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DEPARTMENT OF CHEMISTRY

SYNTHESIS OF A CHIRAL PHOSPHACYCLE TO CATALYZE DEOXYGENATIVE  
CONDENSATION OF  $\alpha$ -KETO ESTERS AND CARBOXYLIC ACIDS VIA  $P^{III}/P^V$  REDOX  
CYCLING

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## ABSTRACT

Previous studies by the Radosevich Group have shown that a phosphetane (i.e. a 4-membered phosphacycloalkane) catalyzes the deoxygenative condensation of  $\alpha$ -keto esters and carboxylic acids to form  $\alpha$ -acyloxy ester products with good functional group compatibility. The reaction proceeds through initial addition of the phosphacycle in its +3 oxidation state to the  $\alpha$ -keto ester in a Kukhtin-Ramirez reaction, followed by subsequent reaction with the carboxylic acid to expel a phosphine oxide byproduct with C-O bond formation. The phosphine oxide, which has phosphorus in the +5 oxidation state, is then reduced *in situ* by a silane reductant back to the starting phosphetane. This thesis describes initial experiments directed toward enantioselective variants of this catalytic reaction using new, chiral phosphacycles as catalysts.

## TABLE OF CONTENTS

LIST OF FIGURES .....	iii
LIST OF TABLES .....	iv
ACKNOWLEDGMENTS .....	v
<b>Chapter 1</b> Introduction.....	1
<b>1.1</b> Trivalent Phosphorus Chemistry .....	1
<b>Chapter 2</b> .....	3
Deoxygenative Condensation of $\alpha$ -Keto Esters and Carboxylic Acids Via $P^{III}/P^V$ Redox Cycling.....	3
<b>2.1</b> Catalytic Phosphacycles .....	3
<b>2.2</b> $\alpha$ -Keto Esters and Carboxylic Acids .....	5
<b>2.3</b> Proposed Mechanism.....	7
<b>2.4</b> Conclusion .....	8
<b>Chapter 3</b> Pursuit of Chiral Phosphacycle.....	9
<b>3.1</b> Goals .....	9
<b>3.2</b> Synthesis of the Chiral Phosphetane.....	9
<b>3.3</b> Exploration of Alternative Phosphacycles.....	11
<b>3.4</b> Conclusion .....	13
<b>Chapter 4</b> Experimental Section.....	15
<b>Appendix A</b> $^1H$ and $^{31}P$ NMR Spectra .....	19
REFERENCES .....	24

## LIST OF FIGURES

<b>Scheme 1.</b> Wittig Reaction.....	1
<b>Scheme 2.</b> Mitsunobu Reaction.....	2
<b>Scheme 3.</b> Appel Reaction .....	2
<b>Figure 4.</b> Catalytic Wittig Cycle .....	3
<b>Scheme 5.</b> Optimized Reaction Conditions.....	4
<b>Scheme 6.</b> Kinetic control and importance of ring strain of catalyst .....	7
<b>Scheme 7.</b> Proposed mechanism for deoxygenative condensation and <i>in situ</i> reduction .....	8
<b>Figure 8.</b> salen(Co) catalysts for asymmetric epoxide ring-opening reactions.....	12
<b>Scheme 9.</b> (i) ( <i>R,R</i> )- <b>28</b> ·OAc, 0.55 eq. H <sub>2</sub> O; (ii) <i>n</i> -BuLi, Et <sub>2</sub> O, PhPH <sub>2</sub> ; (iii) <b>32a/32b</b> , <i>p</i> -TsOH, toluene.....	13

**LIST OF TABLES**

<b>Table 1.</b> Examples with varying carboxylic acid components.....	5
<b>Table 2.</b> Examples with varying $\alpha$ -keto ester components .....	6

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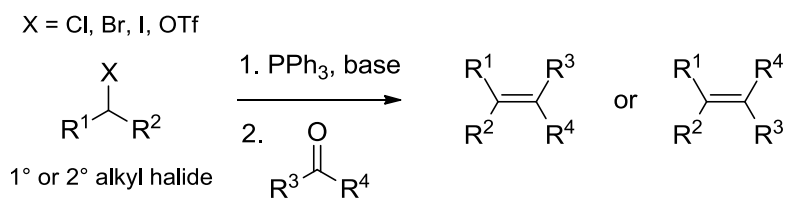
## Chapter 1

### Introduction

#### 1.1 Trivalent Phosphorus Chemistry

Trivalent phosphorus compounds refer to a group of compounds that exhibit a phosphorus atom with a +3 oxidation state. Trivalent phosphorus chemistry was explored as early as 1898 by Michaelis through the formation of carbon-phosphorus bonds in the Michaelis-Arbuzov rearrangement.<sup>1</sup> The rearrangement involves a reaction of an alkyl halide with a trivalent phosphorous ester to yield a dialkyl alkylphosphonate.

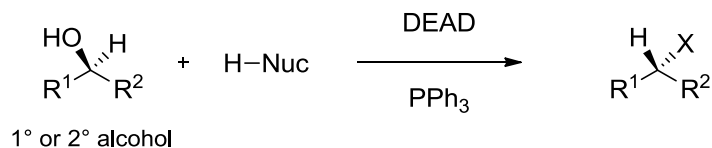
Trivalent phosphorus compounds have featured in extensive applications, and further studies of deoxygenative reactions involving trivalent phosphorus compounds include the Wittig,<sup>2</sup> Mitsunobu,<sup>3</sup> and Appel reactions.<sup>4</sup> The Wittig reaction features the preparation of alkenes from carbonyl compounds (either aldehydes or ketones) through the utilization of phosphonium ylides, most typically generated from triphenylphosphine.



**Scheme 1.** Wittig Reaction

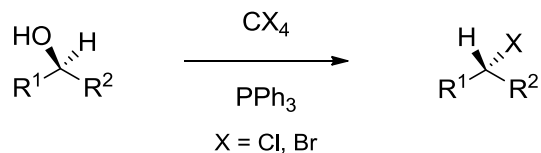
The Mitsunobu reaction is frequently used in the conversion of primary and secondary alcohols to esters and various other products. The reaction functions through the addition of triphenyl phosphine to diethyl azodicarboxylate to generate a dipolar phosphonium intermediate,

which ultimately activates the alcohol oxygen as a leaving group. The extrusion of phosphine oxide via displacement yields the substitution product.



**Scheme 2.** Mitsunobu Reaction

The Appel reaction is used in the halogenation of alcohols via the intermediacy of halophosphonium intermediates formed from a phosphine and a tetrahalomethane. As in the Mitsunobu reaction, a phosphine oxide is formed as the stoichiometric byproduct.



**Scheme 3.** Appel Reaction

The previous reactions all function through a phosphorus(III)-mediated deoxygenative transformation. Recently, the Radosevich group reported a reaction based on the stoichiometric conversion of P<sup>III</sup> to P<sup>V</sup>, involving the deoxygenative condensation of  $\alpha$ -keto esters with protic pronucleophiles.<sup>5</sup> The reactions employ the Kukhtin-Ramirez addition, which features the addition of a trivalent phosphorus to an  $\alpha$ -keto ester to give stable adducts. Protonation of these Kukhtin-Ramirez adducts by the pronucleophile (H-X) gives an intermediate oxyphosphonium.<sup>6</sup> Subsequent displacement by the nucleophile (X<sup>-</sup>) allows the formation of new C-X bonds with expulsion of a phosphine oxide byproduct.

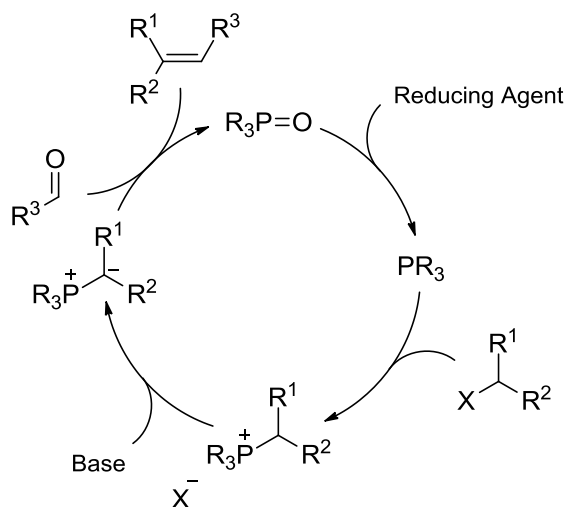


## Chapter 2

### Deoxygenative Condensation of $\alpha$ -Keto Esters and Carboxylic Acids Via $P^{III}/P^V$ Redox Cycling

#### 2.1 Catalytic Phosphacycles

While the stoichiometric Wittig reaction has seen extensive use in organic chemistry, the reaction suffers from a number of limitations including cost efficiency and the removal of the phosphine oxide byproduct. O'Brien developed a catalytic Wittig reaction that relies on the ability of phenylsilane and diphenylsilane to reduce the phosphine oxide byproduct both in the presence of aldehyde and ketones and without unwanted stereochemical consequences on the phosphine.<sup>7</sup>

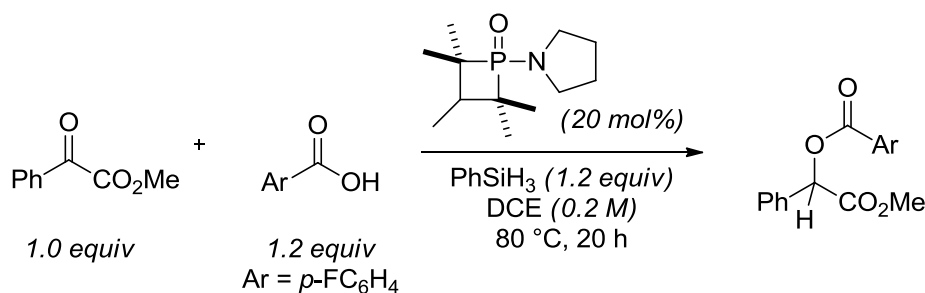


**Figure 4.** Catalytic Wittig Cycle

Small, strained phosphacycles can catalyze the condensation of  $\alpha$ -keto esters and carboxylic acids involving an *in situ* reduction of the phosphine oxide using a silane reductant.<sup>8</sup> The recycling of the phosphine oxide proves cost beneficial, but chiral phosphorus reagents and

enantioselectivity of the  $\alpha$ -acyloxy ester products were only explored using stoichiometric equivalents. The comparison of the  $\alpha$ -acyloxy ester product with the use of stoichiometric and catalytic amounts of the chiral reagent can provide insight into the mechanism of the reduction of the phosphine oxide by silane reductant.

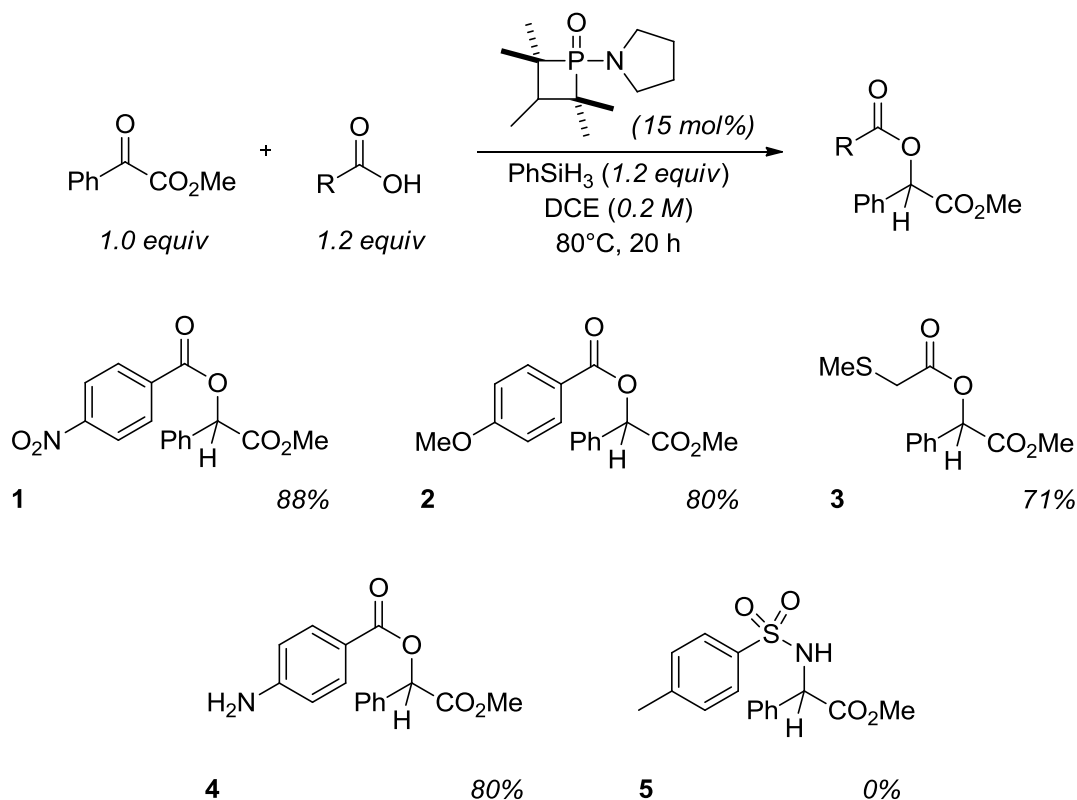
The first portion of this thesis involves the development of phosphacycles that catalyze the condensation of  $\alpha$ -keto esters and protic pronucleophiles with an *in situ* reduction of the phosphine oxide byproduct. For stoichiometric reduction of the phosphine oxide, a number of hydride donors, including lithium aluminum hydride and sodium borohydride prove to be efficient. However, in our system both reduction agents would also cause reduction of the  $\alpha$ -keto ester or the carboxylic acid, resulting in no formation of desired product. Silane-based reductants were chosen for their weaker reduction capabilities and hence higher chemoselectivities.<sup>9, 10</sup> When methyl benzoylformate was reacted with 4-fluorobenzoic acid and a catalytic amount of the phosphetane catalyst in the presence of silane, diphenylsilane, triethyloxysilane, and diethoxymethylsilane all demonstrated insufficiency, but phenylsilane performed the desired reduction of the phosphine oxide effectively without unforeseen complications. After testing a number of different reaction conditions, the reaction conditions were optimized with 1.2 equiv. of phenylsilane in 1,2-dichloroethane at 80 °C.



**Scheme 5.** Optimized Reaction Conditions

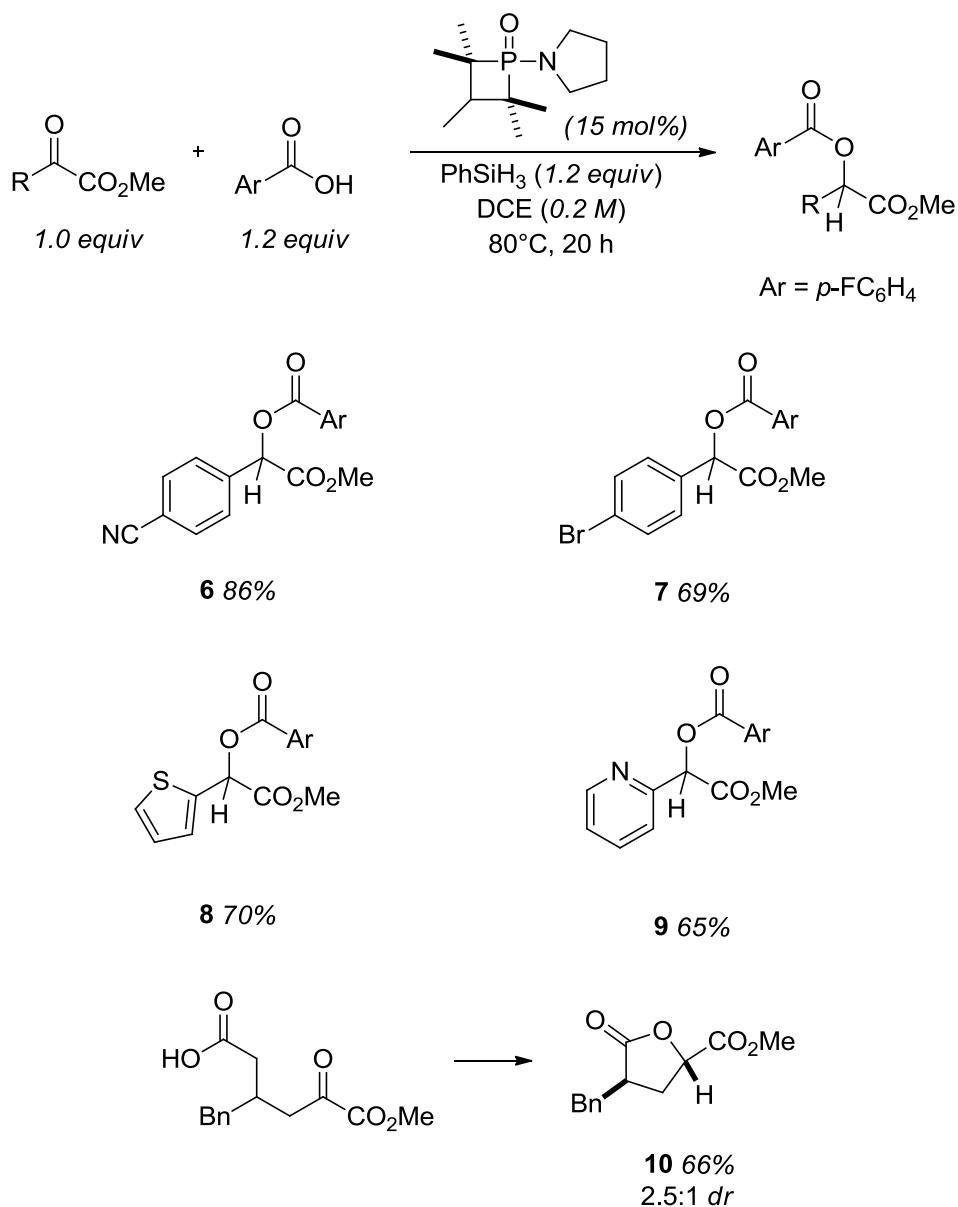
## 2.2 $\alpha$ -Keto Esters and Carboxylic Acids

In terms of the scope of carboxylic acids, a number of benzoic acid derivatives exhibiting electron-rich (**2**) and electron-deficient (**1**) substituents provided desired products with excellent yields. In addition, the low Lewis acidity of the catalyst allowed good compatibility with sulfides (**3**) and anilines (**4**). However, when other pronucleophiles such as N-methyl-*p*-toluenesulfonamide (**5**) were used in place of the carboxylic acids, no significant reactivity was observed. The isolation of the reactivity to only carboxylic acids may be due to the reactive acidity of the proton compared to other pronucleophiles, which would aid in the proton shift between the pronucleophile to the Kukhtin-Ramirez intermediate.



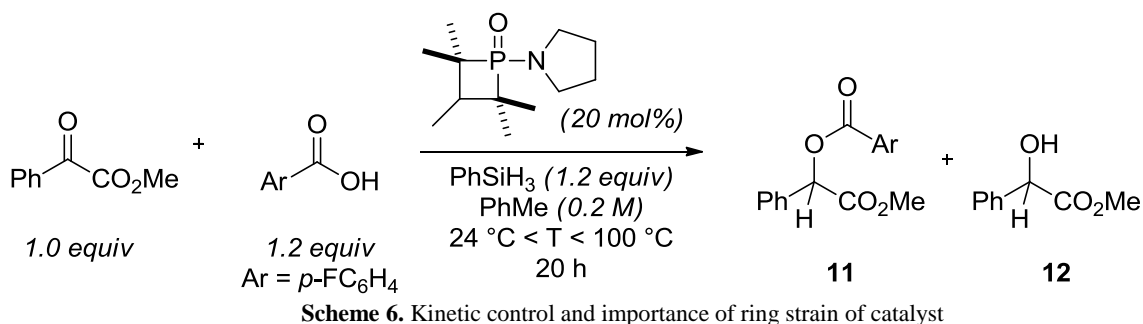
**Table 1.** Examples with varying carboxylic acid components

Reactions also proceeded smoothly with varying  $\alpha$ -keto esters. Benzoylformate functionalities (**6**, **7**) also provided excellent yields, and the reaction exhibited reactivity with hetero-aromatic  $\alpha$ -keto esters (**8**, **9**). In addition, alkyl  $\alpha$ -keto esters demonstrated the ability to intramolecularly react and cyclize with moderate diastereoselectivity (**10**).



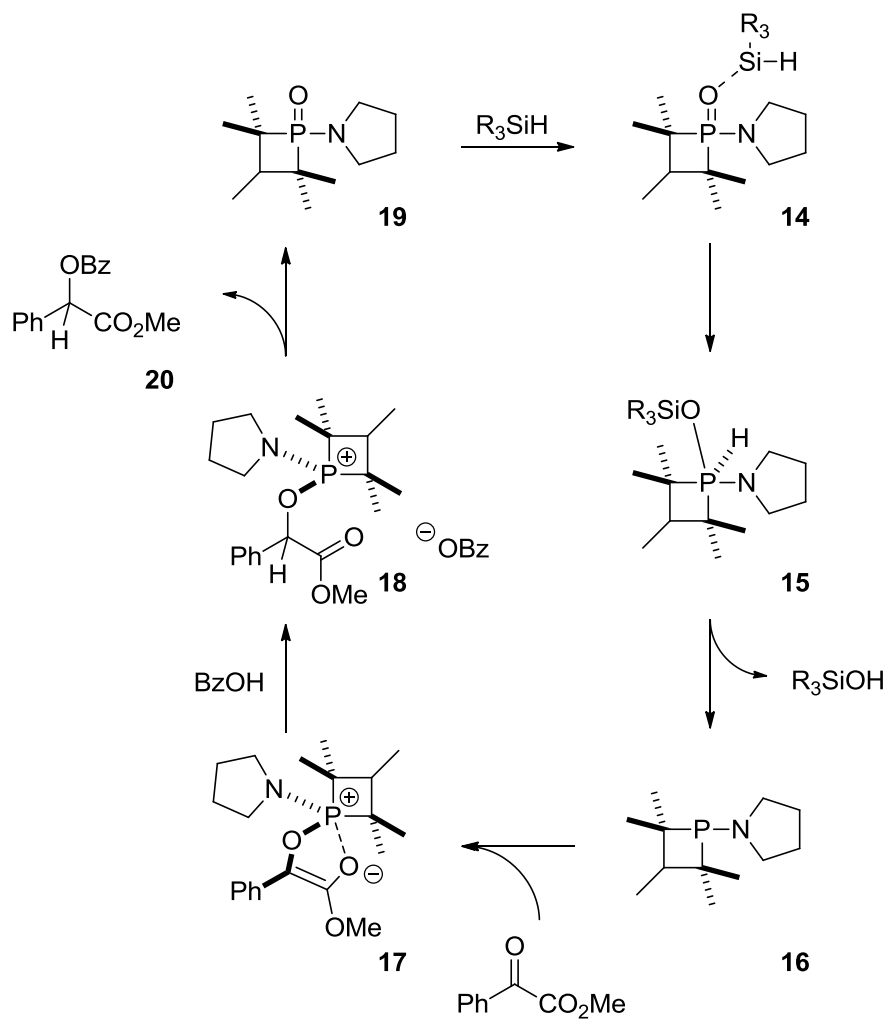
**Table 2.** Examples with varying  $\alpha$ -keto ester components

The Radosevich group also pursued the importance of the torsional ring strain to the  $P^{III}/P^V$  redox cycling. Under conditions slightly differing from ideal reaction conditions (**Scheme 5**), decreasing reaction temperature results in the formation of **12** over the formation of the desired product (**11**). When **12** is subjected to high temperature (100 °C) in similar reaction conditions (**Scheme 6**), product (**11**) is not observed, so the group hypothesized that the products are formed under kinetic control.<sup>8</sup>



### 2.3 Proposed Mechanism

The reaction initiates through the consumption of the phosphine oxide (**19**) by the silane via initial Lewis acid-base interaction (**14**) followed by a hydride shift from silicon to phosphorus (**14**→**15**).<sup>11</sup> Subsequently, the phosphorus(III) species reacts selectively with the  $\alpha$ -keto ester through the Kukhtin-Ramirez addition (**16**→**17**) followed by a proton transfer from the carboxylic acid (**17**→**18**). The deprotonated nucleophile then displaces the phosphine oxide resulting in the observed products (**18**→**19**).



**Scheme 7.** Proposed mechanism for deoxygenative condensation and *in situ* reduction

## 2.4 Conclusion

Because the reaction was only observed to function with carboxylic acids, additional research can investigate and expand the scope of the reaction to include other protic pronucleophiles. In addition, the reaction conditions require a high temperature (80 °C to 100 °C) for an extended period of time (8 to 20 h), so the performance of the catalysis can also receive attention.

## Chapter 3

### Pursuit of Chiral Phosphacycle

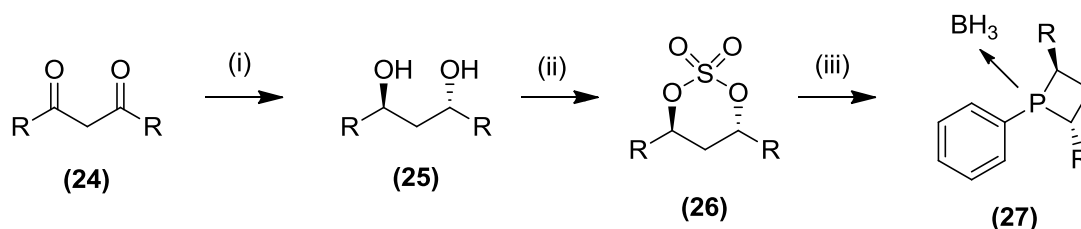
#### 3.1 Goals

While the development of the catalytic reaction represented the ground-work for this thesis, additional research was conducted to obtain a chiral phosphacycle in order to perform the previously investigated catalytic condensation of  $\alpha$ -keto esters and carboxylic acids with an *in situ* reduction of the phosphine oxide with a silane reductant. Utilizing a chiral phosphacycle will allow further investigation of the mechanism of the *in situ* reduction, which current proposed mechanisms involve a hydride shift from the silicon to phosphorus (**Scheme 7**).

#### 3.2 Synthesis of the Chiral Phosphetane

The first phosphacycle target developed (**27**) mimics the phosphetane utilized in the original investigation due to the reported importance of the torsional ring strain to the  $P^{III}/P^V$  cycling.

The synthesis of the chiral phosphetane follows a methodology originally discussed by Marinetti, which initiates with an enantioselective hydrogenation of  $\beta$ -diketones (**24**) in the presence of ruthenium-BINAP complexes.<sup>14</sup> The resulting 1,3-diol (**25**) was converted by sequential treatment with thionyl chloride and  $NaIO_4/RuCl_3$  to the corresponding cyclic sulfate (**26**), which was carried on without purification. The sulfate group was then substituted with phenylphosphine using *n*-butyllithium as base. The resultant phosphacycle was protected with borane to yield the target compound (**27**).



R=(a) Me, (b) *i*Pr

**Scheme 7.** (i) (*S*)-BINAP, RuBr<sub>2</sub> 0.2-0.5%, H<sub>2</sub>, 50 bar, 50 °C, 70h; (ii) (a) thionyl chloride, CCl<sub>4</sub>, reflux 1h, (b) RuCl<sub>3</sub>, NaIO<sub>4</sub>; (iii) (a) PhPH<sub>2</sub>, 2 eq. *n*-BuLi, (b) BH<sub>3</sub>·SMe<sub>2</sub>

The hydrogenation of the 2,6-dimethylheptane-3,5-dione (**24b**) initially failed due to improper heat applied to the pressure reactor. The reactor was initially heated at 50 °C for 72 h, which resulted in no observed product formation, and subsequent reactions were run at 80 °C. Improper release of pressure from the pressure reactor on the initial attempt also caused the reaction mixture to spill within the reactor. The starting material was recovered and the synthesis of the diol (**25b**) was successful with a 57% yield. The product was purified by vacuum distillation, verified by <sup>1</sup>H NMR, and stored as the stable diol (**25b**). In addition, hydrogenation of the pentane-2,4-dione (**24a**), which was executed at 50 °C, was successful with yields of the respective diol (**25a**) 78% and 59%. The product was purified by vacuum distillation and stored as a mixture of the dione (**24a**) and the diol (**25a**), which was determined to be a ratio of 1:12 by <sup>1</sup>H NMR (**Appendix A**).

The mixture of the dione (**24a**) and the diol (**25a**) was carried forward and refluxed with thionyl chloride and carbon tetrachloride followed by an addition of ruthenium(III) chloride and sodium periodate to yield the cyclic sulfate (**26a**), which was confirmed by TLC, with a 24% yield.

For the substitution of the cyclic sulfate (**26a**) with phenylphosphine, initially 1.1 equiv. of *n*-BuLi was added to a dilute solution of PhPH<sub>2</sub> in THF, which was then added to a solution of



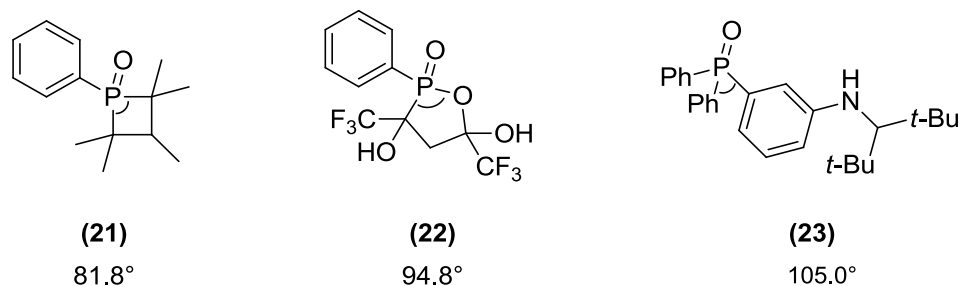
the dimethyl cyclic sulfate (**26a**) before the second 1.1 equiv. of *n*-BuLi was added. The reaction was performed at very low concentrations, and the two additions of *n*-BuLi were added sequentially to avoid the formation of polymers and other undesired products. The initial attempt at synthesizing the phosphine (**27a**) produced no product by  $^{31}\text{P}$  NMR. A subsequent attempt reduced the *n*-BuLi to 1 equiv., but the reaction yielded trace amounts of product by  $^{31}\text{P}$  NMR. A third attempt at the phosphacycle (**27a**) focused on allowing the *n*-BuLi to fully react with the phenylphosphine before addition to the cyclic sulfate (**26a**), but the reaction again failed to produce desired product. The  $^{31}\text{P}$  NMR of the reaction mixture was compared to a  $^{31}\text{P}$  NMR of the pure product attained by Kyle Reichl, a member of the Radosevich group (**Appendix A**). Although the  $^1\text{H}$  NMR of the cyclic sulfate (**26a**) initially demonstrated purity, the compound slowly changed from its original off-white and yellow color to a dark red-brown color, which could indicate possible decomposition. Further  $^1\text{H}$  NMR analysis was not taken prior to the addition of phenylphosphine.

The dimethyl cyclic sulfate (**26a**) was exhausted in the attempts to create the phosphacycle (**27a**), and the procedure was not attempted with the 1,6-dimethylheptane-3,5-diol (**25b**) due to lack of success in the reaction using dimethyl cyclic sulfate (**26a**).

### 3.3 Exploration of Alternative Phosphacycles

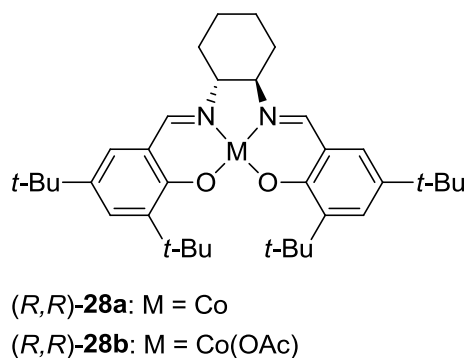
The second phosphacycle target (**33, 34**) was selected due to the oxygen atom increasing torsional strain within the five-membered ring to emulate the strain of a four-membered phosphetane. The four-membered ring (**21**) displays a C-P-C bond angle of  $81.8^\circ$ , while the oxaphospholane (**22**) shows a C-P-O bond angle of  $94.1^\circ$ .<sup>12, 13</sup> While the bond angles still differ

by 15%, both rings exhibit significant torsional strain when compared to the tetrahedral structure of the phosphorus in a phosphine oxide (**23**), which possesses a bond angle of  $105.0^\circ$ .<sup>14</sup>



**Figure 8.** Three phosphine oxide compounds and their respective bond angles

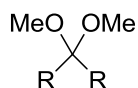
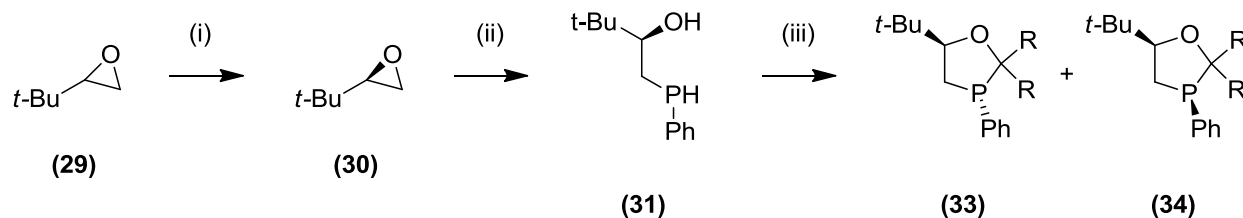
In an exploration of alternative chiral phosphacycles, an oxaphospholane prepared from chiral epoxide (**30**) by Morken was targeted.<sup>16, 17</sup> The synthesis of the chiral oxirane (**27**) involves a kinetic resolution by means of catalytic hydrolysis with an oligomeric (*R,R*)-(salen)Co catalyst (**28b**).<sup>19</sup> The (salen)Co(III) catalyst (*R,R*)-**28b** was prepared by treating a (salen)Co(II) compound (*R,R*)-**28a** with glacial acetic acid while open to air.<sup>16</sup> The resulting oxidized catalyst (*R,R*)-**28b** was utilized in obtaining the enantiomerically pure epoxide (**30**) from the racemic mixture of the terminal epoxide (**29**).



**Figure 8.** salen(Co) catalysts for asymmetric epoxide ring-opening reactions

The use of a synthetic catalyst was chosen due to the procedure utilizing water as the only reagent and affording the enantiomerically pure epoxide in a high yield.<sup>18</sup> The chiral oxirane (**30**) was treated with *n*-BuLi and phenylphosphine to generate the ring-opened *sec*-phosphine

intermediate (**31**). The intermediate (**31**) was refluxed with *p*-toluenesulfonic acid and the dimethoxy compound (**32a**, **32b**) to yield the phosphacycle products (**33**, **34**).<sup>14, 15</sup>



**(32a)**: R = Me

**(32b)**: R = Et

**Scheme 9.** (i) (*R,R*)-**28**·OAc, 0.55 eq. H<sub>2</sub>O; (ii) *n*-BuLi, Et<sub>2</sub>O, PhPH<sub>2</sub>; (iii) **32a/32b**, *p*-TsOH, toluene

The five-membered phosphorus ring (**33**, **34**) was chosen due to the torsional strain provided by the bond angle of the oxygen atom. With the catalyst (*R,R*)-**28b** prepared from (*R,R*)-**28a**, the hydrolytic kinetic resolution of racemic *t*-butyloxirane (**29**) with water was performed. Vacuum transfer of the reaction mixture yielded the enantiomerically pure (*R*)-*t*-butyloxirane (**30**) at a very low yield of <2%. Chiral GC analysis was not performed to characterize the enantiomeric purity due to the low yield of the product. The procedure was not repeated due to exhaustion of starting material.

### 3.4 Conclusion

Due to the success of the synthesis of both the dimethyl and diisopropyl β-diols (**24a**, **24b**) and the improper storage of the dimethyl cyclic sulfate (**25a**), the final step to generating the chiral phosphacycle will be attempted again with confirmed purity of the cyclic sulfate

intermediate. The synthesis of the five-membered oxaphospholane will be resumed once additional racemic terminal epoxide is acquired.

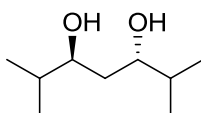
## Chapter 4

### Experimental Section

#### General Procedures

Unless otherwise noted, all reactions were carried out under a N<sub>2</sub> atmosphere using flame-dried glassware. All moisture-sensitive reagents were handled using a dry syringe, and anhydrous solvents were dispensed from a solvent dispensing system. Reagents obtained from commercial sources were used without further purification. Reactions were monitored via TLC and UV light. <sup>1</sup>H NMR spectra were obtained on a 360 or 400 MHz Bruker NMR, and <sup>31</sup>P NMR spectra were obtained on a 360 MHz Bruker NMR.

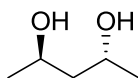
**General Procedure for  $\alpha$ -acyloxy esters.** A 20-mL reaction vial was charged with the carboxylic acid (1.2 equiv.), aminophosphetane *P*-oxide (15 or 20 mol%), and solvent (toluene or 1,2-dichloroethane, 0.2 M). The  $\alpha$ -keto ester substrate (1.0 equiv.) was added to the vial followed by phenylsilane (1.2 equiv.). The vial was sealed and heated to 80°C and monitored with TLC until completion. After allowing the reaction mixture to cool to room temperature, saturated sodium bicarbonate was added, and the biphasic mixture was separated and washed with dichloromethane. The organic layer was dried with anhydrous sodium sulfate and concentrated in vacuo. The crude product was purified using column chromatography (silica gel, 10:1; hexanes: ethyl acetate).



**(*R,R*)-2,6-Dimethyl-3,5-heptanediol (25b).** (*S*)-BINAP (36.1 mg, 0.058 mmol) and [(COD)Ru(2-methylallyl)<sub>2</sub>] (15.3 mg) were added to a 50 mL round bottom flask charged with

anhydrous acetone (5 mL) (distilled over  $K_2CO_3$  and degassed by bubbling  $N_2$  for 30 min.). A solution of HCl in diethyl ether (0.053 mL, 0.106 mmol) was added to the suspension, and the reaction mixture was stirred at room temperature for 40 min. The solvent was removed under vacuum, and the yellow solid residue was used as the catalyst for the hydrogenation reaction.

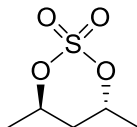
Methanol (10 mL) and 2,6-dimethylheptane-3,5-dione (3.00 g, 19.2 mmol) were added to the reaction vessel, which was placed into a stainless steel pressure reactor under nitrogen. The nitrogen atmosphere was replaced with hydrogen and the pressure reactor was subjected to an initial pressure of 80 bar. The reaction proceeded at 80°C for 70 h. The product was vacuum distilled to yield a white solid (1.75g, 57% yield).  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta=0.90$  (d,  $^3J(H,H)=8$  Hz, 6H;  $CHMe_2$ ),  $\delta=0.95$  (d,  $^3J(H,H)=8$  Hz, 6H;  $CHMe_2$ ),  $\delta=1.59$  (dd,  $^3J(H,H)=6$  Hz, 6 Hz;  $CH_2$ ),  $\delta=1.70$  (m,  $CHMe_2$ ),  $\delta=2.16$  (OH),  $\delta=3.65$  (m,  $CHOH$ ).



**(*R,R*)-pentane-2,4-diol (25a).** (*S*)-BINAP (93.4 mg, 0.15 mmol) and [(COD)Ru(2-methylallyl) $_2$ ] (30 mg, 0.12 mmol) were added to a 100 mL round bottom flask charged with anhydrous acetone (5 mL) (distilled over  $K_2CO_3$  and degassed by bubbling  $N_2$  for 30 min.). A solution of HCl in diethyl ether (0.16 mL, 0.321 mmol) was added to the suspension, and the reaction mixture was stirred at room temperature for 40 min. The solvent was removed under vacuum, and the yellow solid residue was used as the catalyst for the hydrogenation reaction.

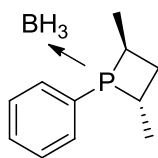
Methanol (10 mL) and pentane-2,4-dione (**24a**) (15 mL, 146 mmol) were added to the reaction vessel, which was placed into a stainless steel pressure reactor under argon. The argon atmosphere was replaced with hydrogen and the pressure reactor was subjected to an initial pressure of 50 bar. The reaction proceeded at 50°C for 70 h. The product was vacuum distilled to

yield a white solid (3.12g, 78% yield; 5.96g, 59% yield) that was determined by  $^1\text{H NMR}$  to be a 12:1 mixture of (**25a**: **24a**).



**(*R,R*)-pentane-2,4-diol cyclic sulfate (26a)**. Thionyl chloride (6.12 ml, 84.4 mmol) was added to a solution of (*R,R*)-pentane-2,4-diol (8.00 g, 76.8 mmol) in  $\text{CCl}_4$  (120 mL). The resulting solution was refluxed for 1h. The solvent was removed by rotary evaporation, and the residue was dissolved in a mixture of  $\text{CCl}_4$  (50 mL), MeCN (50 mL), and water (75 mL) and then cooled to 0 °C.  $\text{RuCl}_3$  (20 mg, 0.1 mmol) and  $\text{NaIO}_4$  (24.4 g, 114 mmol) were also added. The mixture was warmed to room temperature and stirred for about 1h.

Diethyl ether (250 mL) was added and the organic phase was separated, washed with water, and dried over  $\text{MgSO}_4$ . The solution was filtered through a plug of silica gel and distilled to yield an off-white/ light yellow solid (1.05g, 24%)

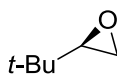


**(*R,R*)-2,4-dimethyl-1-phenylphosphetane borane complex (27a)**. *n*-BuLi (2.5 M, 4.79 mL, 1 equiv.) was added to a solution of  $\text{PhPH}_2$  (11.8 mmol, 10 wt% in THF, 65 mL) at -78 °C, then the mixture was stirred for 1 h before warming to rt. The resulting mixture was added via cannula to a cold (-78 °C) solution of (*R,R*)-pentane-2,4-diol cyclic sulfate in THF (400 mL) over 0.5 h, then stirred for an additional 0.5 h before warming to rt with additional stirring for 1 h. The reaction mixture was then cooled to -78 °C, and an additional 1 equiv. of *n*-BuLi (2.5 M,

4.79 mL) was added and the mixture was stirred for 0.5 h before warming to rt with stirring overnight.  $\text{BH}_3 \cdot \text{SMe}_2$  (1.70 mL, 1.5 eq) was added after cooling to  $-10\text{ }^\circ\text{C}$  and stirred for 0.5 h.

The reaction mixture was filtered through a plug of silica gel before attempted purification with column chromatography (silica gel, 10:1 hexanes: ether), which produced no observed product.

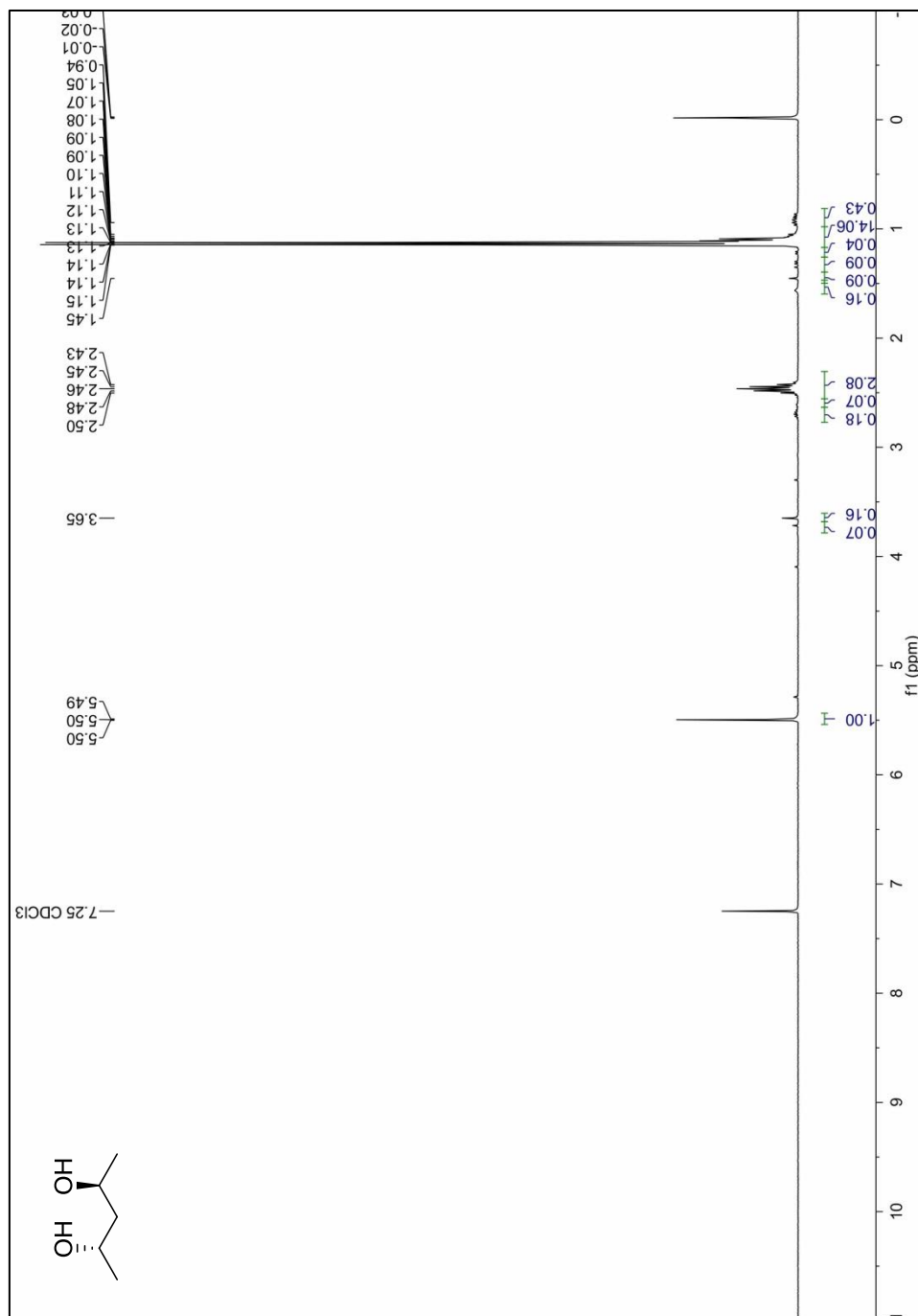
**Pre-oxidation of (*R,R*)-26a with acetic acid (AcOH) [(*R,R*)-28b]**<sup>20</sup> The Co(II)(salen) pre-catalyst (*R,R*)-**28** (483 mg, 800  $\mu\text{mol}$ , 0.02 equiv.) was dissolved in 3 mL of toluene and treated with 500  $\mu\text{L}$  of glacial AcOH. The solution was stirred at room temperature under ambient air for 30 min, during which time the color changed from orange-red to a dark brown. The solution was concentrated in vacuo to leave a crude brown solid which was used without further purification.

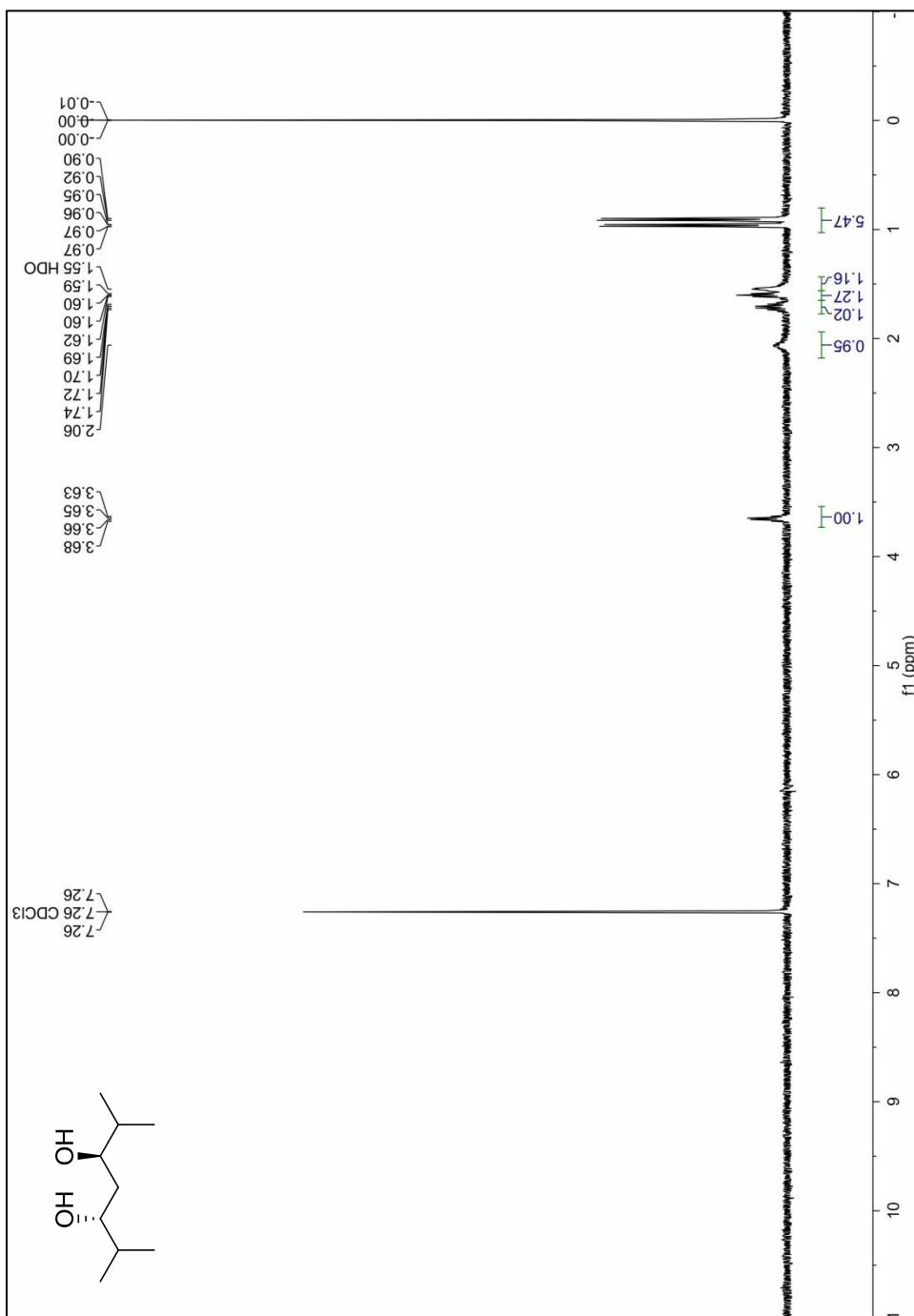


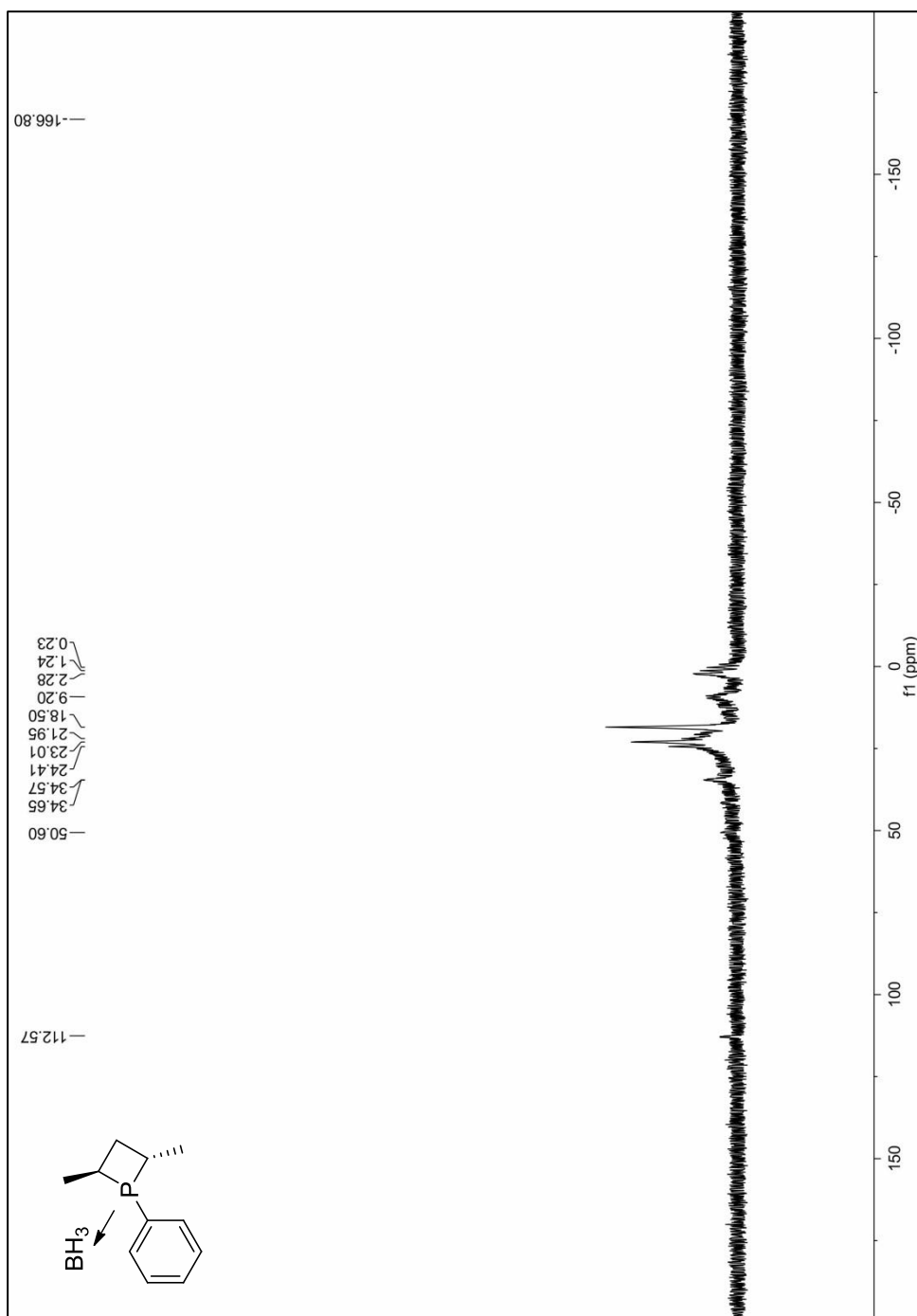
**(*R*)-tert-butyloxirane (30).** The crude catalyst residue (*R,R*)-**28**·OAc (480 mg, 800  $\mu\text{mol}$ ) was treated with ( $\pm$ )-*tert*-butyloxirane (4.88 mL, 4.00 g, 40.0 mmol), followed by ( $\pm$ )-1,2-hexane diol (1.2 mL). The reaction mixture was cooled to  $0\text{ }^\circ\text{C}$ , and  $\text{H}_2\text{O}$  (400  $\mu\text{L}$ , 22 mmol, 0.55 eq) was added in one portion. After 48h, (*R*)-*tert*-butyloxirane was isolated by vacuum transfer into a cooled ( $-78\text{ }^\circ\text{C}$ ) receiving flask to yield a crude, colorless oil.

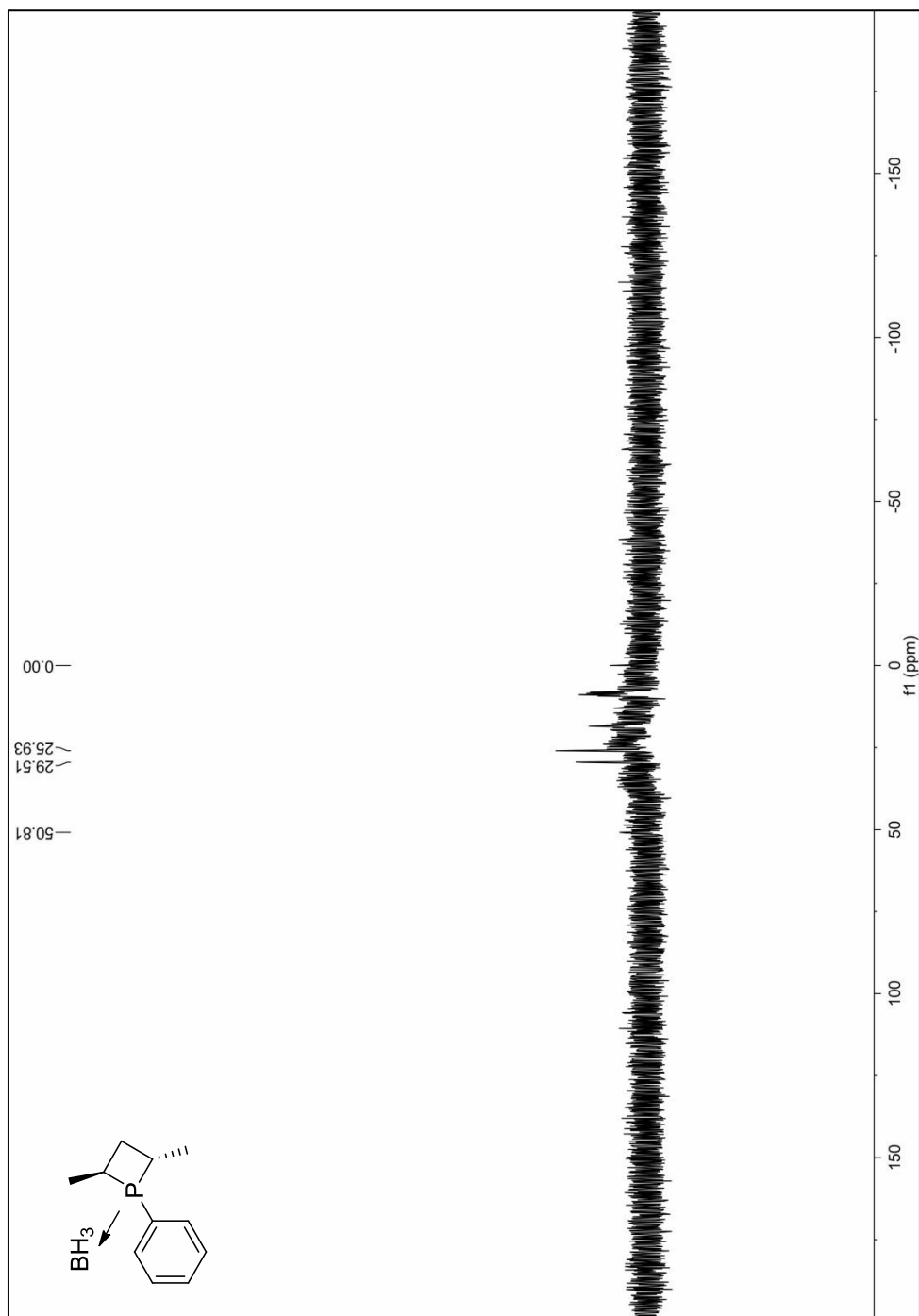


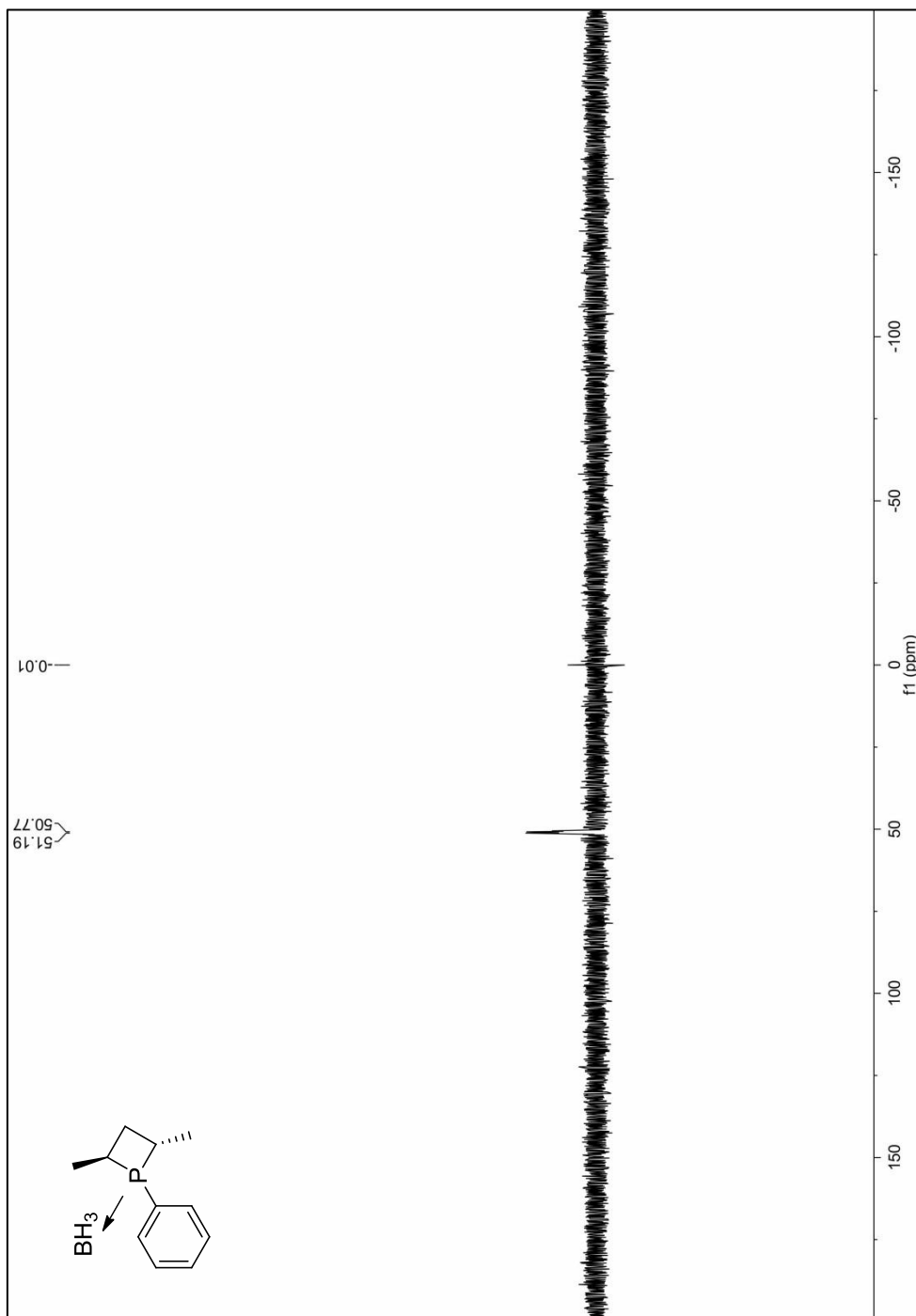
Appendix A  
 $^1\text{H}$  and  $^{31}\text{P}$  NMR Spectra











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### EDUCATION

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**The Pennsylvania State University, The Schreyer Honors College**  
*Eberly College of Science*  
Bachelor of Science Chemistry

Minor in Biology

- Dean's List: Fall 2012 – Fall 2015

**University Park, PA**  
*Graduation: Spring 2016*

### PROFESSIONAL EXPERIENCE

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**GlaxoSmithKline**

*Intern, Bench Chemist (Immuno-Oncology & Combinations DPU)*

- Synthesized, purified, and characterized four drug candidates
- Purified compounds through normal and reverse phase column chromatography
- Characterized compounds through LC-MS, HPLC, LC, and NMR

**Collegeville, PA**

*May 2014–August 2014*

**The Pennsylvania State University, Radosevich Research Group**

*Undergraduate Bench Chemist*

- Synthesized phosphorus catalyst through reduction
- Purified product through column chromatography and characterized products utilizing NMR and GC-MS
- Published as an author on: *J. Am. Chem. Soc.*, **2015**, *137* (2), 616-619

**University Park, PA**

*January 2014–Present*

### LEADERSHIP EXPERIENCE

---

**Penn State Dance Marathon Family Relations Committee**

*Inter-Committee Liaison/ Incentive Development Captain*

- Organized and facilitated programs that increased volunteer interaction with the Four Diamonds Families
- Designed and coordinated orders for four articles of clothing for the captain committee (23 members)
- Updated Four Diamonds Family contacts on a bi-weekly basis with information regarding THON

**University Park, PA**

*September 2015–Present*

**Penn State Dance Marathon Merchandise Committee**

*Special Projects Captain*

- Set up, operated, and organized numerous merchandise sales throughout the year including at THON
- Designed and coordinated orders for five shirts for the captain committee (22 members)
- Created numerous designs and released four products sold through the THON Store

**University Park, PA**

*September 2014–April 2015*

**Penn State Lion Ambassadors**

*Alternative Fundraising THON Chair*

*Tour Guide*

- Created custom apparel graphics (non-project related)
- Designed vectors and graphics for “Be A Part From the Start,” “Campus Showcase,” “Retreat,” and “THON Weekend”
- Guided over 35 prospective and accepted student tours across campus
- Planned and participated in Lion Ambassador projects

**University Park, PA**

*April 2014–April 2015*

*January 2014–Present*

### PUBLICATIONS AND AWARDS

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- Published as an author on: *J. Am. Chem. Soc.* **2015**, *137* (2), 616-619
- A. Miller Endowed Scholarship in Chemistry
- Harry Hayward Academic Excellence Scholarship