Cyclic Alkyl Phosphino Carbenes – A Synthetic Investigation

By: Benjamin Wortman

A thesis submitted to the Department of Chemistry and the Faculty of Science
In partial fulfillment of the requirements for a Bachelor of Science Degree
with Honours in Chemistry

April 19, 2023

Halifax, Nova Scotia

Supervisor and Chemistry Chairperson: Dr. Jason Masuda

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Acknowledgments

Firstly, I would like to thank my supervisor Dr. Jason Masuda. Your role as both my supervisor and professor has taught me valuable skills that helped me in completing my work. More importantly, you have shown me that chemistry can be both educational and entertaining at the same time. I would also like to thank Tanner George and all the time you took to help. My work would not have been able to be done without you and your knowledge of NMR and X-ray crystallography.

Finally, I would like to thank the rest of the Masuda lab, my fellow honours students, and my friends and family. I would have been able to complete my project with out all your help and encouragement.

Abstract

A proposed synthetic pathway to produce a cyclic (alkyl)(phosphino) carbene (CAPC)has been investigated. 1-bromo-2,4,6-tritertbutylbenzene (-2,4,6-tritertbutylbenzene =mes*) was used to produce Mes*PCl_2. A ring closure to form a phosphacycle was performed, a methyl group was added to the phosphorus and was reacted with *N*-bromosuccinimide to form the carbene precursor. The purpose for this synthesis is to attempt to replicate CAACs and improve their properties by replacing nitrogen with phosphorus. A less sterically bulky approach was done using only one *ortho* tBu to allow the use of more sterically bulky substituents at phosphorus. This synthesis provides a start to synthesizing the first CAPC.

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Abbreviations

°	degree
°C	degree Celsius
σ	sigma
π	Pi
Super mesityl	2,4,6-tritertbutylbenzene
Mesityl	2,4,6-trimethylbenzene
Mes*	super mesityl
NBS	*N*-bromosuccinimide
ml	milliliter
g	gram
mg	milligrams
NHC	*N*-heterocyclic carbene
PHC	*P*-heterocyclic carbene
HOMO	highest occupied molecular orbital
LUMO	lowest unoccupied molecular orbital
CAAC	cyclic (alkyl)(amino) carbene
NMR	nuclear magnetic resonance
THF	tetrahydrofuran
DBU	1,8-Diazabicyclo[5,4,0]undec-7-ene
TerMes	2,6-bis(mesityl)benzene
BICAAC	Bicyclic(alkyl)(amino) carbene
SIPr	1,3-Bis(2,6-diisopropylphenyl) imidazolidine

Introduction

There have been big advances in the area of catalysis, largely due to the use of specific ligands called N-heterocyclic carbenes (NHCs) that form metal complexes or just used on their own. NHCs used in catalysis has opened the door for much more new chemistry to be performed as it allows for more reactive catalysts, but also more stable catalysts. Due to the usefulness of NHCs, work has been done to improve NHCs to improve the reactions they are used for. [4] This was done by adding different substituents to the nitrogen atoms and to the backbones as an attempted to alter σ-donor and π-acceptor properties. From this research they discovered a subset of NHCs called cyclic (alkyl)(amino) carbenes (CAACs).[2]

Carbenes

Carbenes are molecules that contain a divalent carbon atom. A divalent carbon atom is a carbon that is bonded to two different groups and has two electrons. These 2 electrons are able to be either in the same orbital or are able to be in different orbitals. This is where the two different types of carbenes come in. The first type of carbene is called a singlet, which is where both the electrons are in the same orbital (Figure 1C). The electrons are located in a hybridized sp^2 orbital. The second type of carbene is called a triplet, which is where both the electrons are in different orbitals (Figure 1B). One electron is located in the hybridized sp^2 orbital while the other electron is located in the p_z orbital of the carbon. Triplet carbenes are typically more reactive than singlet carbenes.[4]

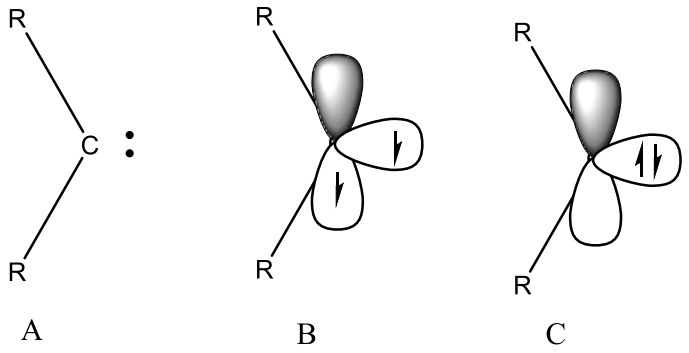
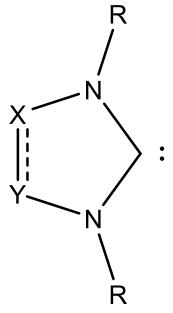


Figure 1: Carbene (A), triplet carbene (B), singlet carbene (C)

N-Heterocyclic Carbenes

NHCs are a type of carbene that form a ring that contain at least one nitrogen atom, typically they contain two nitrogen atoms, along with the divalent carbon. In NHCs, the nitrogen atoms are bonded to different R groups which can help determine the different properties of the carbenes. They can increase donor and acceptor properties or decrease the same properties based on the characteristic of the R group. Looking at the energies of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) is a good way to better understand the donation and accepting properties of NHCs. [1]



X/Y=substituent

Figure 2: Basic structure of an NHCs

The different energies of the HOMO and LUMO play a big part in the σ-donor and π-acceptor potential for the carbene. It is known that the energy of the HOMO determines the σ-donation properties of the carbene and the LUMO determines the π-acceptor properties of the carbene. The best way to tell if a carbene has good σ-donor and π-acceptor properties is by looking at the gap between the HOMO and the LUMO. The smaller the gap between the HOMO and LUMO, the better the σ-donor and π-acceptor properties the carbene will have. Similarly, increasing the gap will have the opposite effect in the donor and acceptor properties of the carbene. The best way to be able to tune this gap is by changing the different alkyl groups on the carbene, both on the nitrogen and the backbone. For example, placing an ethyl group onto the nitrogen will increase the energy of the HOMO more than placing a proton. This is due to an ethyl group being more electron donating then a proton.[1]

In NHCs, the nitrogen atom typically has a planar configuration. This planar configuration of the nitrogen allows proper overlap of the lone pair, in $2p_z$ orbital, of the nitrogen and the empty $2p_z$ orbital of the carbon. Since both orbitals have good overlap, the nitrogen is able to donate electron density through the π-bond to the carbon. The electron density the carbon gets from the nitrogen makes the carbon less π-accepting and less electrophilic. Nitrogen is also quite electronegative, meaning that it is electron withdrawing. This means that the nitrogen is pulling electron density through the σ-bond, lowering the σ-donor capabilities of the carbene. This is one reason why research was being done to improve these properties of NHCs. [2]

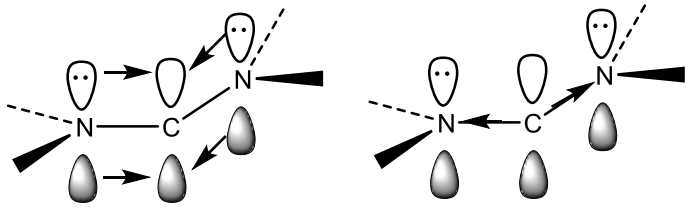


Figure 3: Diagram shows the overlap of the $2p_z$ orbitals of nitrogen and carbon. Not the lone pair on carbon is not shown for clarity

Cyclic (Alkyl)(Amino) Carbenes

As mentioned previously, research is being done on NHCs to help improve the different properties of NHCs. Changing the substituents can have a big impact on the different properties, but removing or switching certain atoms can also be beneficial. Through the research done on NHCs it was determined that removing one of the nitrogen atoms and replacing it with a carbon changes the properties of the carbene. These new NHCs became their own subset called cyclic (alkyl)(amino) carbenes (CAACs). Having only the one nitrogen atom adjacent to the carbene carbon drastically changed how the carbene functioned.[1]

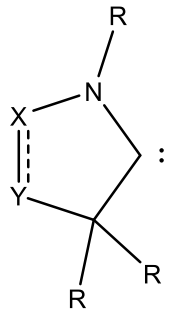


Figure 4: Basic structure of a CAAC

Similar experiments were done on CAACs to determine the σ-donor and π-acceptor properties. Once again, the energies of the HOMO and the LUMO were looked at. Due to the substitution of the electronegative and π-donating nitrogen that is seen in typical NHCs with a σ-donating quaternary carbon leads to the destabilization of the carbene center. This destabilization further alters the σ-donor and π-acceptor properties of the carbene. The σ-donor properties are increased since one of the nitrogen atoms that were pulling electron density away from the

carbon was replaced with a carbon that is able to donate electron density. Similarly, the same nitrogen that was π-donating got replaced with a carbon that is not capable of π-donation, which would mean the carbene carbon would be more willing to accept election density in the p_z orbital, therefore improving π-acceptor properties.[1]

The σ-donor and π-acceptor properties are further confirmed by looking at the energies of the HOMO and LUMO for each carbene. When looking at the energies of the HOMO for CAACs, it is typical to see higher energies, which correspond to the higher σ-doanting properties of the carbene. A similar trend can be seen when looking at the energies of the LUMO for CAACs. Typically, the energy is lower then what is seen in an NHC, which also corresponds to the π-acceptor ability of the CAACs. Changing substituents on both the nitrogen and the adjacent carbon can also change the energy levels of the HOMO and LUMO, similarly how they are changed in an NHC. [1]

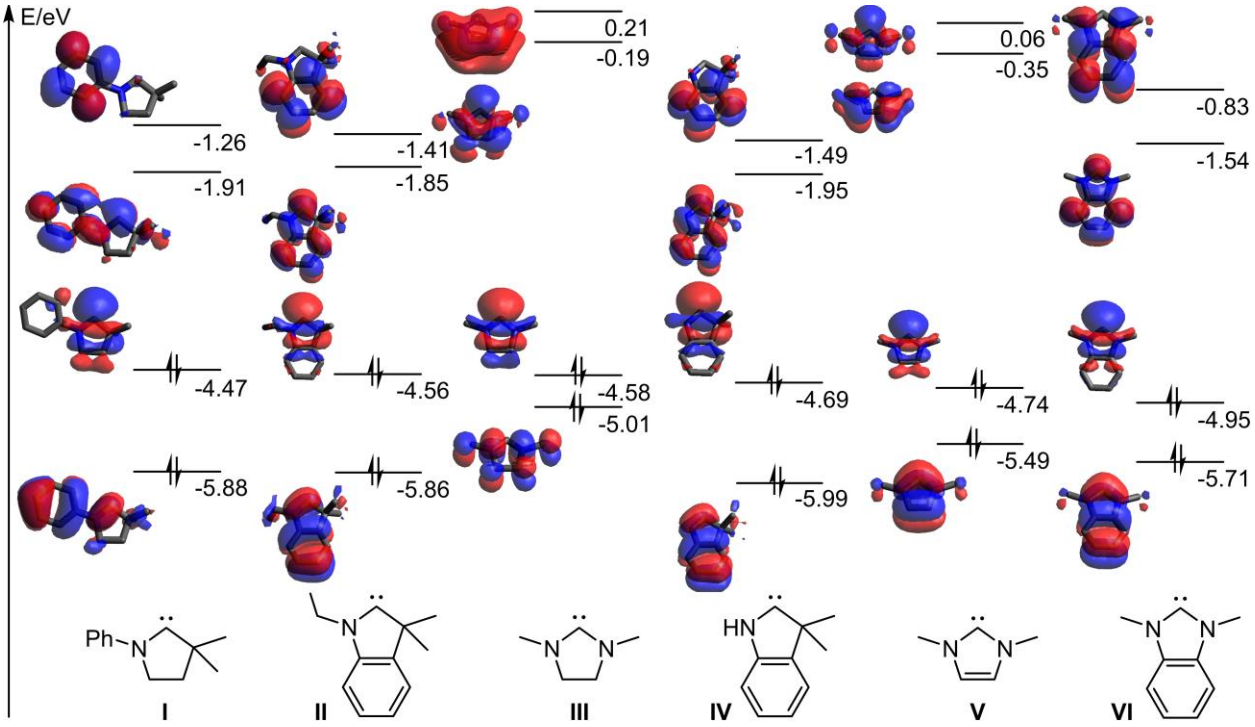
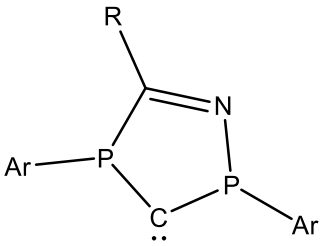


Figure 5: Diagram showing different energy levels of molecular orbitals or different NHCs and CAACs [1]

P-Heterocyclic Carbenes

In doing research to help improve NHCs, research was done looking into what would happen if nitrogen was replaced with a heavier element from the third row such as phosphorus. [3] These new carbenes where the nitrogen was replaced with phosphorus are called P-heterocyclic carbenes (PHCs). Other than PHCs using phosphorus instead of nitrogen, PHCs and NHCs bear a similar structure. From the computational work done on PHCs, it was determined that PHCs could have a higher degree of structural versatility.[5] This work also shows that PHCs would probably have better σ-donor and π-acceptor properties compared to NHCs. Another benefit of using phosphorus instead of nitrogen is the ability to use ^{31}P NMR spectroscopy to follow the reaction be looking at how the signals change. [2]



R=CH_3 or NMe_2
Ar=Mes*

Figure 6: Known PHCs

A problem that comes along with using phosphorus for most singlet carbenes is that phosphorus typically exhibits a trigonal pyramidal geometry. This was not a problem with nitrogen as it is typically planar. The pyramidal configuration of the phosphorus does not give proper π overlap with the empty $2p_z$ orbital on carbon needed for the carbene to be isolable and typically it will be a triplet carbene. For this reason, phosphorus must be forced planar do give

the overlap needed to isolate the carbene. Forcing it to be planar typically also makes the carbene a singlet since there is the sufficient π donation of the phosphorus lone pair to the p_z orbital of the carbene carbon. To force the phosphorus planar, a bulky group, such as 2,4,6-tritertbutylphenyl, also known as super mesityl (Mes*), must be bonded to the phosphorus. This bulky group forces an increase in the bond angle which is why it gets forced into a planar configuration. [6]

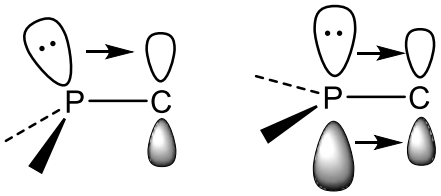


Figure 7: Diagram showing the overlap of the $3p_z$ orbital of the phosphorus and the $2p_z$ of the carbon

Even without a bulky group PHCs can still have good properties that will make them a good carbene. Since phosphorus is bigger than nitrogen, it has a $3p_z$ orbital instead of a $2p_z$ orbital. This means that the phosphorus is not able to donate as much electron density to the carbon. Due to orbital size mismatch this means that the $2p_z$ orbital of the carbon is still filled with less electron density, therefore the π-acceptor properties are better than that of the nitrogen analogues. Phosphorus is also less electronegative than nitrogen is, meaning that the phosphorus pulls less electron density through the σ-bond allowing the carbon to donate more. Meaning that PHCs are better σ-donors. This can also be seen in the HOMO-LUMO gap of the PHCs. Similarly, to NHCs, PHCs can be tuned to have a bigger or smaller gap based on the different substituents in the molecule. If there is a more electron withdrawing group, then the carbon might have lower σ-donor capabilities. [2]

Uses for Carbenes

There are many uses for carbenes, a good amount of which are in catalysis. A significant use for carbenes is as ligands.[3] A good example of a carbene use is as a ligand is in the Grubbs second generation catalyst. The Grubbs catalyst initially had no carbene on it and was still quite useful to catalyze olefin reactions, but when a PCy_3 was replaced with an NHC, the catalyst improved. Adding the NHC allowed the catalyst to be stable in moisture and air, it also made the catalyst more active. [7] Carbenes can also be used as catalyst just on their own. [3] A prime reaction example of a carbene being used as a catalyst on its own is the benzoin condensation reaction. In this reaction, benzaldehyde reacts with an NHC to form an intermediate. Next, another benzaldehyde reacts with the benzaldehyde carbene molecule, where the carbene is kicked out and the two benzaldehydes bond together through the aldehyde substituent. [8]

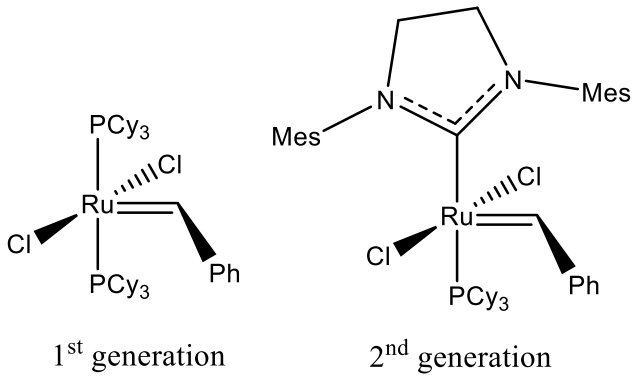


Figure 8: 1st and 2nd generation of Grubbs catalyst

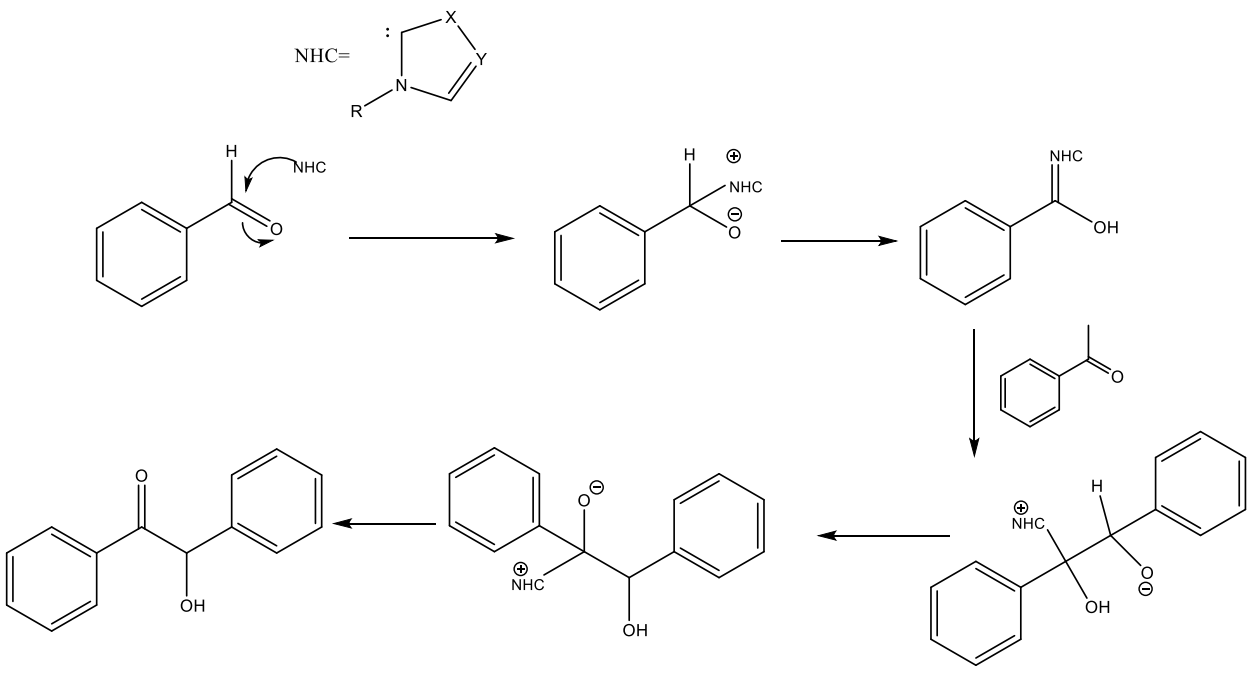


Figure 9: Basic benzoin condensation reaction

Objective

We are trying to create a synthetic path way to a carbene containing a single phosphorus atom adjacent to the carbene carbon. It is already known that replacing one of the nitrogen atoms in an NHC with a carbon that contains alkyl groups increases the π-acceptor and σ-donor properties of the NHCs. Based on this work it is a safe assumption that a similar trend would present itself with PHCs by replacing one of the phosphorus atoms with a carbon containing alkyl groups. For this reason, we are attempting to make the first cyclic alkyl phosphino carbene (CAPC).

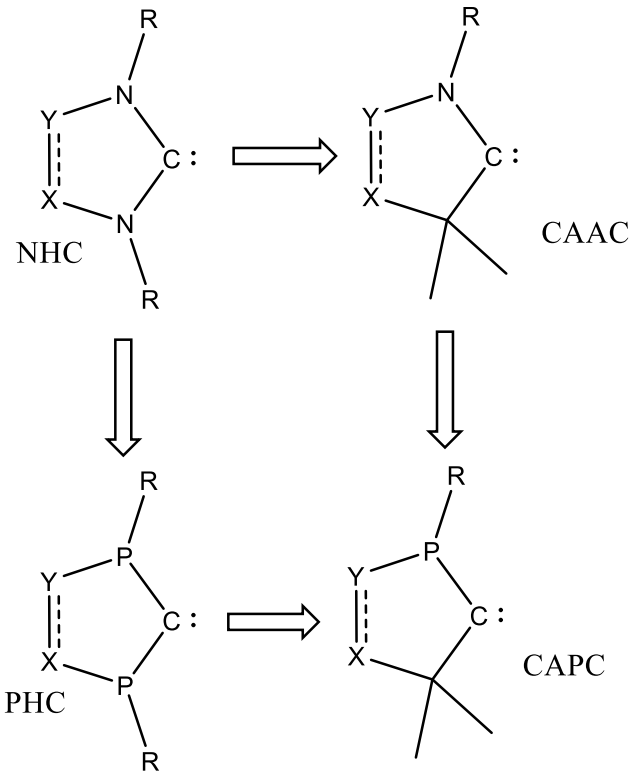
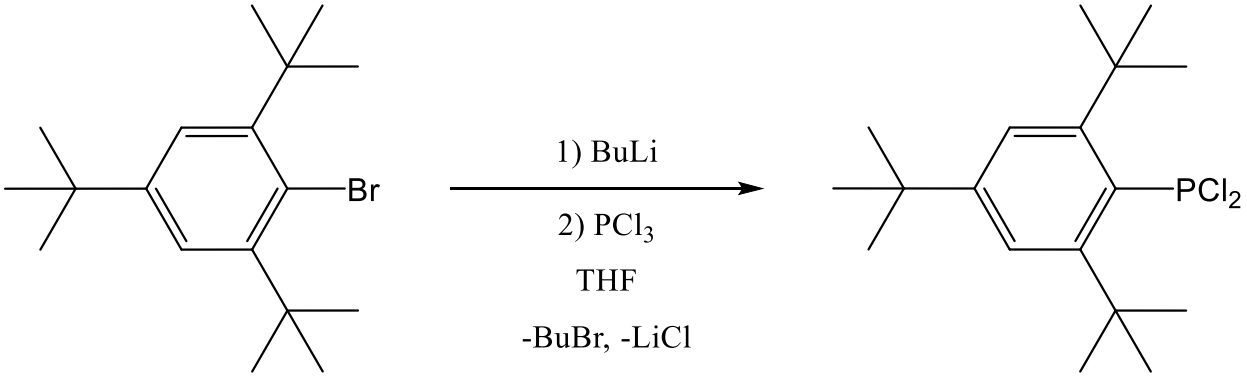


Figure 10: Improvements made on carbenes

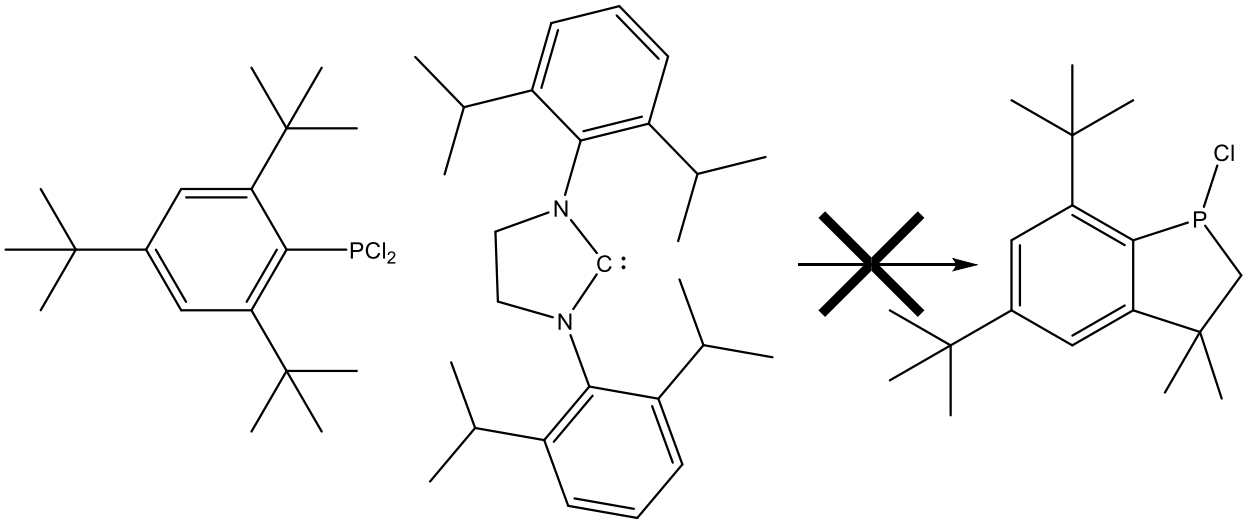
Approach to CAPCs- Method 1

Based on previously reported procedures, the phosphorus dichloride containing the super mesityl was made from super mesityl bromide. This would be the starting material for the synthesis as it contained all the vital substituents needed to produce the desired carbene. It contained only one phosphorus atom, which would make it similar to a CAAC, and had a bulky backbone. It also had the tertbutyl group need to help close the ring. The molecule was made by mixing 1-bromo-2,4,6-tritertbutyl benzene and one equivalent of n-butyl lithium at -78° C. This reaction produced the 1-lithium-2,4,6-tritertbutyl benzene, to which we added phosphorus trichloride to produce super mesityl phosphorus dichloride.

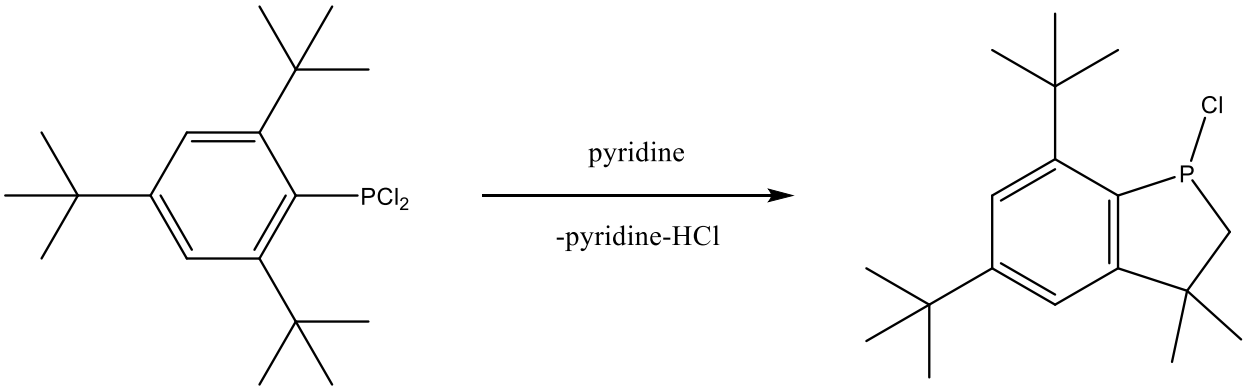


Scheme 1: Synthesis of Mes* PCl_2 (product 1)

The next step in the synthesis was to close the ring with one of the tertbutyl groups and the phosphorus. This reaction has already been done in the literature, but slight changes were made to the procedure. The original procedure was done in toluene with 1 equivalent of pyridine while heating to 100° C. When following reaction progress by ^{31}P NMR spectroscopy we found that the reaction never went to completion. After realizing that the reaction did not work the way it was described in the paper, we decided to try a different base. The same reaction was done using the NHC 1,3-Bis(2,6-diisopropylphenyl) imidazolidine (SiPr) instead of pyridine. This improved the yield slightly but still did not give a quantitative reaction. From here it was decided to slightly change the original procedure to use pyridine as both the solvent and the base with heating to 110° C. We found that this worked much better and greatly increased our yield of the product.[9]



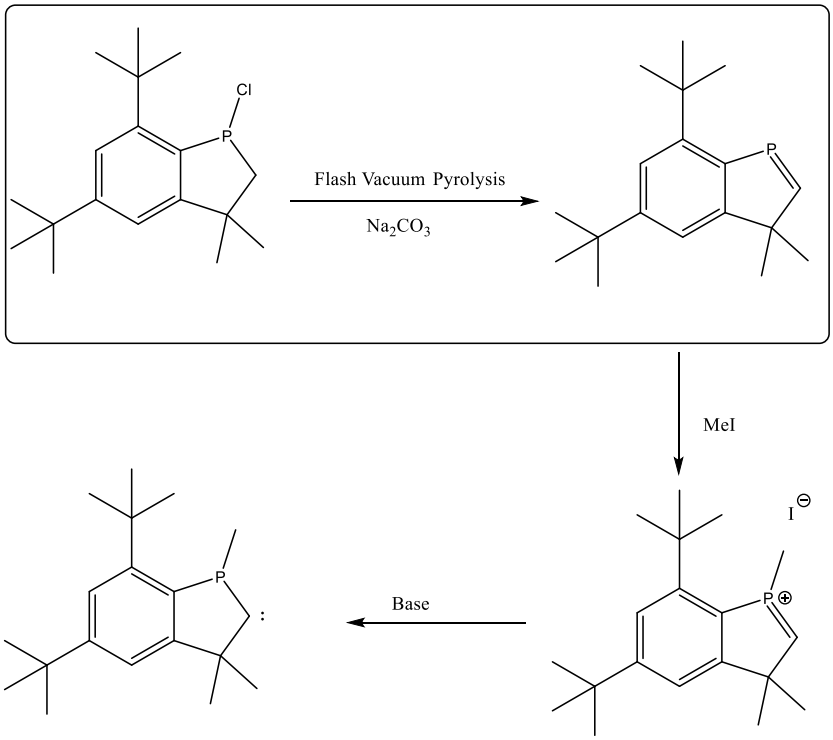
Scheme 2: Mes*PCl_2 reaction with 1,3-Bis(2,6-diisopropylphenyl) imidazolidine (SiPr)



Scheme 3: Synthesis of product 2

The next part of the synthesis proved to be difficult. It was the first roadblock faced when trying to produce the carbene. In this step the formation of the phosphorus carbon double bond was attempted. There was a procedure for doing this in the literature that was successful but was unable to be done in our lab. The procedure involved the use of flash vacuum pyrolysis. The reason this procedure was not doable is because the lab does not have access to the proper equipment required to carry out the procedure. For this reason, alternate methods must be explored to potentially make the phosphorus carbon double bond. We thought that the use of a

stronger base would allow us to create this double bond without the use of the high temperatures from the flash vacuum pyrolysis.[10]



Scheme 4a: Potential pathway to synthesis the carbene

Multiple different bases were used to attempt to make the phosphorus carbon double bond. The bases used were SiPr, BICAAC, Mes* Li, $KN(SiMe_3)_2$, TerMes Li, and DBU (figure 11). Once the formation of the phosphorus carbon double bond was made the next step was going to be to add a methyl group to the phosphorus. A methyl group was chosen since it is was the only group that is big enough to fit on the phosphorus with the tertbutyl group being so close. The methyl group is not big enough to force the phosphorus to be planar, but it is big enough to have a small effect on the stability of the carbene. This being said, the carbene is not stable in air or at room temperature, so the carbene would have to be made at -78° C. [11]

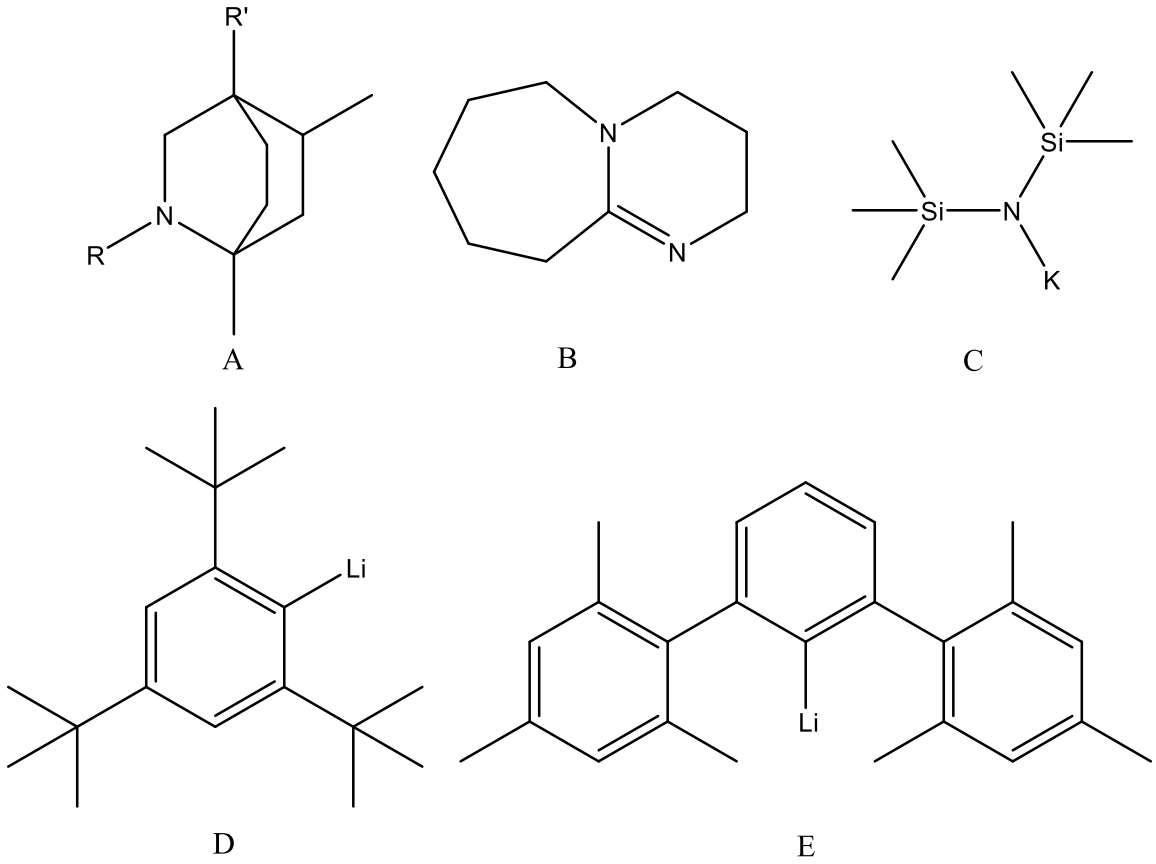


Figure 11: BICAAC (A), DBU (B), $KN(SiMe_3)_2$ (C), Mes* Li (D), TerMes Li (E)

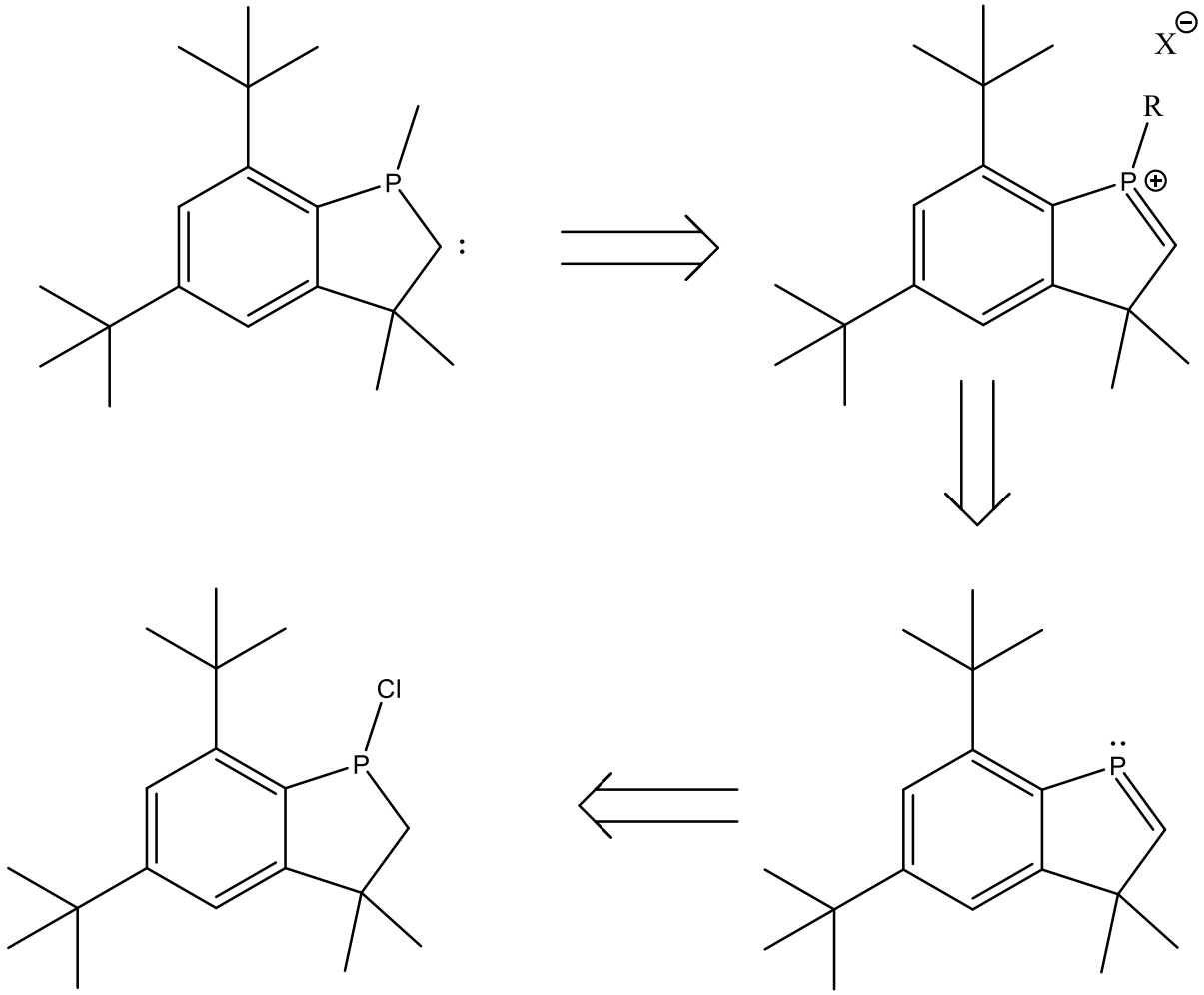


Figure 12: First retrosynthetic pathway to obtain the carbene

Approach to CAPCs- Method 2

As stated before, this pathway was not going to work, so another route was needed. The decision was made to add the methyl group onto the phosphorus first. Adding the methyl group now would have two big advantages to the synthesis. It would add the methyl group onto the phosphorus, which would put us one step closer to making the carbene. It could also make the formation of the phosphorus carbon double bond easier for us in the future.

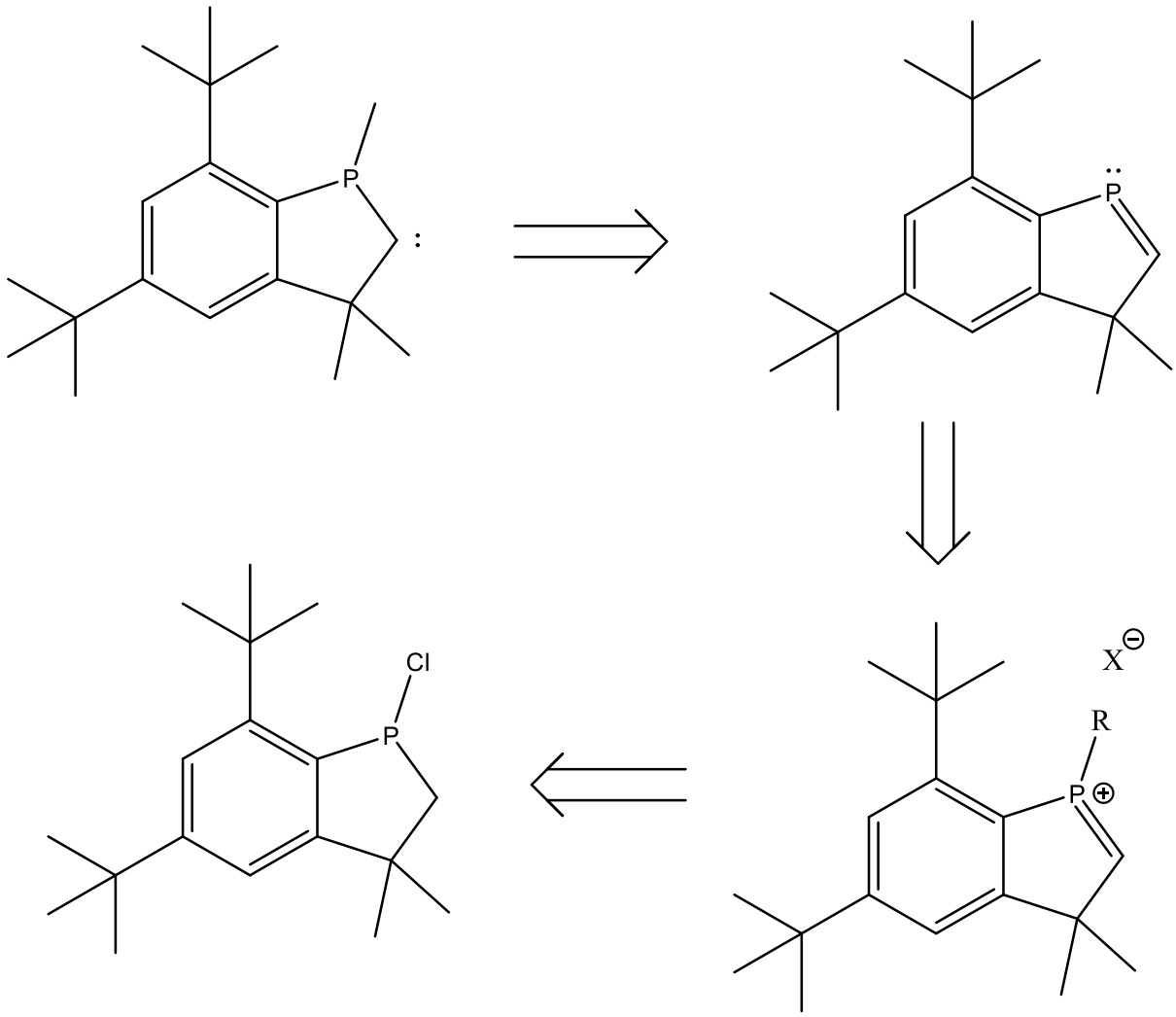
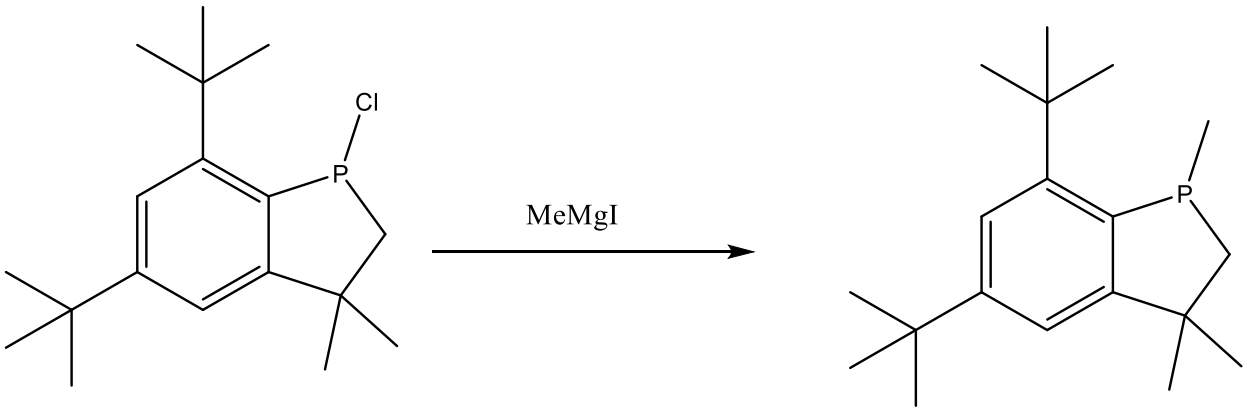


Figure 13: Second retrosynthetic pathway to obtain the carbene

Originally, we attempted to add the methyl group by mixing the product 2 with MeI. After looking at the phosphorus NMR, it was clear that a reaction took place but the chemical shift was not in the area that was expected. Next, a similar reaction was done but instead of using MeI, $(CH_3)_3O(BF_4)$ was used. Once again, the ^{31}P NMR spectroscopy was used to determine if the reaction was successful or not. The ^{31}P NMR spectrum revealed multiple peaks at different intensities. This was a problem since we were looking for only one peak and not multiple. On top of having multiple peaks, none of them were the peak that was anticipated. Finally, we decided

to try a Grignard reagent to see if it would react better. The Grignard reagent of chose was MeMgI. Product 2 was mixed with the Grignard reagent and left to stir. Once the reaction was complete, a ^{31}P NMR spectrum was taken of the reaction. From the ^{31}P NMR spectrum we saw one peak in the area that was expect for a PR_3 molecule.



Scheme 5: Methylation of product 2 to make product 3

The next step was to attempt to form the phosphorus carbon double bond. This step also proved to be difficult. Multiple different routes were tried and only one showed promising results. The first route we decided to take was to use *N*- bromo succinimide (NBS). The idea behind this reaction is the succinimide removes the one of the hydrogens from the carbon adjacent to the phosphorus. These leaves room for two possible products, the first one being the bromine attaching to the carbon or the second being a phosphorus carbon double bong forming and creating a positively charged phosphorus and a negatively charged bromine.

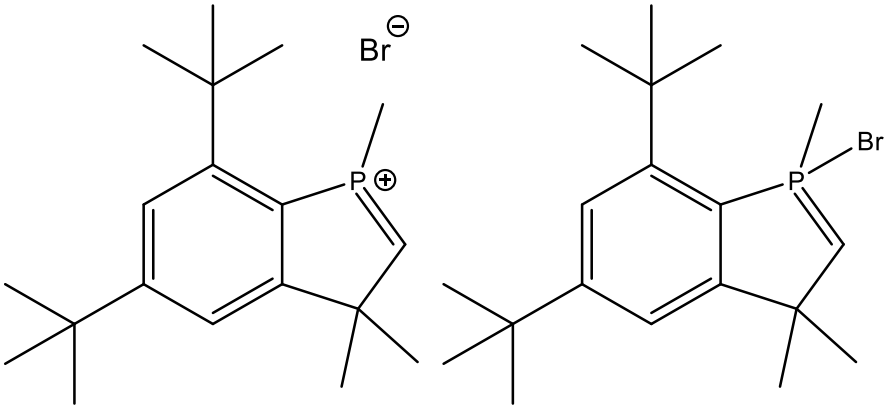
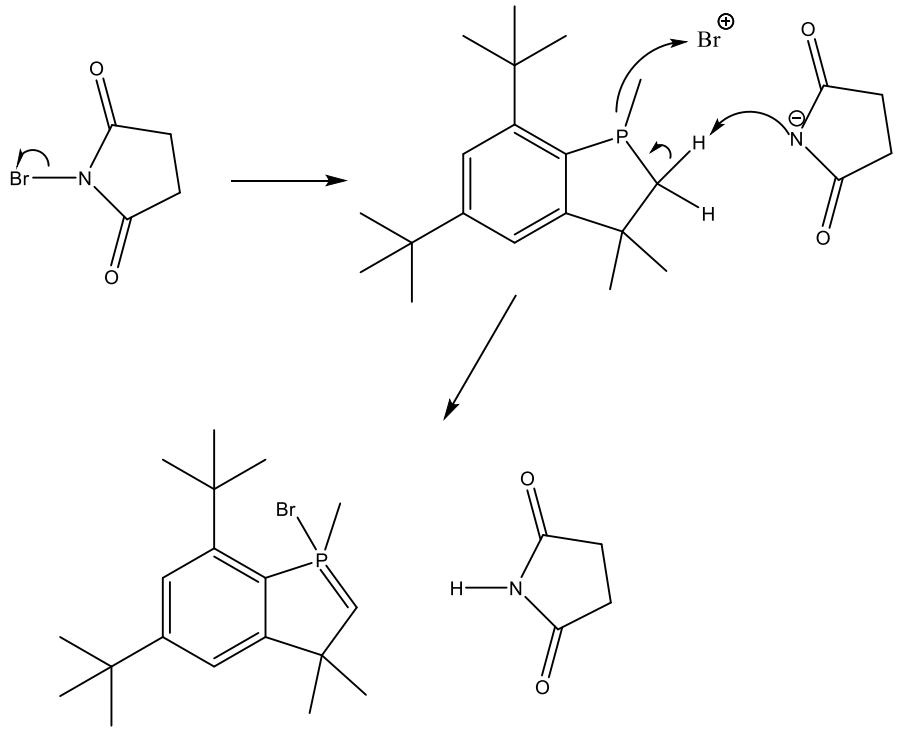
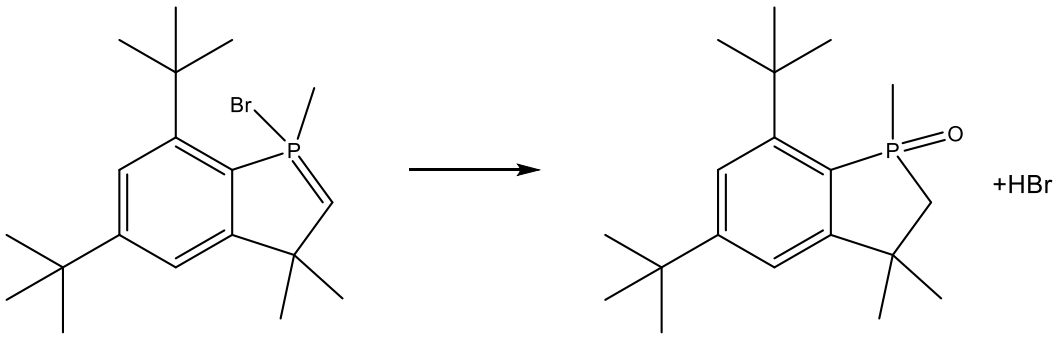


Figure 14: Different possibilities of connectivity

Looking at the NMR we were able to see that the reaction was successful. The only problem was the byproduct succinimide. The desired product and succinimide are both soluble in majority of the same solvents. The best way of removing succinimide is by using water. The only problem with this is that water hydrolyses the phosphorus and turns it from phosphorus(III) to a phosphorus(V) oxide. This method was tested and was confirmed by the shift in ^{31}P NMR peak as well as X-ray crystallography. Pentane was also used to attempt to separate the two products. Pentane only removed the already hydrolyzed product.



Scheme 6: NBS reaction with product 3 to make product 4



Scheme 7: Hydrolysis of product 3 with water

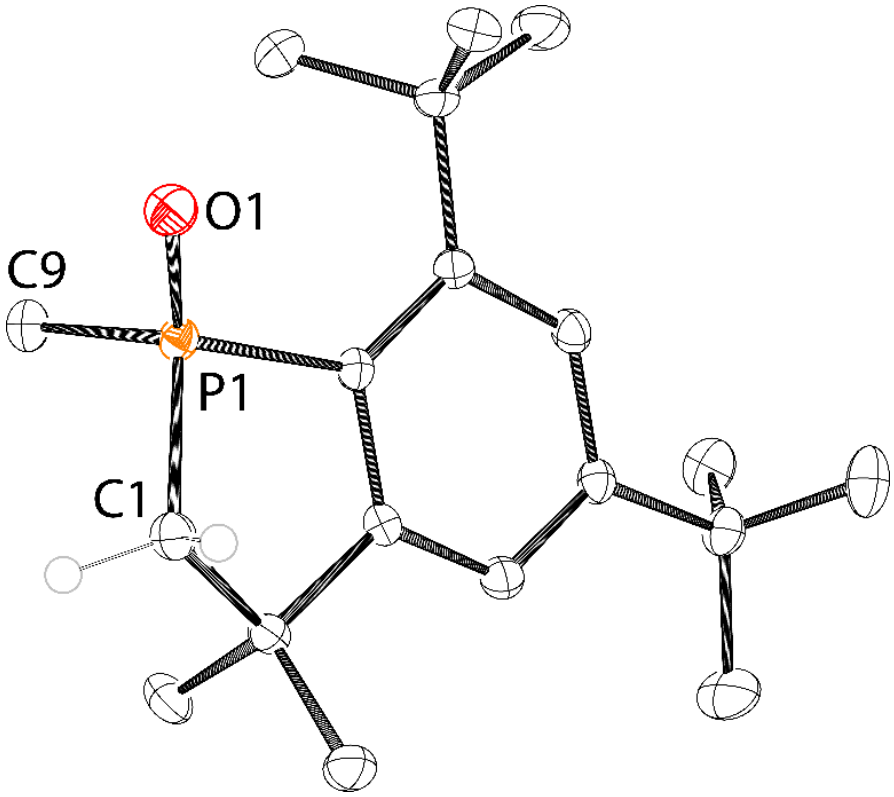
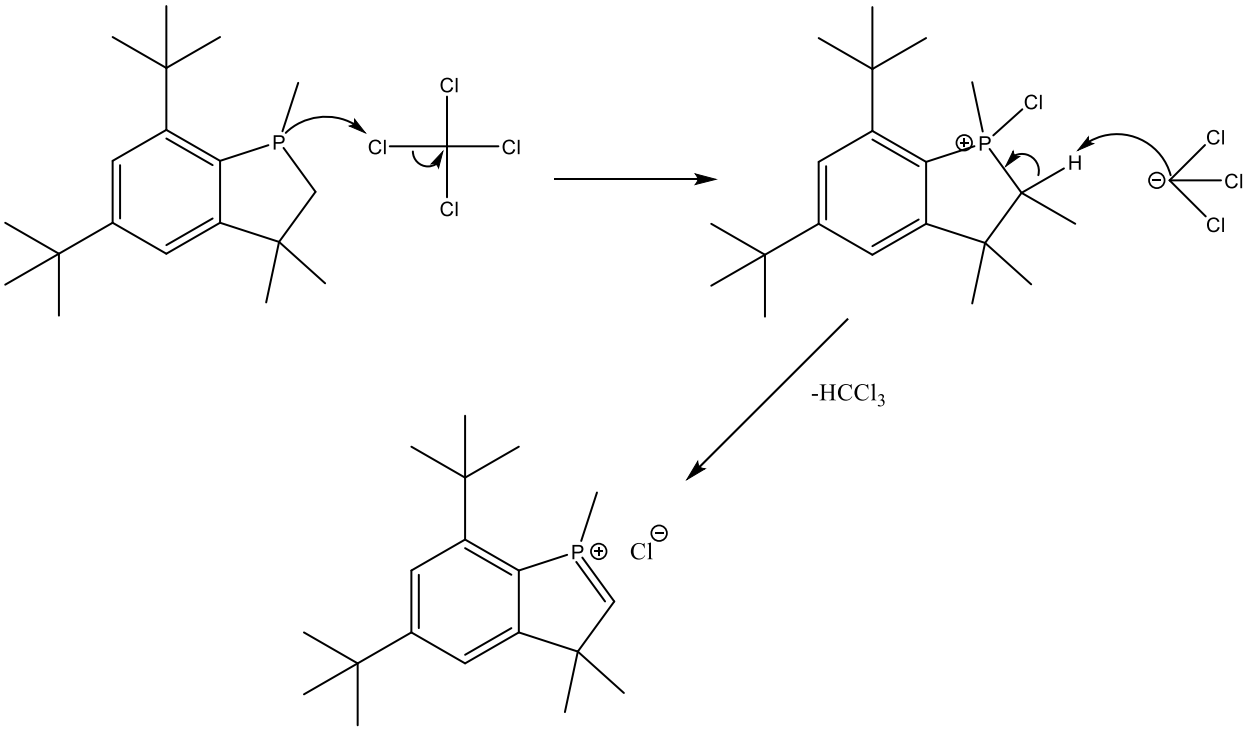


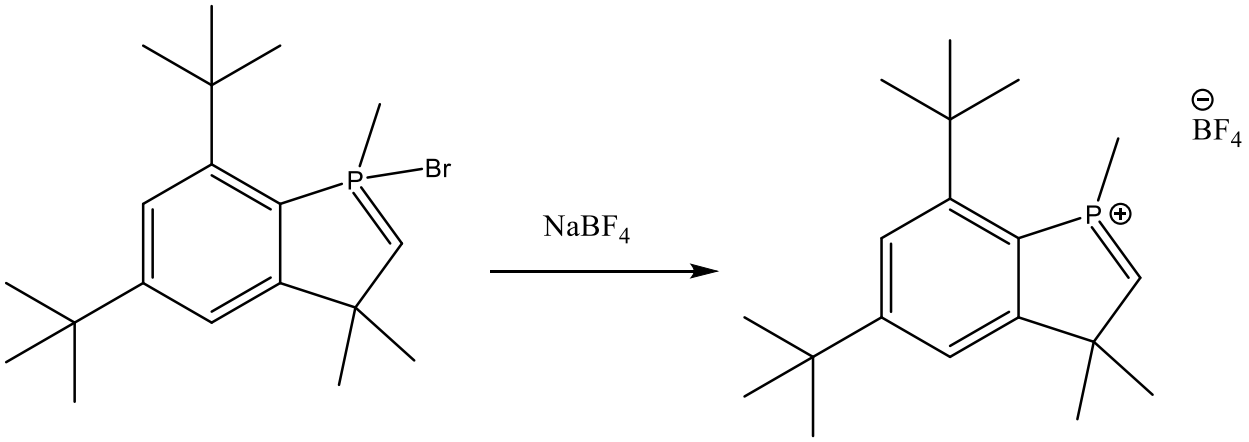
Figure 15: Crystal structure of hydrolysis product 3 (bond lengths in table 1)

Due to the unwanted succinimide product, other reactions were examined. The first one being carbon tetrachloride with product 2. The idea behind using this reagent was to utilize the first step of an Appel reaction.[14] In this reaction a PPh_3 group removes one of the chlorines off of the carbon tetrachloride and produces a carbon trichloride anion. In our case we used product 2 as the phosphorus containing compound to remove the chlorine and produce the anion. The carbocation would then remove one of the protons from the carbene carbon and give a similar product as the NBS reaction. This reaction was unsuccessful in producing the product that was desired. This was determined by looking at the ^{31}P NMR spectrum of the reaction. The NMR revealed many different peaks in a wide range of different chemical shifts. The next reaction that was attempted was sodium tetrafluoroborate and our compound. This reaction was done to

attempt to remove the bromine and create a BF_4 salt to better isolate the compound. This reaction was also determined to be unsuccessful by looking at the ^{31}P NMR spectrum.



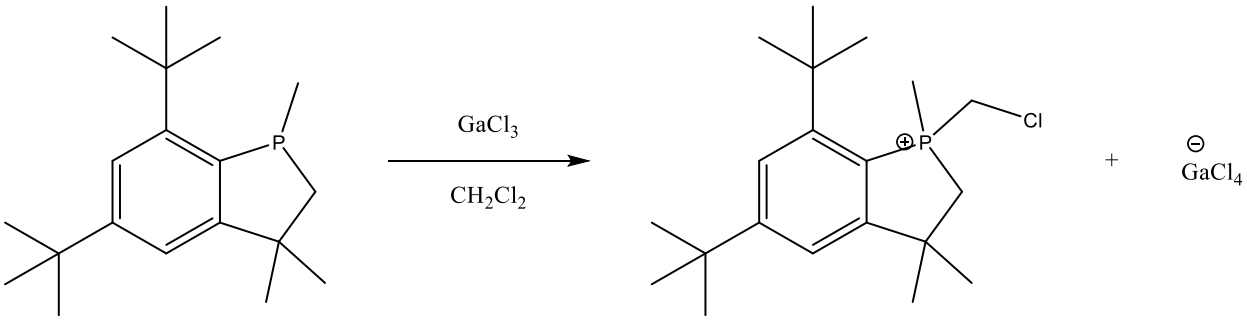
Scheme 8: Reaction of Product 3 with CCl_4 showing similarities to Appel reaction



Scheme 9: Attempted removal of bromide wit $NaBF_4$

After attempting the previous reactions, another idea for removing the succinimide from the product was thought of. The method that was used was sublimation of succinimide. This was done by adding the crude product to a sublimation vessel and lowering it into an oil bath set to 100° C over night. We saw that the succinimide was partially removed by decreased integration values of the succinimide peaks in ^{1}H NMR spectrum.

Alongside trying to remove the succinimide, a crystal structure was also wanted to help show the connectivity of the molecule. Previous attempts were made to obtain a crystal structure, but due to the high symmetry in the compound it was to difficult to model the data from the diffraction experiment. To help break the disorder in the compound, a Lewis acid-base adduct could be made. To do this product 3 was reacted with gallium trichloride in dichloromethane in an attempt to coordinate the gallium to the phosphorus. The ^{31}P NMR spectrum showed one broad peak at -6 ppm. From this reaction we were able to grow crystals and obtain a crystal structure. Instead of the gallium coordination with the phosphorus, it actually removed one of the chlorines from the dichloromethane. This allowed the remaining CH_2Cl cation to coordinate with the phosphorus. Luckily, it was still able to break the disorder and produce a good crystal structure.



Scheme 10: Reaction of product 3 with $GaCl_3$ to obtain crystal structure

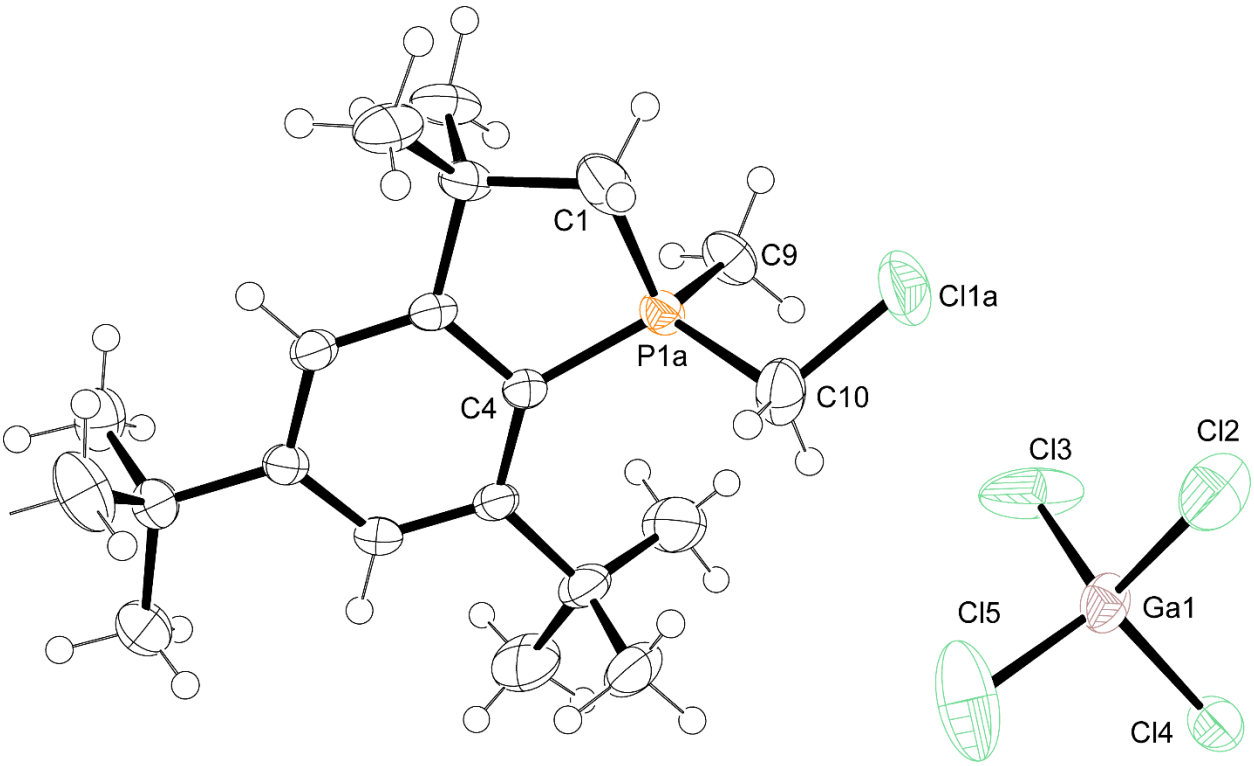


Figure 16: Crystal structure of $GaCl_3$ reaction with compound 3

Approach to CAPCs: method 3

The main disadvantage of this carbene was the inability to make the phosphorus planar. This was due to the bulky tertbutyl group not allowing us to add a bulky group to the phosphorus (Figure 17). To try make the carbene isolable, the phosphorus would need to be forced planar. To achieve this the backbone would need to be changed. A similar synthesis was attempted using ortho tertbutylaniline. With this approach, there are no t-butyl groups on the aryl backbone and would allow for a bulky group, such as Mes*, to be added to the phosphorus.

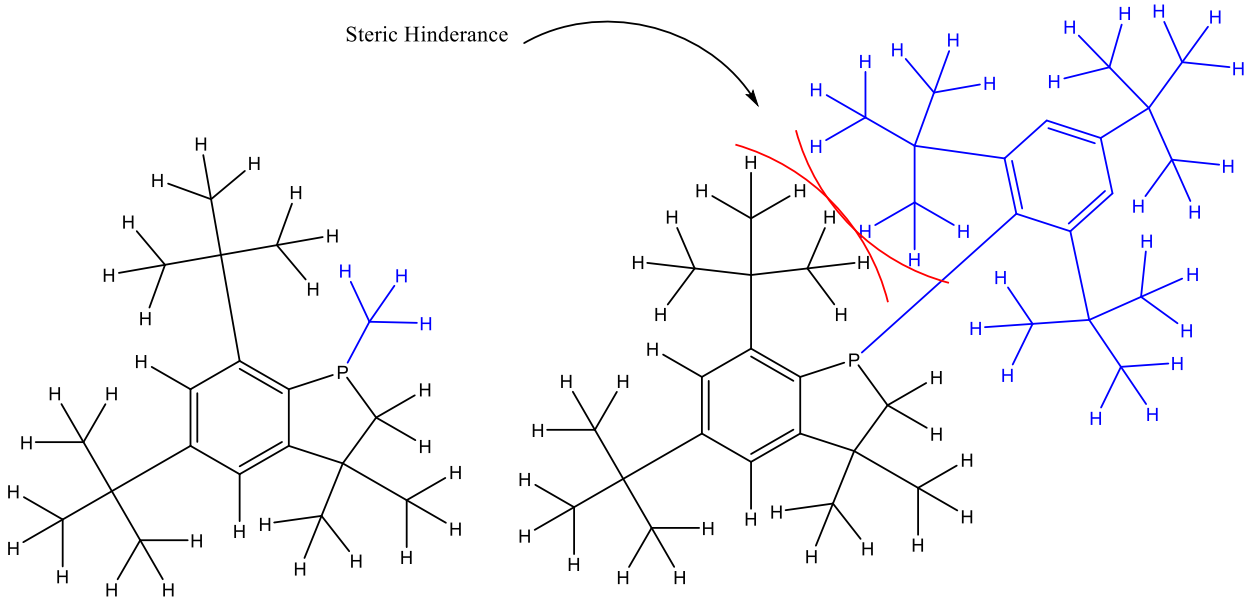
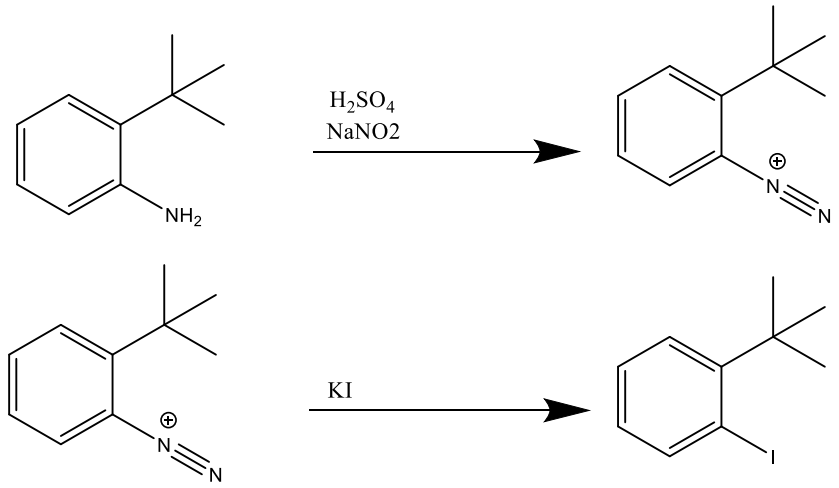


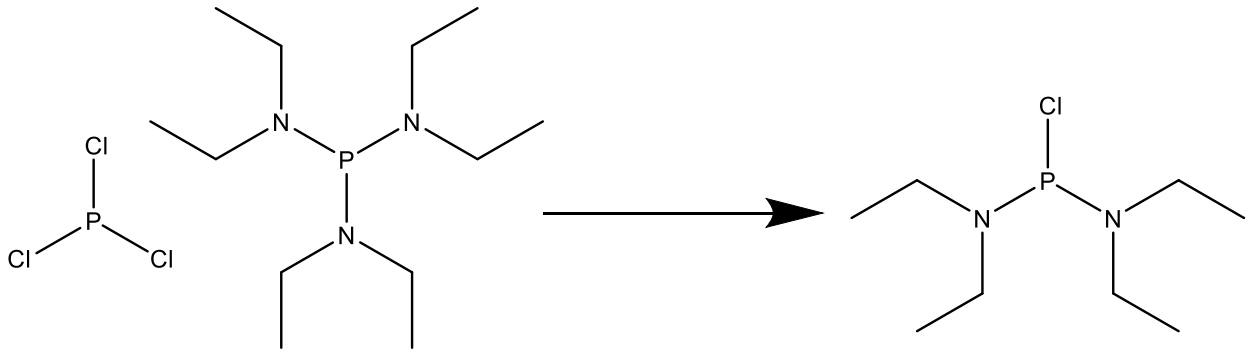
Figure 17: Steric interaction between tert-butyl groups hindering formation of the compound

The synthesis started by removing the NH_2 group from the aniline and replacing it with iodine. This was done by removing the hydrogens and replacing them with another nitrogen by mixing it with sulfuric acid and sodium nitrite. This forms a triple bond between the two nitrogen atoms and gives a formal positive charge to the one bonded to the carbon. Next potassium iodide was added to remove dinitrogen and replace it with iodine. The reason for adding the iodine is to later turn it into a Grignard to help replace it with phosphorus.

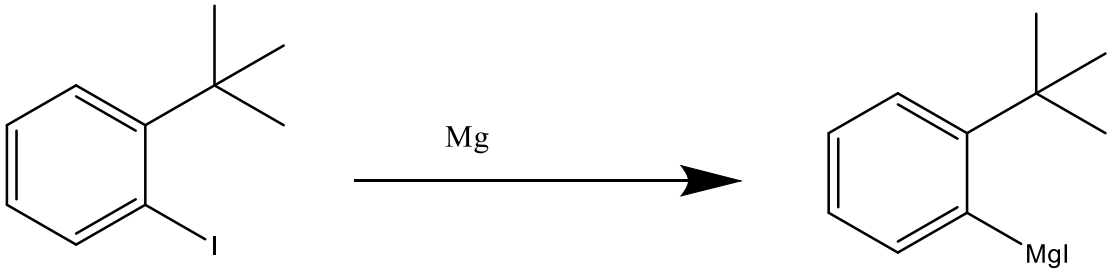


Scheme 11: Synthesis of iodo-ortho-tert-butyl benzene

The next step was to make bis(diethylamino) phosphorus chloride. This will be the molecule replacing the iodine and later converted to phosphorus dichloride. Just adding phosphorus trichloride was an option but it would come with some complications. The main one being it would be hard to control how many equivalents would be added. By adding bis(diethylamino) phosphorus chloride first we would know for sure that only two chlorides would be added. It was made by mixing PCl_3 and $P(NEt_2)_3$. [12]

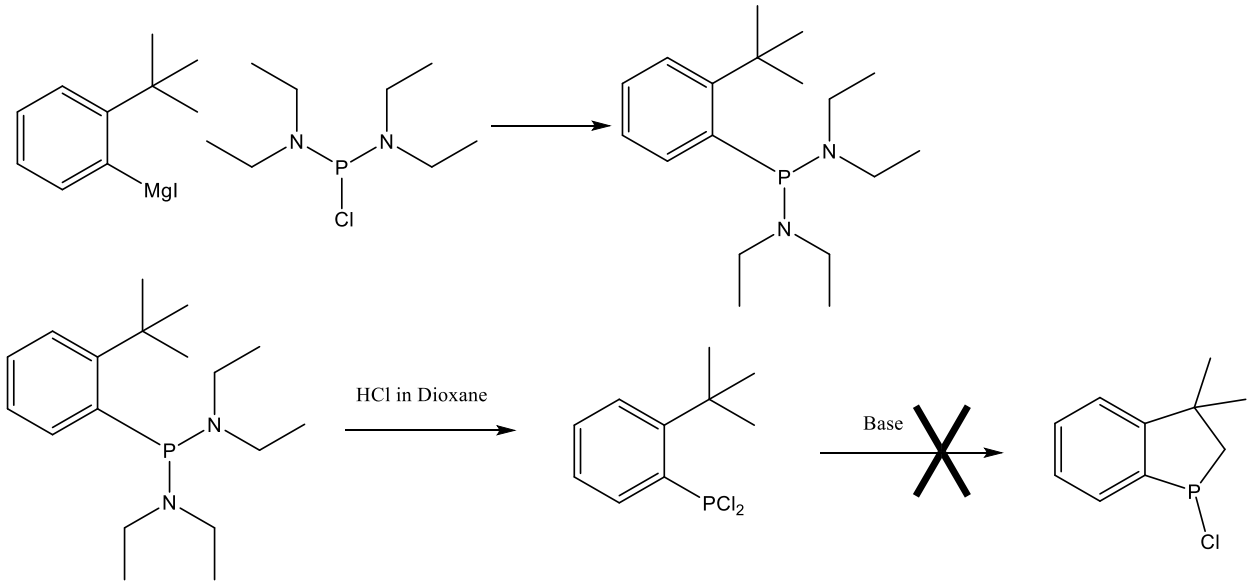


Scheme 12: Synthesis of bis(diethylamino) phosphorus chloride



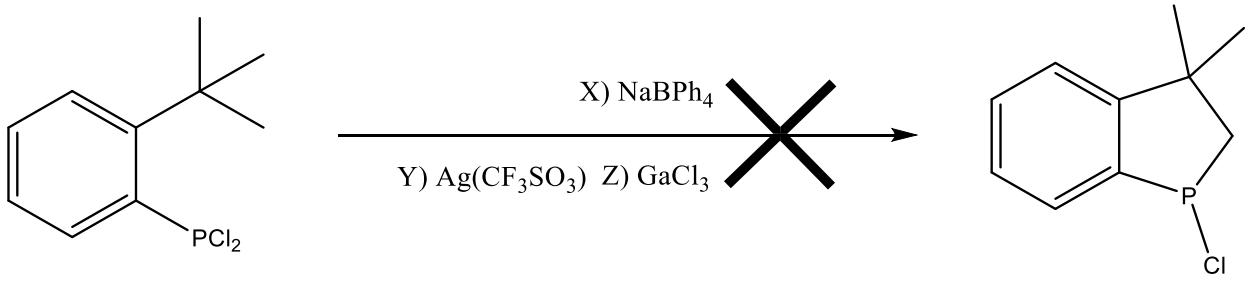
Scheme 13: Synthesis Grignard reagent

The Grignard was made by mixing the one iodine crystal with magnesium metal to activate the metal. The iodine compound was then added to the solution to produce the Grignard. The Grignard was then mixed with the bis(diethylamino) phosphorus chloride to make the phosphorus aryl bond. Once the product was isolated it was reacted with hydrogen chloride in dioxane. This reaction removed both the diethylamino groups and replaces them with two chloride atoms. Once the product was obtained, a small portion was reacted with pyridine to attempt a ring closure. Similar to, the ring closure done on the Mes* version. The reaction was unsuccessful in closing the ring. [13]



Scheme 14: Synthesis of ortho-tBu-PCl_2

Since heating ortho-tert-butyl-PCl_2 in pyridine was unable to close the ring, other reactions were done in an attempt to close the ring. The first reaction was with gallium trichloride. This reaction was done in attempts to remove one of the chlorines to make gallium tetrachloride anion and a phosphorus cation. The phosphorus would remove one of the protons from one of the methyl groups. This would create a CH_2 group that would bond to the phosphorus and close the ring. This reaction was also unsuccessful based on the multitude of peaks shown in the phosphorus NMR. Next sodium tetraphenylborate was used to attempt to remove one of the chorines and replace it with a proton from one of the methyl groups, similar to the gallium reaction. Once again, the reaction was determined to be unsuccessful by looking at the ^{31}P NMR spectrum and seeing no change in the chemical shift. Finally, $Ag(CF_3SO_3)$ was used but it was also determined to be unsuccessful by looking at the ^{31}P NMR spectrum and seeing multiple peaks. More work is needed to find a way to close the ring of the ortho tertbutyl compound.



Scheme 15: Reaction of ortho-tertbutyl PCl_2 with different bases to attempt ring closure

Conclusion

Most of the molecules made were done so by following previously reported procedures with slight changes to better accommodate the desired products. All the reactions were followed and confirmed by ^{31}P and ^{1}H NMR spectroscopy, as well as single crystal X-ray diffraction. A synthetic path was designed to produce the desired carbene and most of the steps were confirmed. More work is still to be done on the Mes* carbene.

Little work was done on the ortho t-butyl compound since none of the route's test for the ring closure were successful.

Future Work

There is still lots of work to be done on this project and even more work to be done in this area of research. For this project, the next step would be to further purify the reaction of the Mes*PMe with NBS to remove the succinimide. Once this is able to be done, work to produce the carbene is able to begin. This reaction would have to be done at -78° C and involve mixing the product with a base to remove the HBr and then reacting it with either $Rh(CO)_2Cl$ or P_5Ph_5. We would be able to use the Rh product to test the σ-donor and π-acceptor properties by looking at the CO stretches in the IR. The σ-donor and π-acceptor properties can also be looked at with the PPh product. By using ^{31}P NMR spectroscopy, we can look at the signal for PPh and determine how good the donor and acceptor properties are. The t-butyl version of the carbene will require more work as it still requires a process for the ring closure. From there, the proposed synthesis is similar to the one used with the Mes* carbene.

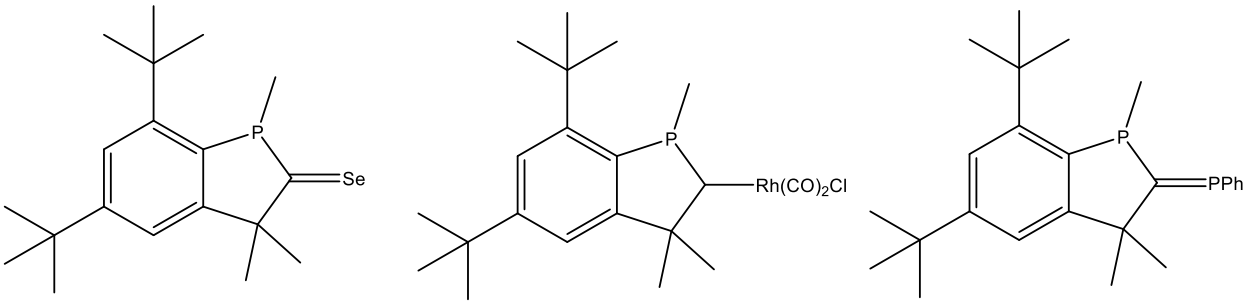


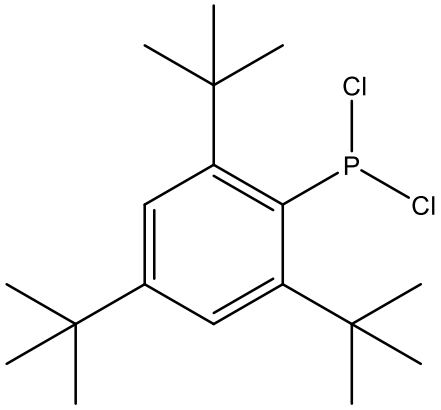
Figure 18: Future compounds to be made

Experimental

Unless otherwise stated, all reactions were done under a dry O_2 free atmosphere of N_2 via Schlenk techniques or using an MBraun UNIlab single station glove box. Pentane, diethyl ether, dichloromethane, tetrahydrofuran were purchased through Sigma-Aldrich and made appropriately anhydrous using an Innovation Technology Grubbs' type solvent purification system or through exposure to drying agents (Na^0, K^0, KH) and subsequent distillation. Sulfuric acid, sodium nitrite, potassium iodide, n-butyl lithium, phosphorus trichloride, pyridine, tris(diethylamino) phosphorus, magnesium, iodine, $KN(SiMe_3)_2$, DBU, MeI, $(CH_3)_3O(BF_4)$, MeMgI, HCl in dioxane, $GaCl_3$, carbon tetrachloride, $NaBF_4$, $NaBPh_4$, and $Ag(CF_3SO_3)$ were bought from Sigma Aldrich. SIPr, BICAAC, NBS, Mes*Br, and TerMes were made previously in the Masuda lab.

Experiment 1

Synthesis of (2, 4, 6)-trit-butyl-1-phosphinodichloride benzene:



16.27g of 1-bromo-2, 4, 6-tritbutyl benzene was added to 125ml of dry THF in a 250ml Schlenk flask with a rubber septum and stir bar. The solution is cooled to -78° C using a dry ice and acetone bath. 22ml of 2.5M n-butyl lithium in hexane was added by syringe over a few minutes and stirred for two hours while maintaining -78° C. The solution was transferred to a 500ml Schlenk flask containing 5ml of PCl_3 in approximately 10 ml of THF using a cannula over 30 minutes. -78° C was maintained for the 30 minutes and the solution was left to stir over night. The solution was dried using a vacuum pump with two traps due to volume of solvent. The product was dissolved in diethyl ether and filtered through celite and dried to give 16.7438g of a slightly yellow opaque powder.

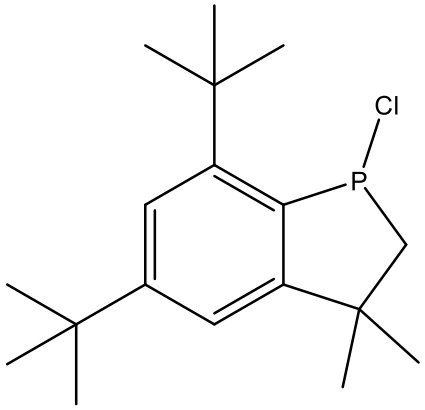
Yield: 96%

^{1}H NMR (500 MHz, C_6D_6) δ: 7.48-7.41 (m, 2H, Aromatic H), 1.59 (s, 18H, o-tBu), 1.15 (s, 9H, p-tBu)

^{31}P NMR (500 MHz, C_6D_6) δ: 152ppm (lit. value 155ppm [9])

Experiment 2

Ring closure of (2, 4, 6)-trit-butyl-1-phosphinodichloride benzene (product 2):



10.775g of (2, 4, 6)-trit-butyl-1-phosphinodichloride benzene was added to a 250ml sealed reaction vessel. Approximately 30ml of pyridine was added to the flask. The flask was then sealed and heated to 110° C overnight. The solution was then dried and dissolved in pentane. The solution was filtered and dried again to give 8.58g of a slightly yellow opaque powder.

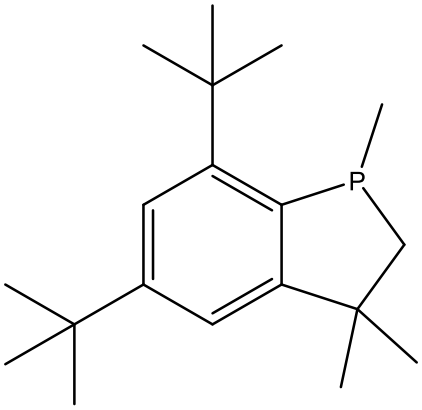
Yield: 89%

^{1}H NMR (500 MHz, C_6D_6) δ: 7.1-7.5 (m, 2H, Aromatic H), 2.33-2.38 (d, 2H, J_H-J_H=15Hz, P-CH_2), 1.65 (s, 9H, o-tBu), (, 6H, 2-CH_3), 1.24 (s, 9H, p-tBu)

^{31}P NMR (500 MHz, C_6D_6) δ: 109ppm (lit. value 111.5ppm [10])

Experiment 3

Methylation of product 2 (Product 3):



3.063g of product 2 were mixed with 2.8ml of MeMgI in a vial. The solution was dried, and the product was extracted with pentane. The product was filtered and dried to give 2.894g of a slightly yellow opaque powder.

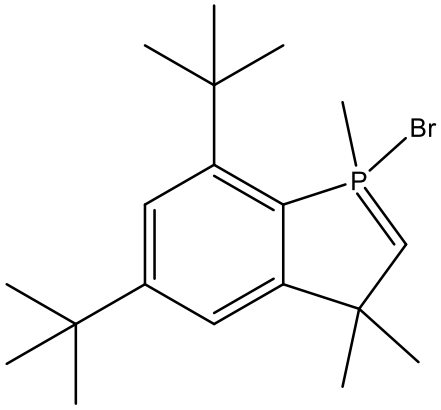
Yield: 99%

^{1}H NMR (500 MHz, C_6D_6) δ: 7.37-7.35 (m, 1H, , J_H-J_H= 2Hz, Aromatic H), 7.12 (d, 1H, , J_H-J_H= 2Hz, Aromatic H), 1.51 (s, 9H, o-tBu), 1.43 (s, 3H, C-CH_3), 1.39 (s, 3H, C-CH_3), 1.36 (s, 9H, p-tBu), 1.348 (s, 2H, P-CH_2), 1.344 (s, 3H, P-CH_3)

^{31}P NMR (500 MHz, C_6D_6) δ: -29 ppm

Experiment 4

Synthesis of product 4:



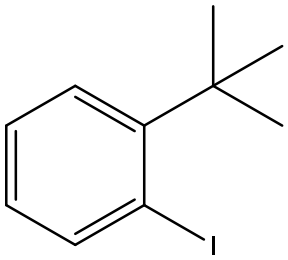
1 gram of product 3 was mixed with 0.674g of NBS in Dichloromethane. Succinimide was not removed so no accurate yield could be recorded. The reaction produced a dark purple opaque powder.

^{1}H NMR (500 MHz, C_6D_6) δ: sample was to dirty to accurately determine peaks

^{31}P NMR (500 MHz, C_6D_6) δ: 67 ppm

Experiment 5

Synthesis of 1-iodo-2-tertbutylbenzene:



11g of 2-tertbutylaniline was dissolved in 3.4M H_2SO_4. 5.25g of $NaNO_2$ was dissolved in approximately 20ml of water and was added to solution over 5 minutes. 37.5g of KI was dissolved in water and was added to the solution. Liquid was decanted off and tar like substance was dissolved in diethyl ether. Extracted the diethyl ether phase in a saltatory funnel into a round

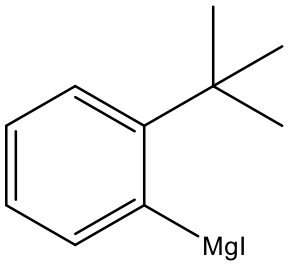
bottom. The solution was dried and dissolved in pentane. The solution was filtered. Column chromatography was done on the solution. 4 different fractions were taken and the first 3 were combined. A second run using 13g of aniline was done. Both runs gave a total of 3.46g of a slightly orange transparent oil.

Yield: 8%

^{1}H NMR (500 MHz, C_6D_6) δ: 8.00-6.78 (m, 4H, aromatic H), 1.53 (s, 9H, tBu)

Experiment 6

Formation of Grignard:

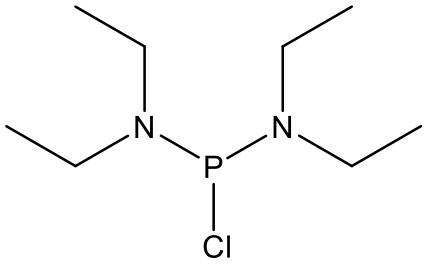


Approximately 50ml of THF was added to a 250ml Schenk flask along with 0.4g of magnesium metal. 1 iodine crystal was added, and the solution was heated. Once all of the iodine had reacted, the iodo-ortho-tertbutyl benzene oil was added to the solution and was heated to boil multiple times over a few days. Reaction was confirmed by the shift in the tert-butyl peak

^{1}H NMR (500 MHz, C_6D_6) δ: 1.27 (s, 9H, o-tBu)

Experiment 7

Synthesis of bis(diethylamino) phosphorus chloride:

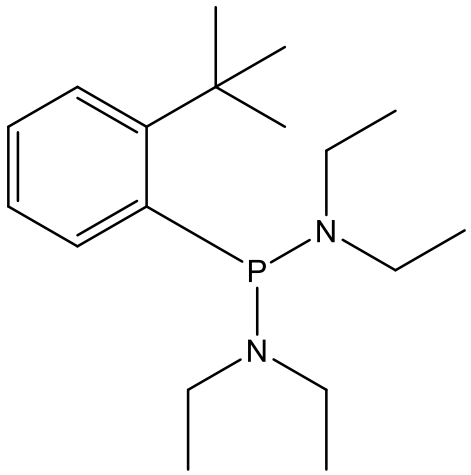


2.19g of tri(diethylamino)phosphorus was mixed with 0.608g of PCl_3 in THF and stirred overnight.

^{31}P NMR (500 MHz, C_6D_6) δ: 153ppm

Experiment 7

Synthesis of ortho-tertbutyl bis(diethylamino)phosphorus benzene:

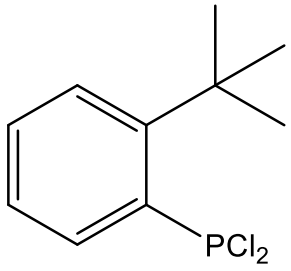


The Grignard product was mixed with the bis(diethylamino) phosphorus chloride and was mixed overnight.

^{31}P NMR (500 MHz, C_6D_6) δ: 92 ppm

Experiment 8

Synthesis of ortho-tertbutyl (phosprousdicloride) benzene:



The ortho-tertbutyl bis(diethylamino)phosphorus benzene was mixed with 9.725ml of HCl in THF. The product was then dried and extracted with pentane. The solution was filtered and dried again giving 3.38g of yellow oil. Distillation was not done leaving impurities cause unrealistic yield.

Crude Yield: 111% (contaminated with excess diethyl amino chloride)

^{1}H NMR (500 MHz, C_6D_6) δ: 8.15-8.10 (m, 1H, Ar-H), 6.78-6.75 (m, 3H, Ar-H), 1.02 (s, 9H, o-tBu)

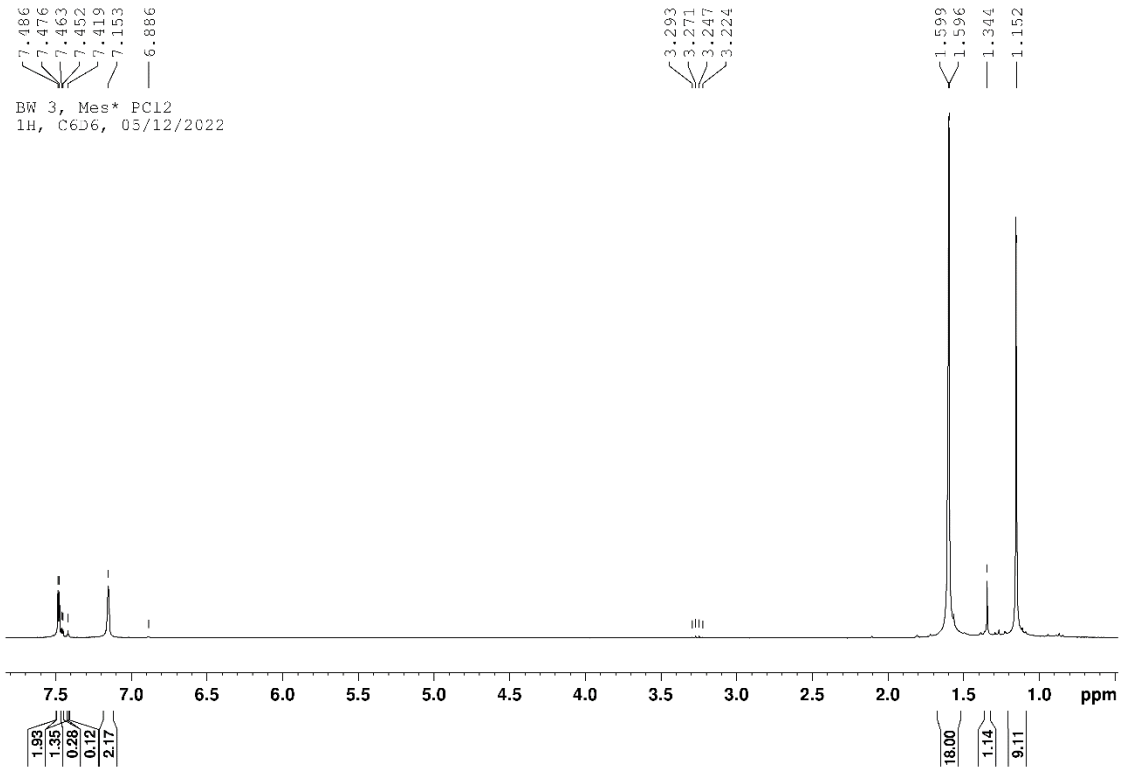
^{31}P NMR (500 MHz, C_6D_6) δ: 165 ppm (lit. value 166ppm [13])

X-ray Crystallography

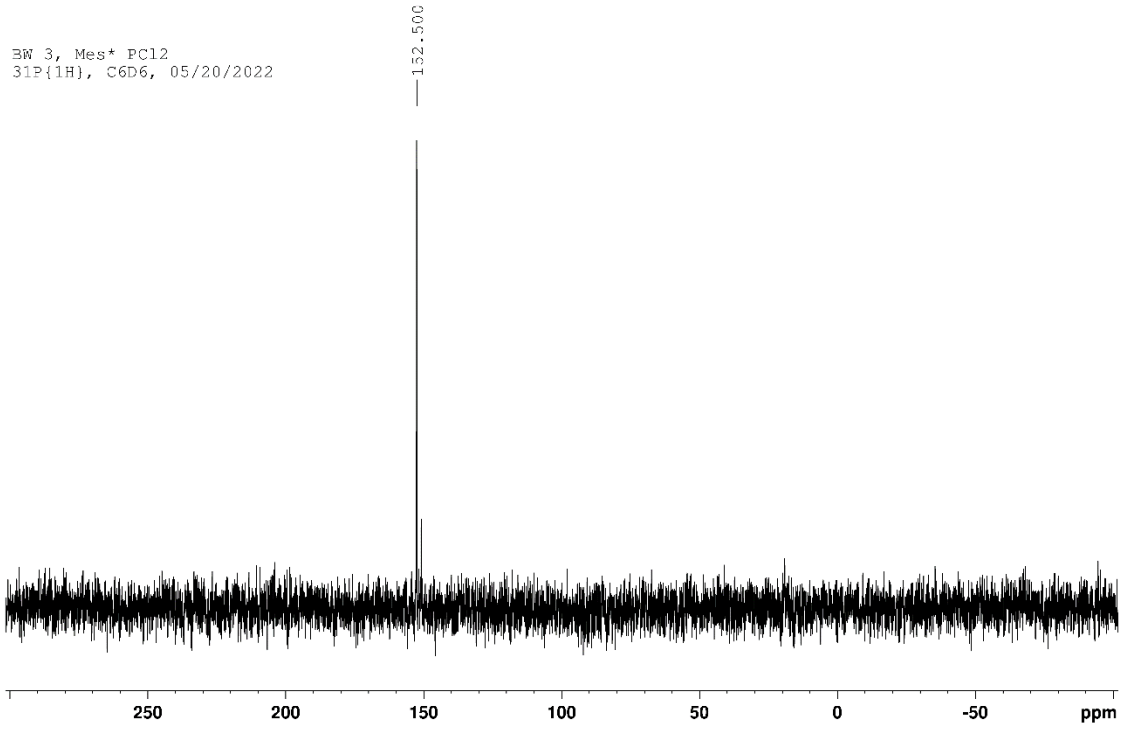
Table 1 Crystallography data

Compound reference	1	2
Chemical formula	$C_{19}H_{31}OP$	$Cl_4Ga•C_{20}H_{33}P1Cl$
Formula Mass	306.41	538.30
Crystal system		
a/Å	6.1064(3)	17.2906(6)
b/Å	18.7075(7)	9.5082(3)
c/Å	15.7703(7)	17.3320(6)
α/°	90	90
β/°	97.977(2)	115.0360(10)
γ/°	90	90
Unit cell volume/Å^3	1784.10(14)	2581.70(15)
Temperature/K	150	125.00
Space group	*P*121/*c*1	*P*121/*c*1
No. of formula units per unit cell, *Z*	4	4
Radiation type	MoKα	MoKα
Absorption coefficient, μ/mm^{-1}	0.153	1.649
No. of reflections measured	45538	89614
No. of independent reflections	4789	7884
R_{int}	0.0601	0.0415
Final R_1 values ($I > 2\sigma(I)$)	0.0489	0.0756
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1038	0.2008
Final R_1 values (all data)	0.0613	0.0883
Final $wR(F^2)$ values (all data)	0.1084	0.2133
Goodness of fit on F^2	1.110	1.063

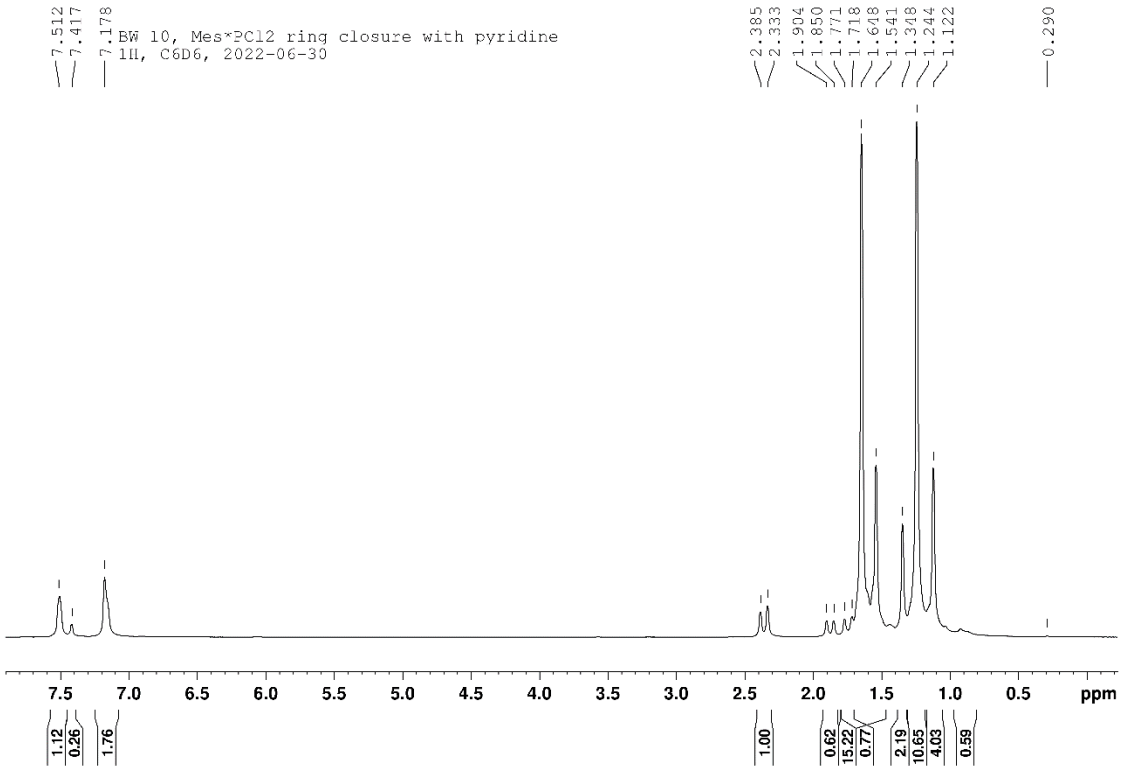
NMR spectrum



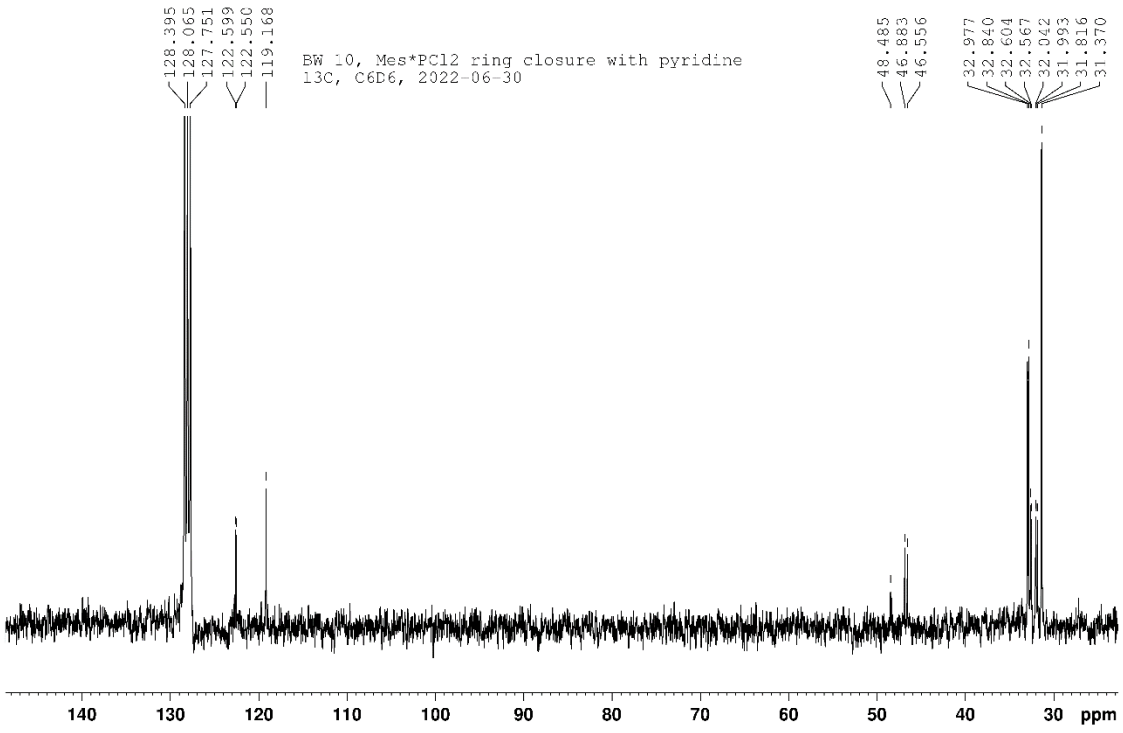
^{1}H NMR spectrum for Mes*PCl_2



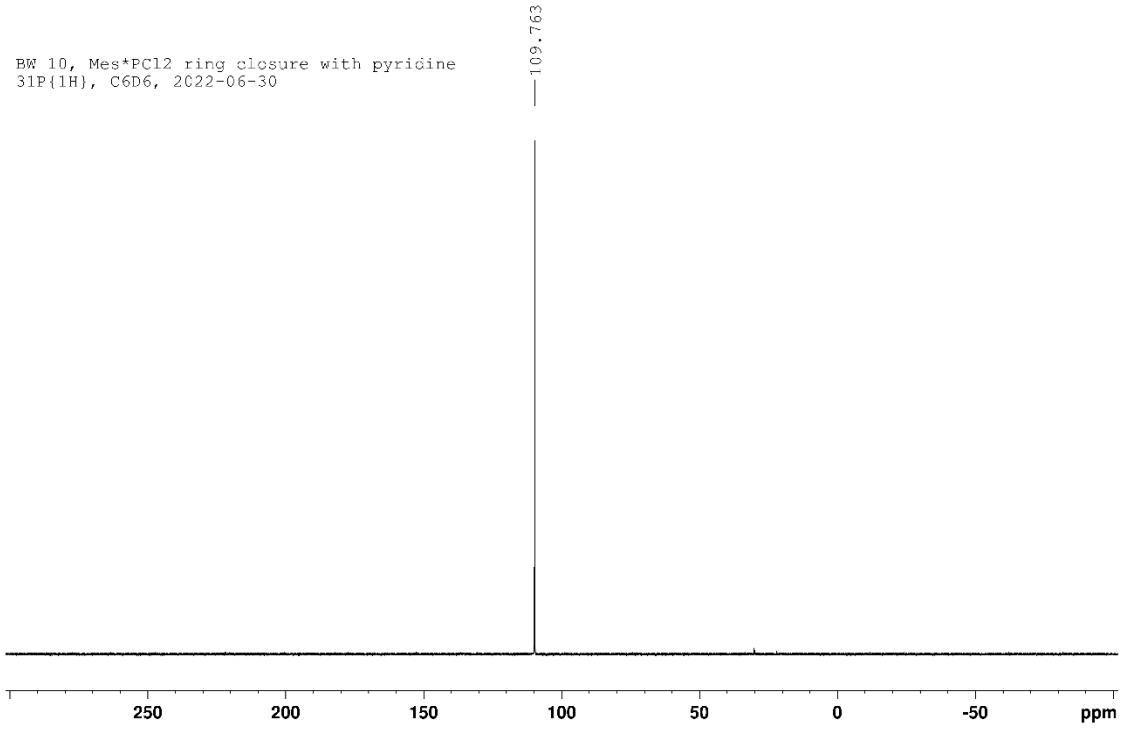
^{31}P {H} NMR spectrum for Mes*PCl_2



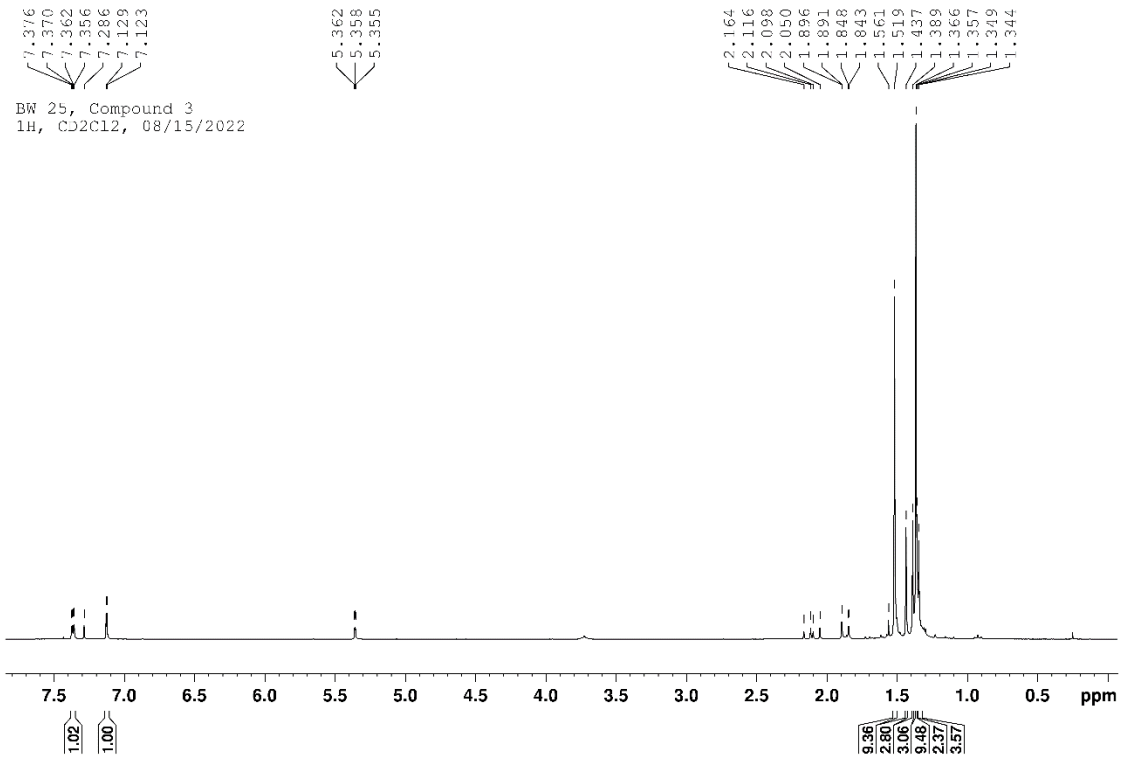
^{1}H NMR spectrum for ring closure of Mes*PCl_2



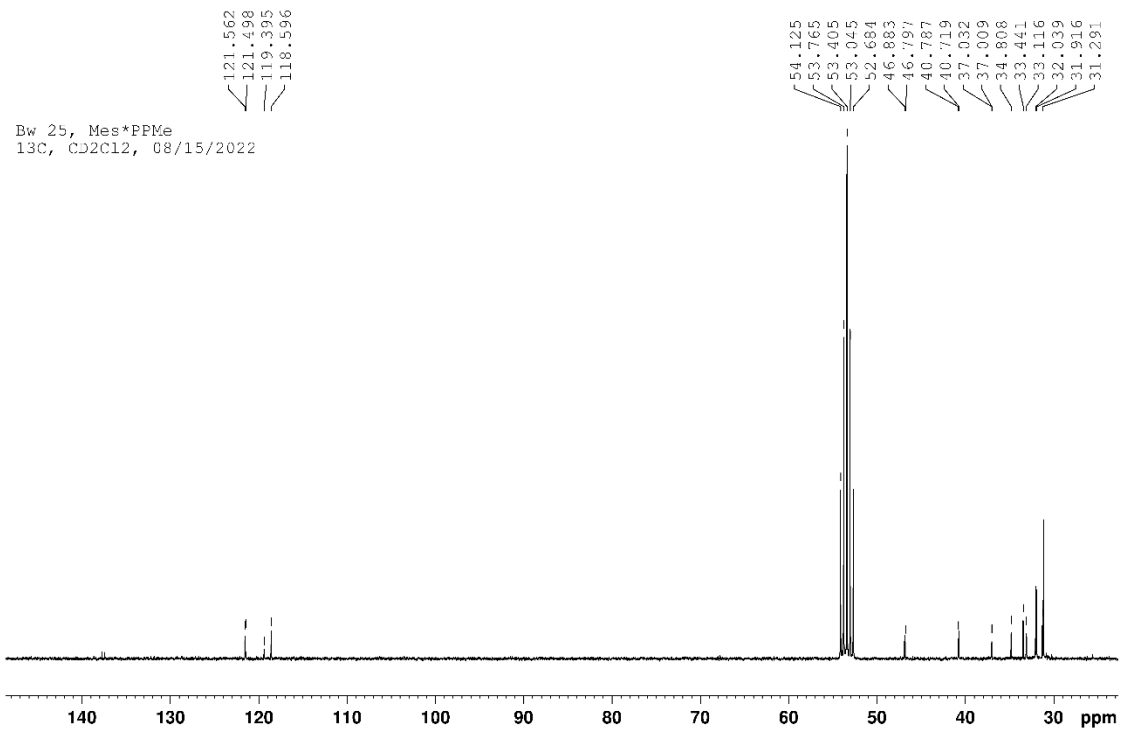
^{13}C NMR spectrum for ring closure of Mes*PCl_2



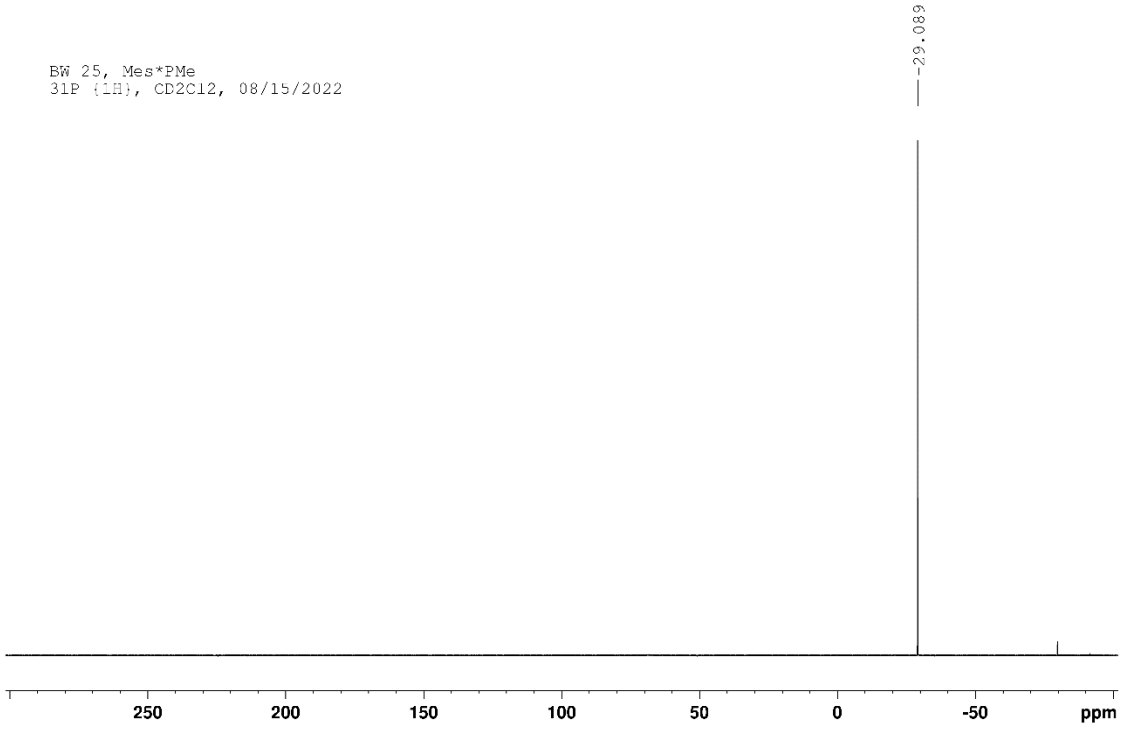
^{31}P {H} NMR spectrum for ring closure of Mes*PCl_2



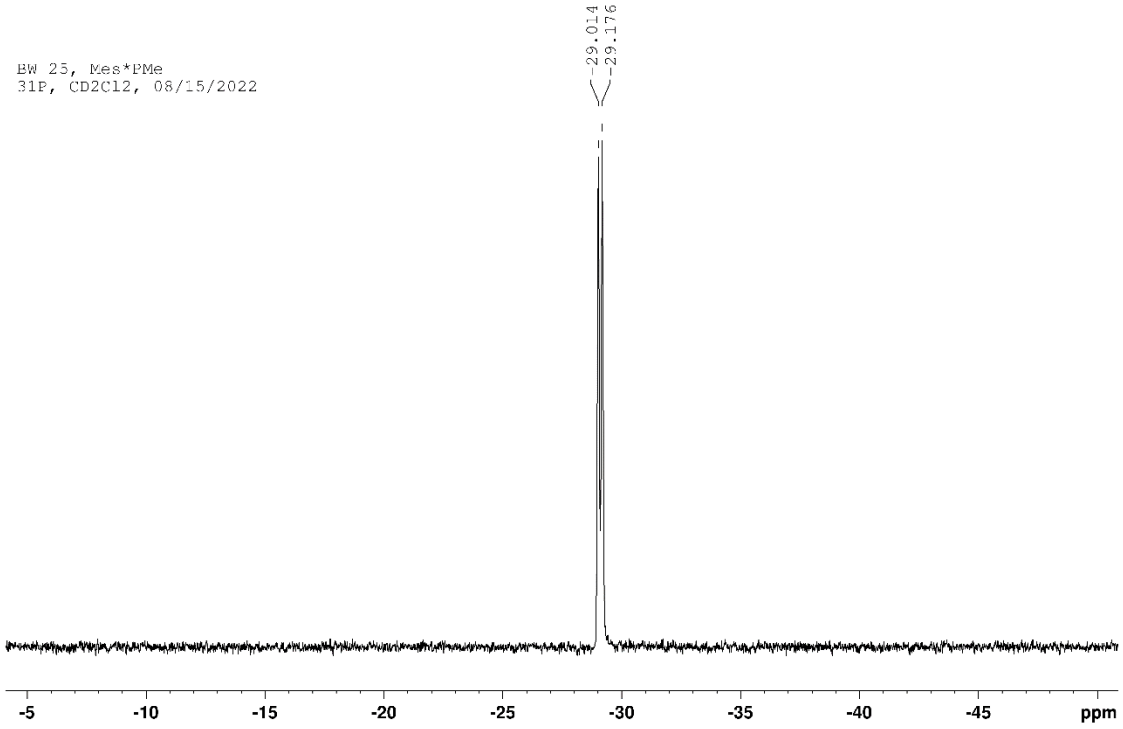
^{1}H NMR spectrum for compound 3



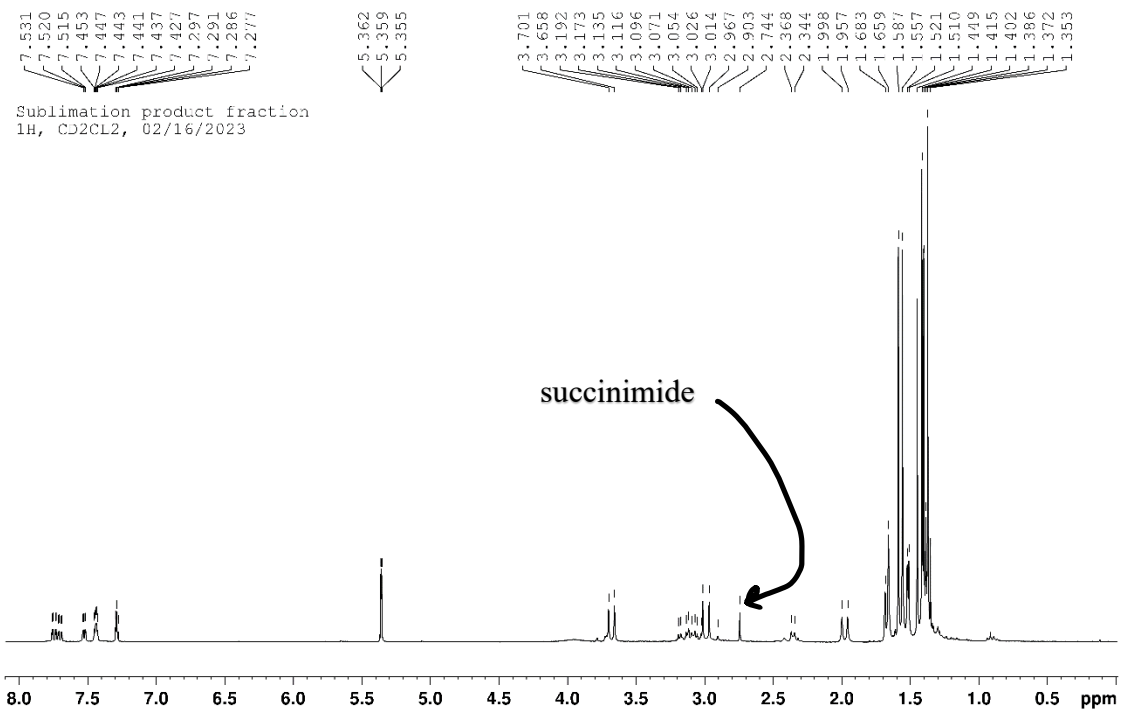
^{13}C NMR spectrum for compound 3



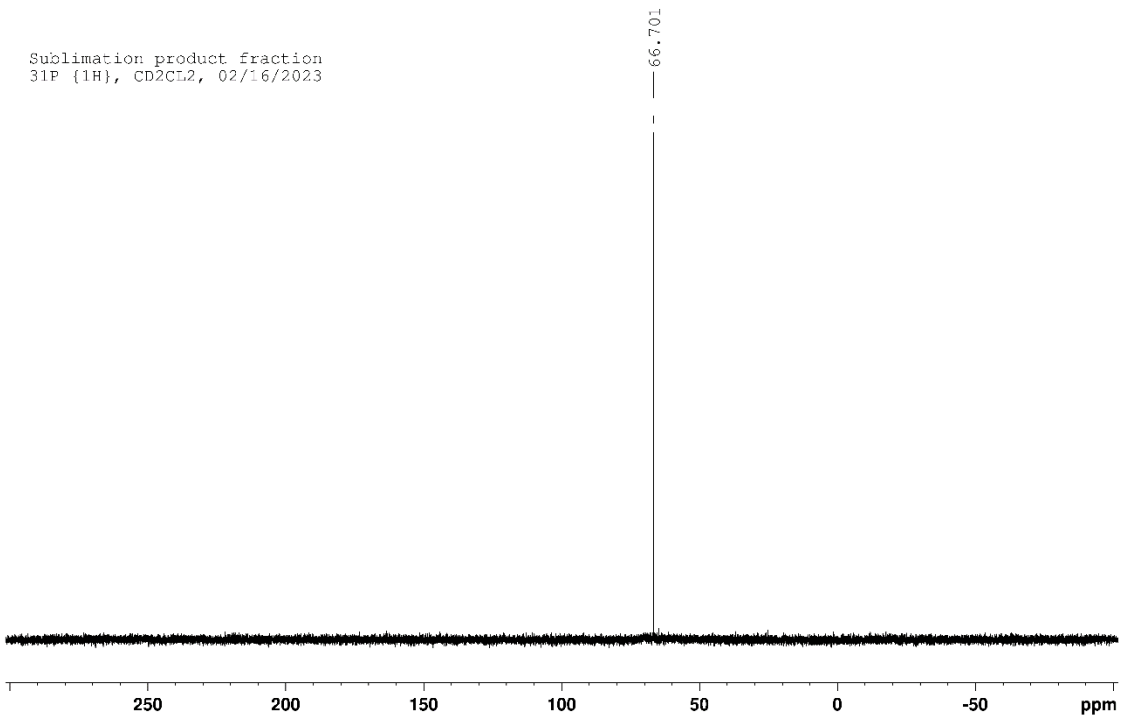
^{31}P {H} NMR spectrum for compound 3



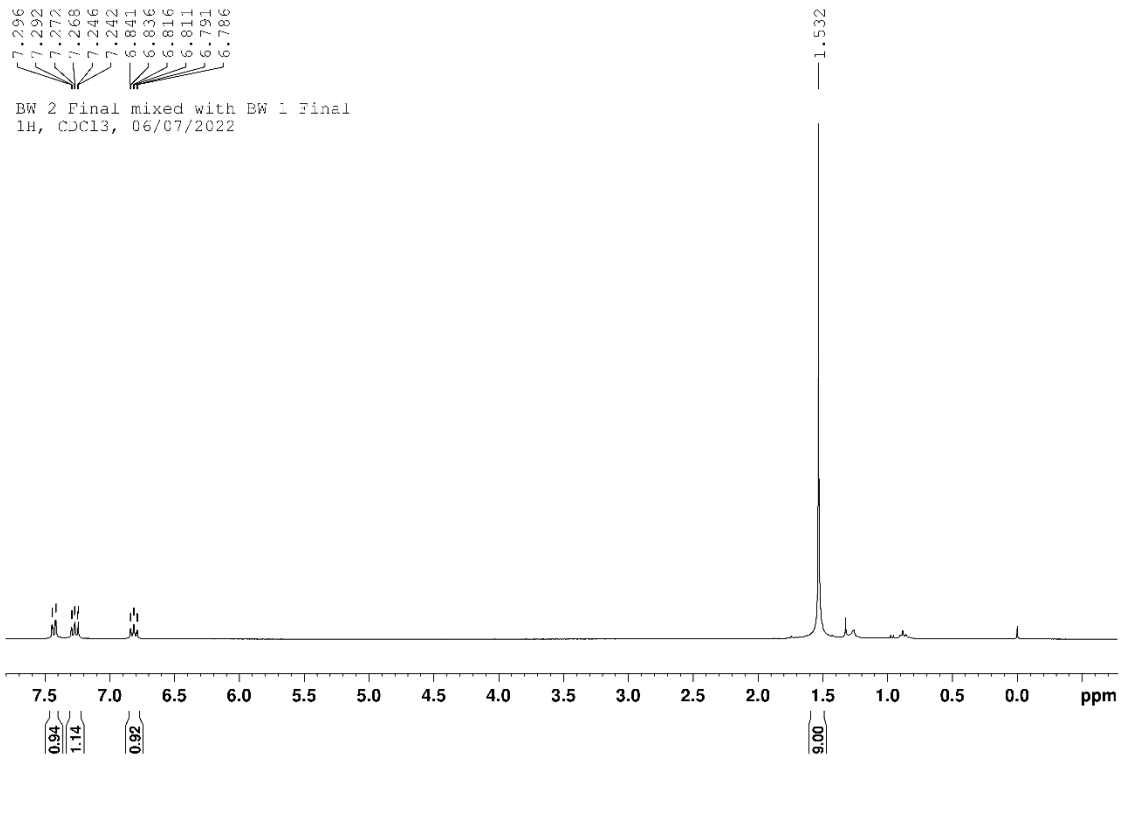
^{31}P NMR spectrum for compound 3



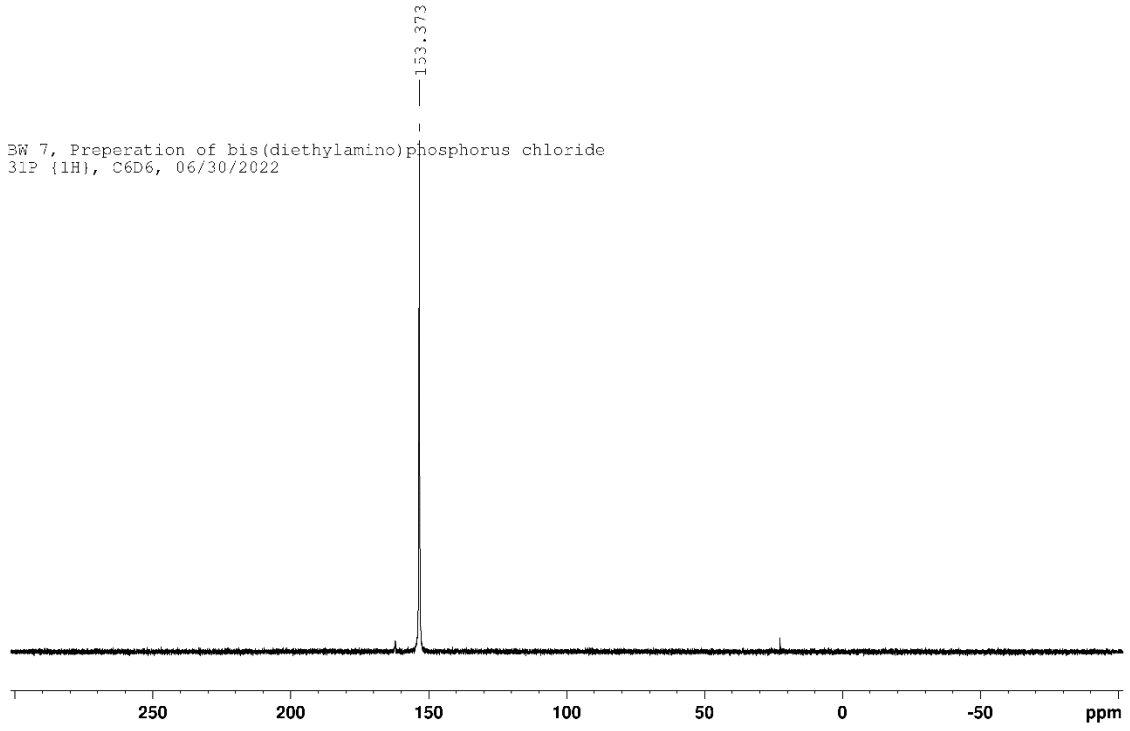
^{1}H NMR spectrum for compound 4



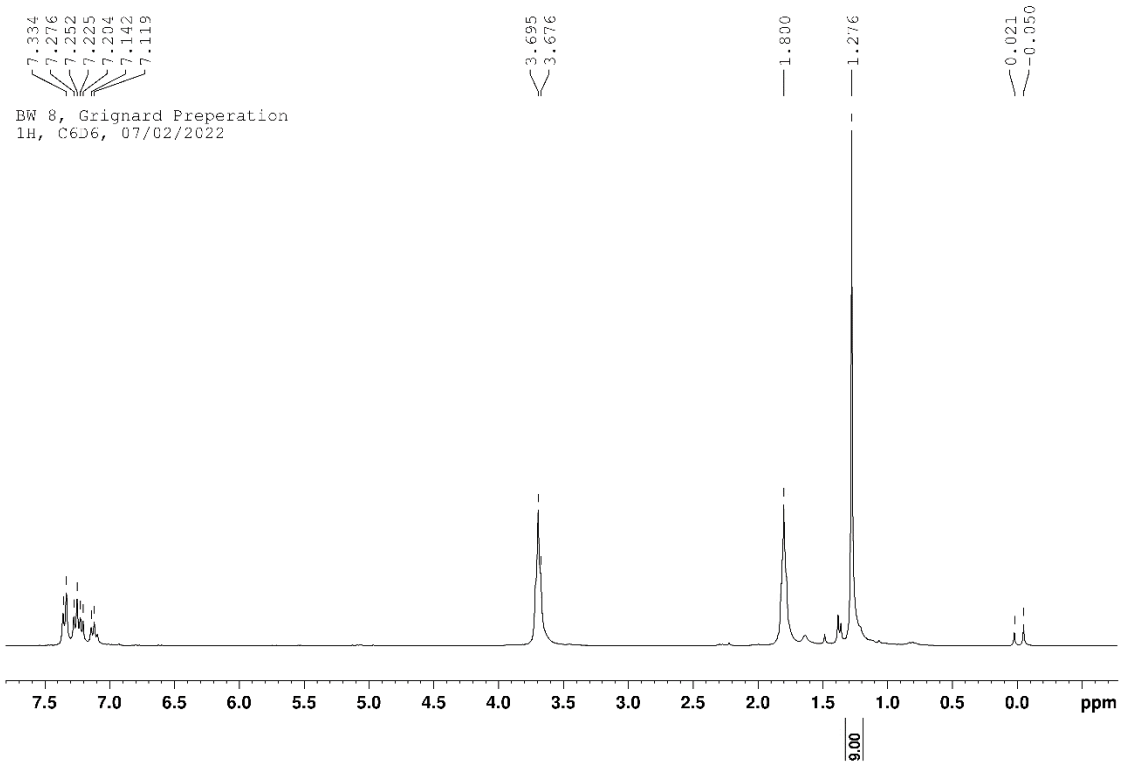
^{31}P {H} spectrum for compound 4



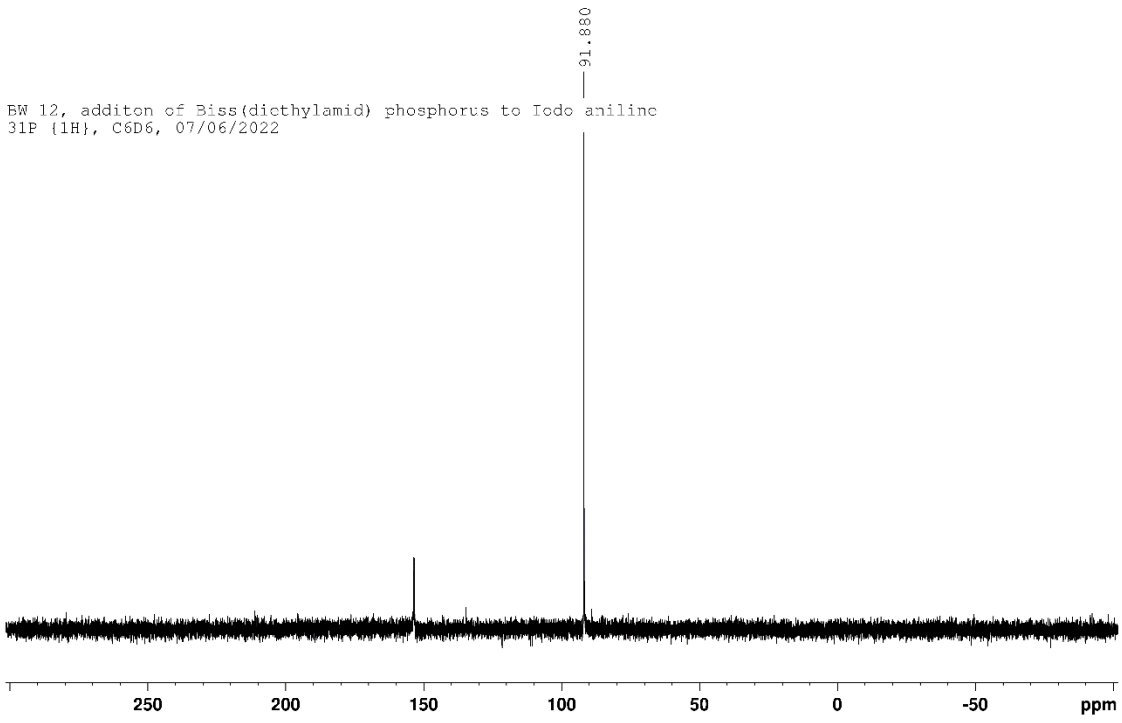
^{1}H NMR spectrum for 1-iodo-2-tertbutylbenzene



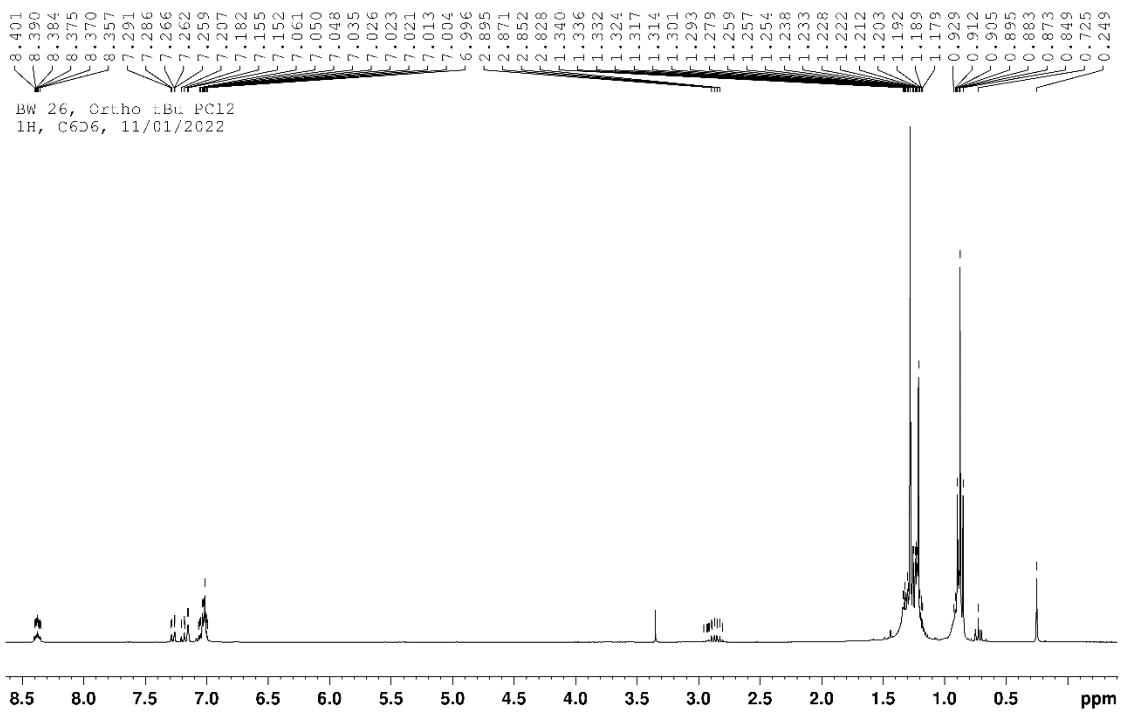
^{31}P {H} NMR spectrum for bis(diethylamino) phosphorus chloride



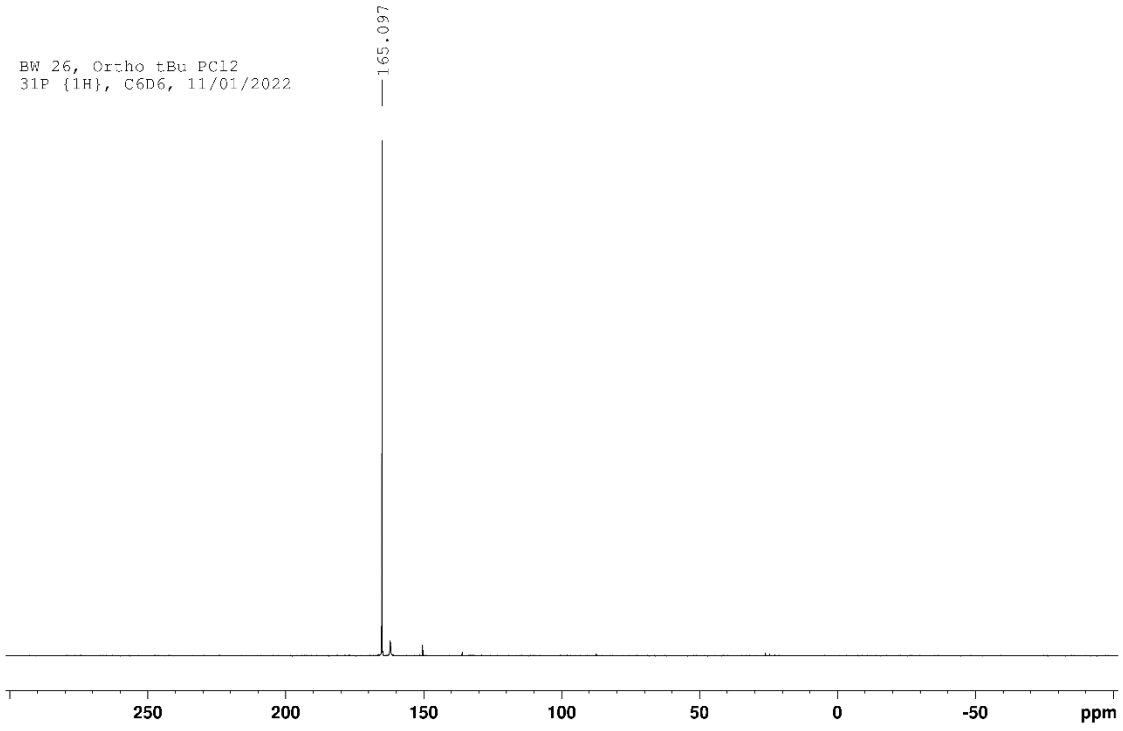
^{1}H NMR spectrum for Grignard formation of o-tBu-C_6H_4MgI



^{31}P {H} NMR spectrum for addition of bis(diethylamino) phosphorus chloride



^{1}H NMR spectrum for ortho-tBu-PCl_2



^{31}P {H} NMR spectrum for ortho-tBu-PCl_2

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