

SYNTHESIS OF FLUOROUS BAr$_f$ AND TRANSFER OF WERNER-TYPE CATIONS INTO THE FLUOROUS PHASE

2.1 Introduction

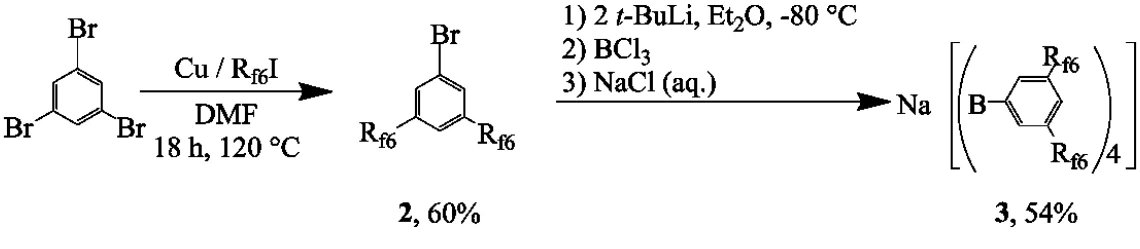
While other modes of transport to the fluorous phase were discussed in the introduction, our targeted method of bringing the Werner-type complexes into the fluorous phase was to pair them with fluorous sodium BAr$_{f6}$. The fluorous BAr$_{f6}$ salt **3** in Scheme 2.1 was first synthesized by van Koten and coworkers.[27] Through copper mediated coupling the arene **1** was prepared from 1,3-diiodobenzene and perfluorohexyliodide. Subsequently **1** was brominated with NBS in concentrated sulfuric acid and trifluoroacetic acid (TFA). After a lithium-halogen exchange using *t*-BuLi, salt metathesis was employed through BCl_3 to generate $Na[B(3,5\text{-}C_6H_3(R_{f6})_2)_4]$ (**3**), in a moderate yield after aqueous workup. The isolated sodium salt was soluble in FC-75, perfluoro(2-butyltetrahydrofuran). The ether successfully solvated the sodium cation and the salt proved to satisfy the "like dissolves like" effect.

Scheme 2.1. Synthesis of **3** reported by van Koten and coworkers.



Bühlmann and coworkers also synthesized **3** using a slightly different procedure presented in Scheme 2.2.[28] The same copper coupling reaction was employed but using 1,3,5-tribromobenzene. By using slightly more than two equivalents of perfluorohexyliodide, the authors obtained **2** in good yields. Compound **3** was then generated in the same manner as van Koten as a sodium salt.

Scheme 2.2. Synthesis of **3** reported by Bühlmann.



2.2 Results: Fluorous BAr_{f6}

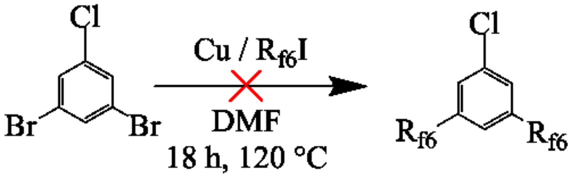
It was our desire not only to reproduce the syntheses of fluorous BAr_{f6} but improve the methodology and synthetic design when possible.

2.2.1 Scouting reactions

2.2.1.1 Adding ponytails to aryl halides

Initial attempts to emulate Büllmann’s synthesis were unsuccessful as the first step gave a mixture of unidentified products. Direct communication with the author resulted in an updated synthesis of **2** that modified the workup procedure. However, the viability of the method could not be confirmed. To promote disubstitution, 1-chloro-3,5-dibromobenzene was used in place of tribromobenzene (Scheme 2.3), while using Büllmann’s coupling conditions. Again, the reaction produced a mixture of unidentified products as assigned by ^1H NMR. Due diligence was served in the reaction sequence by varying several parameters: 1) catalyst loading, 2) activated copper catalyst,[29] 3) equivalents of $R_{f6}I$, 4) reaction time, and 5) reaction temperature. Also, an exhaustive effort was made to separate the products including hot filtration, preparative HPLC, TLC (fluorous, reverse phase, and silica), and sublimation. Every effort to identify or separate the reaction mixture into pure fractions was unsuccessful.

Scheme 2.3. Attempted alternative generation of 1-chloro-3,5-bis(perfluorohexyl)benzene.



Hence, I returned to the van Koten method in Scheme 2.1, which gave **1** in good yields. The reported route dictated that a 1:2 (v/v) mixture of DMSO/C_6F_6 be used as the solvent system and bipy used as a co-catalyst. This is an expensive route since C_6F_6 is over \$2 per gram from VWR International.[30] Also, the recipe called for a reaction time of 6 d at 50 °C. These are not the optimal conditions to obtain **1**. The reaction time is long and the solvent system is costly. However, unlike the Bühlmann synthesis, it was reproducible.

2.2.1.2 Bromination of arenes

van Koten then brominated **1** by reacting with NBS in concentrated sulfuric acid and TFA over a period of 7 d. This synthesis was repeated but only 24% of the brominated product was detected by ^{1}H NMR. The authors isolated a mixture containing **1** and **2** in a 17:83 ratio corresponding to a 54% yield of **2**. This is another opportunity to optimize the reaction since a low purity and yield are obtained after a long reaction time.

2.2.1.3 Generating the borate anion

Subsequent reaction of **2** with *t*-BuLi at –78 °C followed by addition of BCl_3 and workup with saturated sodium chloride gave **3** as a brown oil. The ^{1}H and ^{19}F NMR showed many impurities in the crude product. Bühlmann indicated the product could be recrystallized in perfluororohexanes to give **3**, but this procedure could not be reproduced. Colorless crystals were never isolated even though the product was seen in the ^{1}H NMR spectrum. The crude reaction mixture is shown in Figure 2.1.

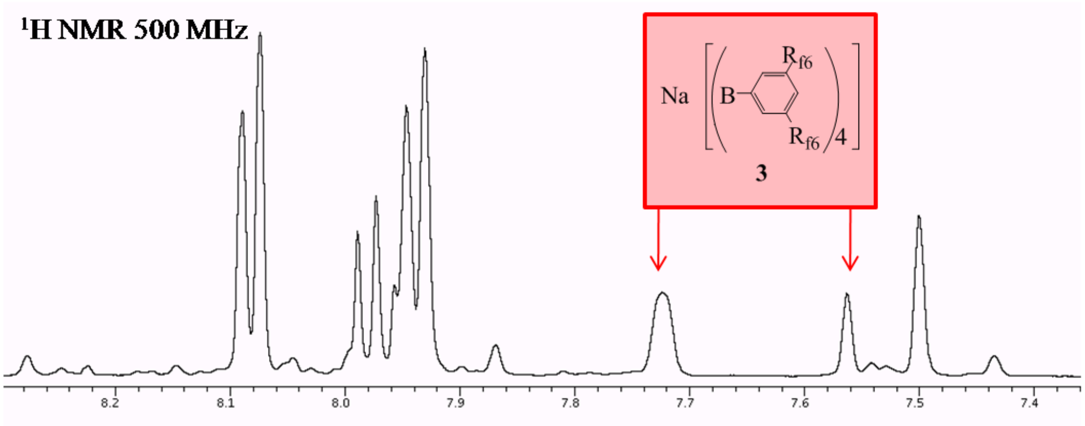
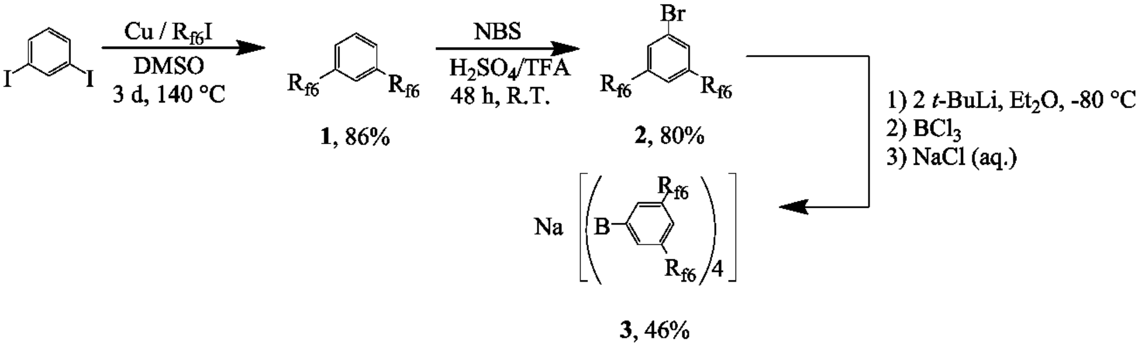


Figure 2.1. Crude reaction mixture confirming the production of **3**.

2.2.2 Improved synthesis of Na[B(3,5-$C_6H_3(R_{f6})_2)_4]_3$ (3)

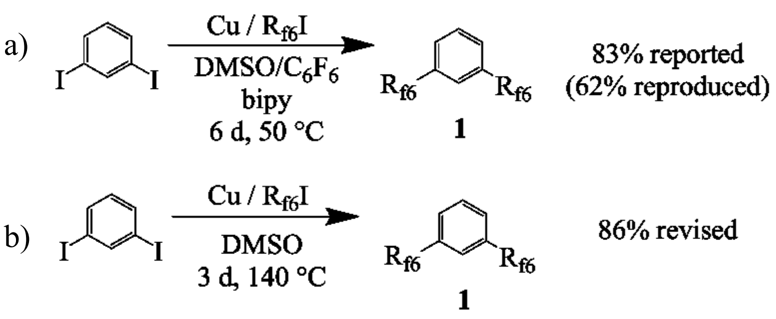
Even though Bühlmann's synthesis was more direct, **2** was never obtained with any confidence or reproducibility. Hence, the longer synthesis posed by van Koten was the method we followed. The reaction sequence in Scheme 2.4 shows the improved, reliable synthesis of fluorous BAr_{f6}.

Scheme 2.4. Improved synthesis of **3** by the Gladysz group.



In the first step of the synthesis, we improved the system by tweaking conditions to use only DMSO as the solvent where van Koten used a mixture of DMSO and C_6F_6. The co-catalyst bipy was discarded and the reaction time was shortened, but at the cost of an elevated temperature. The two reaction sequences are compared in Scheme 2.5. Compound **1** can now be prepared in similar yield to van Koten but at lower cost and shorter reaction times.

Scheme 2.5. a) van Koten synthesis of **1** and b) improved synthesis by our group.



The bromination of **1** by the van Koten method was successful but gave low yields and low purity. A literature search revealed a related bromination of 1,3-bis(trifluoromethyl)benzene involving only a slight variation in solvent ratio and addition method.[31] Whereas van Koten called for a 0.6:1.0 ratio (v/v) of H_2SO_4:TFA, Dolbier and coworkers used a 0.4:1.0 ratio (v/v) H_2SO_4:TFA. Also, the van Koten synthesis stretched the reaction out for 7 d while adding NBS in intervals of 2 d. Dolbier added NBS every hour over the course of 8 h then stirred the reaction for 2 d. Following the Dolbier report, **2** was isolated spectroscopically pure in 80% yield. The van Koten synthesis reports a 54% non-isolated yield, and under the Dolbier conditions, roughly the same conversion was seen in only 6 h and 6 additions of NBS. After the full 2 d, **1** was completely converted to the brominated species. Figure 2.2 shows the production of **2** during the reaction sequence as analyzed by ^{1}H NMR. Compound **2** was isolated as a white, waxy solid that did not require further purification.

The final product, **3**, was synthesized in the same manner as van Koten and Bühlmann but with a few alterations to the workup procedure. Since the crude reaction mixture could not be recrystallized from perfluororohexanes to give the product, column chromatography was attempted. An ether fraction was eluted from the column and elution with acetone gave another fraction. ^{1}H NMR confirmed the ethereal fraction to

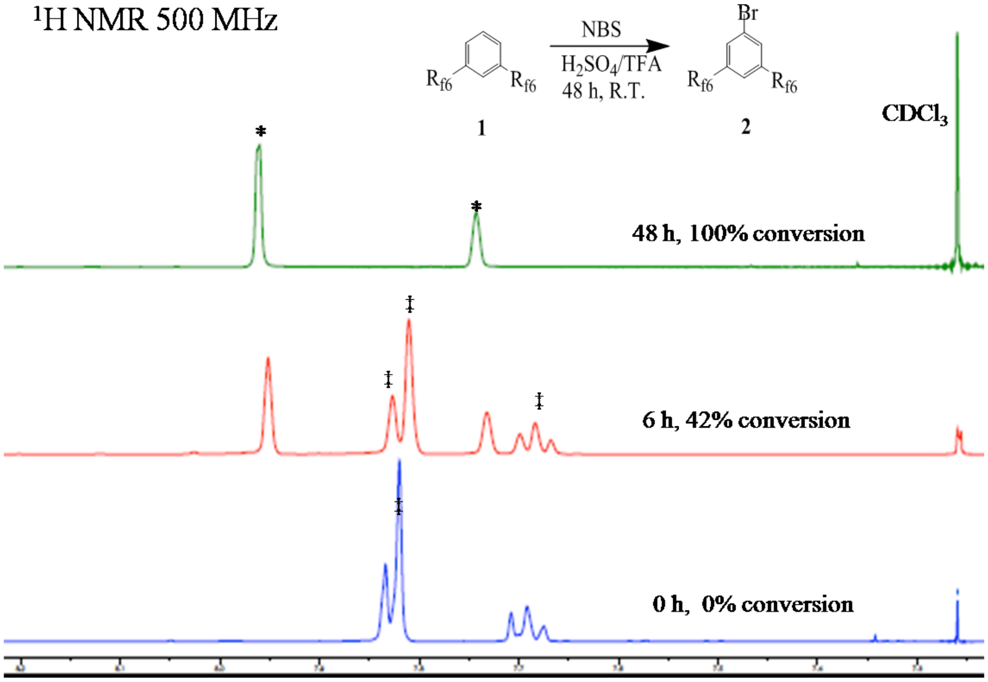


Figure 2.2. ^{1}H NMR spectra following the reaction of **1** with NBS; * denotes a peak from **1**, while ‡ denotes a peak from **2**.

be the impurities seen in the crude NMR, whereas the acetone fraction contained **3**. It is interesting that even after removal of the solvent and heating drying in a pistol to 110 °C under high vacuum overnight, the product showed traces of water and acetone. Recrystallization from FC-75 gave the product as light brown crystals at low temperature, but upon warming to room temperature it became a waxy oil. After heating the material to 200 °C under vacuum the ^{1}H NMR still showed water and acetone. A control sample of tetrabutylammonium bromide was prepared in acetone-d_6. The ^{1}H NMR spectrum of this salt did not display acetone or water further supporting **3** as a solvate.

The improved synthesis confirms the production of **1**, **2**, and **3** through ^{1}H NMR intuitive assignments and confirms the data presented in the literature.[15,27] The ^{1}H NMR spectrum of **1** aligns nicely to reported data showing three signals which correlate to the three unique hydrogen environments. The spectrum also shows a broadening of peaks corresponding to long range ^{1}H-^{19}F coupling. The production of **2** was followed by ^{1}H NMR shown in Figure 2.2. Compound **1** can be clearly identified and its peaks are diminishing as two new peaks appear. These correlate nicely to the two sets of protons in **2** which integrate in a 2:1 ratio. After salt metathesis with BCl_3, a shift in the ^{1}H NMR signal is seen as the aryl protons adjacent to the reactive site move upfield from 7.94 to 7.71 ppm. However, ^{13}C NMR spectroscopy is the best tool to identify the borate anion through identification of the signal at 167.3 ppm that shows ^{11}B-^{13}C coupling (49.8 Hz).

2.3 Results: Fluorous Werner-type Complexes

Werner-type complexes have not been previously solubilized in fluorous media. By using phase transfer techniques, $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ (**4**, Figure 2.3) and $[Co(\mathit{R,R}\text{-}chxn)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ (**5**) were prepared from the corresponding cobalt chloride salt and **3**.

*2.3.1 [Co(en)$_3$][B(3,5-C$_6$H$_3$(R$_{f6}$)$_2$)$_4$]$_3$ (**4**)*

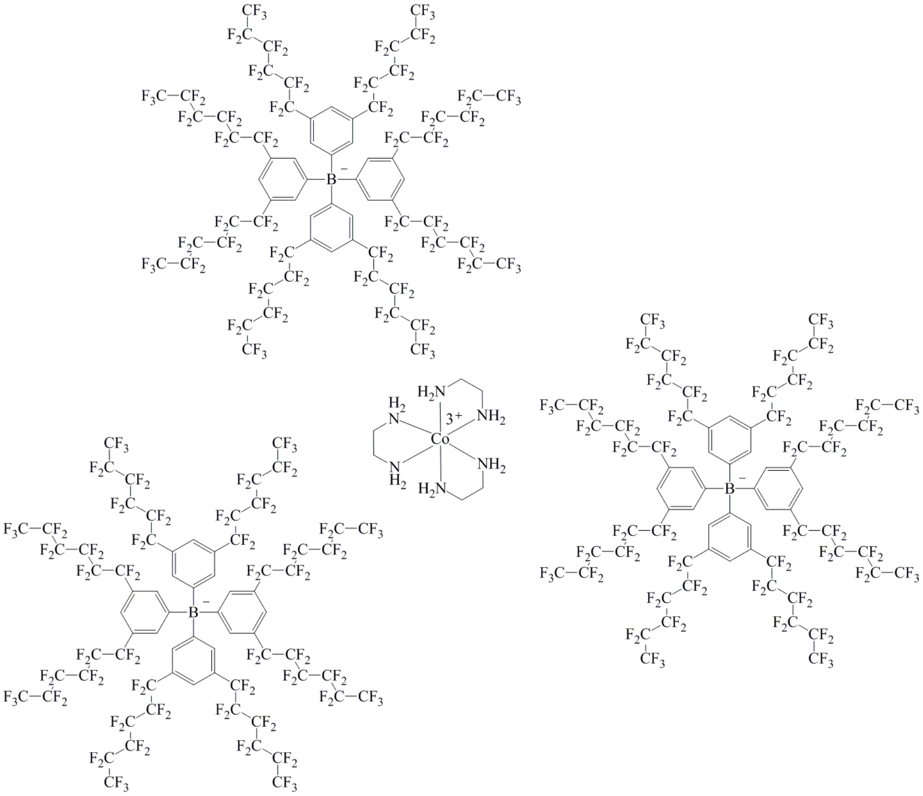


Figure 2.3. Complex **4**, $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$.

2.3.1.1 Preparation and analysis

The salt was prepared by stirring an aqueous solution of $[Co(en)_3]Cl_3$ and a solution of **3** in perfluoromethylcyclohexane (PFMC) at room temperature for 10 min. The characteristic yellow color of the cobalt complex was present in the aqueous phase; however after stirring, the color was transferred to the fluorous phase signaling the transfer of the Werner cation into the fluorous phase by salt formation with the fluorous borate anion. Figure 2.4 shows the phase transfer process.

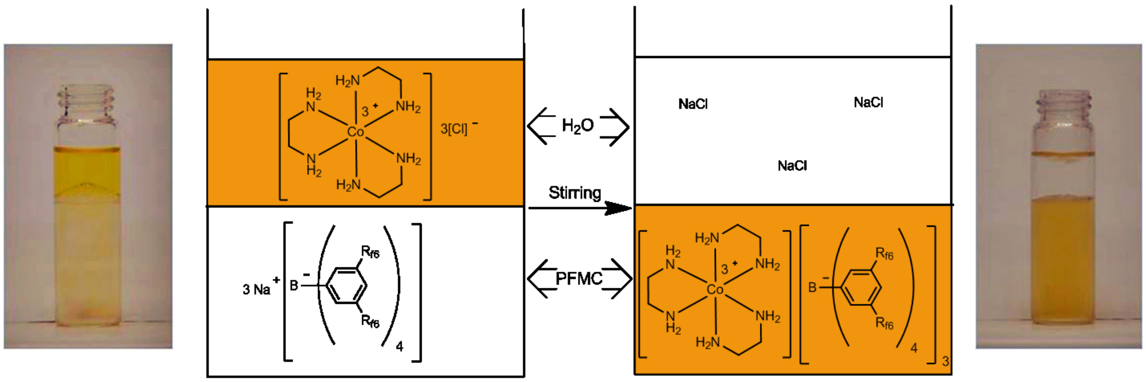


Figure 2.4. Anion exchange with **3** to generate **4**.

The fluorous phase was extracted and the solvent removed to give $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ (**4**) as an orange oil. The ^1H NMR spectrum of **4** can be recorded in acetone-d_6 and the signals are consistent with the aromatic hydrogens present in **3** and show the ethylenediamine shifts analogous to the $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ system.[21] Shown in the ^1H NMR spectrum of **4** in Figure 2.5, fluorous BAr_{f6} brings 6 eq. of acetone and 15-20 eq. of water into the fluorous phase, the latter evidenced by a peak at 2.81 ppm. It is not presently known if this acetone plays any part in the stability of **4**. Also, closely related cobalt amine complexes can be unstable in the absence of water.[21,32] Integration of the anion to cation shows a 2:1 ratio illustrated in the ^1H NMR below.

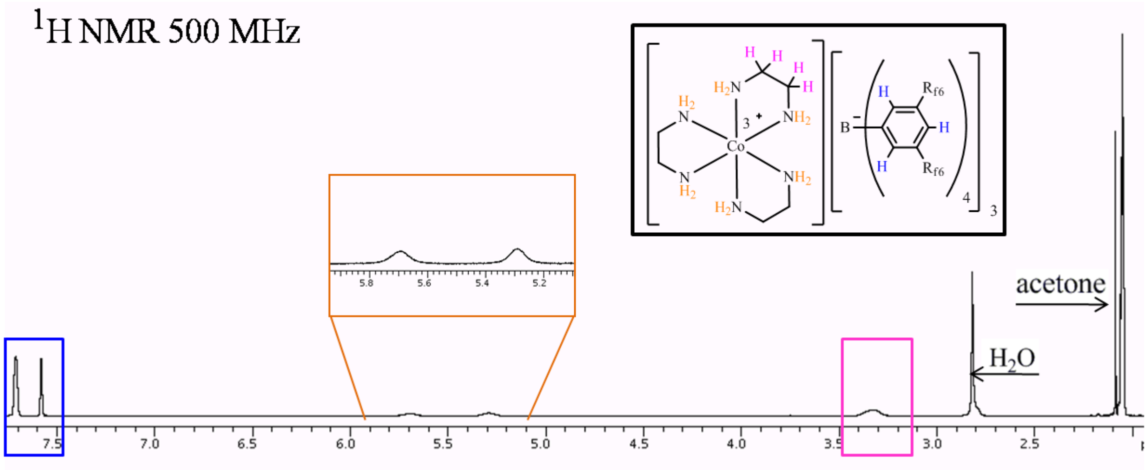


Figure 2.5. ^{1}H NMR of **4** in acetone-d_6.

After biphasic salt metathesis, the UV-Vis spectrum was obtained for each phase and presented in Figure 2.6.

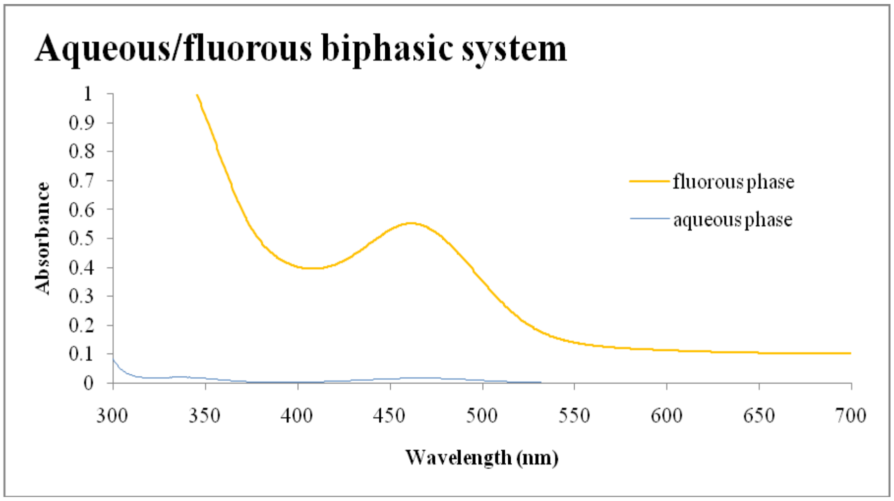


Figure 2.6. UV-Vis spectra of **4** in fluorous and aqueous phases after fluorous biphasic salt metathesis.

The $[Co(en)_3]Cl_3$ complex in water shows a ligand to metal absorption at 466 nm which is also present in the fluorous phase confirming UV-Vis spectroscopy as a viable probe to detect **4** in the fluorous phase.

Elemental analysis of **4** did not agree with the calculated values for the salt. However, ^1H NMR integration was used to determine the amount of water and acetone contained in the sample and when included in the calculated analysis, the values were in close agreement. Table 2.1 shows the experimental values with the calculated simulations.

Table 2.1. Elemental analysis of **4**.

		Calculated	
Element	Found	**4**	**4** •6(acetone)•15 H_2O
C	30.99	30.20	30.51
H	0.80	0.67	1.33
N	0.94	0.95	0.89
F	64.35	67.14	62.74

2.3.1.2 Solubility of ***5*** *in organic and fluorous media*

Compound **4** was soluble in a number of fluorous and organic solvents (Table 2.2).

Table 2.2. Solubility of **4** at 23 °C.

Solvent	Solubility
Acetone	Soluble
Benzene	Insoluble
CH_2Cl_2	Soluble
DMSO	Insoluble
Et_2O	Soluble
Solvent	Solubility
Methanol	Soluble
Toluene	Insoluble
FC-70	Soluble
FC-72	Soluble
FC-75	Soluble

*2.3.1.3 Partition coefficients of **4** in organic and fluorous media*

The partition coefficient of **4** in H_2O/PFMC was determined by UV-Vis spectroscopy. A worked example to find ε and the partition coefficient is presented in the experimental section. The extinction coefficient of **4** was determined to be 213 $M^{-1}cm^{-1}$ at 460.5 nm. The partition coefficient of **4** in the H_2O/PFMC system was determined to be 1.0:99.0.

Several other solvents were tested to determine the partition coefficients and the results were very similar to those in PFMC. Table 2.3, shown below, summarizes the results of this investigation.

Table 2.3. Partition coefficient of **4** in different biphasic systems at 23 °C.

Solvents		Partition Coefficient
Phase 1	Phase 2	
Water	PFMC	1.0:99.0
Toluene	PFMC	<0.7:>99.3
Water	FC-72	4.3:95.7
Water	FC-75	1.7:98.3

2.3.2 Partition coefficients of rac-$[Co(en)_3][BAr_f]_3$ *in fluorous media*

As discussed in the general introduction, the trication $[Co(en)_3]^{3+}$ was made soluble in organic media by creating the salt $[Co(en)_3][BAr_f]_3$. With the synthesis of fluorous BAr_{f6}, an organic/fluorous biphasic system can be envisioned where the cobalt complex has preferable solubility in one phase. Therefore, standard solutions of $[Co(en)_3][BAr_f]_3$ were prepared in CH_2Cl_2 and the extinction coefficient at 469 nm was determined to be 101 $M^{-1}cm^{-1}$.

A biphasic solution containing $[Co(en)_3][BAr_f]_3$ in CH_2Cl_2 and **3** in PFMC was prepared. The phase transfer process is shown in Figure 2.7.

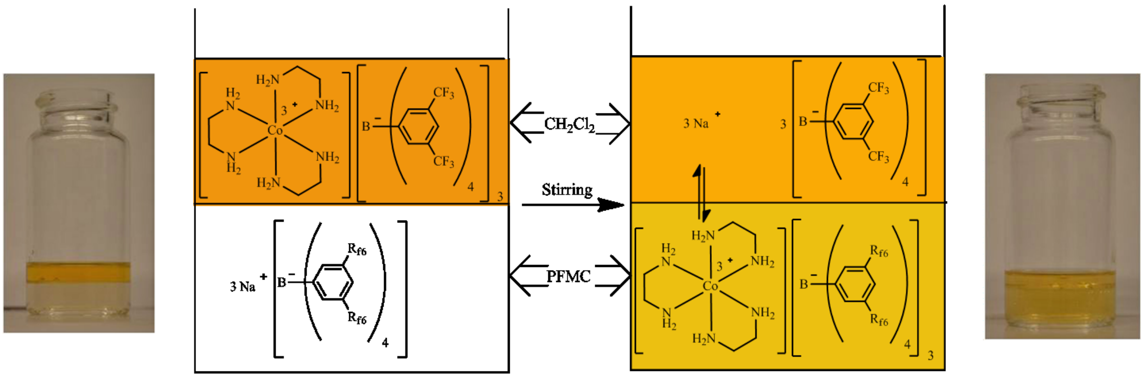


Figure 2.7. Partition of $[Co(en)_3]^{3+}$ in organic/fluorous biphasic system.

After stirring, the UV-Vis spectrum of each layer was obtained. From the absorbance at 460 nm, the partition coefficient of the CH_2Cl_2/PFMC system was determined to be 42:58.

*2.3.3 [Co(R,R-chxn)$_3$][B(3,5-C$_6$H$_3$(R$_{f6}$)$_2$)$_4$]$_3$ (**5**)*

2.3.3.1 Preparation and analysis

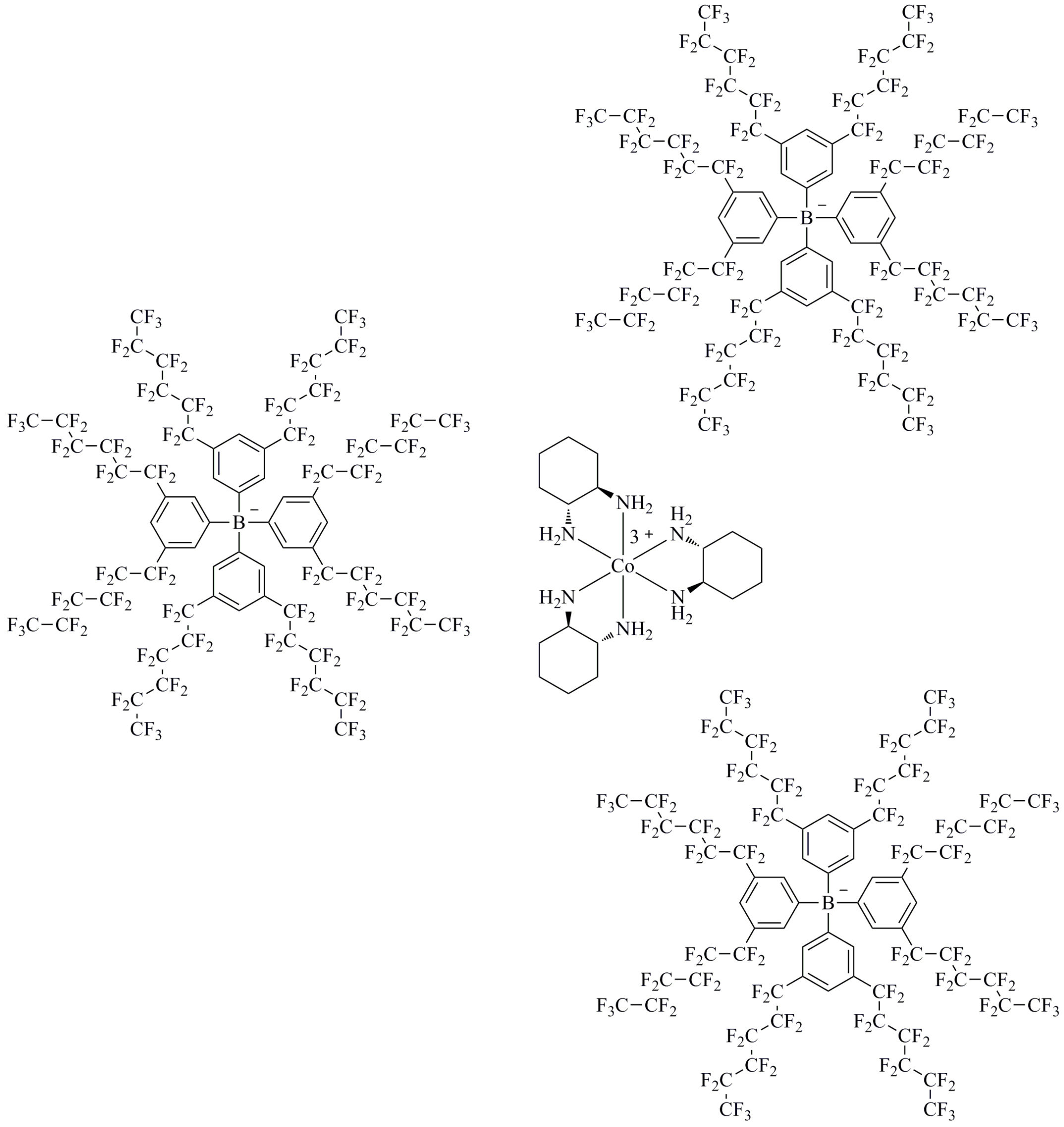


Figure 2.8. Compound **5**, [Co(chxn)$_3$][B(3,5-C$_6$H$_3$(R$_{f6}$)$_2$)$_4$]$_3$.

Compound **5** (Figure 2.8) was prepared by biphasic anion exchange in the same manner as **4**. A representation of the anion exchange process is shown in Figure 2.9. Unlike **4**, after removal of the fluorous solvent a sticky, orange solid was obtained. The salt displays ^{1}H NMR shifts consistent with the analogous $[Co(chxn)_3][B(3,5\text{-}C_6H_3(CF_3)_2)_4]_3$ complex[21] and **3**. Also consistent with **4**, compound **5** contains 6 equivalents of acetone at 2.08 ppm and 15-20 eq. H_2O at 2.82 ppm as depicted in the spectrum in Figure 2.10.

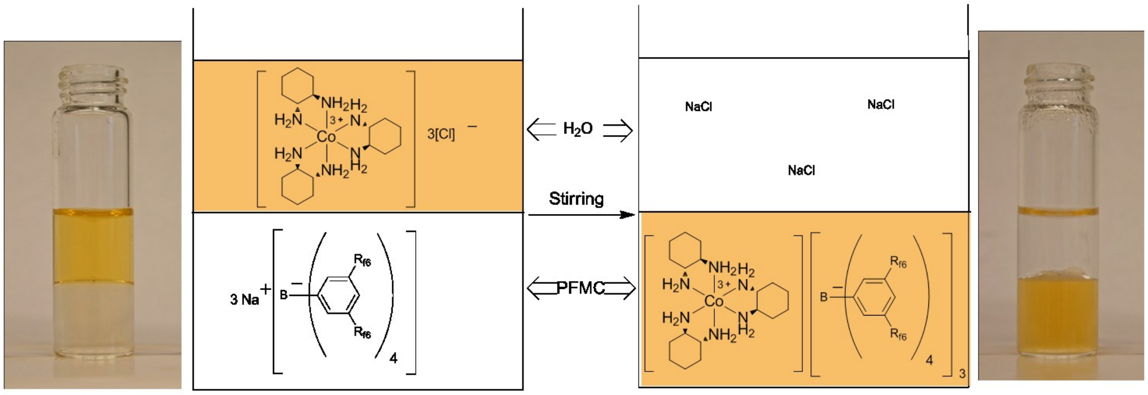


Figure 2.9. Anion exchange with **3** to generate **5**.

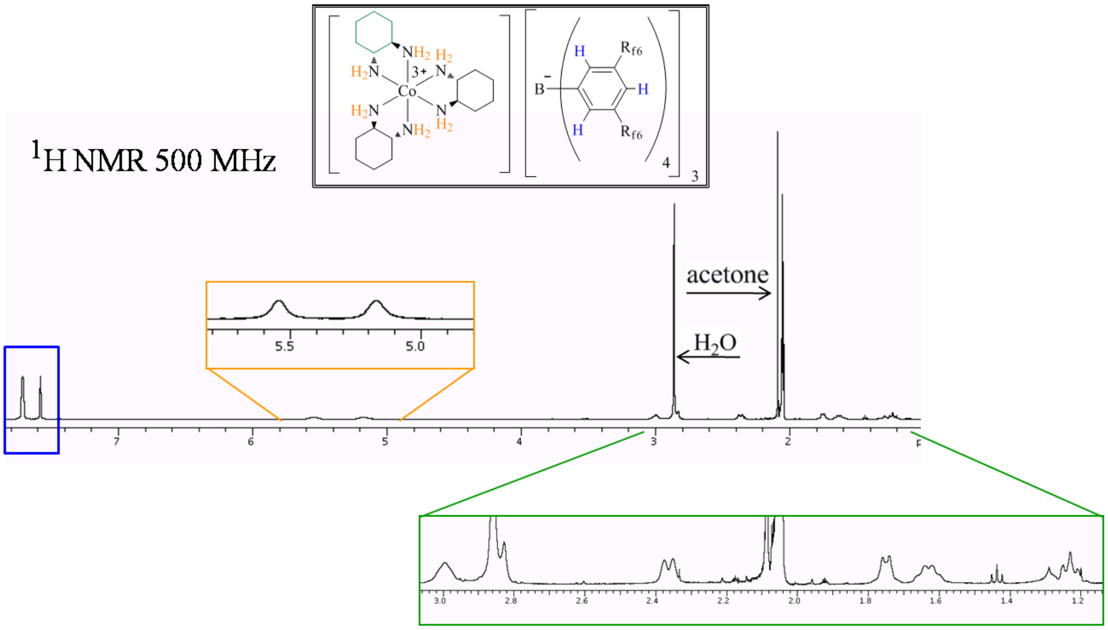


Figure 2.10. ^{1}H NMR of **5** in acetone-d$_6$.

The elemental analysis of **5** was much the same as **4**. The salt alone did not agree with the calculated values and ^{1}H NMR integration was used to determine the amount of water and acetone contained in the sample. When 15 molecules of water and 3 molecules of acetone were included, the values agreed within 1%. Table 2.4 shows the experimental values with the calculated simulations.

*2.3.3.2 Solubility of **5** in organic and fluorous media*

Compound **5** was soluble in several fluorous and organic solvents as shown in Table 2.5.

Table 2.4. Elemental analysis of **5**.

		Calculated	
Element	Found	**5**	**5** •3(acetone)•15 H_2O
C	31.80	31.26	31.49
H	0.99	0.87	1.51
N	0.91	0.93	0.87
F	61.66	65.92	61.68

Table 2.5. Solubility of **5** at 23 °C.

Solvent	Solubility
Acetone	Soluble
Benzene	Insoluble
CH_2Cl_2	Soluble
DMSO	Insoluble
Et_2O	Soluble
Methanol	Soluble
Toluene	Insoluble
FC-70	Soluble
FC-72	Soluble
FC-75	Soluble

*2.3.3.3 Partition coefficients of **5** in organic and fluorous media*

The extinction coefficient of **5** was determined to be 34.3 $M^{-1}cm^{-1}$ by UV-Vis spectroscopy. The partition coefficient of **5** in H_2O/PFMC and toluene/PFMC were determined in the same manner as **4**. The results of the investigation are presented in Table 2.6.

Table 2.6. Partition coefficient of **5** in different biphasic systems at 23 °C.

Solvents		Partition Coefficient
Phase 1	Phase 2	
Water	PFMC	1.0:99.0
Toluene	PFMC	<0.7:>99.3

2.4 Discussion

*2.4.1 Synthesis of $Na[B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ (**3**)*

Strictly following the literature procedure, **3** could not be obtained. Problems persisted during the copper mediated coupling step of Bühlmann's synthesis and in the bromination step of van Koten's synthesis. However, the improved method developed during the course of this thesis is a reliable and efficient way to generate **3**. The copper mediated coupling was not adversely affected by removing C_6F_6 and bipy from the equation (Scheme 2.5). Early reports of this type of copper mediated coupling used a single solvent system, DMSO or DMF, without any additives to achieve a wide range of perfluorinated products.[33-36] Thrower suggests a mechanism for this transformation that is reproduced in Figure 2.11.[33]

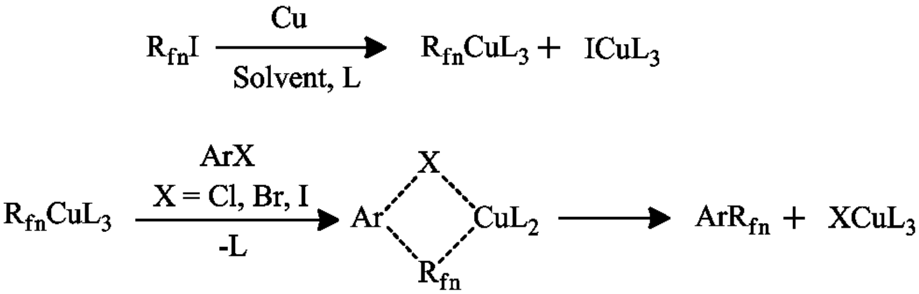


Figure 2.11. Proposed mechanism of copper mediated coupling of perfluoroalkyl iodides with aryl halides.

Thrower suggests the coordinating solvent plays a vital role in the perfluoroalkylation process. The key is to find a solvent that neither binds too strongly or weakly to copper. The solvent must help stabilize the perfluoroalkylcopper species and also dissolve the cuprous halides, keeping the copper clean and available. Thrower analyzed a variety of solvents and found DMSO met the requirements the best.[33] One reason a mixed solvent system might be attractive is that the C_6F_6 acts as an inert diluent. It promotes the perfluoroalkylation by limiting the coordination of solvent to the copper catalyst and promoting the formation of perfluoroalkylcopper species. Eapen found that bidentate ligands such as 2-2'-bipyridine (bipy) coordinate to the copper in place of the solvent and suppresses side reactions.[36] This was a useful trick when trying to add ponytails to less reactive haloarenes. Even so, elevated temperatures and extended reaction times are needed to combat the low reactivity of bromo- and chloroarenes. In our experience the best route for perfluoroalkylation was to keep the process simple. Iodoarenes have the highest reactivity which allows the use of the most optimal solvent system and no added catalyst.

Small traces of water and acetone remain even after heating **3** to 200 °C under oil pump vacuum. This suggests the binding of solvent molecules to the sodium cation.

2.4.2 Syntheses of ***4*** *and* ***5***

The syntheses of **4** and **5** involved straight forward salt metathesis. Interestingly, when comparing the integration of the fluorous BAr_{f6} anion with the Werner-type cation, a 3:1 ratio is not strictly observed. Looking again at Figure 2.5, the integration of the amine peaks (5.68 and 5.29 ppm) to the *para* hydrogen fluorous BAr_{f6} peak (7.58 ppm), a 2:1 ratio of anion to cation is observed. This would lead to the possibility of a $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_2Cl$ species present in the fluorous phase. This would mean that when the Werner cation is coordinated to two fluorous anions it transfers, with a chloride, to the fluorous phase.

Table 2.7 compares these possibilities using elemental analysis. The calculated value in each variation is equivalent within 1% for every element except for fluorine. For the chloride species, the fluorine content is close to the experimental value. However, when the observed water and acetone are factored in, the fluorine content is almost 5% below the experimental value. Another way of looking at this is to focus on the amount of chlorine that would be expected from $[Co(en)_3][B(3,5C_6H_3(R_{f6})_2)_4]_2Cl$ or $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_2Cl$•6(acetone)•$15H_2O$. In the first compound, cobalt and boron would represent 0.98% and 0.36% respectively. This accounts for 98.4% of the mass (30.99 (found C) + 0.80 (found H) + 0.94 (found N) + 64.35 (found F) + 0.98

(calculated Co) + 0.36 (calculated B)), leaving ample room for a chlorine. The situation is similar with the second compound (98.3 % of mass accounted for without chlorine).

Table 2.7. Elemental analysis calculated for the variations of **4**.

		Calculated			
Element	Found	**4**	**4**•6(acetone)•$15H_2O$	$[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_2Cl$	$[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_2Cl$•6(acetone)•$15H_2O$
C	30.99	30.20	31.49	30.02	30.48
H	0.80	0.67	1.51	0.79	1.72
N	0.94	0.95	0.87	1.40	1.27
F	64.35	67.14	61.68	65.85	59.70
Co	a	0.67	0.62	0.98	0.89
B	a	0.37	0.34	0.36	0.33
Cl	a	0	0	0.59	0.54

[a]No analysis was conducted.

Regardless, the working supposition is that the complex can be treated as $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ even though the present data does not fully support this conclusion. The same issue can be seen when integrating the cation vs. anion signals in the ^1H NMR of **5** (Figure 2.10). However, like compound **4**, the elemental analysis better supports a 3:1 ratio of anion to cation. In all reality, the average ratio of anion to cation might lie somewhere in between 2:1 and 3:1 for both **4** and **5**.

*2.4.3 Partitioning of **4** and **5***

The partition coefficients determined in Tables 2.3 and 2.6 show the ability of fluorous anion to keep the Werner cation in the fluorous phase evidenced by the very high partitions toward the fluorous phase. An interesting twist is seen when organic soluble $[Co(en)_3][BAr_f]_3$ competes with fluorous soluble $[Co(en)_3][B(B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$ complex, Figure 2.7. The partition coefficient of 42:58 shows a slight preference for the fluorous phase.

In *The Handbook of Fluorous Chemistry* Gladysz dedicated a chapter to partition coefficients involving non-fluorous, partially-fluorinated, fully-fluorinated, and fluorous tagged compounds.[37] This leads to an easy comparison of compounds **4** and **5** with other fluorous transition metal complexes. Table 2.8 compares several entries from the book and the partition coefficients determined through the course of this work.

Table 2.8. Selected partition coefficients of several fluorous transition metal complexes.

Entry	Solute	Solvent System	Partition coefficient
1	$[\mathbf{Co}(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$(**4**)	$CF_3C_6F_{11}:CH_3C_6H_5$	>99.3:<0.7
2	$[\mathbf{Co}(\mathit{R,R}\text{-}chxn)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3$(**5**)	$CF_3C_6F_{11}:CH_3C_6H_5$	>99.3:<0.7
3	$[\mathbf{Co}(en)_3][BAr_f]$/ $[\mathbf{Co}(en)_3][B(C_6H_3\text{-}3,5\text{-}(R_{f6})_2)_4]_3$	$CF_3C_6F_{11}:CH_3C_6H_5$	58:42
4	$[(R_{f6}(CH_2)_2)_3P]_2\mathbf{Rh}(Cl)$	$CF_3C_6F_{11}:CH_3C_6H_5$	99.86:0.12
5	$[(R_{f6}(CH_2)_2)_3P]_2\mathbf{Ir}(Cl)(CO)$	$CF_3C_6F_{11}:CH_3C_6H_5$	>99.7:<0.3
6	$[(R_{f6}(CH_2)_2)_3P]_2\mathbf{Ni}(Cl)_2$	$CF_3C_6F_{11}:CH_3C_6H_5$	98.8:1.2
7	$\mathbf{Fe}[C_5H_3((CH_2)_2R_{f6})_2]_2$	$CF_3C_6F_{11}:CH_3C_6H_5$	98.6:1.4
8	$[\mathbf{Rh}(COD)(Ar_2P(CH_2)_nPAr_2)]^+ X^-$		
a	$Ar = 4\text{-}C_6H_4[Si(CH_3)_2(CH_2)_2R_{f6}]$ $X = [B(3,5\text{-}C_6H_3(R_{f6})_2)_4]^-$; n = 2	$CF_3C_6F_{11}:CH_3C_6H_5$	97.1:2.9
b	$X = [B(4\text{-}C_6H_3R_{f6})_4]^-$; n = 2	$CF_3C_6F_{11}:CH_3C_6H_5$	98.5:1.5
c	$X = [BF_4]^-$; n = 2	$CF_3C_6F_{11}:CH_3C_6H_5$	98.4:1.6
d	$Ar = C_6H_5$ $X = [B(3,5\text{-}C_6H_3(R_{f6})_2)_4]^-$; n = 4	$CF_3C_6F_{11}:CH_3C_6H_5$	41:59
9[38]	$[\mathbf{Ru}(bipy)_3][(R_fCO_2)_2H]_2$	$C_{10}F_{18}{}^a:CH_2Cl_2$	97.5:2.5

$^aC_{10}F_{18}$ = perfluorodecalin

Entries 4-6 contain fluorous alkyl phosphines and entry 7 has two fluorous tagged cyclopentadiene fragments. All of these transition metal complexes demonstrate very high fluorophilicity. When comparing the new compounds, entries 1 and 2, to these known fluorous transition metal complexes we can see that the fluorophilicity is maintained when the fluorous moiety is moved from the ligand scaffold to the coordinating anion. Also, we can compare the two new compounds to van Koten's series of fluorous borates (as described in Chapter I) in entries 8a-d. For 8a-c, the ligand scaffold contains four ponytails but the anion varies in its fluorophilicity. Entry 8d has the same rhodium backbone, but with a slightly longer bidentate chain length and no ponytails contained in the ligand set.

In entries 8a-c it is seen that changing the fluorophilicity of the anion does not enhance the overall partitioning of the compound. Even the BF_4^- complex (entry 8c) has a high fluorophilicity. It isn't until the fluorous ponytails are removed (entry 8d) that we can see the true effect of the coordinating anion. Looking back at entries 1 and 2, again the fluorophilicity is rooted solely in the anion. In this case the cobalt trication complexes benefit from partnering three fluorous BAr_{f6} anions that shift the partition drastically to the fluorous phase.

Vincent and coworkers recently published an article that takes the common $[Ru(bipy)_3]^{2+}$ dication, which shows no partitioning into fluorous media by itself, and added 2 eq. of a fluorous carboxylate.[38] When a stoichiometric amount of acid with respect to the carboxylate anion was added, the $[Ru(bipy)_3]^{2+}$ transferred almost quantitatively to the fluorous phase. Figure 2.12 is a representation of the $[Ru(bipy)_3][(R_fCO_2)_2H]_2$ species, a partition coefficient for which is given in entry 9 of Table 2.8. The authors suggest the highly fluorous carboxylate anions create a self-assembled network around the dication and stabilize the complex through hydrogen-bond interactions even in the midst of the highly non-polar fluorous solvent. This example lends great credit to the quantitative transfer of the cobalt complexes in this work. The higher oxidation states of both the ruthenium and cobalt allow multiple fluorous anions to associate, making the net fluorophilicity of the compound very high.

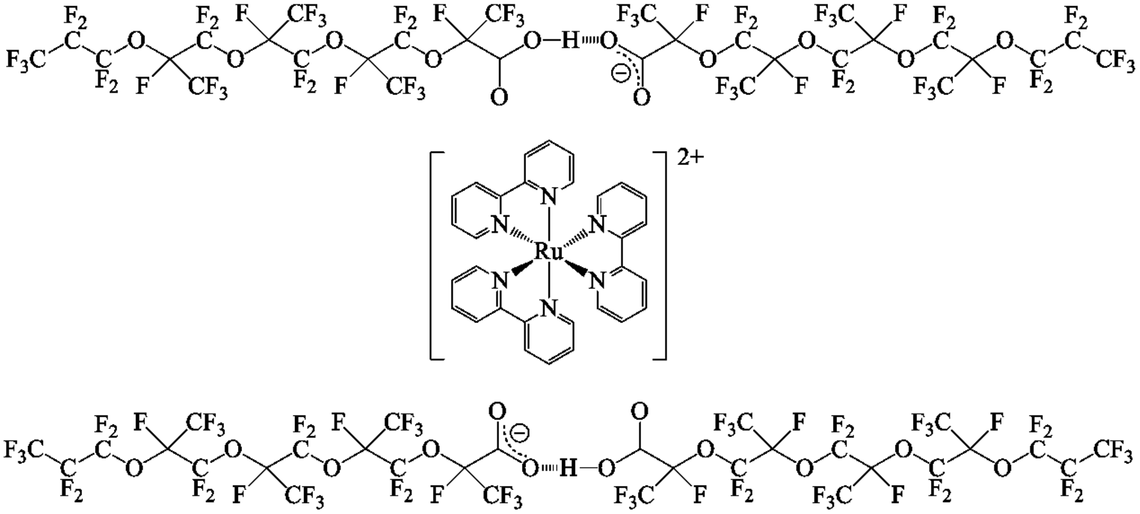


Figure 2.12. Vincent's $[Ru(bipy)_3][(R_fCO_2)_2H]_2$ complex.

CHAPTER III

CONCLUSION AND EXPERIMENTAL

3.1 Conclusion

A reliable method to synthesize **3** was presented. This improved synthesis will be beneficial to the greater scientific community as fluorous chemistry grows to expand the scope of "naked" cations in the fluorous phase. In this work, the fluorous BAr_{f6} anion was paired with two Werner-type cations but the facile anion exchange that it displayed can be applied to a wide range of substrates. Within the scope of Werner-type complexes, this work constitutes a significant stride toward developing a series of compounds that bring the concept of organocatalysis into fluorous media. New compounds **4** and **5** show high preferences for the fluorous phase. These data provide an available baseline for future Werner-type salt metathesis with fluorous BAr_{f6}.

3.2 Experimental

3.2.1 General experimental

All reactions were carried out under air unless noted. All workups were carried out in air. Chemicals were treated as follows: DMSO and DMF were distilled from CaH_2; all other solvents were purified using a Glass Contour solvent purification system; 1,3,5-tribromobenzene (Acros, 98%), copper (100 mesh 99.5%, Alfa Aesar), perfluorohexyliodide (SynQuest Labs, 98%), hexafluorobenzene (TCI, 99%), 1-chloro-

3,5-dibromobenzene (AK Scientific, 98%), 1,3-diiodobenzene (Alfa Aeser, 98%), *N*-bromosuccinimide (Alfa Aesar, 99%), sulfuric acid (EDM, 95%), trifluoroacetic acid, (Alfa Aesar, 99.5%), *t*-butyl lithium (Alfa Aesar, 1.74 M), boron trichloride (Acros, 1 M), sodium chloride (EDM, 98%), FC-75 (Alfa Aeser, 99%), FC-72 (Apollo Scientific, 98%), FC-70 (Acros, 99%), PFMC (ABCR, 90%), and toluene (Mallincknodt, 98%) were used as received.

NMR specta were recorded on a Varian 500 MHz spectrometer at ambient probe temperatures and referenced as follows: ^{1}H: residual internal $CHCl_3$ (δ = 7.26 ppm) or acetone-d_5 (2.05 ppm); ^{13}C: internal $CDCl_3$ (δ = 77.2 ppm) or acetone-d_6 (29.8 ppm). The highly coupled ^{13}C signals of the fluorinated carbons are not listed. Melting points were recorded with a Stanford Research Systems (SRS) MPA100 (Opti-Melt) automated melting point system. Microanalyses were conducted by Atlantic Microlabs.

3.2.2 Experimental procedures

1,3-bis(perfluorohexyl)benzene.[27] Under a N_2 atmosphere, a Schlenk flask was charged with copper (7.03 g, 0.110 mol), diiodobenzene (7.09 g, 21.5 mmol), and DMSO with stirring. The mixture was heated to 140 °C and perfluorohexyliodide (10.2 mL, 47.1 mmol) was added dropwise over 15 min. After 3 d, the mixture was cooled to room temperature and deionized water (100 mL) added. The solid was extracted with CH_2Cl_2 (3 × 100 mL), which was washed with water (100 mL) and then brine (100 mL). The solution was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The yellow oil was dissolved in perfluorohexane (5 mL), which was extracted with acetone (2 × 20 mL). The solvent was removed from the fluorous phase by rotary evaporation to give **1** as a light yellow oil (9.46 g, 13.2 mmol, 61%). ^{1}H NMR (δ, 1:1

v/v $CDCl_3/C_6F_6$) 7.89 (s, 1H), 7.88 (s, 2H), 7.76 (t, J = 8.06 Hz, 1H). These data agreed with those in the literature.[27]

1-bromo-3,5-bis(perfluorohexyl)benzene (2).[27,28] A round-bottomed flask was charged with **1** (5.85 g, 8.20 mmol), sulfuric acid (6.6 mL), and TFA (16.8 mL) with stirring. Then a portion of NBS (2.27 g, 12.7 mmol total) was added every hour for 8 h. After an additional 40 h, the mixture was poured over ice (300 g) and aqueous NaOH was added until a pH of 7 was reached. The mixture was extracted with CH_2Cl_2 (3 × 100 mL). The extracts were combined and dried ($MgSO_4$). The solvent was removed by rotary evaporation to give **2** as a white solid (4.94 g, 6.22 mmol, 80 %), mp 39.8-41.6 °C. ^1H NMR (δ, 1:1 v/v $CDCl_3/C_6F_6$) 7.94 (s, 2H), 7.72 (s, 1H). These data agreed with those in the literature.[27,28]

$Na[B(C_6H_3\text{-}3,5(R_{f6})_2)_4]$ (3).[27,28] A round-bottomed flask was charged with **2** (1.84 g, 2.32 mmol) and Et_2O (100 mL). The mixture was cooled to –78 °C. After 10 min, *t*-BuLi (3.0 mL, 1.74 M, 5.22 mmol) was added dropwise over 15 min with stirring. After an additional hour, BCl_3 (0.50 mL, 1.0 M, 0.50 mmol) was added. After an additional hour, the cooling bath was removed. After 12 h, the solution was poured into water (100 mL), and NaCl was added until saturation. The mixture was extracted with Et_2O (3 × 50 mL). The extracts were dried ($MgSO_4$), and the solvent was removed by rotary evaporation. Then FC-72 (5 mL) was added, and the solution was extracted with acetone (2 × 5 mL). The acetone was removed by rotary evaporation. The brown oil was chromatographed on a silica gel column (10 × 1.5 cm). A fraction was eluted with Et_2O and another with acetone. The acetone was removed by rotary evaporation, which gave a brown oil that was recrystallized from FC-75 and dried in a drying pistol (refluxing toluene) to give **3**·3(acetone)·H_2O as a light brown waxy solid (0.7632 g, 0.2480 mmol, 49%). ^1H NMR (δ, acetone-d_6) 7.71 (s, 8H), 7.58 (s, 4H). These data agreed with those in the literature.[27,28]

The acetone and water stoichiometry estimated by NMR was unchanged after drying under vacuum at 198 °C (ethylene glycol drying pistol) and fit the microanalysis reasonably well. Elemental analysis: Calculated for $C_{72}H_{12}BF_{104}Na\bullet3(acetone)\bullet H_2O$: C, 31.60; H, 1.05; F, 64.18. Found: C, 30.89; H, 0.69; F, 63.93.

$[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3\cdot6(acetone)\cdot xH_2O$ (x = 15-20) **(4).** A round-bottomed flask was charged with a solution of **3** (0.1270 g, 0.04401 mmol) in PFMC (3 mL). Then an aqueous solution of $[Co(en)_3]Cl_3$ (1.313 mL, 0.01089 M, 0.01429 mmol) was added with vigorous stirring. After 10 min, the lower fluorous phase was separated and dried ($MgSO_4$). The solvent was removed by rotary evaporation to afford $[Co(en)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3\cdot6(acetone)\cdot xH_2O$ (x = 15-20) as an orange oil (0.01214 g, 0.01309 mmol, 92%). ^1H NMR (δ, acetone-d_6): BAr_{f6}^- at 7.71 (s, 24H), 7.58 (s, 12H); $[Co(en)_3]^{3+}$ at 5.68 (br s, 6H, N$\underline{H}$H'), 5.29 (br s, 6H, NH$\underline{H'}$), 3.30 (br s, 12H, CH_2), 2.90 (s, 30-40H depending on sample, H_2O), 2.08 (s, 24H, acetone); $^{13}C\{^1H\}$ NMR (δ, acetone-d_6) BAr_{f6}^- at 161.6 (q, $^1J_{BC}$ = 49.8 Hz), 137.5 (s), 128.2 (m), 121.4 (s); $[Co(en)_3]^{3+}$ at 46.2 (s). Elemental analysis: Calculated for $C_{222}H_{59}CoB_3F_{312}N_6\bullet6(acetone)\bullet15H_2O$: C, 29.92; H, 1.16; N, 0.91; F, 63.92. Found: C, 30.99; H, 0.79; N, 0.94; F, 64.35.

$[Co(R,R\text{-}chxn)_3][B(3,5\text{-}C_6H_3(R_{f6})_2)_4]_3\cdot6(acetone)\cdot xH_2O$ (x = 15-20) **(5).** A round-bottomed flask was charged with a solution of **3** (0.0955 g, 0.0330 mmol) in PFMC (2.375 mL). Then an aqueous solution of $[Co(R,R\text{-}chxn)_3]Cl_3$ (2.190 mL, 0.004955 M, 0.01018 mmol) was added with vigorous stirring. After 10 min, the lower fluorous phase was separated and dried ($MgSO_4$). The solvent was removed by rotary evaporation to afford an orange oil (0.0844 g, 0.00894 mmol, 89%). ^1H NMR (δ, acetone-d_6) BAr_{f6}^- at 7.71 (s, 24H), 7.57 (s, 12H); $[Co(R,R\text{-}chxn)_3]^{3+}$ at 5.54 (br s, 6H, N$\underline{H}$H'), 5.17 (br s, 6H, NH$\underline{H}$'), 2.99 (br s, 6H, CHN), 2.86 (s, 30-40H depending on sample, H_2O), 2.08 (s, 24H, acetone), 2.35 (m, 6H, 2CH), 1.74 (m, 6H, 2CH), 1.62 (m, 6H, 2CH), 1.25 (m, 6H, 2CH). $^{13}C\{^{1}H\}$ NMR (δ, acetone-d_6) BAr_{f6}^{-} at 161.6 (q, $^{1}J_{BC}$ = 49.8 Hz), 137.5 (s), 128.3 (m), 121.4 (s); $[Co(chxn)_3]^{3+}$ at 61.5 (s), 33.5 (s), 24.5 (s). Elemental analysis: Calculated for $C_{234}H_{78}B_3CoF_{312}N_6$•6(acetone)•15$H_2O$: C, 30.93; H, 1.35; N, 0.89; F, 62.81. Found: C, 31.80; H, 0.99; N, 0.91; F, 61.66.

3.2.3 Partition coefficient

Standard Solutions. A standard solution of **4** (0.2732 g, 0.0296 mmol) in PFMC (5.938 mL) was prepared (0.00500 M). This was diluted in a series of volumetric flasks to give 0.00119 and 0.000282 M solutions. The UV-Vis absorptions at 460 nm were measured. The three solutions gave absorbances (A) of 1.0795, 0.2440, and 0.0601, indicating good agreement with Beer's law and an extinction coefficient (ε) of 215 $M^{-1}cm^{-1}$ (R = 0.999).

Partitioning. To determine the partition coefficient of the biphasic system, **4** in PFMC (0.0358 mmol in 4.750 mL; 0.00753 M) and water (4.750 mL) were stirred vigorously for 10 min at 23 °C. A UV-Vis spectrum of an aliquot of each phase was recorded. The absorbance at 460 nm was used to determine the mmol of **4** in the aqueous and fluorous phases following A = ε l c. In this example, the absorbance of the fluorous phase was 1.0269 and the aqueous phase 0.0114 (the more dilute solution also showed the characteristic d-d transitions of the trication at ca 270 nm, ruling out any substantial contribution of an impurity to the 460 nm absorption). This corresponds to a 0.00478 M solution containing 0.0227 mmol of **4** in the fluorous phase and 0.0000530 M solution containing 0.000252 mmol of **4** in the aqueous phase. The ratio of **4** in the fluorous phase to the total amount of **4** present in both phases is 0.0227/0.0229×100 = 99.0%. Partitioning of **4** into the aqueous phase is 0.000252/0.0229×100 = 1.0%. The ratio of the partitioning of **4** in the fluorous phase to that in the aqueous phase, 99.0:1.0, represents the partition coefficient of the biphasic system, sometimes written as 99 where $P_{FBS} = c_{fluorous\ phase}/c_{other\ phase}$. The total recovery of the system is 0.0236 mmol, 65%.

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