UNIVERSITY OF CALIFORNIA

Santa Barbara

Reactions of Homogeneous Gold Catalysis: Ligand Design, Alkynes, and Gold-Carbenes

A Thesis submitted in partial satisfaction of the requirements for the degree Master of Science in Chemistry

by

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June 2016

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March 2016

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ACKNOWLEDGEMENTS

Firstly, I would like to express my gratitude to my advisor, Professor Liming Zhang. His great passion for organic chemistry and positive attitude inspired me to work hard and to persevere, especially through medical challenges. He always had good advice, even when it was difficult to hear.

I would also like to express my gratitude and appreciation to the members of my committee: Professors Daniel Little, Javier Read de Alaniz, and Norbert Reich. Their dedication and personalities have provided a wonderful atmosphere in the UCSB Chemistry department.

I would like to express sincere gratitude and appreciation to my undergraduate advisors and mentors: Professor Phil Baran, who instilled strong interest in organic chemistry, particularly in total synthesis, and Professor Carlos Guerrero.

I am indebted to the group members in the Liming group, both former and current. This work would not have been possible without the inspiring collaboration within the Liming group, in particular Zhixun Wang, Zhitong Zheng, and Youliang Wang. Special thanks go to Dr. Kegong Ji, with whom I worked closely for a period of time, and Mallarie Stevens of the chemistry administration for all of her patient help.

My family and friends have been extremely supportive and understanding of my graduate school journey. In particular I thank Jeff Heckey and Dayton Horvath for their unswerving friendship, support, adventures, and countless barbeques. Special thanks also goes to my siblings, who have lent invaluable insights, discussions, and support. I'd also like

to express my deep gratitude and sincere appreciation to my mother for her unwavering support, encouragement, understanding, and her positive persistent pursuit of life.

To my father, may he rest in peace, who taught me how to build and create, I think you would be proud.

ABSTRACT

Reactions of Homogeneous Gold Catalysis:

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The last decade has seen a rapid rise in the developments in homogeneous gold catalysis. The soft Lewis acidity of cationic gold(I) complexes towards alkynes and allenes and the easy access to gold carbene intermediates via oxidation have produced a diverse range of synthetically versatile transformations. In my thesis, several novel methodologies have been explored and developed, including: (1) The design of novel new ligands to enable highly efficient gold-catalyzed nucleophilic addition reactions, including the development of *P,S*-bidentate ligands, which enabled the generation of tris-coordinated gold carbene species, and provided high selectivity and yields for propargylic ether to undergo a 1,2-C–H insertion; (2) The highly regioselective oxidation of carboxylates of primary and secondary propargylic alcohols, undergoing 1,2-acyloxy migrations over a 1,2-C–H migration, with selectivity was greatly enhanced by using the *P,S*-bidentate ligand, with ratios ranging from 16 to over 300; (3) An investigation into the effects of α-oxo gold-carbene electrophilicity on product selectivity of propargylic ethers to undergo 1,2-alkyl-migration versus 1,2-C–H insertion, along with the application of said 1,2-alkyl migration to both ring expansion and

the migration of a propargylic sp^2 substituents; excellent regioselectivities were obtained for the gold catalyzed oxidation of propargylic ethers while selecting for the hydride migration.

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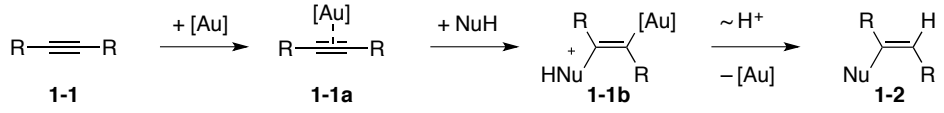
1. Introduction and Theory

1.1 Basic Chemistry of Homogeneous Au(I) Catalysis

Homogeneous gold catalysis has, in the last decade, seen a rapid evolution in the methods developed[1] and uses in natural synthesis.[2, 3] The most common reactivity pattern in gold-catalyzed organic reactions is the nucleophilic addition to C-C π-bonds. The π-bonds of alkynes, allenes, or olefins coordinate to gold complexes, and this very efficiently activates them for the attack of a nucleophile. Alkynes are the most successful and most frequently used reaction partners for gold catalysts,[4] although allenes were among the first substrates used, and they are still quite popular. An example of the mechanism for a simple nucleophile is shown in Scheme 1-1. First, the gold interacts with the π-system to form structure **1-1a**, then the nucleophile attacks the activated π-system. There is much evidence[1] that the nucleophile adds *anti* to gold to deliver a vinyl gold species **1-1b**, but as an exemption, the nucleophile adds *syn* in the case of norbornene compounds.[5] The organogold intermediate **1-1b** undergoes protodemetallation of the gold catalyst to give the addition product **1-2**.

Scheme 1-1: General Form of Cationic Gold(I) Catalyzed Nucleophilic Attack



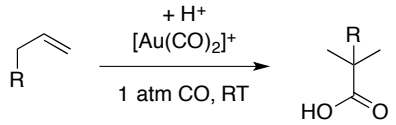
In most gold catalyzed reactions, which proceed via organogold-intermediates containing a carbon-gold single bond, an acidic media is required, to invoke the required protodemetallation step. The proton may be from a catalytic amount of a Brønsted acid as a co-catalyst, or it may be generated in situ previously in the reaction pathway. In fact, there

was a discussion for a long time on the role of the protons in gold catalysis, as it was suspected in some cases that the proton was the true catalyst.[6]

Cationic gold is able to substitute for Brønsted acids in acid-catalyzed addition and elimination reactions, as it has a similar activation effect on the π-system as shown by Hashmi et. al.[7-8] Where *p*-toluenesulphonic acid shows an identical catalytic activity as $AuCl_3$ in the three-fold reaction of α,β-unsaturated aldehydes[9] and the two-fold reaction of aryl aldehydes with electron-rich arenes.[10] Quite similar results for hydroamination of alkenes were found with both a gold catalyst and triflic acid,[11-12] as well as for the addition of different oxygen nucleophiles. However these are the few examples of equivalent reactivity. There are more examples of protons playing the role of co-catalysts.

First used in a low-pressure Koch-Haaf reaction,[13-14] the collaboration of a strong Brønsted acid and the gold catalyst is indicated by a significantly lower pressure of 1 atm versus the usual 100 atm.

Scheme 1-2: Example of Low Pressure CO Insertion

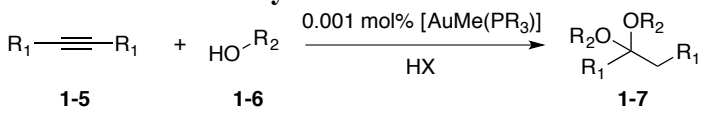


1-3 **1-4**

When a Brønsted acid is used as the co-catalyst, the activity of the gold catalyst increases for reaction following the general mechanism of Scheme 1-2, and sometimes is required for reactivity. For example, in Scheme 1-3, showing the conversion of **1-5** and **1-6** to **1-7** with a strong Brønsted acid co-catalyst, the TOF, or Turn Over Frequency, of the gold catalyst increased almost linearly with the concentration of H^+.[15] The TOF is the frequency

or speed at which the catalyst completes a catalytic cycle. A low TOF means a slower reaction, longer reaction time, and a higher chance of side reactions.

Scheme 1-3: Addition of Alcohol to Alkyne

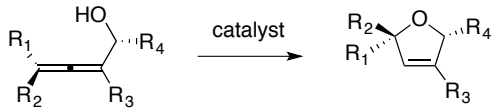


1-5 **1-6** **1-7**

In 1998, for the hydroamination of alkynes, acidic promoters were considered crucial for gold catalysis, as neither the gold complexes nor the acids alone were found to be adequate.[16] The current mechanistic understanding is that a strongly acidic proton is essential for a fast proto-demetallation step. Acid can also be added in stoichiometric amounts, and is mostly done when the product gains protons, or when the organo-gold bond is particularly strong.

For a number of reactions, especially those reported in recent years, gold catalysts are superior to Brønsted acid catalysts. Stradiotto reported in 2010 an acid-free hydroamination reaction, progressing through a intramolecular proto-demetallation step with no net pH change over the course of the reaction.[17] The example in Scheme 1-4 is the cyclization of α-hydroxyallenes to 2,5-hidydrofurans.[18]

Scheme 1-4: Example of Gold(I) Catalyzed Cyclization



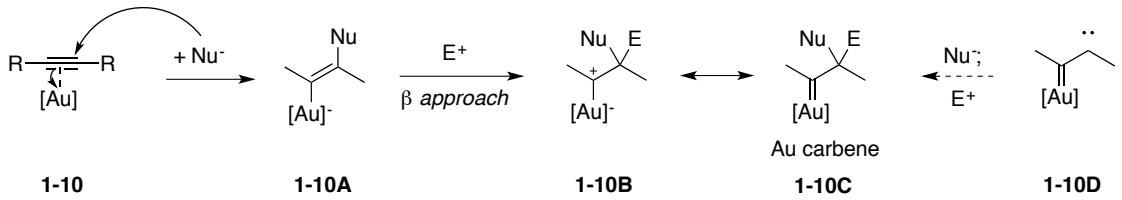
1-8 **1-9**

Notice that the cyclization reaction has no net pH change, as the mechanism formally requires the transfer of a proton from the hydroxyl group to the new olefin. The presence of acid has also been reported to shift the product ratio, for example, by hydrolysis of the final product of the gold catalysis.[19] The formation of gold carbenes is another reaction class that does not utilize acid.

The increased popularity in its use as a catalyst can be attributed to the potent and versatile reactivities of gold complexes. There are the renown soft Lewis acidity of cationic gold(I) species towards alkynes and allenes, as well as the ready access to gold carbene intermediates, which have a diverse library of transformations. Gold(I) carbenes are arguably the most versatile intermediates of gold catalysis, enabling access to a diverse range of functional products from often simple substrates.[20]

Scheme 1-5 shows a generalized mechanism to making gold carbenes from alkynes. In the first stage, coordination with cationic gold complex greatly promotes the attack of a nucleophile to the π-bond of the alkyne **1-10**, giving the alkenyl gold intermediate **1-10A**. While formally it is possible for the Au-C(sp^2) bond in this intermediate to react with an incoming electrophile (i.e. α approach), the alternative attack at the β approach, at the distal end of the alkene from gold, would generate a gold-substituted carbocation **1-10B**. Electron back donation from the metal center would stabilize the electron-deficient trivalent carbon center and produce the gold carbene intermediate **1-10C**. Although gold is measured as the most electronegative metal in the Pauling scale,[21] density field (DFT) calculation have suggested that such back-donation have a similar stabilization effect offered by a directly substituted MeO-group.[22]

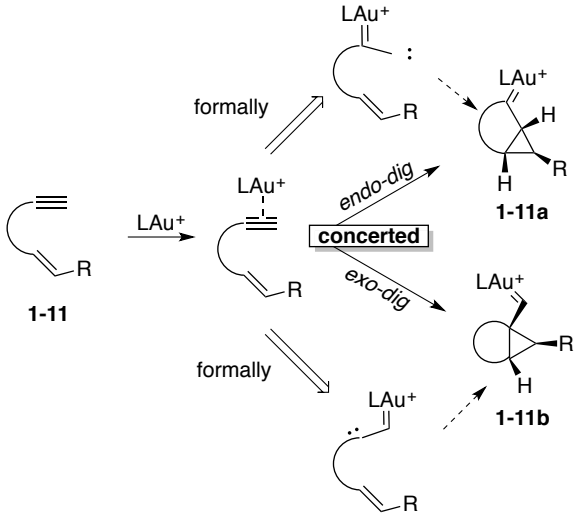
Scheme 1-5: General Outline of Gold Carbene Formation



Interestingly the overall conversion to a gold carbene of type **1-10C** from an alkyne is identical in a formal sense to first producing the hypothetical intermediate α-carbene gold carbene **1-10D** and reacting it with a nucleophile and an electrophile at its free carbene center. Hence, a gold-coordinated alkyne, before producing the gold carbene intermediate, is formally equivalent to the general structure **1-10D**. This formalism is a good model for envisioning bond formations produced by the generation of the gold carbene, and can be used to discover further reactions.

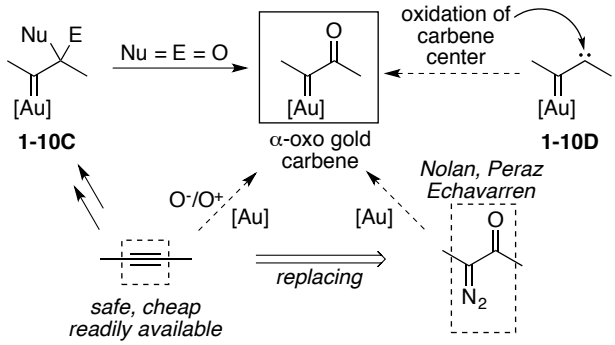
The initial nucleophilic attack and subsequent approach of the electrophile could occur in a single step. Gold-catalyzed enyne cycloisomerizations, outlined in Scheme 1-6, have been a rich area of research, and the formalism between the gold-activated alkyne and α-carbene gold carbenes is nicely demonstrated.[23-24]

Scheme 1-6: Gold-catalyzed en-yne Cycloisomerization



If both the nucleophile and electrophile are oxygen, a α-oxo gold carbene is generated (Scheme 1-7). Formally, this can be modeled as the oxidation of the carbene center of structure **1-10D**.

Scheme 1-7: Alkyne as a Surrogate to Diazo Compounds

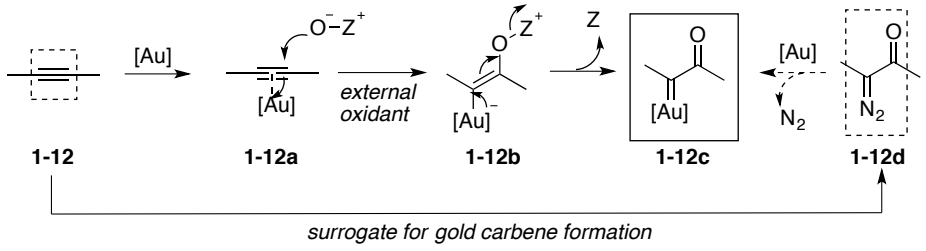


The principle and most reliable strategy to generate α-oxo metal carbenes/carbenoids is through metal-catalyzed dediazotizations of diazo carbonyl compounds, which are versatile compounds that can transform via challenging and highly valuable routes, such as C-H

insertion, ylide formation, and cyclopropanation reactions.[25] Methods using Rh catalyst with chiral ligands allow for enantioselective transformations, which are synthetically valuable. These methods, however, are less desirable due to the hazardous nature of the diazo carbonyl compounds, via the high energy held within these compounds and the potential for explosions. Consequently, this family of reactions is only safely performed on a small scale, and it takes considerable engineering ingenuity to perform safely on a larger scale, but it has been done.[26-27] Preparation of these compounds also requires energetic reagents, increasing the hazard level, and often require multiple steps unless the methylene group is fairly acidic[25]. A safer, shorter, and less harsh method for the generation of corresponding metal carbenes would be synthetically beneficial.

This oxidative version of formation, summarized in Scheme 1-8, giving the α-oxo gold carbene/carbenoid, can be used to generate the same intermediate from an alkyne instead of a diazo carbonyl. Hence, for gold catalysis, alkynes can replace the use of hazardous α-diazo carbonyl compounds.

Scheme 1-8: Alkyne as a Surrogate to Diazo Compounds via Oxidation

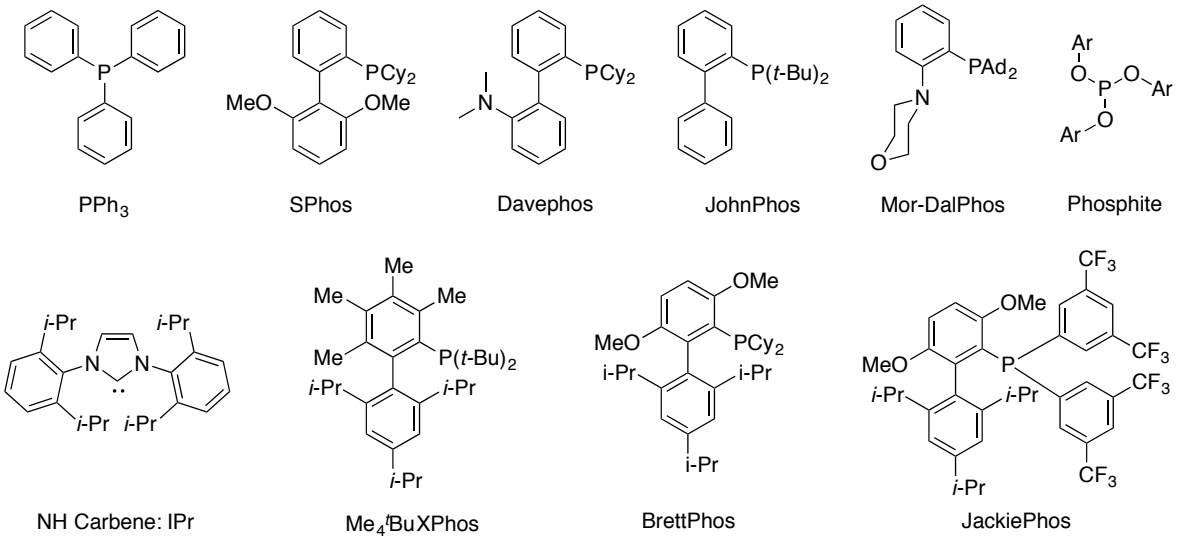


2. Ligand Design and Reactivity Studies

2.1 Introduction

Ligands play the critical role in gold-catalyzed reactions of stabilizing the cationic gold center, and significant variation of the reactivity of the metal center can be preformed by varying the ligand used. Catalyzed reactions with high efficiency, excellent chemo-, regio- and stereoselectivity depend heavily on selecting the correct ligand. Recently a review summarized ligand effects as applied to homogeneous gold catalysis.[28] Several popular ligands are presented in Scheme 2-1, which are also utilized in various reactions throughout this work.

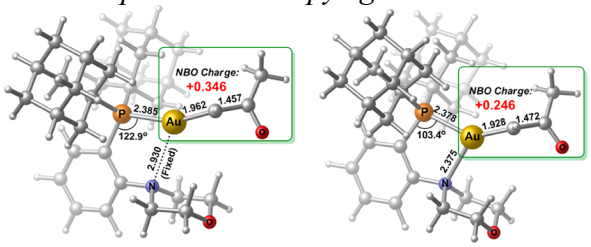
Scheme 2-1: Commonly Used Ligands for Gold(I) Catalysis



2.2 Background of Bidentate Phosphine Ligands

The behavior of the Mor-DalPhos ligand may be used as an example of the function of a *P,N*–bidentate ligand. Originally developed by Stradiotto for Pd catalysis,[29] its potential usefulness for gold chemistry was also demonstrated by the same group.[17] When used to generate a gold carbene, it was found to produce much better results, giving high yields over previous moderate ones.[30] However, the full usefulness is not realized until the catalyst complex is examined. Counter to the typical linear coordination undergone by cationic gold species, the *P,N*-bidentate nature of Mor-DalPhos enables the formation of a tris-coordinated gold carbene. Tris-coordinated gold complexes are well known, although their use in gold catalysis is rare.[31-32] This results in a much less electrophilic species due to addition electron density donation from the nitrogen atom, and should react more selectively. Therefore, the interference of solvents and other weaker nucleophiles are reduced, giving much higher yields. DFT calculations support this argument, as the third coordination causes the gold carbene to be more stable, as seen in Scheme 2-2 in the shorter coordination bonds within the catalyst complex, the lower NBO (non-bonding orbital) charge, and the overall lower energy state granted by the Au-N coordination.

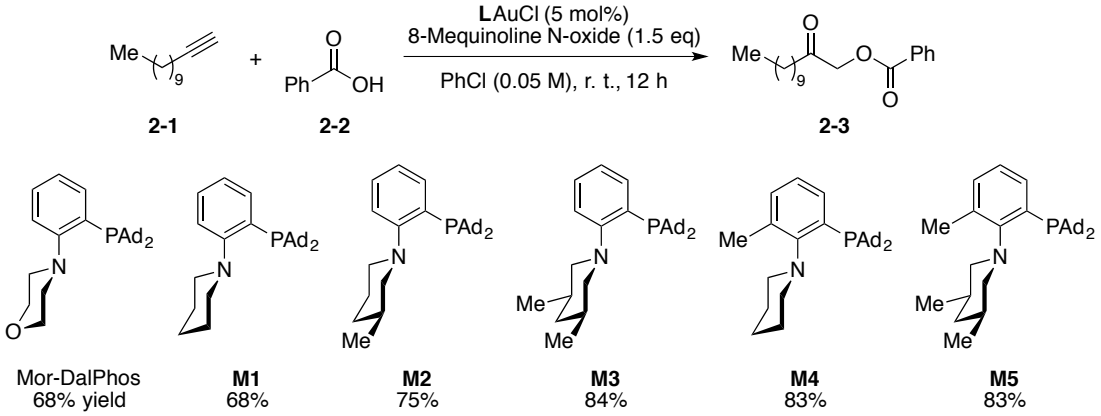
Scheme 2-2: Partially Optimized Structure of Bis-coordinated Gold Carbene
Bis-coordinated gold carbene **L** with fixed Au-N distance of 2.930 Å and the fully optimized tris-coordinated gold carbene **M**. The relative energies are in kcal/mol. Calculated at PBE1PBE/6-311+G** level[30]. *Open Access Copyright ©2014 ACS*[20].



L (0.0 kcal/mol) M(-5.4 kcal/mol)

An example of further modification of MorDal-Phos ligand, seen in Scheme 2-3, was done later by the Zhang group to improve the geometries of the complex.[33] Locking the pendant ring into fixed chair conformation dramatically improved the yield of carboxylic acid trapping of the gold carbene. This shows that the main concerns in designing this type of *P,N*-ligand is the steric shielding of the highly electrophilic gold carbene and maintaining the correct conformer for bis-coordination.

Scheme 2-3: Modification of MorDal-Phos



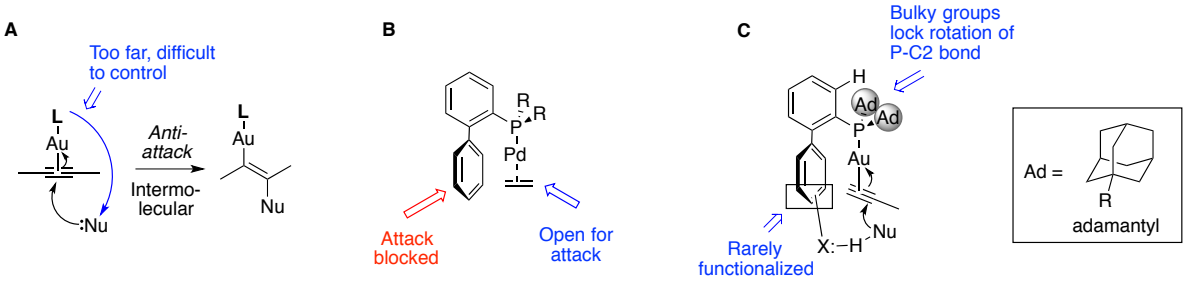
2.3 Background of Biaryl-phosphine Ligands

Bulky and electron-rich biarylphosphines were originally developed by Buchwald,[34-36] and are extremely useful for Pd catalysis,[37, 38] as the ridged backbone creates a steric wall, which blocks all attack from that side, while leaving the reaction center uninhibited. These ligands have been applied in gold catalysis in the past with much success,[39-46] however modification remains relatively unexplored with few examples.[47] In Pd catalysis, substitution of the lower half of the second phenyl ring (outlined in Scheme 2-4) is generally undesired due to the square planar Pd(II) complexes, where higher substitution would

merely crowd the reaction center. The exceptions are SPhos with a C3' sulfonate and XPhos with C4' sulfonate to increase catalyst aqueous solubility.[48] Bis-coordinated gold(I) complexes are linear in structure, rather than square planar, which logically leads to a different ligand design philosophy from that for Pd catalysis.

Scheme 2-4: Ligand Design for Highly Efficient Gold Catalysis.

(A) *Anti*-attack at gold(I)-activated alkyne by nucleophile. (B) The advantage of the (1,1'-biphenyl)-2-ylphosphine framework. (C) The general concept for quasi-intramolecular, ligand-directed nucleophilic attack.



There are several positions on the ligand where changes could be made based on the geometries of the ligand metal center and substrate to each other. Making the P-C2 rotation more rigid and locked by placing bulky substituents on the phosphorus, would force the P-Au-alkyne linear complex to lay parallel across the pendant phenyl ring. This would place the alkyne substrate directly alongside that ring. Should functional groups (FGs) be attached to these distant locations, they would be positioned to interact with the catalyzed reaction of the substrate. If these FGs were to be H-bond acceptors, they could direct neutrally charged nucleophiles, such as MeOH, by H-bonding between the FG and the acidic proton of the nucleophile. This stabilization would give a high preference for a quasi-intramolecular anti-attack on the activated alkyne. The resulting proton would also be stabilized and positioned for the rapid protonation of the gold-carbon bond in the catalyst transition state.

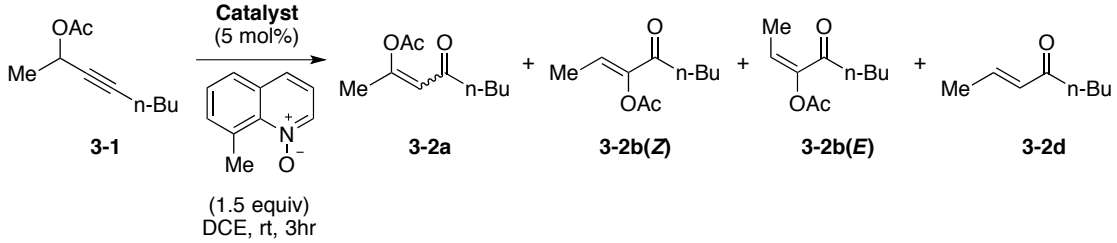
The choice of such a functional group follows the optimization of these two properties: the initial H-bonding to the nucleophile versus the later protonation of the gold-carbon bond. The deciding property would then be the pK_a of the protonated directing group, but only relative to the strength of the gold-carbon bond and the acidic proton of the nucleophile. The pK_a values of various nucleophiles are well known, as are the general pK_a values of possible functional groups. However, the thermo kinetic properties of the gold-carbon bond in such a situation are not so easily predicted. Hence experimental optimization is required to find the best FG. The directing FG should also be capable of handling a broad substrate scope, and the conversion to a quasi-intramolecular attack from an original intermolecular process would accelerate reaction and give higher catalyst TONs, equating to higher catalyst efficiency as a lower catalyst load would be required.

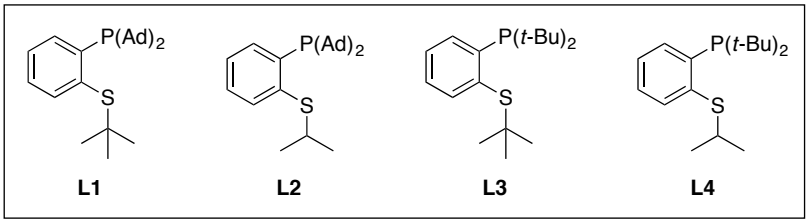
2.4 Bidentate Ligand Research

Research efforts have been focused following the described design logic, which centered foundationally on nitrogen in MorDal-Phos functioning as a Lewis base to the Lewis acid nature of cationic gold. Research was driven forward by theorizing whether other ligands developed with various other Lewis base groups would also function well. Hence, the development of a variety of ligands was pursued laboriously.

The promising ligands developed in the Zhang group were eventually published, however, it does not tell the whole story of the development. The development of the following ligands remained for the most part unpublished due to poor performance results in model reactions, however their study remains foundationally instrumental in the developed understanding used to design later catalysts.

Scheme 2-5: Bidentate Phosphine Ligand Results





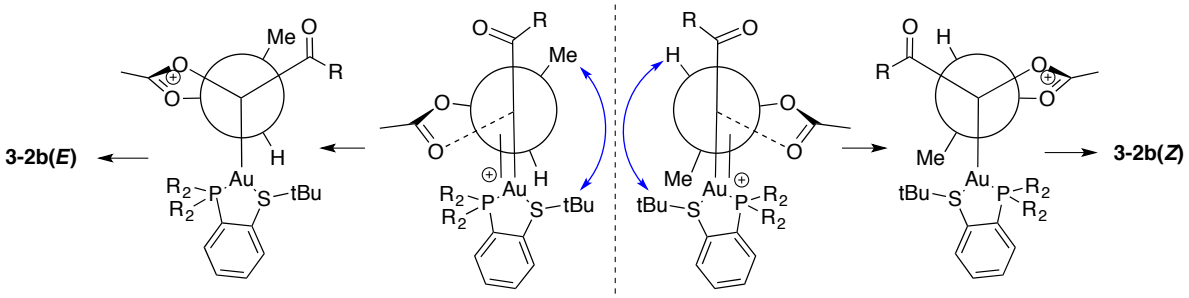
Entry	Catalyst	3-1	3-2b(*Z*)	3-2b(*E*)	3-2a	3-2d
1[1]	**L1**AuNTf$_2$	1.2%	91.5%	7.1%	<0.1%	<0.1%
2[1]	**L1**AuNTf$_2$	7.5%	84.6%	7.1%	0.4%	0.3%
3[1]	**L2**AuCl/AgNTf$_2$	87.7%	10.2%	0.6%	0.4%	1.0%
4[2]	**L2**AuCl/AgNTf$_2$	98.0%	1.7%	<0.1%	NA	<0.2%
5[1]	**L3**AuCl/AgNTf$_2$	<0.1%	91.2%	7.2%	0.3%	1.2%
6[2]	**L3**AuCl/AgNTf$_2$	<0.1%	92.0%	7.1%	<0.1%	0.7%
7[1]	**L4**AuCl/AgNTf$_2$	8.4%	83.1%	6.3%	0.2%	2.0%
8[2]	**L4**AuCl/AgNTf$_2$	50.9%	45.2%	3.4%	NA	0.5%
9[1]	Mor-DalPhosAuCl/AgNTf$_2$	21.3%	60.4%	8.2%	0.4%	9.7%

[1]**L**AuNTf$_2$ generated in situ by the addition of AgNTf$_2$ to **L**Au, prior to adding reactancts.
[2]**L**AuNTf$_2$ prepared in DCM prior to reaction, and resulting AgCl filtered off before concentration, then reactants added.
*Percentage is percent of total 1H NMR integration across these five peaks.

As seen in Scheme 2-5, the best results came from the *t*-butyl sulfane FG, combined with the diadamantyl and di-*t*-butyl phosphine, with the latter performing slightly better in this case. Comparison of the isopropyl functionalization of the sulfane with the *t*-butyl revealed that *t*-butyl shows a much higher selectivity for product ratios (best amount of **3-2b(*Z*)** over others). This shows the steric bulk of the sulfanyl group is key in directing the reaction. The mechanism of this reaction is expanded further in chapter 3, so Scheme 2-6 has a brief outline of the gold-carbene transition stage involved. From this point the reaction

proceeds via 2,3-acetoxyl migration to give the desired product. The isopropyl group would allow more freedom in rotation and orientation for the substrate. It should be noted here that the synthesis of **L3** and **L4** were originally designed by another member of the Zhang lab, Kegong Ji.[30]

Scheme 2-6: Transition State Selection for *Z* over *E*.

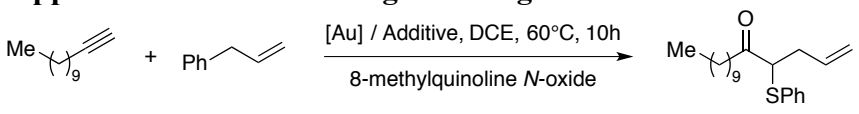


The directing effects of the sterically bulky groups on the phosphine and sulfane can explain the high selection of the *Z* over *E* isomer. If the sterically bulky group is too large, the catalyst is inhibited, however, if the group is too small, the catalyst becomes less selective as the bond geometries are not locked in place. Adamantyl groups are overall larger than the *t*-butyl, but sterically tied back away from the center, thus giving the catalyst center slightly more freedom of motion. The implication for the ligand is such that the adamantyl groups will lock the orientation of the phosphorous aromatic bond causing the Au-P orientation to occur in the same as the aromatic ring. This would put the sulfane in a perfect position to coordinate its lone electrons with the gold to form the bidentate complex, and the geometry gives a high preference to remain as the bis-coordinated complex.

Before the study it was unclear whether allowing the substrate more freedom in orientation would improve the efficiency of the catalyst, as sterically bulky groups tend to

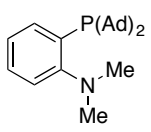
slow down catalysis. However, as seen from the results in Scheme 2-5, the reaction prefers to be in as much of a locked conformation as possible, in order to achieve high product selectivity.

Scheme 2-7: Application of Bidentate Ligand Design

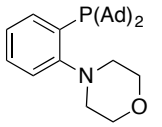


2-4 **2-5** **2-6**

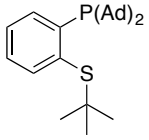
Entry	[Au] (y%)	2a/3 (equiv.)	Additive (1.5 y%)	Yield (conversion)
1	$Ph_3PAuNTf_2$	2.0/1.5	–	5% (70%)
2	$BrettPhosAuNTf_2$	2.0/1.5	–	5% (89%)
3	Me-DalPhosAuCl	2.0/1.5	$NaBAr^F{}_4$	86% (>99%)
4	Mor-DalPhosAuCl	2.0/1.5	$NaBAr^F{}_4$	87% (>99%)
5	**L1**AuCl	2.0/1.5	$NaBAr^F{}_4$	88% (>99%)
6	**L1**AuCl	1.5/1.3	$NaBAr^F{}_4$	83% (>99%)
7	**L1**AuCl, rt	1.5/1.3	$NaBAr^F{}_4$	34% (80%)



Me-DalPhos



Mor-DalPhos



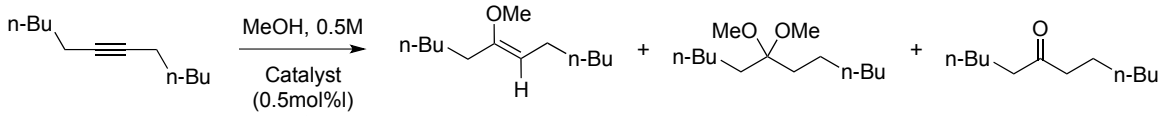
L1

As outlined in Scheme 2-7, the *t*-butyl sulfane ligand **L1** was utilized in the Chemical Communication work "Expanding the horizon of intermolecular trapping of in situ generated a-oxo gold carbenes: efficient oxidative union of allylic sulfides and terminal alkynes via C–C bond formation" by Jiabin Li, et. al.[49] In the reaction of allylic sulfides and terminal alkynes, the developed *t*-butyl sulfane phosphine ligand showed a slightly higher activity than Mor-DalPhos, along with allowing for lower excess loadings of reactants to starting material. This study expanded the scope of external nucleophiles that can be trapped by a α-oxo gold carbene.

2.5 Application of Biaryl Phosphine Ligand Design

In the addition of methanol to an internal alkyne there are three possible products as seen in Scheme 2-8. There is a single addition product **2-8**, which is the first product formed and is more desirable. The second product **2-9**, a methoxy acetal, forms from the addition of the second methoxy group into the first product. The carbonyl product **2-10** forms from the hydrolysis of the acetal product by water.

Scheme 2-8: Biaryl Ligand Model Reaction



2-7
dodec-6-yne

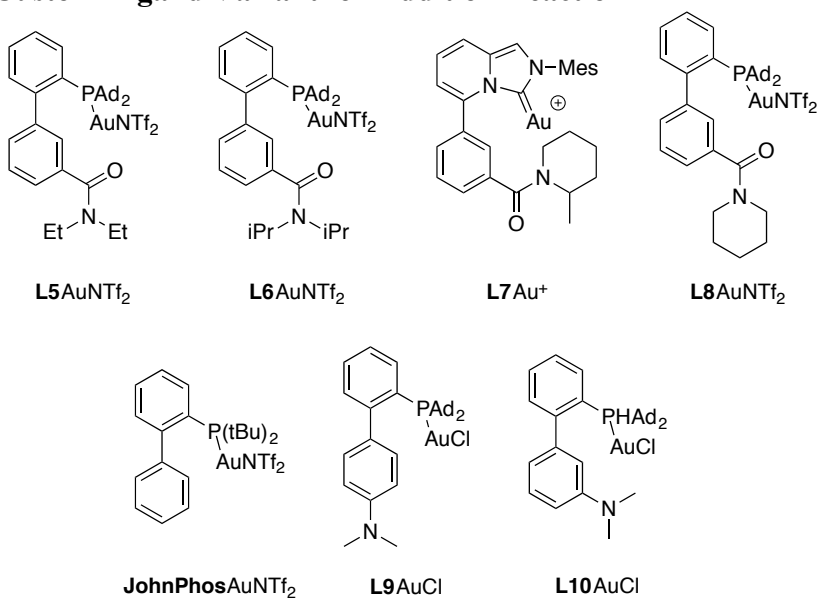
2-8
Methoxy-ene

2-9
Acetal

2-10
Hydration

In the ligand design experiments we were interested to see how such a simple model reaction of nucleophilic addition was affected by ligand structural modifications of the standard biaryl phosphine ligand. As such, the reaction was performed with a variety of ligands while measuring the product ratios by 1H NMR to show the reaction kinetics. The charts of results are placed in the appendix, and discussed here.

Scheme 2-9: Custom Ligand Variant for Addition Reaction



Firstly, ligand **L5** with a diethyl amide on the secondary ring, showed a mild reactivity with a high preference for the single addition methoxy-ene **2-8** (75% peak yield at 25hrs), and was slow to produce the acetal and hydration products. Ligand **L6**, very similar to the first but with a di-isopropyl amide, performed very similarly but on a longer reaction time (peak yield of **2-8**, 70%, at 49hrs). It logically follows that the additional steric bulk of the isopropyl groups slightly inhibited the rate of the catalytic process. Ligand **L7** produced no reaction, but the purpose of this ligand was to show that the phosphine structure was important to the high yield and fast reaction time.

Ligand **L8**, similar to **L5** and **L6** with a piperidin-amide substituent, showed a much higher reaction speed to both **L5** and **L6** (6 hr peak amount of **2-8**, 65%, versus 30 hrs and 45 hrs respectively). This can be attributed to the six-membered piperidine ring representing sterically a more tied-back and compacted version of the diethyl amide of **2-8**, with less freedom of motion. However, this faster reaction time also seemed to greatly increase the

amount of acetal **2-9** generated, giving lower selectivity for **2-8**. JohnPhos, a basic biaryl ligand developed by Buchwald, was used as a control as it has no substituents on the secondary ring. It showed a preference for product **2-8**, but at the peak yield (62%) it had also generated a considerate amount of acetal (28%) and hydrolysis (10%) products.

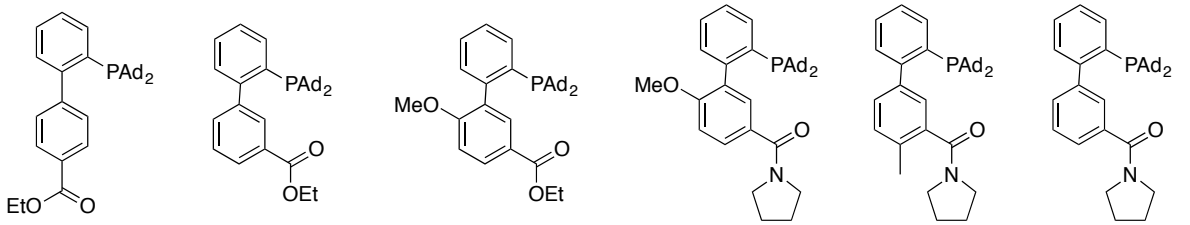
Ligand **L9**, with a para-dimethylamine substituent on the secondary ring, showed a unique activity by being highly selective to the acetal over the single addition product **2-8**. This result is interesting mainly in contrast to ligand **L10**, where the dimethylamine is moved to the meta position, which showed a higher preference for **2-8** initially, with the acetal yield increasing over time. All of these results are included as Figure 6-1 to Figure 6-6 in the experimental section.

These results showed substituents at the *meta*-position of the secondary ring are positioned to better promote the production of single addition products over the acetal and hydration products with higher selectivity than ligands without a substituent group. Further research was based on this realization, and developing the model that such a substituent would actually direct the nucleophile towards bonding.

2.6 Biaryl Phosphine Ligand Modification and Variants

In the course of furthering research for the lab as a whole, I produced several variations of the nucleophile directing group ligands. Variations **L11** and **L12** replaced the amide group of **L5** with a ethyl ester, to show whether or not it was a conjugated carbonyl that was key, or the amide specifically, and how important the amide was to the selectivity.

Scheme 2-10: Biaryl Phosphine Ligand Variants.



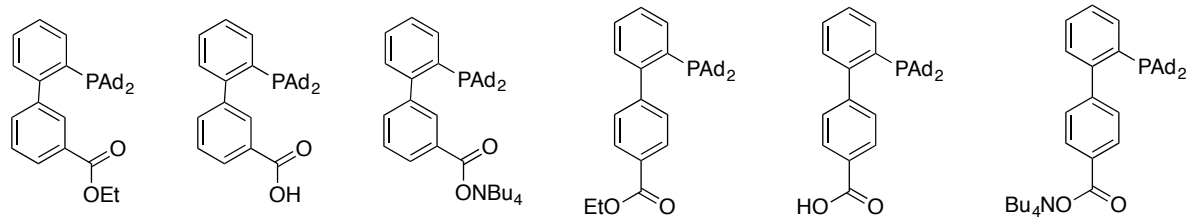
The ester carbonyl would form a weaker H-bond with incoming nucleophiles, which would cause them to be slower to react. However, the protonation of the gold-carbon bond would proceed much faster, due to the lower pK_a of the resulting acid.

In **L13**, a methoxy group was added *para* to the substituent, which would donate electron density into the carbonyl via conjugation, thereby increasing the Lewis basicity of the carbonyl, causing it to have a stronger directing effect. Variant **L14** followed the same logic, but for the amide. Variant **L15** added a methyl group *ortho* to the amide susbstituent, with the hypothesis of using sterics between the pyrrolidine ring and the methyl group to restrict the freedom of rotation around the aryl-carbonyl bond, and hopefully lock the amide in the correct position to interact with the incoming nucleophile. The study and use of these variants and many others were taken up by other researchers in the group, and this field of research eventually led to the 2014 publication in Nature Communication by Yanzhao Wang, et. al.[50]

A final variant of the biaryl nucleophile-directing phosphine ligands was produced, with a much more basic directing group, in the form of an anionic free carboxylate. Such a ligand would, in theory, produce a much stronger hydrogen bonding to any incoming nucleophile, as it is much more basic than an amide, and as the resulting acid is a carboxylic acid, it

should be adequate to protonate the gold-carbon bond, especially due to its close proximity. The synthesis of such a ligand was not without its difficulties, and did spawn two other variations, the unadorned ethyl ester, and the carboxylic acid, which were also tested by other members of the group in their research. The ligand was produced in both the *meta*- and *para*-substituted variants, for completeness of variation.

Scheme 2-11: Carboxylate Phosphine Ligands



L11 **L17** **L18** **L12** **L19** **L20**

The difficulty with synthesizing **L18** and **L20** came from the inherent scenario of adding an anion carboxylate to a cationic gold ligand and maintaining stability of the complex. How would one go about it? Here, the free benzoic acid was subjected to tetrabutylammonium hydroxide in MeOH and DCM, and the change in structure verified. It was then complexed with cationic gold(I) chloride dimethylsulfide in a mixture of solvents (1:1:1 DCM:MeCN:MeOH), and the complex verified by ^{31}P NMR and MS. At this point, the gold cation was stabilized by the chloride, which is known to prevent the catalyst from reacting. Upon removal of the chloride in a solution of $AgNTf_2$ in the same solvent mixture, the resulting compound did not behave as expected, as it did not produce any reaction when subjected to the model reaction.

The TOF-ESI mass of **L18**AuCl showed a secondary peak with double the mass (ES-$((Au\text{-}L)_2+H^+)$: 1461) without the tetrabutylammonium counterion, which would suggest

once the stabilizing ions are removed, the catalyst will form a dimer. The ^{31}P NMR of **L18**$AuNTf_2$ immediately after isolation showed a minor doublet peak downfield of the major peak, still within the range for gold-phosphine complex. This could mean the phosphorous atom was conjugating with another NMR active atom, such as if another NMR active atom had bonded with the gold.

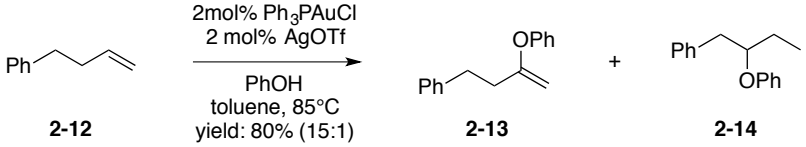
The catalyst is proposed to have formed a dimer complex upon removal of the protecting chloride. This conclusion is also supported by the in situ removal of the chloride by $AgNTf_2$ producing some initial reaction activity, albeit with very low yield, before stopping. This ligand was tested by other members in further experiments and gave overall underwhelming results, most probably due to the bis-complexing tendency giving a low catalyst turn over number. However, there was no further investigation into this phenomenon, therefore whether a dimer is formed cannot be known for certain.

2.7 Nucleophile Addition to Alkenes

The attraction of a gold catalyzed nucleophilic addition to an alkene was primarily that it had not been very explored in literature. Gold coordinates to alkenes, just as readily as to alkynes. What matters or differs is what happens next, if gold is able to activate it for electrophilic addition.

There is evidence that alkenes are activated by Au(I),[51] hence there was interest in investigating whether this activation was enough for a nucleophile addition. Initially, it was not known if alkenes reacted with gold catalysts with an alkyne present. It was later shown that at high enough temperatures the intermolecular addition of weak nucleophiles like phenols and carboxylates to unactivated alkenes proceeded.[52]

Scheme 2-12: Insertion of Phenol to Terminal Alkene

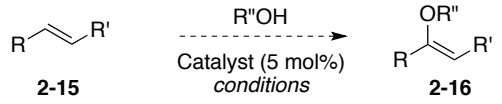


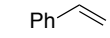
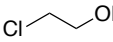
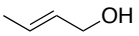
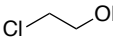
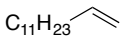
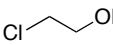
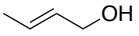
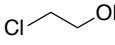
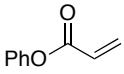
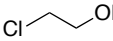
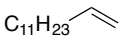
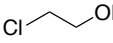
2-12 **2-13** **2-14**

It was of interest whether the recently developed ligands were capable of performing addition under milder conditions. A model reaction was chosen, in which an alkene was reacted with a primary alcohol in the presence of a catalyst. Several starting alkenes with differing structures were selected, to hopefully collect the results simultaneously.

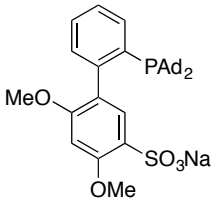
The alkenes selected were styrene, a terminal conjugated alkene **2-15a**, the polarized internal alkene **2-15b**, and the terminal alkene **2-15c**. Phenyl acrylate, structure **2-15d**, was later used to represent a conjugated system. The dnucleophiles chosen were methanol as solvent, and 2-chloroethanol in DCE, as 2-chloroethanol was expected to perform better as a nucleophile, based on the lower pK_a value.[53] The catalyst chosen first was silver(I) complexed to the designed phosphine ligands, then later cationic gold-phosphine catalysts. As the silver was expected to be less reactive, the reactions were heated to 60°C. However, despite all variations, no reaction was ever observed.

Scheme 2-13: Results of Addition to Alkene

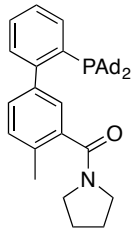


Entry	Starting Alkene	Alcohol	Catalyst	Conditions	Result
1		 0.2M	**L21**$AgNTf_2$	60°C, DCE	*NR observed*
2	**2-15a**	MeOH 0.1M	**L15**$AgNTf_2$	60°C	*NR observed*
3		 0.2M	**L21**$AgNTf_2$	60°C, DCE	*NR observed*
4	**2-15b**	MeOH 0.1M	**L15**$AgNTf_2$	60°C	*NR observed*
5		 0.2M	**L21**$AgNTf_2$	60°C, DCE	*NR observed*
6	**2-15c**	MeOH 0.1M	**L15**$AgNTf_2$	60°C	*NR observed*
7		MeOH, rt	**L9**AuCl, $AgNTf_2$	rt	*NR observed*
8		MeOH, rt	**L16**AuCl, $AgNTf_2$	rt	*NR observed*
9	**2-15b**	 0.2M	**L16**AuCl, $AgNTf_2$	rt, DCE	*NR observed*
10		MeOH, rt	**L9**AuCl, $AgNTf_2$	rt	*NR observed*
11		MeOH, rt	**L16**AuCl, $AgNTf_2$	rt	*NR observed*
12	**2-15d**	 0.2M	**L16**AuCl, $AgNTf_2$	rt, DCE	*NR observed*
13		MeOH, rt	**L9**AuCl, $AgNTf_2$	rt	*NR observed*
14		MeOH, rt	**L16**AuCl, $AgNTf_2$	rt	*NR observed*
15	**2-15c**	 0.2M	**L16**AuCl, $AgNTf_2$	rt, DCE	*NR observed*

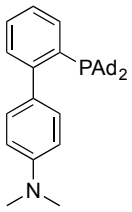
Ligands:



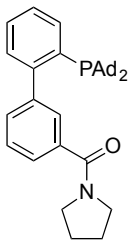
L21



L15



L9



L16

In retrospect, avenues are evident where this study could have been expanded to be made more thorough, but at the time the lack of any positive results caused the project to be put on hold. If this project were to be continued, a rigorous investigation of higher temperatures

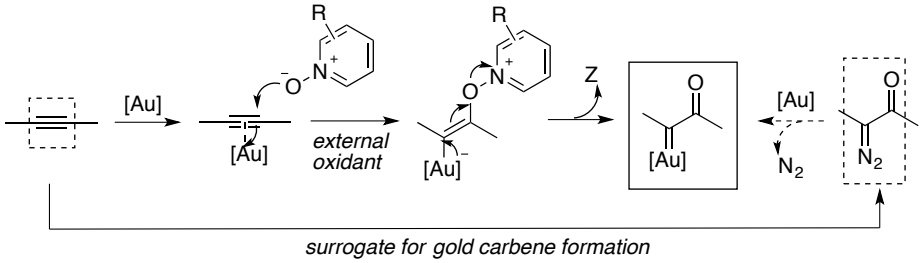
would be recommended, although too high of temperatures would destabilize the phosphine catalysts. A broader scope of catalysts, not merely focusing on the nucleophile directing aspect, should also be tested, such as ones that give a more electron rich or electron poor metal center. In summary, the collected results in no way represent anything beyond an initial investigation into mild conditions for the addition of nucleophiles to alkenes, and are presented to aid in further studies.

3. Regioselective Oxidation of Propargylic Carboxylates

3.1 Background

In 2010,[54] Zhang group reported the generation of α-oxo gold carbenes from intermediates of gold-catalyzed intermolecular oxidation of alkynes. Mild pyridine *N*-oxides and 8-substituted quinoline *N*-oxides were used as external oxidants, for a safer alternative strategy to dediazotization (Scheme 3-1).

Scheme 3-1: Alkyne as a Surrogate to Diazo Compounds via Oxidation

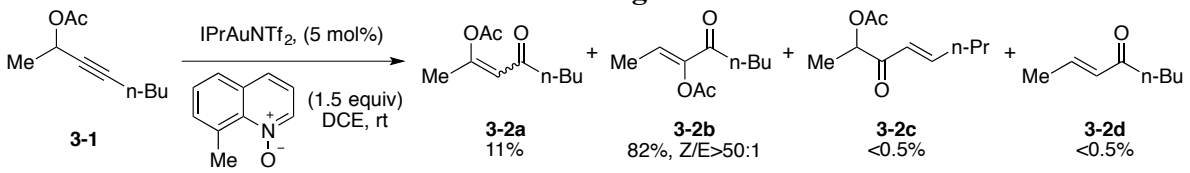


Internal alkynes present an additional challenge compared to terminal alkynes; that of control of the regioselectivity of the oxidation. Synthetically useful regioselectivity has been shown to be gained if the two sides of the C–C triple bond are biased by steric bulk and/or conjugation. However, this has limited use, as the structure of the desired synthetic product limits this steric bias. In the interests of improving the regioselective of this oxidation with different alkynes, propargylic carboxylates were explored, as they provided an induced electronic bias, and a reliable synthesis of α-carboxy α,β-unsaturated ketones and aldehydes was developed.

3.2 Initial Investigation

The initial development by Kegong Ji, a member of Zhang group, subjected propargylic acetate **3-1** to previously developed conditions: $IPrAuNTf_2$ (5 mol %), and 8-methyl quinoline *N*-oxide (1.5 equiv) in 1,2-dichloroethane at ambient temperatures. The reaction yielded the α-acetoxyenone **3-2b** (Z/E >50:1) and the isomeric **3-2a** in a combined yield of 92% along with <0.5% of the enone **3-2d**. **3-2b** was favored over **3-2a** by a factor of ~7:1. The isomer **3-2c** was only detected in trace amounts, showing an exceptional level of regioselectivity in the oxidation of this type of internal alkyne.

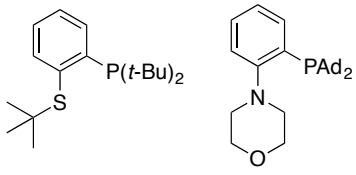
Scheme 3-2: Model Reaction for Initial Investigation

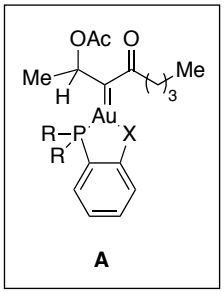


3.3 Study, Results and Discussion

To improve the low product selectivity of the reactions, as initial results of $IPrAuNTf_2$ gave ~7:1 product ratio, several bidentate ligands were screened, the results of which were presented in Scheme 2-6. The previously presented bulky *P,S*-bidentate ligand **L3** was found to reach a product ratio of **3-2b** to **3-2a** >200:1. The *P,N*-bidentate ligand MorDalPhos gave a similarly high selectivity, but a lower Z/E ratio. The higher attenuation of the electrophilicity of the gold carbene by the tris-coordinated gold complex **A** in Scheme 3-3 is credited for the increase in product selectivity.

Scheme 3-3: Summary of Ligand Results



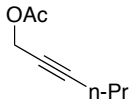
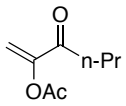
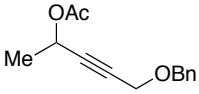
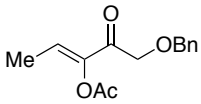
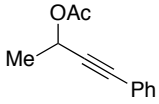
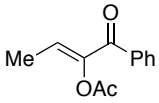
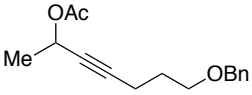
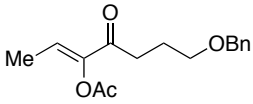


	L3	Mor-DalPhos
3-2b (Z/E)	97% (13:1)	93% (~7:1)
3-2a	<0.5%	<0.5

A

From the initial model reaction, the new catalyst system was applied to several substrates that reacted with poor selectivity under the $IPrAuNTf_2$ system, according to the prior substrate screening performed by Kegong Ji. As seen in Scheme 3-4, the product ratios were greatly improved, however the Z/E ratio never exceeded far above 10. Entry 1 was not expected to see much improvement in product ratios, due to the simplicity of the structure not being as affected by the steric directing groups. The return of the propargylic methyl group (Entry 2-4) allowed the effect of the steric directing groups again, as it locked the rotation of the C-C bond adjacent to gold carbene in the orientation required for the 2,3-acetoxy migration. This kinetic direction gave the high yield of the migration product, but the results show it also inhibited rotation to the thermodynamically preferred Z conformer.

Scheme 3-4: Results of *P,S*-Bidentate Catalyst System L3AuNTf$_2$

Entry	Starting Carboxylate	Major Product	% yield (major) Ratio (major/minor) Z/E ratio (major)
1	 **3-3**	 **3-4**	70% >16/1
2	 **3-5**	 **3-6**	60% 250/1 Z/E=13
3	 **3-7**	 **3-8**	75% 40/1 Z/E=3.9
4	 **3-9**	 **3-10**	75% >300/1 Z/E=10

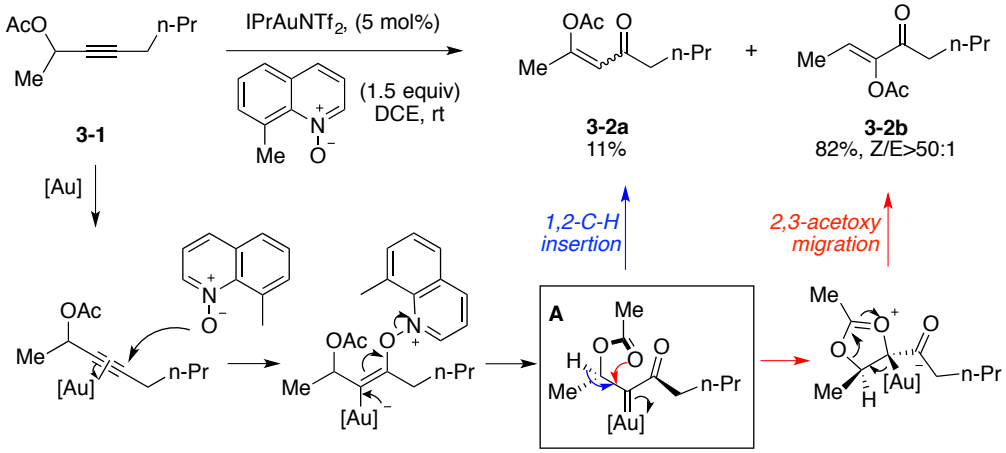
When published in Beilstein Journal of Organic Chemistry,[55] these results were presented along with the IPr-gold catalyst results. The conclusion was that it was not one catalyst system that was the best overall, but together the two made a robust means to perform this transformation.

3.4 Mechanism

In order to understand the transition from this brief investigation to later research, a understanding of the mechanism steps involved was required. The mechanism proposed in the article for the formation of **3-2b** and **3-2a** followed divergent pathways from the α-oxo gold carbene **A**. **3-2b** resulted from a two-step 2,3-acetoxy migration,[56-57] and **3-2a** was likely the product of a concerted 1,2-C-H insertion to the carbene.[58] The selection of the *Z* isomer of **3-2b** as preferred followed from the carbene conformation **A**, seen in Scheme 2-5, which minimized the steric interaction between Me, the acetate group, and the sterically

bulky *tert*-butyl groups of the ligand. The intramolecular version of this reaction has already been reported.[59]

Scheme 3-5: Proposed Mechanism of 2,3-Acetoxy Migration



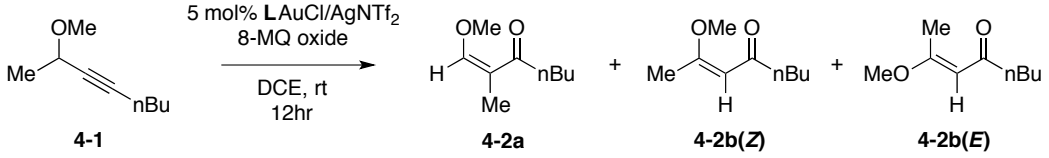
These conclusions eventually led to the proposition that if these types of α-oxo gold carbenes will undergo a 1,2-hydride shift, it might be possible to selectively undergo a 1,2-alkyl shift instead. This would lead to *α,β*-unsaturated carbonyl products with potentially complex substituted at both the α and β positions. Having one-step access to such a complex and synthetically useful product from the simple alkyne would be great benefit to the library of chemistry knowledge, and would be useful synthetically.

4. Regioselectivity as Enabled by α-Oxo Gold-Carbene Electrophilicity

4.1 Investigation of 1,2-Alkyl Shift

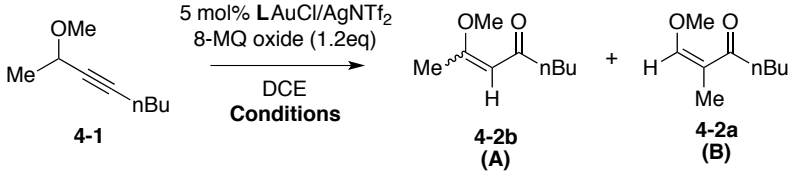
Following the mechanism of the previous project, the hydride shift was an expected side reaction. However, with the carboxylate replaced with a methoxy to prevent the acetoxy migration, it would also be possible for the methyl group to undergo a 1,2 shift. The methoxy is required to give electronic preference for directing the oxidation.

Scheme 4-1: Model Reaction for 1,2-Methyl Shift

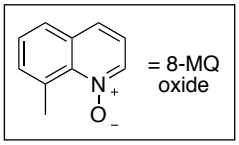


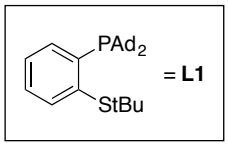
The investigation was separated into two different routes. The investigation of optimizing the 1,2-hydride shift was pursued later by myself and Kegong Ji, following my initial results while working on the alkyl shift. We eventually published the hydride shift work in Journal of Organometallic Chemistry in 2014,[60] and while the alkyl shift work was initially promising, it produced mainly lack-luster results. The reasoning for the catalyst choice seen in Scheme 4-2 followed that as an electron rich metal center produced a high preference for the hydride shift, perhaps an electron poor metal center would produce a preference for the alkyl shift. This was indeed found to be the case.

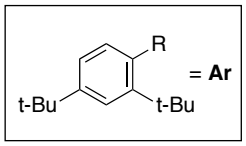
Scheme 4-2: Initial Screening Results of 1,2-Methyl Shift



Catalyst	Conditions	NMR Ratio (A:B)
L1-AuCl	rt	43.7:1, 25:1 E/Z for **A**
$(C_6F_5)_3PAuCl$	rt, 2hr	1:3.3
	60C, 30min	1:1.54
	-20°C 12hr	1:2
	rt, THF solvent	1:1.04
	-20°C, THF	1:1.28
$(\mathbf{Ar}O)_3PAuNTf_2$	rt, 2h	1:3.3
	-20°C, 12h	1:2.4
IPrAuCl	rt, 3h	1.95:1
JackiePhosAuNTf$_2$	rt	1.85:1

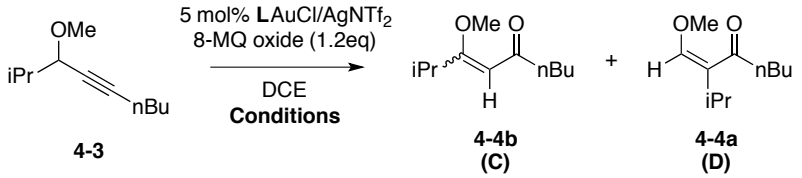






Upon testing various catalysts in the above model reaction, there was a direct correlation found with the electron density of the metal center versus the product ratio. The more electron rich the gold center, as seen in the PS-bidentate ligand, the more the ratio favored the hydride shift, up to 40:1. The more electron poor the gold center, with electron drawing groups attached to the phosphine, such as with the $(ArO)_3P$ phosphite ligand, the more the methyl shift was favored, up to 3:1. Exchanging the propargylic methyl group with an isopropyl gave an expected lower preference for the alkyl shift, given the increased steric congestion around the metal center.

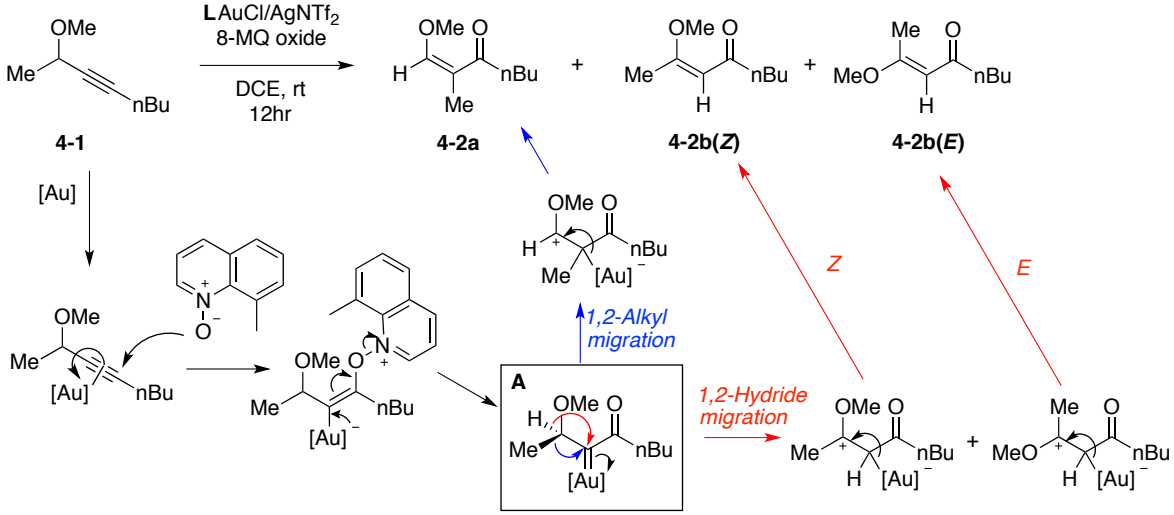
Scheme 4-3: Screening for 1,2-Isopropyl Shift



Catalyst	Conditions	NMR Ratio (C:D)
L1-AuCl	rt, 5hr	77:1, 6:1 E/Z for **C**
$(C_6F_5)_3PAuCl$	rt, 3hr	1:1.25
$(\mathbf{Ar}O)_3PAuNTf_2$	rt, 3h	1:1.77
IPrAuCl	rt, 3h	2.4:1
JackiePhosAuNTf$_2$	rt	1:1.4

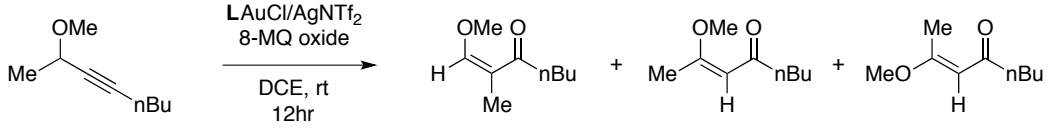
The proposed mechanism for the transformation is shown in Scheme 4-4. Upon activation by the gold catalyst, and subsequent oxidation, the gold carbene species **A** in Scheme 4-4 is generated. From here, there are two possible routes. 1,2-alkyl migration of the methyl group into the gold carbene produces the alkyl shift product. A 1,2-hydride migration, followed by elimination gives either the E-hydride shift product **4-2b(*E*)**, or the Z-hydride shift product **4-2b(*Z*)**.

Scheme 4-4: Mechanism for 1,2-Alkyl Shift



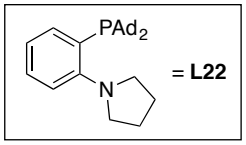
Interestingly enough, screening with various catalysts gave a variable product ratio, depending on the ligand used. Election-deficient ligands, such as the first three entries in Scheme 4-5, saw a increase in selection for the alkyl shift, while electron donating ligands, such as PN and PS bidentate type, saw an increase in selection for the **4-2b(*Z*)** product. Ligands not characterized as electron rich or poor, and instead direct more via sterics, such as triphenylphosphine or IPr, produced more of a mixture of products.

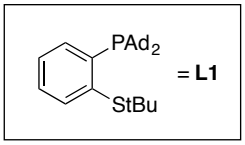
Scheme 4-5: Spectrum of Reactivity for Gold Catalysts

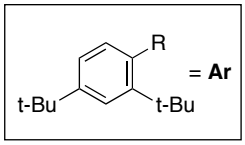


4-1 **4-2a** **4-2b(*Z*)** **4-2b(*E*)**

Catalyst	4-2a	4-2b(*Z*)	4-2b(*E*)
$(C_6F_5)_3PAuCl$	44%	26%	2%
(**Ar**O)$_3$PAuNTf$_2$	62%	trace	11%
PPh_3AuCl	53%	18%	7%
$Me_4{}^tBuXPhosAuCl$	11%	64%	trace
$JackiePhosAuNTf_2$	31%	2%	35%
$MorDalPhosAuNTf_2$	3%	49%	28%
L1-AuCl	3%	76%	1%
L22-AuCl	2%	78%	2%
IPrAuCl	28%	56%	2%







All NMR yields based on terminal Me group
Reactions proceed until sm consumed, or 12hr

Anhydrous conditions (dry, $NaBArF_4$ instead of $AgNTF_2$) yielded poorer results, supporting the conclusion that gold catalysis often requires catalytic water to aid in reaction. Testing of other oxidants, besides 8-methyl quinoline oxide, also gave poorer results, with increased side reactions, slower reaction times, or lower product yields.

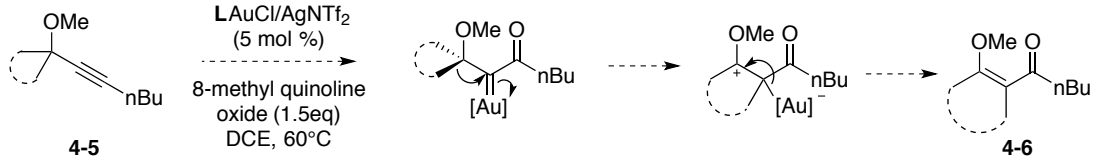
These results while initially promising, presented an unavoidable obstacle in the form of attempting to create a more electron poor ligand. A 3:1 product ratio was a promising initial result, however it would not yet synthetically useful. Attaching more electron withdrawing groups to phosphine, would eventually produce a ligand that did not have enough electron density to coordinate to cationic gold. There is no clear literature evidence of successfully creating a more electron withdrawing ligand for gold catalysis, especially one strong enough to bring the alkyl shift product ratio much above 10:1, without which the reaction remains synthetically inefficient. Overall, this was determined to be a dead end as far as producing a synthetically useful reaction.

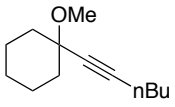
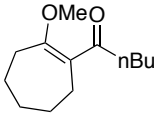
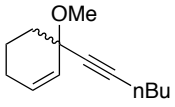
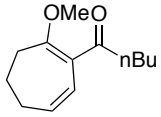
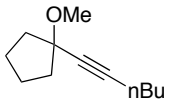
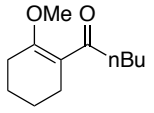
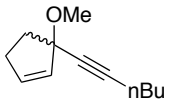
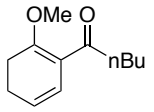
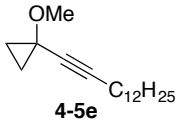
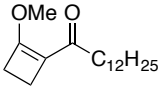
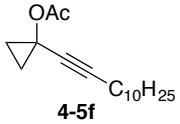
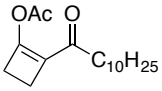
4.2 Application for Ring Expansion

Attention was turned to ring expansion. If the catalysts were not strong enough to produce a good result with a methyl shift, perhaps the removal the H-substituent to migrating from a tertiary center would serve as a sufficient driving force. Compounds **4-5a** through **4-5d** were made to test this hypothesis, and were subjected to a number of different catalyst and oxidant conditions. It was concluded that there was a misjudgment in starting hypothesis made in the selection of these compounds, as at no point was the desired product **4-6** generated.

Thermodynamically a ring expansion from 5-membered such as **4-5c** and **4-5d** to 6-membered rings would be favorable, as 6-membered rings have lower ring strain energy. However, kinetically the driving force of reacting with the gold-carbene was found to be inadequate to overcome the energy barrier. Cyclohexane **4-5a** and cyclohexene **4-5b** in Scheme 4-6 performed similarly. Another explanation would be poor orbital overlap of the tertiary center with the gold-carbene due to sterics of bond rotation.

Scheme 4-6: Ring Expansion Application



Entry	Starting Material	Desired Product	Catalyst
1	 4-5a	 4-6a	IPrAuCl/AgNTf$_2$ **L1**AuCl/AgNTf$_2$ PPh$_3$AuCl/AgNTf$_2$ BrettPhosAuCl/AgNTf$_2$ (C$_6$F$_5$)$_2$PAuCl/AgNTf$_2$
2	 4-5b	 4-6b	IPrAuCl/AgNTf$_2$ **L1**AuCl/AgNTf$_2$ IPrAuCl/NaBArF$_4$ **L1**AuCl/NaBArF$_4$
3	 4-5c	 4-6c	IPrAuCl/AgNTf$_2$ **L1**AuCl/AgNTf$_2$ IPrAuCl/NaBArF$_4$ **L1**AuCl/NaBArF$_4$ PPh$_3$AuCl/AgNTf$_2$ BrettPhosAuCl/AgNTf$_2$ (C$_6$F$_5$)$_2$PAuCl/AgNTf$_2$
4	 4-5d	 4-6d	IPrAuCl/AgNTf$_2$ **L1**AuCl/AgNTf$_2$ IPrAuCl/NaBArF$_4$ **L1**AuCl/NaBArF$_4$
5	 4-5e	 4-6e	IPrAuCl/AgNTf$_2$ PPh$_3$AuCl/AgNTf$_2$ BrettPhosAuCl/AgNTf$_2$
6	 4-5f	 4-6f	(**Ar**O)$_3$PAuNTf$_2$ Et$_3$PAuNTf$_2$ MorDalPhosAuNTf$_2$

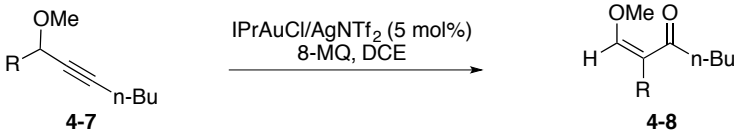
The last two substrates, cyclopropyl structures **4-5e** and **4-5f** in Scheme 4-6, were thought to most certainly undergo a ring expansion, as similar reactions have been documented as catalyzed by cationic gold,[61] albeit without the tertiary acetate substitution. The methoxy group was replaced with the stronger electron withdrawing acetate

group, to facilitate the desired reaction through electronics. However, the only product formed was an unsubstituted enone product, still bearing the cyclopropyl ring, which was hypothesized to be the oxidation product on the electronically disfavored side. With no generation of the cyclobutene product, it may be that the tertiary acetate caused too much steric crowding near the alkyne, and prevented the desired reaction from occurring. For the same reasons as stated in the following section, this research remains incomplete.

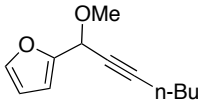
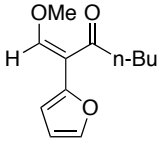
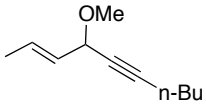
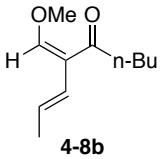
4.3 Selection of the sp^2 1,2-Alkenyl Shift

The final stage in this project followed the idea that while a sp^3 1,2-alkyl shift may not be favorable, perhaps a sp^2 1,2-alkenyl shift would be. Two substrates were chosen, one with a furan-substituent and another with a simple unconjugated alkene, and bother were screened under a variety of catalysts. Reaction under the described conditions led to an initial result of a 90% NMR yield for the furan, and a 50% NMR yield for the propargylic alkene group. Reproduction of these results proved difficult, however, giving a 50-70% yield for the furan and 20-40% yield for the alkenyl shift in later trials. These roadblocks contributed to the project being shelved and as this was at the end of my time in the Zhang lab and at UCSB, completion was not reached.

Scheme 4-7: sp^2 1,2-Shift Results



4-7 4-8

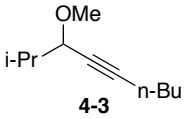
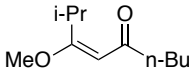
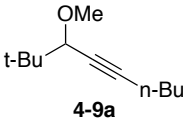
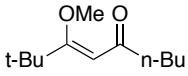
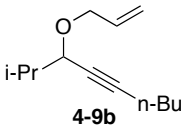
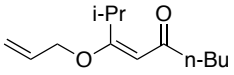
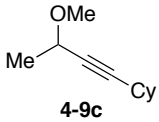
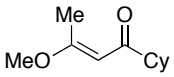
Entry	1	2	Temp	Initial NMR yield
1	 4-7a	 4-8a	rt	>90%
2	 4-7b	 4-8b	60°C	50%

This methodology should be investigated further, as it would allow for rapid access to α-alkenyl-β-alkoxy-α,β-unsaturated ketones from the aldehyde in two steps. These types of substrates would prove very useful synthetically, as it would allow for easy generation of highly substituted α,β-unsaturated carbonyls.

4.4 Eventual Publication of 1,2-Hydride Shift

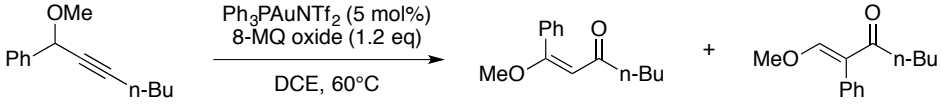
With the ongoing lack of publishable results for the alkyl migrations, attention was turned towards the hydride shift. The reaction scope of the hydride migration was examined in Scheme 4-8, using the sulfane-containing **L1**AuCl catalyst. The catalyst system performed well with sterically more demanding alkyl groups (entry 1-2 and 4), and did react with an allyl ether (entry 3). The products were generated as a mixture of double bond geometries, the ratio of which appears to be directed by sterics and dipole-dipole repulsion.

Scheme 4-8: Hydride shift by PS-Ligand

Entry	1	2	Yield (isolated)	*E/Z* (by ^{1}H NMR)
1	 **4-3**	 **4-4**	63%	10:1
2	 **4-9a**	 **4-10a**	67%	1:3.6
3	 **4-9b**	 **4-10b**	78%	3.6:1
4	 **4-9c**	 **4-10c**	73%	6:1

This work, as with the previous two sections, was performed at the end of my time at UCSB, and did not reach full completion. Later, Kegong Ji completed the investigation of the 1,2-hydride shift, and showed an 89% isolated yield for the 1,2-shift of a propargylic phenyl group under similar conditions to the reactions I had performed.

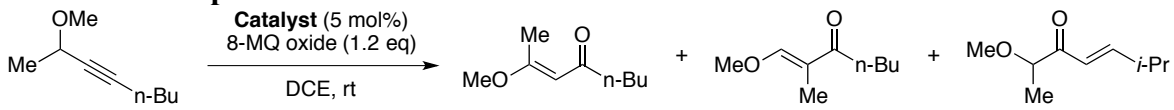
Scheme 4-9: Published 1,2-Phenyl Shift



Kegong utilized the previous study I had made of the spectrum of reactivities, in Scheme 4-5, and used the initial discovery to optimize for the hydride shift (Scheme 4-10) using the

pyrrolidine-containing **L22**$AuNTf_2$ catalyst. He applied it to several substrate examples, selecting for the hydride shift over the alkyl. These examples are presented in our publication.

Scheme 4-10: Optimization of Conditions for Publication



4-1

	4-2b	**4-2a**	**4-2c**
$Ph_3PAuNTf_2$	30%	50%	<3%
(^{t}BuXPhos)$AuNTf_2$	53%	29%	4%
(Mor-DalPhos)$AuNTf_2$	71%	2%	<2%
L22-$AuNTf_2$	82%	2%	<3%

5. Conclusions

A novel ligand design has been realized of the *P,S*-bidentate type. It enables the generation of tri-coordinated and less electrophilic gold carbene species, and provides greater selectivity and yields for reactions involving α-oxo gold carbene intermediates. Application in 1,2-acyloxy migrations and the addition of external nucleophiles has produced highly efficient and selective results under mild conditions.

A study of the nucleophilic addition of methanol to a gold-activated alkyne with a variety of biarylphosphine catalysts demonstrates the impact of substituents on the secondary ring. Substituents at the *meta*-position react faster and with better selectivity than unsubstituted or *para*-substituted ligands.

Several new biarylphophine catalysts variants were synthesized for the purpose of examining the impact of structure modifications on ligand performance.

A novel carboxylate substituted phosphine ligand was synthesized, however it was found to have low performance.

An initial investigation was performed into applying the developed catalysts to the gold-activated addition of a nucleophile to an alkene. A variety of substrates were tested, however, no reaction was ever observed.

A gold-catalyzed, highly regioselective oxidation of carboxylates of primary and secondary propargylic alcohols has been realized for compounds with electron-withdrawing carboxy moiety to induce polarization of the C–C triple bond. The α-oxo gold carbene intermediates generated selectively underwent 1,2-acyloxy migrations over 1,2-C–H migration, and the selectivity was greatly enhanced by using the *P,S*-bidentate ligand, with

ratios ranging from 16 to over 300. α-Acyloxy-α,β-unsaturated ketones/aldehydes can be obtained with fair to excellent yields.

A study of the effects of α-oxo gold-carbene electrophilicity on product selectivity has been performed. Under mild conditions propargylic ethers can undergo selective 1,2-migration of either the propargylic alkyl group, by utilizing an electron-withdrawing ligand to form a highly electrophilic gold carbene species, or the propargylic hydrogen, by utilizing an electron-donating ligand to form a less electrophilic gold carbene species.

The application of the 1,2-alkyl migration to ring expansion was examined, and it was found that propargylic tertiary centers do not undergo an alkyl migration, possibly due to steric crowding of the reaction center and poor orbital overlap for migration.

The application of the 1,2-alkyl shift to the migration of a propargylic sp^2 substituent was examined, and was found in good yields. This methodology would allow for rapid access to α-alkenyl-β-alkoxy-α,β-unsaturated ketones from the aldehyde in two steps.

Excellent regioselectivities were obtained for the gold catalyzed oxidation propargylic ethers. The regioselectivity is driven by polarization of the C–C triple bond by α-alkoxy groups, with ratios typically ranging from 10 to >50. The developed *P,S*-bidentate ligand enables the minimization of competing alkyl group migration to the gold carbene center over the desired hydride migration.

To conclude, the mild condition, good efficiency, and broad reaction scope, with general tolerance of functional groups, of oxidative gold catalysis to rapidly access α,β-unsaturated ketones from readily accessible propargyl ethers without the use of hazardous diazo compounds provides a valuable retrosynthetic tool for synthetic design, especially considering the synthetic versatility of this enone moiety.

6. Experimental

6.1 General Information and Disclaimer

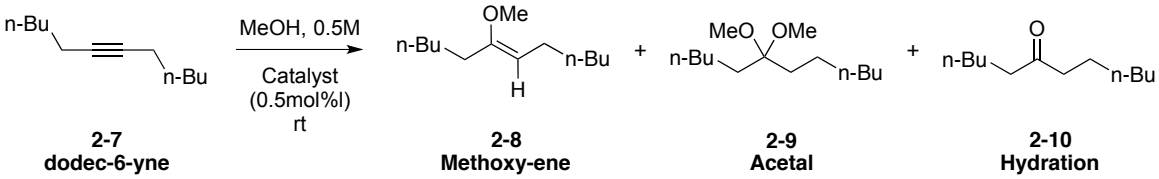
1,2-Dichloroethane (HPLC grade), ethyl acetate (ACS grade), hexanes (ACS grade) and diethyl ether (ACS grade) were purchased from Fisher Scientific and used without further purification. Anhydrous tetrahydrofuran in Pure-Pac^{TM} from Aldrich was used directly without further purification. Commercially available reagents were used without further purification. Reactions were monitored by thin layer chromatography (TLC) using silicycle pre-coated silica gel plates. Flash column chromatography was performed over silicycle silica gel (230–400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian 500 MHz Unity plus spectrometer and a Varian 600 MHz spectrometer using residue solvent peaks as internal standards. 31P NMR was performed on Varian 400 MHz spectrometer. Infrared spectra were recorded with a Perkin Elmer FT-IR spectrum 2000 spectrometer and are reported in reciprocal centimeter (cm^{-1}). Mass spectra were recorded with Micromass QTOF2 Quadrupole/Time-of-Flight Tandem mass spectrometer using electron spray ionization.

DMF is *N*, *N*-dimethylformamide; DCM, dichloromethane; Dippf, bis(diisopropylphosphinyl)ferrocene; Tol, toluene; DMS, dimethylsulfide; MeCN, acetonitrile; DMSO, dimethylsulfoxide.

Disclaimer: NMR spectra and characterization data is presented ‘as is’, with no additional characterization information available, due to sudden halt in research caused by medical illness on the part of the author. Displayed ^{1}H NMR integrations might sum to a higher value and spectra may contain additional peaks due to impurities.

6.2 Chapter 2 Experimental

General Procedure A: Addition of MeOH to Alkyne



2-7
dodec-6-yne

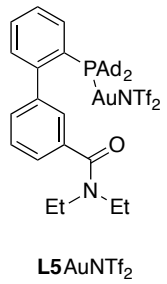
2-8
Methoxy-ene

2-9
Acetal

2-10
Hydration

The catalyst (0.002mmol) and MeOH (0.8ml, 0.5M to alkyne, not anhydrous) were combined in a screw-cap vial. 82µl of 6-dodecyne (0.388mmol) were added, and the solution was stirred at room temperature and monitored by TLC (25:1 hexanes:EtOAc). At the chosen times, 0.1ml samples were removed and worked up by the addition of tetrabutylammonium chloride solution (0.2ml, 0.100M in MeOH), followed by concentration and dried on high vacuum before NMR.

Figure 6-1: Results of L5AuNTf$_2$



L5AuNTf$_2$

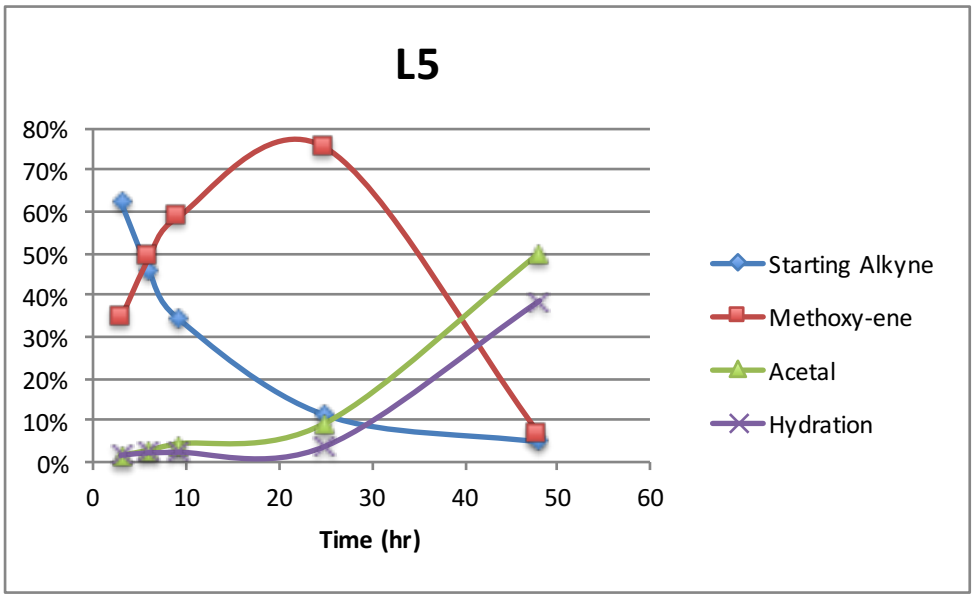
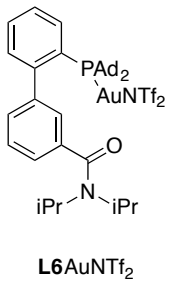


Figure 6-2: Results of L6AuNTf$_2$



L6AuNTf$_2$

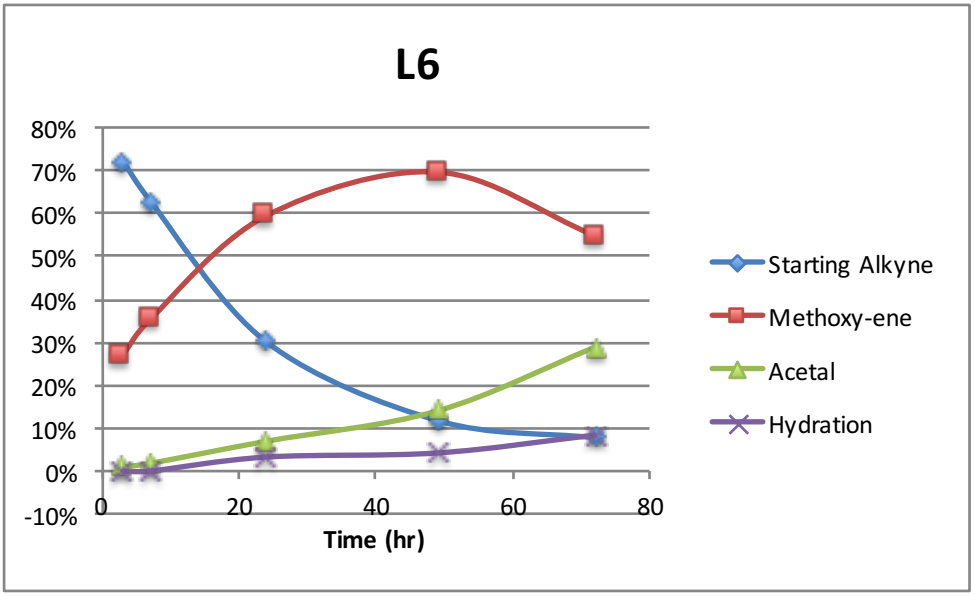
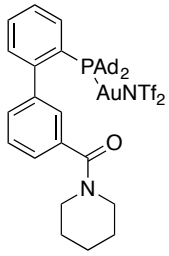


Figure 6-3: Results of L8AuNTf$_2$



L8AuNTf$_2$

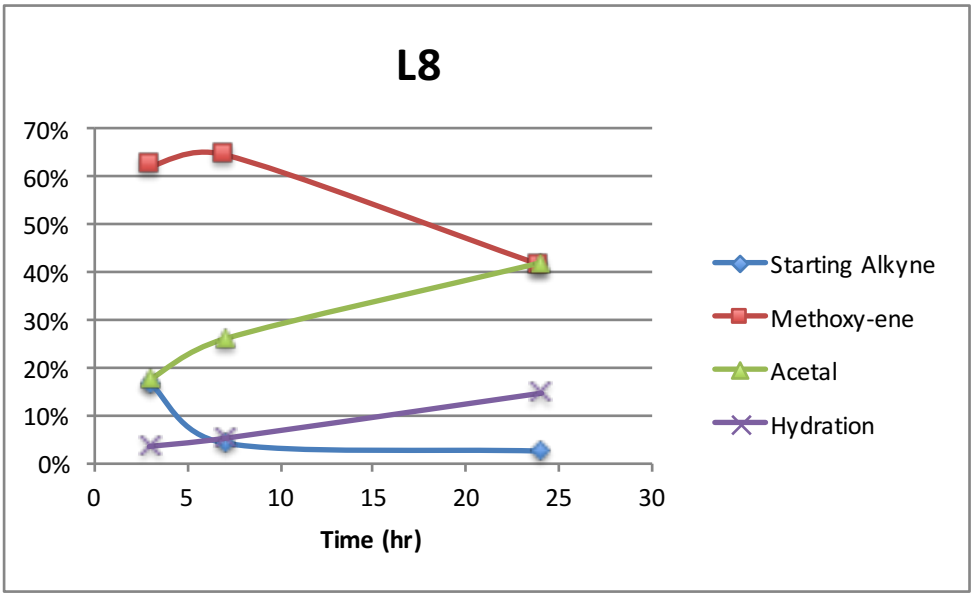


Figure 6-4: Results of JohnPhosAuNTf$_2$

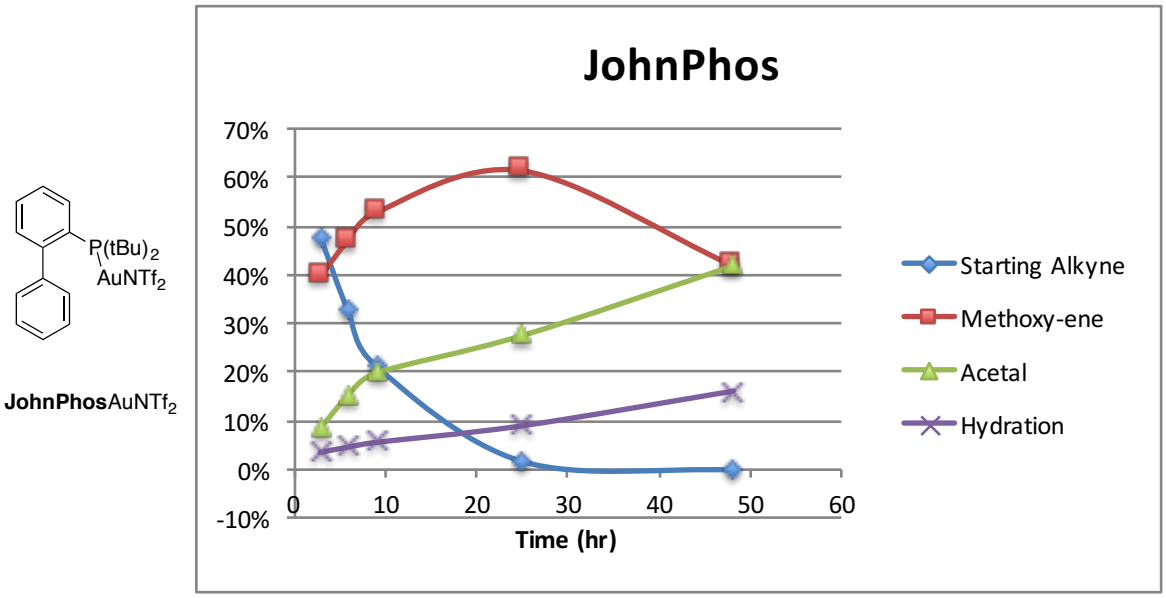


Figure 6-5: Results of L9AuCl

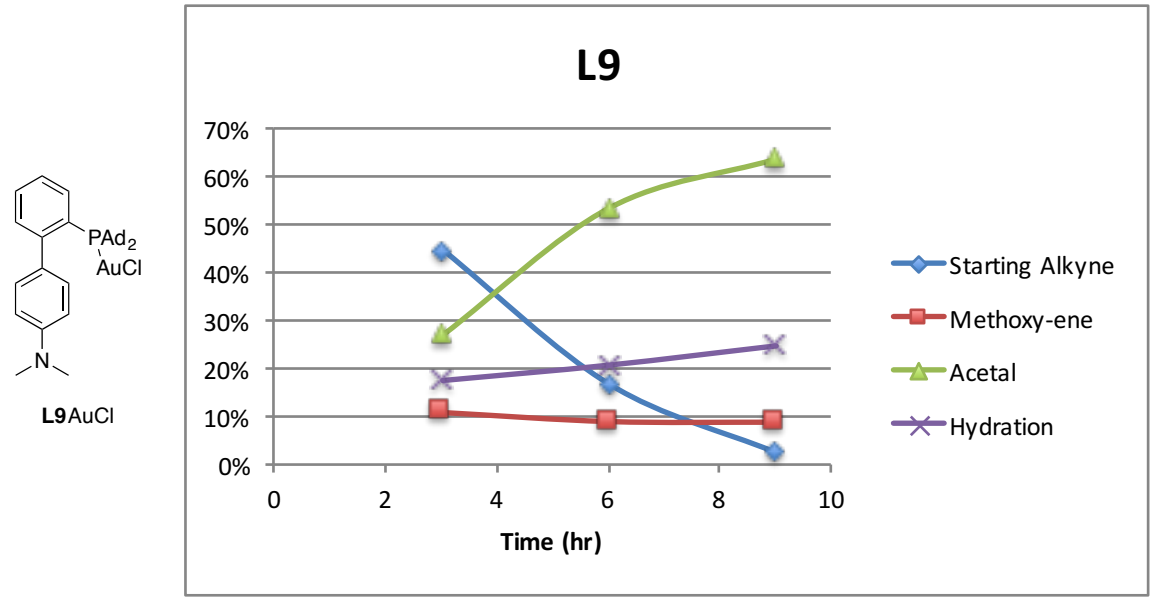
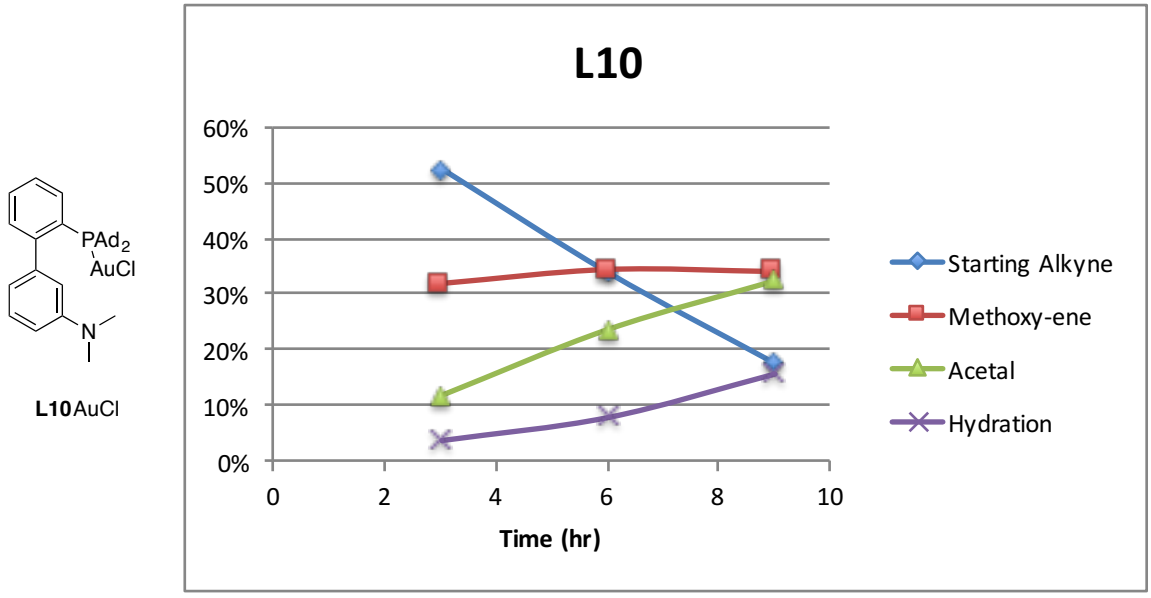


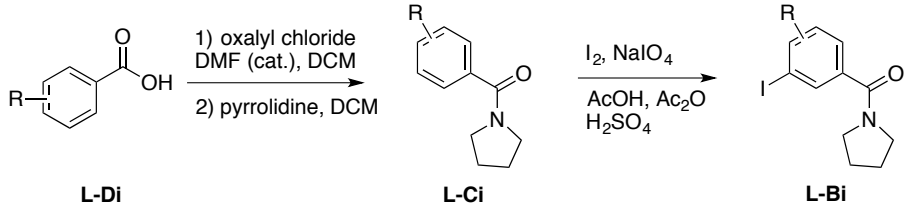
Figure 6-6: Results of L10AuCl



General Procedure B: Synthesis of Phosphine Ligands

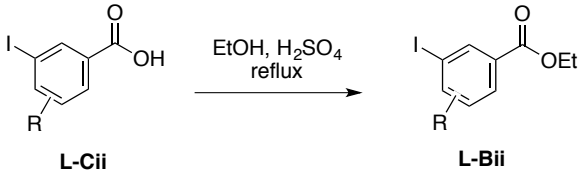
To a dispersion of 10 mmol **L-Di** (1 equiv) in 50 mL dry CH_2Cl_2 was added 25 mmol oxalyl chloride (2.5 equiv) and three drops of DMF, and the mixture was stirred for 2 - 4 h at room temperature. The reaction mixture was evaporated under reduced pressure and dried under vacuum to yield corresponding benzoyl chloride, which was dissolved in 50 mL dry CH_2Cl_2 again and cooled in an ice bath. A 10 mL CH_2Cl_2 solution containing 15 mmol amine (1.5 equiv) and 20 mmol Et_3N (2 equiv) was then added and the reaction mixture was stirred at room temperature under a nitrogen atmosphere. After 1 h, the solution was treated with 50 mL water and 100 mL DCM, and the organic phase was separated, dried, evaporated, and then purified by column chromatography to yield compound **L-Ci** in 90 - 95% yield.

Scheme 6-1: Synthesis of Coupling Partner L-Bi, for Ligands L14-15



The second step outlined in Scheme 6-1 is a literature procedure[62] and was performed as follows: 5.28mmol of **L-Ci** was slowly added to a solution of acetic anhydride (1.886ml, 2.8M to **L-Ci**), $NaIO_4$ (5.76mg, 0.51eq) and I_2 (235mg, 0.35eq) in acetic acid (3.77ml, 2.6M to **L-Ci**) and sulfuric acid (2.03ml, 2.6M to **L-Ci**) at room temperature. After stirring for 30min, reaction was heated to 40°C for 6-24hr, and monitored by TLC (2:1 hexanes:EtOAc) after mini-workup of 0.1ml of reaction solution (wash with saturated $Na_2CO_{3\,(aq)}$/EtOAc, check organic layer) for completion. Once all starting material **L-Ci** was completely consumed, the reaction was diluted with 100ml H_2O and extracted 3x with DCM. Then the organic layer was washed with sat. $Na_2CO_{3\,(aq)}$, dried over Na_2SO_4, filtrated, evaporated, and purified by flash chromatography (9:1 → 1:1 hexanes:EtOAc) to give **L-Bi** in 80% yield.

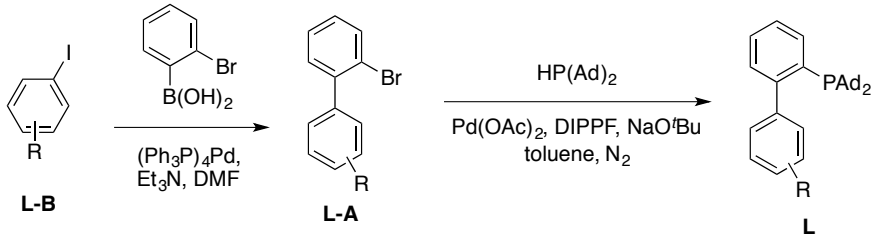
Scheme 6-2: Synthesis of Coupling Partner L-Bii, for Ligands L11-13, L17-20



Iodobenzoic acid **L-Cii** (5.37mmol, 1.0eq) was added at room temperature to a flask fitted with reflux condenser. Ethanol (26.9ml, 0.2M) and concentrated sulfuric acid (0.268ml, 20M to **L-Cii**) were added, and the reaction was heated to reflux (95°C) overnight

(12hr). Once all starting material consumed by TLC (2:1 EtOAc:hexanes), reaction was removed from heat, quenched after cooling with sat. $NaHCO_{3\,(aq)}$, diluted with EtOAc, and washed with DI water. The aqueous layer was back-extracted 3x with EtOAc, and the organic layer washed with brine, dried with $MgSO_4$, filtered and concentrated. **L-Bii** isolated with no further purification as a clear oil, in 80-95% yield.

Scheme 6-3: Cross-Coupling Synthesis of Phosphine Ligands

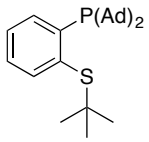


A mixture of 8 mmol **L-B** (1 equiv), 8.8 mmol 2-bromophenylboronic acid (1.1 equiv) and 24 mmol Et_3N (3 equiv) in 40 mL DMF was stirred and bubbled with N_2 gas for 15 minutes, and then 0.4 mmol $Pd(PPh_3)_4$ (5 mol %) was added; the reaction mixture was heated at 90 °C for 4 - 8 h under nitrogen atmosphere. Once TLC indicated **B** was completely consumed, the reaction was diluted with 500 mL Et_2O and washed with water to remove DMF. Then the organic layer was dried over $MgSO_4$, filtrated, evaporated, and then purified by column chromatography to yield product **L-A** in 85 - 92% yield.

Under nitrogen atmosphere **L-A** (2 mmol, 1 equiv), $Pd(OAc)_2$ (0.04 mmol, 2 mol%), DiPPF (1,1'-bis(diisopropyl- phosphino)ferrocene, 0.06 mmol, 3 mol%), *t*-BuONa (2.4 mmol, 1.2 equiv) and 5 mL dry toluene were added to a flame-dried Schlenk flask and the resulting suspension was stirred until apparently homogeneous. Added di(1-adamantyl)phosphine (2.2 mmol, 1.1 equiv), the flask was heated at 110°C in oil bath for 20

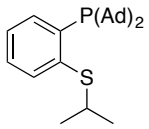
hours, which then was cooled to room temperature, and purified by column chromatography without work-up to yield the final ligand **L** in 60-80% yield.

L1



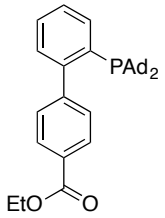
This compound was prepared from 2-bromobenzenethiol according to the literature procedure[63] to give the (2-bromophenyl)(tert-butyl)sulfane and step 2 in Scheme 6-3 of General Procedure B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 1H), 7.70 – 7.64 (m, 1H), 7.30 – 7.22 (m, 2H), 2.00 – 1.87 (m, 18H), 1.66 (s, 12H), 1.39 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ143.75, 140.51, 137.17, 136.77, 128.12, 125.67, 48.02, 41.97, 37.89, 37.21, 31.98, 29.12. ^{31}P NMR ($CDCl_3$, 162 MHz) δ 23.33. IR(neat): 2902, 2848, 1451, 1362, 1301, 908, 733. ESI($M+H^+$):467.24.

L2



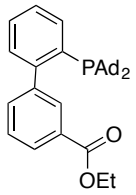
This compound was prepared from 2-bromobenzenethiol according to the literature procedure[63] to give the (2-bromophenyl)(isopropyl)sulfane and step 2 in Scheme 6-3 of General Procedure B. ^{1}H NMR (400 MHz, $cdcl_3$) δ 7.86 (d, J = 23.6 Hz, 1H), 7.76 – 7.41 (m, 2H), 7.36 (s, 1H), 3.86 – 3.70 (m, 1H), 2.39 – 1.61 (m, 28H), 1.23 (t, J = 7.3 Hz, 5H). ^{31}P NMR (162 MHz, $cdcl_3$) δ 17.43 (s).

L11



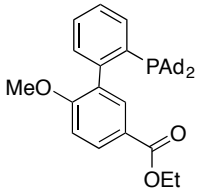
This compound was prepared from 4-iodobenzoic acid according to General Procedure B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 – 7.88 (m, 3H), 7.48 – 7.34 (m, 4H), 4.36 (q, *J* = 7.3 Hz, 2H), 2.00 – 1.59 (m, 32H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{31}P NMR (162 MHz, $cdcl_3$) δ 20.50 (s).

L12



This compound was prepared from 3-iodobenzoic acid according to General Procedure B. ^{1}H NMR (400 MHz, $cdcl_3$) δ 8.10 – 7.89 (m, 2H), 7.72 – 7.58 (m, 1H), 7.56 – 7.29 (m, 5H), 4.46 – 4.29 (m, 2H), 2.06 – 1.52 (m, 32H), 1.45 – 1.32 (m, 3H). ^{31}P NMR (162 MHz, $cdcl_3$) δ 20.57 (s).

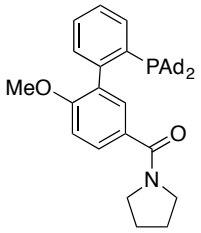
L13



This compound was prepared from 4-methoxybenzoic acid according to General Procedure B. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 – 8.09 (m, 1H), 7.86 (t, *J* = 4.1 Hz, 1H), 7.65 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.28 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.24 –

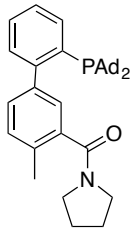
7.21 (m, 1H), 7.01 – 6.98 (m, 1H), 4.37 – 4.34 (m, 2H), 3.85 (s, 3H), 1.94 – 1.70 (m, 32H), 1.39 – 1.36 (m, 3H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 44.15 (s) [HPAd$_2$ impurity], 24.46 (s).

L14



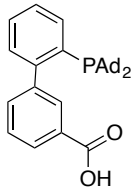
This compound was prepared from 4-methoxybenzoic acid according to General Procedure B. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.84 (t, *J* = 12.3 Hz, 1H), 7.64 – 7.57 (m, 1H), 7.34 (ddt, *J* = 18.5, 12.6, 9.2 Hz, 2H), 7.24 – 7.15 (m, 2H), 6.95 – 6.87 (m, 1H), 3.73 (d, *J* = 6.9 Hz, 3H), 3.68 – 3.48 (m, 4H), 1.95 – 1.61 (m, 32H).

L15



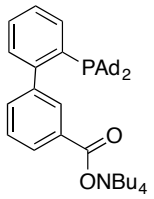
This compound was prepared from 2-methylbenzoic acid according to General Procedure B. ^{1}H NMR (400 MHz, cdcl$_3$) δ 7.86 (d, *J* = 7.4 Hz, 1H), 7.33 (dt, *J* = 16.2, 7.8 Hz, 2H), 7.25 – 7.23 (m, 1H), 7.22 – 7.06 (m, 3H), 3.66 (t, *J* = 6.9 Hz, 2H), 3.34 (t, *J* = 6.6 Hz, 2H), 2.40 – 2.32 (m, 3H), 1.94 – 1.60 (m, 32H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 20.44 (s).

L17



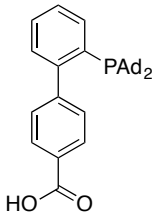
This compound was prepared from **L12** according to literature procedure[64]. ^{1}H NMR (400 MHz, cdcl$_3$) δ 8.04 (dt, *J* = 7.6, 1.5 Hz, 1H), 7.99 (s, 1H), 7.91 (d, *J* = 7.2 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.45 (dd, *J* = 13.2, 5.6 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.31 – 7.27 (m, 1H), 1.97 – 1.54 (m, 32H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 20.43 (s).

L18



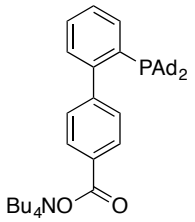
This compound was prepared from **L17** by titration with tetrabutylammonium hydroxide (1.0 equiv, 40% solution in MeOH) in 3ml DCM and 3ml MeOH, monitoring with ^{1}H NMR for a 1:1 ratio based on ^{1}H integration. ^{1}H NMR (400 MHz, cdcl$_3$) δ 8.09 – 7.70 (m, 4H), 7.33 – 7.21 (m, 4H), 3.37 (t, *J* = 8.7 Hz, 8H), 3.23 (s, 8H), 1.93 – 1.50 (m, 32H), 1.35 (d, *J* = 6.8 Hz, 8H), 0.98 – 0.87 (m, 12H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 20.37 (s).

L19



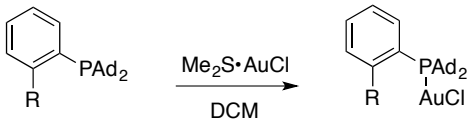
This compound was prepared from **L11** according to literature procedure[64]. ^{1}H NMR (400 MHz, cdcl$_3$) δ 8.02 (d, *J* = 7.8 Hz, 2H), 7.86 (d, *J* = 7.4 Hz, 1H), 7.36 – 7.28 (m, 2H), 7.23 – 7.16 (m, 3H), 1.82 (q, *J* = 12.6 Hz, 14H), 1.64 (d, *J* = 21.2 Hz, 18H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 20.37 (s).

L20



This compound was prepared from **L17** by titration with tetrabutylammonium hydroxide (1.0 equiv, 40% solution in MeOH) in 3ml DCM and 3ml MeOH, monitoring with ^{1}H NMR for a 1:1 ratio based on ^{1}H integration. ^{1}H NMR (400 MHz, cdcl$_3$) δ 8.06 (d, *J* = 8.1 Hz, 2H), 7.87 (d, *J* = 7.4 Hz, 1H), 7.40 – 7.29 (m, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 3.47 – 3.26 (m, 8H), 2.24 (s, 8H), 1.85 (q, *J* = 13.0 Hz,14H), 1.64 (s,18H), 1.51 – 1.36 (m, 8H), 0.99 (t, *J* = 7.3 Hz, 12H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 20.37 (s).

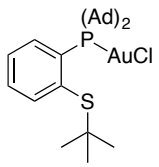
General Procedure C: Coordination of Au(I) to Phosphine Ligand



L **L**AuCl

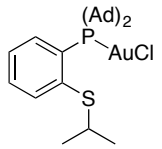
To a solution of 1 mmol ligand **L** in 5 mL anhydrous DCM was added dimethylsulfide gold (I) chloride (294.5 mg, 1 mmol). The mixture was stirred for 30 min at room temperature and the solvent was evaporated off under reduced pressure to give the desired gold catalyst **L**AuCl as white to light beige solid in quantitative yield.

L1AuCl



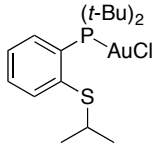
This compound was prepared according to General Procedure C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 – 7.83 (m, 2H), 7.51 – 7.42 (m, 2H), 2.20 – 2.10 (m, 12H), 1.98 (s, 6H), 1.67 (s, 12H), 1.50 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.54, 140.29, 135.61, 130.40, 130.06, 127.10, 52.02, 42.66, 42.22, 36.51, 31.75, 28.81. ^{31}P NMR (162 MHz, $CDCl_3$) δ 62.45. IR(neat): 2906, 2851, 1447, 1301, 1162, 914, 730. ESI(L1Au^{+}): 663.16.

L2AuCl



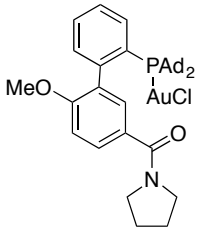
This compound was prepared according to General Procedure C. ^{1}H NMR (400 MHz, $cdcl_3$) δ 7.86 (d, J = 23.6 Hz, 1H), 7.76 – 7.41 (m, 2H), 7.36 (s, 1H), 3.86 – 3.70 (m, 1H), 2.39 – 1.61 (m, 28H), 1.23 (t, J = 7.3 Hz, 5H). ^{31}P NMR (162 MHz, $cdcl_3$) δ 64.35 (s), 60.66 (s).

L4AuCl



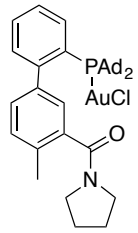
This compound was prepared according to General Procedure C. ^{1}H NMR (400 MHz, $cdcl_3$) δ 7.93 – 7.31 (m, 4H), 3.91 – 3.68 (m, 1H), 1.50 (dt, J = 40.6, 7.3 Hz, 18H), 1.39 (s, 3H), 1.24 (dd, J = 18.0, 6.7 Hz, 3H). ^{31}P NMR (162 MHz, $cdcl_3$) δ 65.83 (s), 59.56 (s).

L14AuCl



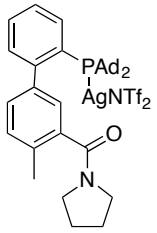
This compound was prepared according to General Procedure C. ^{31}P NMR (162 MHz, cdcl$_3$) δ 62.60 (s).

L15AuCl



This compound was prepared according to General Procedure C. ^{1}H NMR (600 MHz, cdcl$_3$) δ 8.87 – 8.65 (m, 1H), 7.91 (ddd, *J* = 25.3, 19.3, 11.7 Hz, 1H), 7.78 – 7.53 (m, 3H), 7.48 – 7.39 (m, 1H), 6.66 – 6.26 (m, 1H), 3.39 – 3.22 (m, 1H), 3.15 (s, 3H), 3.11 – 3.06 (m, 1H), 2.39 – 2.33 (m, 1H), 2.24 – 2.15 (m, 1H), 2.14 – 0.93 (m, 32H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 61.36 (s).

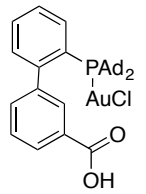
L15AgNTf$_2$



L15 AgNTf$_2$

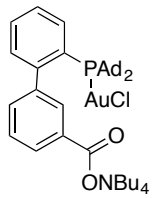
This compound was prepared according to General Procedure C, with the change of adding anhydrous silver(I) triflimide (1mmol), instead of dimethylsulfide gold (I) chloride. ^{1}H NMR (400 MHz, cdcl$_3$) δ 7.89 (dd, *J* = 9.7, 4.4 Hz, 1H), 7.60 – 7.47 (m, 3H), 7.34 – 7.28 (m, 1H), 7.21 (d, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 5.9 Hz, 1H), 3.65 (t, *J* = 6.7 Hz, 2H), 3.45 – 3.34 (m, 1H), 3.20 – 3.09 (m, 1H), 2.43 (s, 3H), 2.14 – 1.64 (m, 32H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 51.71 (d, *J* = 52.0 Hz), 47.21 (d, *J* = 52.4 Hz). ESI (L15Ag^{+}):672.36

L17AuCl



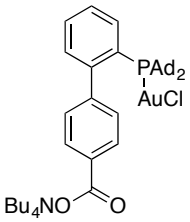
This compound was prepared from **L17** according to General Procedure C. ^{1}H NMR (400 MHz, cdcl$_3$) δ 8.27 (d, *J* = 7.8 Hz, 1H), 7.89 (s, 1H), 7.84 (s, 1H), 7.55 (dd, *J* = 9.7, 5.5 Hz, 3H), 7.39 – 7.29 (m, 2H), 2.07 (d, *J* = 59.6 Hz, 18H), 1.67 (s, 14H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 61.37 (s).

L18AuCl



This compound was prepared from **L18** according to General Procedure C, using a mixture of DCM, MeOH, and MeCN (1ml:1ml:1ml) as solvent. ^{1}H NMR (400 MHz, cdcl$_3$) δ 8.19 (d, *J* = 7.8 Hz, 1H), 8.03 (s, 1H), 7.82 (t, *J* = 7.2 Hz, 1H), 7.45 (p, *J* = 7.2 Hz, 2H), 7.33 (dt, *J* = 15.2, 4.8 Hz, 2H), 7.11 (d, *J* = 7.4 Hz, 1H), 3.39 – 3.29 (m, 8H), 2.30 – 2.06 (m, 8H), 2.07 – 1.91 (m, 11H), 1.67 (dd, *J* = 28.6, 19.6 Hz, 18H), 1.52 – 1.40 (m, 8H), 1.00 (t, *J* = 7.3 Hz, 12H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 61.66 (s). ESI(-) (M-NBu$_4^+$):729.21

L20AuCl



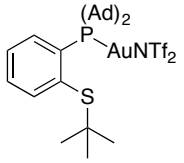
This compound was prepared from **L20** according to General Procedure C, using a mixture of DCM, MeOH, and MeCN (1ml:1ml:1ml) as solvent. ^{1}H NMR (400 MHz, cdcl$_3$)

δ 8.15 (d, *J* = 7.9 Hz, 2H), 7.91 – 7.81 (m, 1H), 7.50 (dd, *J* = 9.0, 5.6 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 3.35 (s, 8H), 2.11 (t, *J* = 20.9 Hz, 12H), 2.02 (t, *J* = 12.3 Hz, 8H), 1.67 (s, 22H), 1.42 (dd, *J* = 23.9, 6.4 Hz, 8H), 0.99 (t, *J* = 7.0 Hz, 12H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 61.49 (s).

General Procedure D: Synthesis of L18AuNTf$_2$ and similar structures

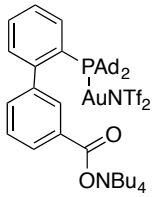
To a solution of 0.8 mmol catalyst **L**AuCl in 4 mL anhydrous DCM was added Silver bis(trifluoromethanesulfonyl)imide (309 mg, 0.8 mmol). The mixture was stirred for 20 min at room temperature and the precipitating silver chloride was filtered. The solvent was evaporated off under reduced pressure to give the desired gold complex **L**AuNTf$_2$ in quantitative yield.

L1AuNTf$_2$



This compound was prepared according to General Procedure D. ^{1}H NMR (400 MHz, cdcl$_3$) δ 7.90 (s, 2), 7.52 (s, 2H), 2.53 – 1.56 (m, 32H), 1.47 (d, *J* = 4.6 Hz, 9H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 65.17 (s), 58.59 (s).

L18AuNTf$_2$



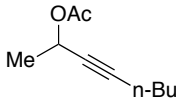
This compound was prepared according to General Procedure D, using a mixture of DCM (2ml anhydrous) and MeCN (2ml anhydrous) as solvent. ^{1}H NMR (400 MHz, cdcl$_3$) δ 8.14 (d, *J* = 7.9 Hz, 1H), 8.05 – 7.81 (m, 2H), 7.59 (s, 1H), 7.55 – 7.42 (m, 2H), 7.29 (d, *J* = 4.0 Hz, 1H), 7.14 (d, *J* = 7.4 Hz, 1H), 3.15 (dd, *J* = 10.1, 7.0 Hz, 8H), 2.40 – 1.89 (m, 20H), 1.69 (t, *J* = 20.4 Hz, 12H), 1.65 – 1.55 (m, 8H), 1.47 – 1.37 (m, 8H), 1.00 (t, *J* = 7.3 Hz, 12H). ^{31}P NMR (162 MHz, cdcl$_3$) δ 57.74 (d, *J* = 4.6 Hz), 57.21 (s).

6.3 Chapter 3 Experimental

General Procedure E: Preparation of propargylic acetate

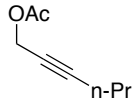
To a solution of the propargylic alcohol (2.0 mmol), pyridine (1.65 mL, 20.0 mmol) and catalytic amount of DMAP in anhydrous CH_2Cl_2 (6.0 mL) at 0 °C, was slowly added acetyl chloride (0.29 mL, 4.0 mmol). The reaction was stirred at the same temperature for 30 min before being diluted with hexanes (30 mL). The solid precipitates were filtered off and the filtrate obtained was concentrated. The residue was purified through silica gel flash column chromatography (hexanes/ethyl acetate = 20/1) to yield the desired acetate.

3-1



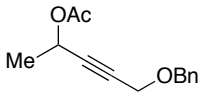
This known compound **3-1** was prepared in 90% yield through the General Procedure E and its spectroscopic data were in accordance with the literature data.[65] . ^{1}H NMR (500 MHz, CDCl$_3$) δ 5.43 (qt, *J* = 6.6, 2.0 Hz, 1H), 2.19 (td, *J* = 7.1, 2.0 Hz, 2H), 2.06 (s, 3H), 1.51 – 1.43 (m, 5H), 1.40-1.36 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 169.96, 85.54, 78.53, 60.84, 30.53, 21.88, 21.81, 21.15, 18.33, 13.55

3-3



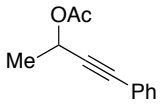
This compound **3-3** was prepared in 88% yield through the General Procedure E. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.66 (dt, *J* = 2.2, 1.1 Hz, 2H), 2.21-2.09 (m, 2H), 2.09 (s, 3H), 1.53 (h, *J* = 7.3 Hz, 2H), 0.97 (t, *J* = 7.3Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.37, 87.54, 74.00, 52.86, 21.84, 20.82, 20.71, 13.43. IR(neat): 3392, 2969, 1749, 1380, 1226, 1033. ESI(M+Na^+): 163.01.

3-5



This compound **3-5** was prepared in 85% yield through General Procedure E. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.27 (m, 5H), 5.50 (qt, *J* = 6.7, 1.6 Hz, 1H), 4.58 (s, 2H), 4.20 (d, *J* = 1.6 Hz, 2H), 2.08 (s, 3H), 1.51 (d, *J* = 6.7 Hz, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 169.87, 137.28, 128.41, 128.09, 127.87, 84.95, 80.66, 71.61, 60.30, 57.26, 21.32, 21.04. ESI(M+Na^+): 255.11.

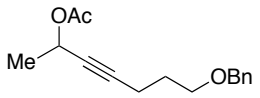
3-7



This known compound **3-7** was prepared in 95% yield through General Procedure E and its spectroscopic data were in accordance with the literature data.[65] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 – 7.40 (m, 2H), 7.36 – 7.26 (m, 3H), 5.69 (q, *J* = 6.7 Hz, 1H), 2.11 (s, 3H),

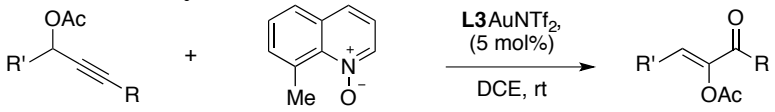
1.58 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 131.84, 128.55, 128.21, 122.25, 87.39, 84.53, 60.79, 21.50, 21.10

3-9



This compound **3-9** was prepared in 90% yield through General Procedure E. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 5H), 5.42 (dt, J = 8.6, 4.7Hz, 1H), 4.51 (s, 2H), 3.55 (t, J = 6.2 Hz, 2H), 2.34 (td, J = 7.1, 1.9 Hz, 2H), 2.06 (s, 3H), 1.86 – 1.74 (m, 2H), 1.44 (d, J = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.95, 138.44, 128.33, 127.56, 127.52, 84.77, 78.92, 72.92, 68.66, 60.75, 28.59, 21.75, 21.14, 15.53. IR(neat): 2989, 2937, 2859, 1740, 1371, 1235, 1106, 1060, 1019, 944, 737. ESI(M+Na^+): 283.15.

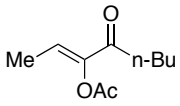
General Procedure F: Gold-catalyzed oxidation/acetoxy migration reaction of propargyl acetates to α-acetoxyenones



A **8-MQ** (1.5 equiv) **B**

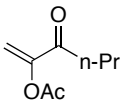
8-methylquinoline-*N*-oxide **8-MQ** (0.36 mmol, 1.2 equiv) and **L3**AuNTf2 (13.1 mg, 0.015 mmol, 5 mol %) were added in this order to a solution of the propargyl acetates **A** (0.3 mmol) in DCE (6 mL) at room temperature. The reaction mixture was stirred at the same temperature until the propargyl acetates was completely consumed. The reaction mixture was concentrated under vacuum. The residue was purified by chromatography on silica gel (eluent: hexanes/ethyl acetate) to afford the desired α-acetoxyenones **B**.

3-2b



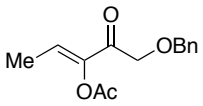
The compound **3-2b** was prepared in 82 % yield according to the General Procedure F (eluents: ethyl acetate: hexanes = 1: 10). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.53 (q, J = 7.0 Hz, 1H), 2.59 (t, J = 7.4 Hz, 2H), 2.24(s, 3H), 1.77 (d, J = 7.0 Hz, 3H), 1.58 (p, J = 7.4 Hz, 2H), 1.31 (h, J = 7.4 Hz, 2H), 0.89 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.71, 168.52, 147.05, 126.84, 36.76, 26.20, 22.24, 20.22, 13.79, 11.69. IR(neat): 2961, 2875, 1764, 1688, 1371, 1207, 1033. ESI(M+Na^+): 207.09.

3-4



The compound **5b** was prepared in 80 % yield according to General Procedure F (eluents: ethyl acetate: hexanes = 1: 10). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.90 (d, J = 2.4 Hz, 1H), 5.58 (d, J = 2.4 Hz, 1H), 2.64 (t, J = 7.3 Hz, 2H), 2.23 (s, 3H), 1.67 (h, J = 7.4 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.14, 168.89, 151.63, 113.05, 39.39, 20.42, 17.39, 13.61. IR(neat): 2967, 1729, 1687, 1374, 1207, 1044, 750. ESI(M+Na^+):157.08.

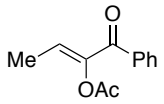
3-6



The compound **3-6** was prepared in 60% yield according to General Procedure F (eluents: ethyl acetate: hexanes = 1: 10). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 6.60 (q, J = 7.1 Hz, 1H), 4.59 (s, 2H), 4.38 (s, 2H), 2.26 (s, 3H), 1.78 (d, J = 7.1 Hz, 3H).

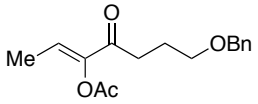
^{13}C NMR (151 MHz, $CDCl_3$) δ 190.35, 168.45, 145.22, 137.10, 128.61, 128.46, 128.07, 127.98, 73.23, 71.64, 20.22, 11.72. ESI(M+Na^+): 271.09.

3-8



The compound **3-8** was prepared in 75% yield according to General Procedure F (eluents: ethyl acetate: hexanes = 1: 10). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 6.24 (q, *J* = 6.9 Hz, 1H), 2.27 (s, 3H), 1.85 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 189.65, 168.56, 146.63, 136.91, 132.19, 129.90, 129.17, 128.16, 20.31, 11.80. IR(neat): 3065, 2938, 1760, 1664, 1371, 1275, 1020, 846, 777, 709. ESI(M+Na^+): 227.06.

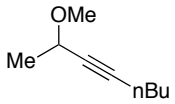
3-10



The compound **3-10** was prepared in 75% yield according to General Procedure F (eluents: ethyl acetate: hexanes = 1: 10). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.24 (m, 5H), 6.56 (q, *J* = 7.1 Hz, 1H), 4.48 (s, 2H), 3.50 (t, *J* = 6.1 Hz, 2H), 2.74 (t, *J* = 7.2 Hz, 2H), 2.26 (s, 3H), 1.99 – 1.88 (m, 2H), 1.77 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.29, 168.50, 146.96, 138.37, 128.28, 127.55, 127.47, 127.16, 72.78, 69.06, 33.63, 24.14, 20.20, 11.69. IR(neat): 3346, 2859, 1760, 1683, 1369, 1201, 1027, 805, 735. IR(neat): 3346, 2859, 1760, 1683, 1369, 1201, 1027, 805, 735. ESI(M+Na^+): 299.12.

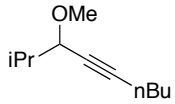
6.4 Chapter 4 Experimental

4-1



This compound was prepared according to literature procedure[66]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70-3.68 (m, 1H), (t, *J* = 7.4 Hz, 2H), 3.99 (sept, 1H), 3.63 (s, 3H), 2.40 (t, *J* = 6 Hz, 2H), 1.58 (q, *J* = 6 Hz, 2H), 1.33 (sext, *J* = 12 Hz, 2H), 1.04 (d, *J* = 6 Hz, 6H), 0.91 (t, *J* = 6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 87.00, 77.41, 77.26, 56.51, 33.01, 30.90, 29.69, 21.91, 18.57, 18.37, 17.68, 13.57. IR(neat): 2960, 2931, 2874, 1467, 1351, 1203, 1094, 760. GC-MS (M-H): 167

4-3

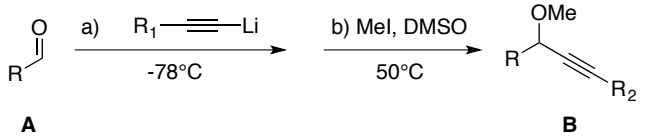


This compound was prepared according to literature procedure[66]. ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.70-3.68 (m, 1H), (t, *J* = 7.4 Hz, 2H), 3.99 (sept, 1H), 3.63 (s, 3H), 2.40 (t, *J* = 6 Hz, 2H), 1.58 (q, *J* = 6 Hz, 2H), 1.33 (sext, *J* = 12 Hz, 2H), 1.04 (d, *J* = 6 Hz, 6H), 0.91 (t, *J* = 6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 87.00, 77.41, 77.26, 56.51, 33.01, 30.90, 29.69, 21.91, 18.57, 18.37, 17.68, 13.57. IR(neat): 2960, 2931, 2874, 1467, 1351, 1203, 1094, 760. GC-MS (M-H): 167.

General Procedure G: Synthesis of Propargyl Ethers

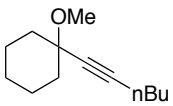
The general synthesis of the 2-methoxy-3-yne framework structure is outlined in Scheme 6-4. The preparation follows literature procedure[67] .

Scheme 6-4: Synthesis Outline for 2-Methoxy-3-yne Framework



To a solution of terminal alkyne (0.0115 mmol) in dry tetrahydrofuran (6.76 mL) at -78°C was added n-butyllithium (2.5M in hexanes, 4 mL, 0.01 mmol) slowly. The solution was stirred for 10 min, then warmed to 0°C. After stirring for 10 mins, the solution was re-cooled to -78°C and a solution of carbonyl **A** (0.01 mmol) in dry tetrahydrofuran (0.5 mL) were added dropwise via syringe. After addition, the cooling bath was removed and the reaction solution was stirred at room temperature for 3 h. MeI (1.5eq) dissolved in DMSO (10ml, 1.5M to MeI) was added and the reaction heated at 50°C for 6hr. TLC (95% hex:EtOAc). The cold mixture was hydrolyzed and extracted with pentane. The organic layer was washed once with saturated aqueous ammonium chloride. dried over magnesium sulfate and concentrated. The resulting oil was distilled on Kuegel Rohr (110°C) under vacuum to give propargylic ester **B**.

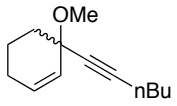
4-5a



This compound was prepared from cyclohexanone according to General Procedure G, with the addition of anhydrous LiBr (0.5eq, 4M solution in dry THF) prior to addition of carbonyl. ^{1}H NMR (600 MHz, cdcl$_3$) δ 3.34 (s, 3H), 2.23 (t, J = 7.0 Hz, 2H), 1.89 – 1.80 (m,

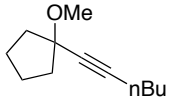
2H), 1.62 (dd, J = 12.1, 4.3 Hz, 2H), 1.58 – 1.47 (m, 8H), 1.42 (dq, J = 14.2, 7.1 Hz, 2H), 0.91 (t, J = 7.3 Hz, 3H).

4-5b



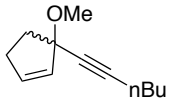
This compound was prepared from cyclohex-2-en-1-one according to General Procedure A, with the addition of anhydrous LiBr (0.5eq, 4M solution in dry THF) prior to addition of carbonyl. ^{1}H NMR (600 MHz, cdcl$_3$) δ 5.81 (ddd, J = 36.7, 20.2, 6.8 Hz, 2H), 3.37 (s, 3H), 2.22 (t, J = 7.1 Hz, 2H), 2.08 – 1.96 (m, 2H), 1.94 – 1.86 (m, 2H), 1.81 – 1.65 (m, 2H), 1.55 – 1.47 (m, 2H), 1.42 – 1.33 (m, 2H), 0.88 (t, J = 7.0 Hz, 3H).

4-5c



This compound was prepared from cyclopentanone according to General Procedure G, with the addition of anhydrous LiBr (0.5eq, 4M solution in dry THF) prior to addition of carbonyl. ^{1}H NMR (600 MHz, cdcl$_3$) δ 3.31 (s, 3H), 2.22 (t, J = 7.0 Hz, 2H), 1.95 (ddd, J = 8.6, 7.9, 3.6 Hz, 2H), 1.86 – 1.77 (m, 2H), 1.76 – 1.63 (m, 4H), 1.53 – 1.45 (m, 2H), 1.45 – 1.36 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H).

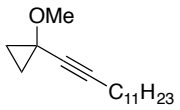
4-5d



This compound was prepared from cyclopent-2-en-1-one according to General Procedure G, with the addition of anhydrous LiBr (0.5eq, 4M solution in dry THF) prior to

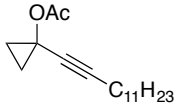
addition of carbonyl. ^{1}H NMR (600 MHz, cdcl$_3$) δ 6.01 (dd, *J* = 5.1, 2.6 Hz, 1H), 5.85 (dd, *J* = 4.9, 2.5 Hz, 1H), 3.34 (s, 3H), 2.53 – 2.46 (m, 1H), 2.43 – 2.36 (m, 1H), 2.26 – 2.20 (m, 2H), 2.17 (tt, *J* = 17.3, 8.9 Hz, 1H), 1.54 – 1.48 (m, 2H), 1.39 (dd, *J* = 21.6, 15.2 Hz, 2H), 0.87 (dd, *J* = 13.5, 6.5 Hz, 3H).

4-5e



This compound was prepared from 1-Ethoxy-1-trimethylsiloxycyclopropane according to literature procedure[68], followed by an in-situ trapping of the propynylmagnesium bromide with MeI (3.0eq) dissolved in DMSO (1M to **4-5e**) and heated at 45°C for 6hr. TLC (95% hex:EtOAc) rf:0.95. The cold mixture was hydrolyzed and extracted with DCM. The organic layer was dried over magnesium sulfate and concentrated. Purified with flash chromatography (loading in hexanes, elude 5% EtOAc in hexanes). ^{1}H NMR (400 MHz, cdcl$_3$) δ 5.30 (s, 1H), 3.37 (s, 3H), 2.22 (dt, *J* = 14.1, 7.1 Hz, 2H), 1.54 – 1.45 (m, 2H), 1.43 – 1.33 (m, 2H), 1.26 (s, 14H), 1.00 – 0.93 (m, 2H), 0.90 – 0.83 (m, 5H).

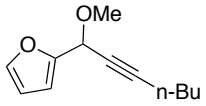
4-5f



This compound was prepared from 1-Ethoxy-1-trimethylsiloxycyclopropane according to literature procedure[68], to give the 1-(1-propyny1)cyclopropanol, which was then protected with acetyl group following literature procedure[69]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 – 2.13 (m, 2H), 2.03 (d, *J* = 11.3 Hz, 3H), 1.52 – 1.43 (m, 2H), 1.27 (d, *J* = 20.7 Hz, 15H), 1.15 – 1.06 (m, 4H), 0.89 – 0.86 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.41 (s), 83.98

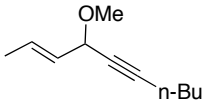
(s), 78.55 (s), 48.67 (s), 32.12 (s), 31.81 (s), 29.75 (d, J = 7.7 Hz), 29.54 (s), 29.31 (s), 29.07 (s), 28.75 (s), 22.88 (d, J = 3.3 Hz), 21.32 (s), 19.06 (s), 15.92 (s), 14.33 (s).

4-7a



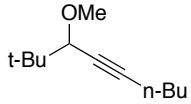
This compound was prepared from furan-2-carbaldehyde according to General Procedure G. ^{1}H NMR (600 MHz, cdcl$_3$) δ 7.41 (d, J = 0.6 Hz, 1H), 6.50 – 6.44 (m, 1H), 6.35 (dd, J = 2.8, 1.7 Hz, 1H), 5.17 (s, 1H), 3.38 (s, 3H), 2.33 – 2.26 (m, 2H), 1.61 – 1.50 (m, 2H), 1.49 – 1.40 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H).

4-7b



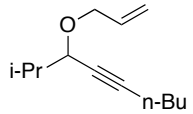
This compound was prepared from but-2-enal according to General Procedure G. ^{1}H NMR (600 MHz, cdcl$_3$) δ 5.87 (tt, J = 13.2, 6.5 Hz, 1H), 5.56 – 5.49 (m, 1H), 4.43 – 4.37 (m, 1H), 3.33 (s, 3H), 2.23 (ddd, J = 7.5, 6.3, 1.9 Hz, 2H), 1.72 (dd, J = 9.2, 4.2 Hz, 3H), 1.54 – 1.47 (m, 2H), 1.40 (dq, J = 14.3, 7.2 Hz, 2H), 0.90 (td, J = 7.3, 3.9 Hz, 3H).

4-9a



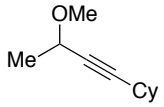
This compound was prepared according to literature procedure[66]. ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.49 (d, J = 2.2 Hz, 1H), 3.39 (s, 3H), 2.24 (td, J = 6.9, 2.1 Hz, 2H),1.55 – 1.47 (m, 2H), 1.47 – 1.36 (m, 2H), 0.96 (s, 8H), 0.91 (t, J = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 86.88, 80.92, 77.59, 57.27, 35.42, 30.93, 25.77, 21.93, 18.39, 13.58. IR(neat): 2958, 2905, 2873, 2607, 2221, 1465, 1392, 1327, 1009, 876. GC-MS (M-H): 181.

4-9b



This compound was prepared according to literature procedure[66]. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.92 (ddt, *J* = 15.4, 10.9, 5.7 Hz, 1H), 5.29 (dq, *J* = 17.2, 1.8 Hz, 1H), 5.17 (dd, *J* = 10.6, 1.6 Hz, 1H), 4.28 – 4.20 (m, 1H), 3.94 (dd, *J* = 12.7, 6.2 Hz, 1H), 3.84 (dt, *J* = 5.6, 1.9 Hz, 1H), 1.90 (dq, *J* = 13.2, 6.6 Hz, 1H), 1.54 – 1.47 (m, 2H), 1.46 – 1.38 (m, 2H), 0.98 (dd, *J* = 14.6, 6.7 Hz, 6H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 134.89, 116.82, 86.84, 77.67, 74.65, 69.49, 33.17, 30.89, 29.69, 21.91, 18.66, 18.39, 17.83, 13.58. IR(neat): 3081, 2960, 2932, 2873, 1648, 1467, 1383, 1367, 1083, 1029, 921. GC-MS (M-H): 193.

4-9c

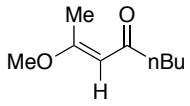


This compound was prepared according to literature procedure[66]. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.07 (qd, *J* = 6.5, 1.7 Hz, 1H), 3.38 (s, 3H), 2.40 (dq, *J* = 8.7, 4.4, 3.8 Hz, 1H), 1.83 – 1.74 (m, 2H), 1.69 (ddq, *J* = 9.5, 6.9, 3.5, 2.9 Hz, 2H), 1.55 – 1.46 (m, 1H), 1.39 (d, *J* = 6.6 Hz, 3H), 1.35 – 1.23 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 89.85, 79.54, 67.01, 55.92, 32.70, 28.95, 25.88, 24.79, 22.37. IR(neat): 2985, 2932, 2855, 2233, 1731, 1679, 1449, 1330, 1115, 969, 934. GC- MS (M-H): 165.

General Procedure H: Gold-catalyzed oxidation of propargyl ethers

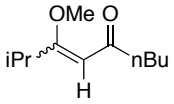
8-methylquinoline-*N*-oxide (0.36 mmol, 1.2 eq) and **L1**AuNTf2 (0.015 mmol, 5 mol %) were added in this order to a solution of the propargyl ethers **1** (0.3 mmol) in DCE (0.05M) at room temperature. The reaction mixture was stirred at the same temperature until the propargyl ethers was completely consumed. The reaction mixture was concentrated under *vacuum*. The residue was purified by chromatography on silica gel (eluent: hexanes/ethyl acetate) to afford the desired *β*-alkoxy-*α,β*-unsaturated ketones **2**.

4-2b(*E*)



The compound **4-2b(*E*)** was prepared in 82 % yield according to General Procedure H. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.45 (s, 1H), 3.64 (s, 3H), 2.45 – 2.36 (m, 2H), 2.28 (s, 3H), 1.61-1.56 (m, 2H), 1.36-1.30 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.77, 172.47, 98.86, 55.27, 44.40, 26.94, 22.46, 19.58, 13.92. IR(neat): 2959, 2932, 1682, 1589, 1400, 1266, 1068, 925, 866. ESI(M+Na^+):179.10.

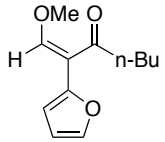
4-4b



The compound **4-4b** was prepared in 63 % yield according to General Procedure H. (*E*/*Z* ration 10:1). The crude product was purified with ethyl acetate: hexanes = 1: 10. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.31 (s, 1H), 3.99 (hept, *J* = 6.9 Hz, 1H), 3.63 (s, 3H), 2.43 – 2.37 (m, 2H), 1.61 – 1.54 (m, 2H), 1.33 (hept, *J* = 7.4 Hz, 2H), 1.05 (d, *J* = 6.8 Hz, 6H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.43, 179.90, 97.08, 55.33, 44.59, 29.49,

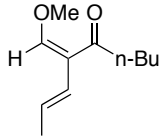
26.96, 22.45, 19.59, 13.94. IR(neat): 2963, 2934, 2874, 1678, 1584, 1468, 1107, 1073, 749. ESI(M+Na^+):207.1383.

4-8a



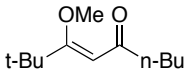
This compound was prepared according to General Procedure H, using instead IPrAuCl/$AgNTf_2$ as a catalyst. ^{1}H NMR (600 MHz, $cdcl_3$) δ 7.56 (d, *J* = 6.9 Hz, 1H), 7.34 (s, 1H), 6.50 (d, *J* = 3.3 Hz, 1H), 6.44 (dd, *J* = 3.2, 1.8 Hz, 1H), 3.92 (s, 3H), 2.56 (dd, *J* = 15.9, 8.3 Hz, 2H), 1.59 – 1.52 (m, 2H), 1.32 – 1.26 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H).

4-8b



This compound was prepared according to General Procedure H, using instead IPrAuCl/$AgNTf_2$ as a catalyst and heating to 60°C. ^{1}H NMR (600 MHz, $cdcl_3$) δ 7.20 (s, 1H), 6.35 – 6.27 (m, 1H), 6.18 (d, *J* = 16.1 Hz, 1H), 3.90 (s, 3H), 2.53 (dd, *J* = 13.8, 6.5 Hz, 3H), 1.81 (d, *J* = 6.6 Hz, 3H), 1.62 – 1.55 (m, 2H), 1.32 (dd, *J* = 15.4, 7.3 Hz, 2H), 0.91 (dd, *J* = 9.3, 5.3 Hz, 3H).

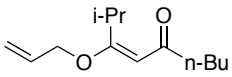
4-10a



The compound **4-10b** was prepared in 67 % yield according to General Procedure H (*E/Z* ratio 1:3.6). The crude product was purified with ethyl acetate: hexanes = 1: 10. ^{1}H NMR (600 MHz, MHz, $CDCl_3$) δ 5.48 (s, 1H), 3.84 (s, 3H), 2.44 – 2.39 (t, *J* = 6 Hz, 2H), 1.57 (pent, *J* = 7.5 Hz, 1H), 1.33 (hept, *J* = 7.4 Hz, 1H), 1.12 (s, 4H), 0.91 (t, *J* = 7.4 Hz,

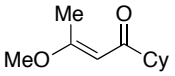
2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.37, 179.58, 101.27, 62.86, 44.06, 38.38, 28.09, 27.11, 22.44, 13.92. IR(neat): 2936, 2873, 1679, 1590, 1481, 1411, 1372, 1350, 1079, 1037, 929, 820. ESI(M+Na^+): 221.16.

4-10b



The compound **4-10c** was prepared in 78 % yield according to General Procedure H (*E/Z* ratio 3.6:1). The crude product was purified with ethyl acetate: hexanes = 1: 10. ^{1}H NMR (600 MHz, MHz, $CDCl_3$) δ 5.95 (ddd, *J* = 22.0, 10.3, 5.1 Hz, 1H), 5.37 (dd, *J* = 17.3, 1.8 Hz, 1H), 5.30 (s, 1H), 5.27 (d, *J* = 10.6 Hz, 1H), 4.31 (d, *J* = 5.2 Hz, 2H), 4.00 (p, *J* = 6.8 Hz, 1H), 2.41 – 2.35 (m, 2H), 1.62 (td, *J* = 10.9, 10.4, 6.9 Hz, 1H), 1.32 (hept, *J* = 7.4 Hz, 2H), 1.08 (d, *J* = 7.2 Hz, 6H), 0.91 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.48, 178.60, 131.95, 117.52, 98.01, 77.21, 68.33, 44.63, 29.60, 26.97, 22.44, 19.68, 13.95. IR(neat): 2962, 2933, 1679, 1468, 1396, 1359, 1206, 1167, 1068, 870, 771. ESI(M+Na^+): 233.16.

4-10c



The compound **4-10d** was prepared in 73 % yield according to General Procedure H (*E/Z* ratio 6:1). The crude product was purified with ethyl acetate: hexanes = 1: 10. ^{1}H NMR (500 MHz, MHz, $CDCl_3$) δ 5.48 (s, 1H), 3.65 (s, 3H), 2.28 (s, 3H), 1.86 – 1.76 (m, 4H), 1.41 – 1.16 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 202.84, 173.05, 97.94, 55.29, 52.21, 29.14, 25.97, 25.91, 19.69. IR(neat): 2930, 2854, 1677, 1588, 1488, 1399, 1264, 1095, 929, 892. ESI(M+Na^+): 205.1.

7. References

1. Hashmi, A. S. K., Gold-catalyzed organic reactions. *Chemical Reviews* **2007,** *107* (7), 3180-3211. DOI: 10.1021/cr000436x.

2. Hashmi, A. S. K.; Rudolph, M., Gold catalysis in total synthesis. *Chemical Society Reviews* **2008,** *37* (9), 1766-1775. DOI: 10.1039/b615629k.

3. Hashmi, A. S. K.; Wang, T.; Shi, S.; Rudolph, M., Regioselectivity Switch: Gold(I)-Catalyzed Oxidative Rearrangement of Propargyl Alcohols to 1,3-Diketones. *Journal of Organic Chemistry* **2012,** *77* (17), 7761-7767. DOI: 10.1021/jo301381z.

4. Hashmi, A. S. K., Homogeneous gold catalysts and alkynes: A successful liaison. *Gold Bulletin* **2003,** *36* (1), 3-9.

5. Hutchings, G. J., VAPOR-PHASE HYDROCHLORINATION OF ACETYLENE - CORRELATION OF CATALYTIC ACTIVITY OF SUPPORTED METAL CHLORIDE CATALYSTS. *Journal of Catalysis* **1985,** *96* (1), 292-295. DOI: 10.1016/0021-9517(85)90383-5.

6. Hashmi, A. S. K., Homogeneous gold catalysis: The role of protons. *Catalysis Today* **2007,** *122* (3-4), 211-214. DOI: 10.1016/j.cattod.2006.10.006.

7. Hashmi, A. S. K.; Schwarz, L.; Choi, J. H.; Frost, T. M., A new gold-catalyzed C-C bond formation. *Angewandte Chemie-International Edition* **2000,** *39* (13), 2285-2288. DOI: 10.1002/1521-3773(20000703)39:13<2285::aid-anie2285>3.0.co;2-f.

8. Hashmi, A. S. K.; Frost, T. M.; Bats, J. W., Highly selective gold-catalyzed arene synthesis. *Journal of the American Chemical Society* **2000,** *122* (46), 11553-11554. DOI: 10.1021/ja005570d.

9. Nair, V.; Vidya, N.; Abhilash, K. G., Gold(III) chloride promoted addition of electron-rich heteroaromatic compounds to the C=C and C=O bonds of enals. *Tetrahedron Letters* **2006,** *47* (17), 2871-2873. DOI: 10.1016/j.tetlet.2006.02.130.

10. Nair, V.; Abhilash, K. G.; Vidya, N., Practical synthesis of triaryl and triheteroarylmethanes by reaction of aldehydes and activated arenes promoted by gold(III) chloride. *Organic Letters* **2005,** *7* (26), 5857-5859. DOI: 10.1021/o1052423h.

11. Mertins, K.; Lovel, I.; Kischel, J.; Zapf, A.; Beller, M., Gold-catallyzed benzylation of arenes and heteroarenes. *Advanced Synthesis & Catalysis* **2006,** *348* (6), 691-695. DOI: 10.1002/adsc.200505433.

12. Li, Z.; Zhang, J.; Brouwer, C.; Yang, C.-G.; Reich, N. W.; He, C., Bronsted acid catalyzed addition of phenols, carboxylic acids, and tosylamides to simple olefins. *Organic Letters* **2006,** *8* (19), 4175-4178. DOI: 10.1021/ol0610035.

13. Xu, Q.; Imamura, Y.; Fujiwara, M.; Souma, Y., A new gold catalyst: Formation of gold(I) carbonyl, Au(CO)(n) (+) (n=1,2) in sulfuric acid and its application to carbonylation of olefins. *Journal of Organic Chemistry* **1997,** *62* (6), 1594-1598. DOI: 10.1021/jo9620122.

14. Xu, Q., Metal carbonyl cations: generation, characterization and catalytic application. *Coordination Chemistry Reviews* **2002,** *231* (1-2), 83-108. DOI: 10.1016/s0010-8545(02)00115-7.

15. Teles, J. H.; Brode, S.; Chabanas, M., Cationic gold(I) complexes: Highly efficient catalysts for the addition of alcohols to alkynes. *Angewandte Chemie-International Edition* **1998,** *37* (10), 1415-1418. DOI: 10.1002/(sici)1521-3773(19980605)37:10<1415::aid-anie1415>3.0.co;2-n.

16. Hayashi, T.; Tanaka, K.; Haruta, M., Selective vapor-phase epoxidation of propylene over Au/TiO2 catalysts in the presence of oxygen and hydrogen. *Journal of Catalysis* **1998,** *178* (2), 566-575. DOI: 10.1006/jcat.1998.2157.

17. Hesp, K. D.; Stradiotto, M., Stereo- and Regioselective Gold-Catalyzed Hydroamination of Internal Alkynes with Dialkylamines. *Journal of the American Chemical Society* **2010,** *132* (51), 18026-18029. DOI: 10.1021/ja109192w.

18. Hoffmann-Roder, A.; Krause, N., Gold(III) chloride catalyzed cyclization of alpha-hydroxyallenes to 2,5-dihydrofurans. *Organic Letters* **2001,** *3* (16), 2537-2538. DOI: 10.1021/ol016205+.

19. Zhang, L. M.; Wang, S. Z., Efficient synthesis of cyclopentenones from enynyl acetates via tandem Au(I)-catalyzed 3,3-rearrangement and the Nazarov reaction. *Journal of the American Chemical Society* **2006,** *128* (5), 1442-1443. DOI: 10.1021/ja057327q.

20. Zhang, L., A Non-Diazo Approach to alpha-Oxo Gold Carbenes via Gold-Catalyzed Alkyne Oxidation. *Accounts of Chemical Research* **2014,** *47* (3), 877-888. DOI: 10.1021/ar400181x.

21. Pauling, L., *The Nature of the Chemical Bond and the Structure of Molecules and Crystals; an Introduction to Modern Structural Chemistry*. 3 ed.; Cornell University Press: Ithaca, NY: 1960.

22. Benitez, D.; Shapiro, N. D.; Tkatchouk, E.; Wang, Y.; Goddard, W. A., III; Toste, F. D., A bonding model for gold(I) carbene complexes. *Nature Chemistry* **2009,** *1* (6), 482-486. DOI: 10.1038/nchem.331.

23. Zhang, L.; Sun, J.; Kozmin, S. A., Gold and platinum catalysis of enyne cycloisomerization. *Advanced Synthesis & Catalysis* **2006,** *348* (16-17), 2271-2296. DOI: 10.1002/adsc.200600368.

24. Jimenez-Nunez, E.; Echavarren, A. M., Gold-catalyzed cycloisomerizations of enynes: A mechanistic perspective. *Chemical Reviews* **2008,** *108* (8), 3326-3350. DOI: 10.1021/cr0684319.

25. Doyle, M. P. M., M. A.; Ye, T., *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*. Wiley; New York: 1998.

26. Archibald, T. G., Large-scale use of diazomethane in pharmaceutical production. *Chimica Oggi-Chemistry Today* **2000,** *18* (6), 34-38.

27. Rossi, E.; Woehl, P.; Maggini, M., Scalable in Situ Diazomethane Generation in Continuous-Flow Reactors. *Organic Process Research & Development* **2012,** *16* (5), 1146-1149. DOI: 10.1021/op200110a.

28. Gorin, D. J.; Sherry, B. D.; Toste, F. D., Ligand effects in homogeneous Au catalysis. *Chemical Reviews* **2008,** *108* (8), 3351-3378. DOI: 10.1021/cr068430g.

29. Lundgren, R. J.; Peters, B. D.; Alsabeh, P. G.; Stradiotto, M., A P,N-Ligand for Palladium-Catalyzed Ammonia Arylation: Coupling of Deactivated Aryl Chlorides, Chemoselective Arylations, and Room Temperature Reactions. *Angewandte Chemie-International Edition* **2010,** *49* (24), 4071-4074. DOI: 10.1002/anie.201000526.

30. Luo, Y.; Ji, K.; Li, Y.; Zhang, L., Tempering the Reactivities of Postulated alpha-Oxo Gold Carbenes Using Bidentate Ligands: Implication of Tricoordinated Gold Intermediates and the Development of an Expedient Bimolecular Assembly of 2,4-Disubstituted Oxazoles. *Journal of the American Chemical Society* **2012,** *134* (42), 17412-17415. DOI: 10.1021/ja307948m.

31. Ito, H.; Takagi, K.; Miyahara, T.; Sawamura, M., Gold(I)-phosphine catalyst for the highly chemoselective dehydrogenative silylation of alcohols. *Organic Letters* **2005,** *7* (14), 3001-3004. DOI: 10.1021/ol050979z.

32. Ito, H.; Saito, T.; Miyahara, T.; Zhong, C.; Sawamura, M., Gold(I) Hydride Intermediate in Catalysis: Dehydrogenative Alcohol Silylation Catalyzed by Gold(I) Complex. *Organometallics* **2009,** *28* (16), 4829-4840. DOI: 10.1021/om900445w.

33. Ji, K.; Zhao, Y.; Zhang, L., Optimizing P,N-Bidentate Ligands for Oxidative Gold Catalysis: Efficient Intermolecular Trapping of alpha-Oxo Gold Carbenes by Carboxylic Acids. *Angewandte Chemie-International Edition* **2013,** *52* (25), 6508-6512. DOI: 10.1002/anie.201301601.

34. Fors, B. P.; Watson, D. A.; Biscoe, M. R.; Buchwald, S. L., A highly active catalyst for Pd-catalyzed amination reactions: Cross-coupling reactions using aryl mesylates and the highly selective monoarylation of primary amines using aryl chlorides. *Journal of the American Chemical Society* **2008,** *130* (41), 13552-+. DOI: 10.1021/ja8055358.

35. Anderson, K. W.; Tundel, R. E.; Ikawa, T.; Altman, R. A.; Buchwald, S. L., Monodentate phosphines provide highly active catalysts for Pd-catalyzed C-N bond-

forming reactions of heteroaromatic halides/amines and (H)N-heterocycles. *Angewandte Chemie-International Edition* **2006,** *45* (39), 6523-6527. DOI: 10.1002/anie.200601612.

36. Billingsley, K.; Buchwald, S. L., Highly efficient monophosphine-based catalyst for the palladium-catalyzed Suzuki-Miyaura reaction of heteroaryl halides and heteroaryl boronic acids and esters. *Journal of the American Chemical Society* **2007,** *129* (11), 3358-3366. DOI: 10.1021/ja068577p.

37. Mauger, C. C.; Mignani, G. A., Synthetic applications of Buchwald's phosphines in palladium-catalyzed aromatic-bond-forming reactions. *Aldrichimica Acta* **2006,** *39* (1), 17-24.

38. Schlummer, B.; Scholz, U., Palladium-catalyzed C-N and C-O coupling - A practical guide from an industrial vantage point. *Advanced Synthesis & Catalysis* **2004,** *346* (13-15), 1599-1626. DOI: 10.1002/adsc.200404216.

39. Ye, L.; He, W.; Zhang, L., A Flexible and Stereoselective Synthesis of Azetidin-3-ones through Gold-Catalyzed Intermolecular Oxidation of Alkynes. *Angewandte Chemie-International Edition* **2011,** *50* (14), 3236-3239. DOI: 10.1002/anie.201007624.

40. Wang, Y.; Ji, K.; Lan, S.; Zhang, L., Rapid Access to Chroman-3-ones through Gold-Catalyzed Oxidation of Propargyl Aryl Ethers. *Angewandte Chemie-International Edition* **2012,** *51* (8), 1915-1918. DOI: 10.1002/anie.201107561.

41. Nieto-Oberhuber, C.; Lopez, S.; Echavarren, A. M., Intramolecular 4+2 cycloadditions of 1,3-enynes or arylalkynes with alkenes with highly reactive cationic phosphine Au(I) complexes. *Journal of the American Chemical Society* **2005,** *127* (17), 6178-6179. DOI: 10.1021/ja042257t.

42. Leyva, A.; Corma, A., Isolable Gold(I) Complexes Having One Low-Coordinating Ligand as Catalysts for the Selective Hydration of Substituted Alkynes at Room Temperature without Acidic Promoters. *Journal of Organic Chemistry* **2009,** *74* (5), 2067-2074. DOI: 10.1021/jo802558e.

43. Wang, C.; Han, Z.-Y.; Luo, H.-W.; Gong, L.-Z., Highly Enantioselective Relay Catalysis in the Three-Component Reaction for Direct Construction of Structurally Complex Heterocycles. *Organic Letters* **2010,** *12* (10), 2266-2269. DOI: 10.1021/ol1006086.

44. Lopez-Carrillo, V.; Echavarren, A. M., Gold(I)-Catalyzed Intermolecular 2+2 Cycloaddition of Alkynes with Alkenes. *Journal of the American Chemical Society* **2010,** *132* (27), 9292-9294. DOI: 10.1021/ja104177w.

45. Wang, T.; Zhang, J., Chemoselective C-C Bond Cleavage of Epoxide Motifs: Gold(I)-Catalyzed Diastereoselective 4+3 Cycloadditions of 1-(1-Alkynyl)oxiranyl Ketones and Nitrones. *Chemistry-a European Journal* **2011,** *17* (1), 86-90. DOI: 10.1002/chem.201002395.

46. Barabe, F.; Levesque, P.; Korobkov, I.; Barriault, L., Synthesis of Fused Carbocycles via a Selective 6-Endo Dig Gold(I)-Catalyzed Carbocyclization. *Organic Letters* **2011,** *13* (20), 5580-5583. DOI: 10.1021/ol202314q.

47. Henrion, G.; Chavas, T. E. J.; Le Goff, X.; Gagosz, F., Biarylphosphonite Gold(I) Complexes as Superior Catalysts for Oxidative Cyclization of Propynyl Arenes into Indan-2-ones. *Angewandte Chemie-International Edition* **2013,** *52* (24), 6277-6282. DOI: 10.1002/anie.201301015.

48. Anderson, K. W.; Buchwald, S. L., General catalysts for the Suzuki-Miyaura and Sonogashira coupling reactions of aryl chlorides and for the coupling of challenging substrate combinations in water. *Angewandte Chemie-International Edition* **2005,** *44* (38), 6173-6177. DOI: 10.1002/anie.200502017.

49. Li, J.; Ji, K.; Zheng, R.; Nelson, J.; Zhang, L., Expanding the horizon of intermolecular trapping of in situ generated alpha-oxo gold carbenes: efficient oxidative union of allylic sulfides and terminal alkynes via C-C bond formation. *Chem Commun (Camb)* **2014,** *50* (31), 4130-3. DOI: 10.1039/c4cc00739e.

50. Wang, Y.; Wang, Z.; Li, Y.; Wu, G.; Cao, Z.; Zhang, L., A general ligand design for gold catalysis allowing ligand-directed anti-nucleophilic attack of alkynes. *Nature Communications* **2014,** *5*. DOI: 10.1038/ncomms4470.

51. Brown, T. J.; Dickens, M. G.; Widenhoefer, R. A., Syntheses, X-ray Crystal Structures, and Solution Behavior of Monomeric, Cationic, Two-Coordinate Gold(I) pi-Alkene Complexes. *Journal of the American Chemical Society* **2009,** *131* (18), 6350-+. DOI: 10.1021/ja90115827.

52. Yang, C. G.; He, C., Gold(I)-catalyzed intermolecular addition of phenols and carboxylic acids to olefins. *Journal of the American Chemical Society* **2005,** *127* (19), 6966-6967. DOI: 10.1021/ja050392f.

53. Bruice, T. C.; Bruno, J. J.; Brandon, N. E.; Fife, T. H., HYDROXYL GROUP CATALYSIS .2. REACTIVITY OF HYDROXYL GROUP OF SERINE - NUCLEOPHILICITY OF ALCOHOLS AND EASE OF HYDROLYSIS OF THEIR ACETYL ESTERS AS RELATED TO THEIR PKA. *Biochemistry* **1962,** *1* (1), 7-&. DOI: 10.1021/bi00907a002.

54. Ye, L.; Cui, L.; Zhang, G.; Zhang, L., Alkynes as Equivalents of alpha-Diazo Ketones in Generating alpha-Oxo Metal Carbenes: A Gold-Catalyzed Expedient Synthesis of Dihydrofuran-3-ones. *Journal of the American Chemical Society* **2010,** *132* (10), 3258-+. DOI: 10.1021/ja100041e.

55. Ji, K.; Nelson, J.; Zhang, L., Gold-catalyzed regioselective oxidation of propargylic carboxylates: a reliable access to alpha-carboxy-alpha,beta-unsaturated ketones/aldehydes. *Beilstein J Org Chem* **2013,** *9*, 1925-30. DOI: 10.3762/bjoc.9.227.

56. Mamane, V.; Gress, T.; Krause, H.; Furstner, A., Platinum- and gold-catalyzed cycloisomerization reactions of hydroxylated enynes. *Journal of the American Chemical Society* **2004,** *126* (28), 8654-8655. DOI: 10.1021/ja048094q.

57. Harrak, Y.; Blaszykowski, C.; Bernard, M.; Cariou, K.; Mainetti, E.; Mouries, V.; Dhimane, A. L.; Fensterbank, L.; Malacria, M., PtCl2-catalyzed cycloisomerizations of 5-En-1-yn-3-ol systems. *Journal of the American Chemical Society* **2004,** *126* (28), 8656-8657. DOI: 10.1021/ja0474695.

58. Lu, B.; Li, C.; Zhang, L., Gold-Catalyzed Highly Regioselective Oxidation of C-C Triple Bonds without Acid Additives: Propargyl Moieties as Masked alpha,beta-Unsaturated Carbonyls. *Journal of the American Chemical Society* **2010,** *132* (40), 14070-14072. DOI: 10.1021/ja1072614.

59. Murai, M.; Kitabata, S.; Okamoto, K.; Ohe, K., Gold-catalysed cycloisomerisation reactions of 2-(2-propynyl)pyridine N-oxides leading to indolizinones. *Chemical Communications* **2012,** *48* (61), 7622-7624. DOI: 10.1039/c2cc32628k.

60. Ji, K.; D'Souza, B.; Nelson, J.; Zhang, L., Gold-Catalyzed Oxidation of Propargylic Ethers with Internal C-C Triple Bonds: Impressive Regioselectivity Enabled by Inductive Effect. *J Organomet Chem* **2014,** *770*, 142-145. DOI: 10.1016/j.jorganchem.2014.08.005.

61. Li, C.-W.; Pati, K.; Lin, G.-Y.; Abu Sohel, S. M.; Hung, H.-H.; Liu, R.-S., Gold-Catalyzed Oxidative Ring Expansions and Ring Cleavages of Alkynylcyclopropanes by Intermolecular Reactions Oxidized by Diphenylsulfoxide. *Angewandte Chemie-International Edition* **2010,** *49* (51), 9891-9894. DOI: 10.1002/anie.201004647.

62. Kraszkiewicz, L.; Sosnowski, M.; Skulski, L., Oxidative iodination of deactivated arenes in concentrated sulfuric acid with I-2/NaIO4 and KI/NaIO4 iodinating systems. *Synthesis-Stuttgart* **2006,** (7), 1195-1199. DOI: 10.1055/s-2006-926374.

63. Harkins, S. B.; Peters, J. C., Amido-bridged Cu2N2 diamond cores that minimize structural reorganization and facilitate reversible redox behavior between a Cu(1)Cu(1) and a class III delocalized Cu(1.5)Cu(1.5) species. *Journal of the American Chemical Society* **2004,** *126* (9), 2885-2893. DOI: 10.1021/ja037364m.

64. Khurana, J. M.; Chauhan, S.; Bansal, G., Facile hydrolysis of esters with KOH-methanol at ambient temperature. *Monatshefte Fur Chemie* **2004,** *135* (1), 83-87. DOI: 10.1007/s00706-003-0114-1.

65. Wang, S.; Zhang, L., A highly efficient preparative method of alpha-ylidene-beta-diketones via Au-III-catalyzed acyl migration of propargylic esters. *Journal of the American Chemical Society* **2006,** *128* (26), 8414-8415. DOI: 10.1021/ja062777j.

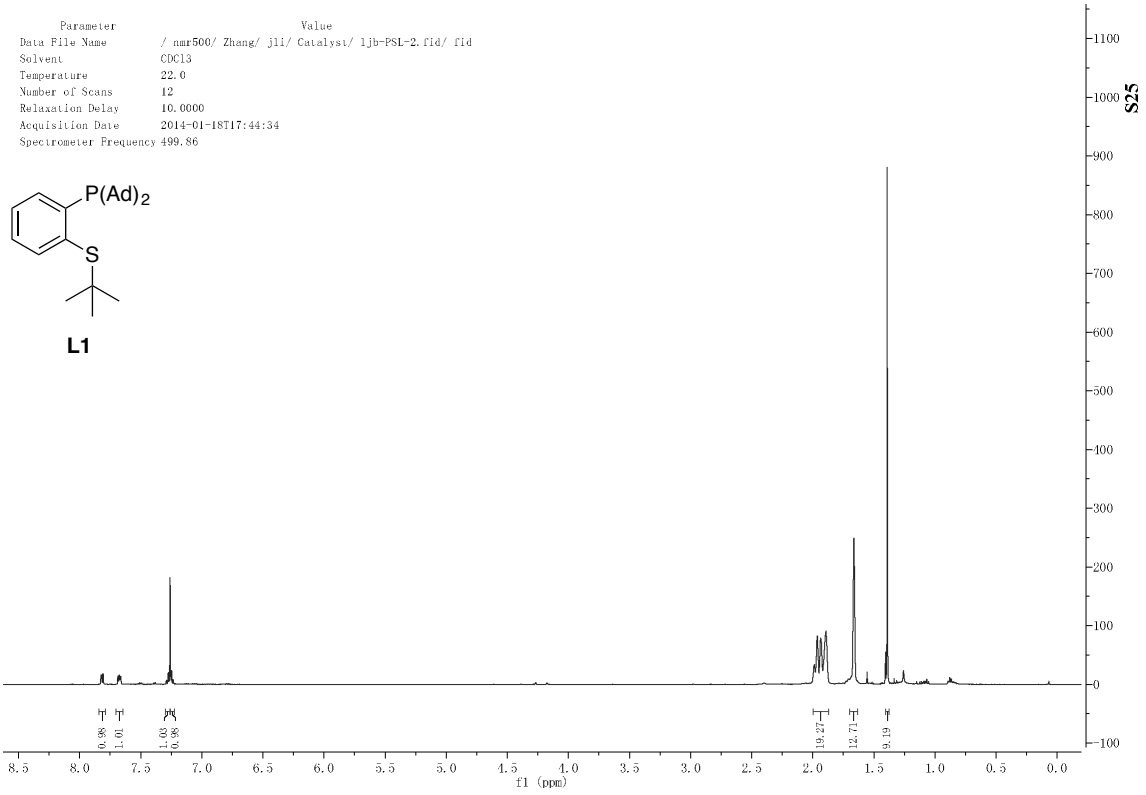
66. Kabalka, G. W.; Slayden, S., DIRECTIVE EFFECTS IN HYDROBORATION OF ISOMERIC METHOXY-2-HEXYNES. *Journal of Organometallic Chemistry* **1975,** *93* (1), 33-38. DOI: 10.1016/s0022-328x(00)94141-x.

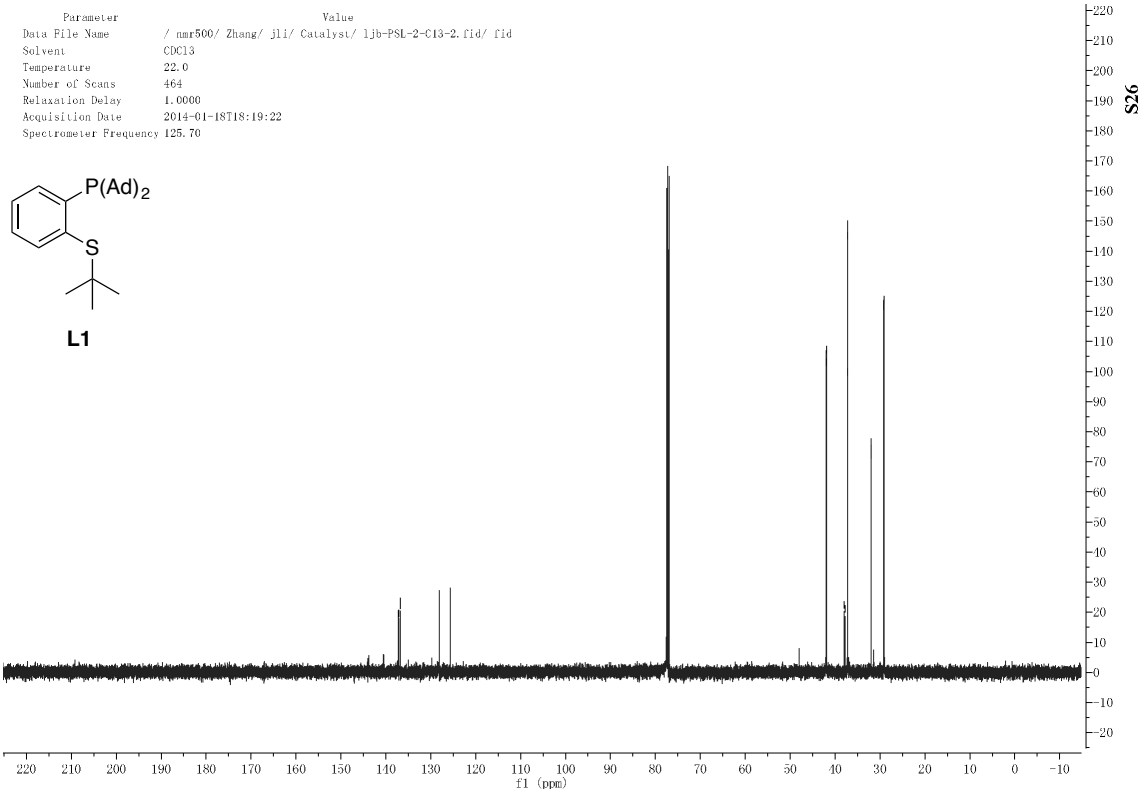
67. Tanaka, K.; Sasaki, K.; Takeishi, K.; Hirano, M., Cationic P(OPh)(3)- or PPh3-Rhodium(I) complex-catalyzed isomerizations of 5-alkynals to delta-alkynyl ketones, cyclopent-1-enyl ketones, and cyclohexenones. *European Journal of Organic Chemistry* **2007,** (34), 5675-5685. DOI: 10.1002/ejoc.200700550.

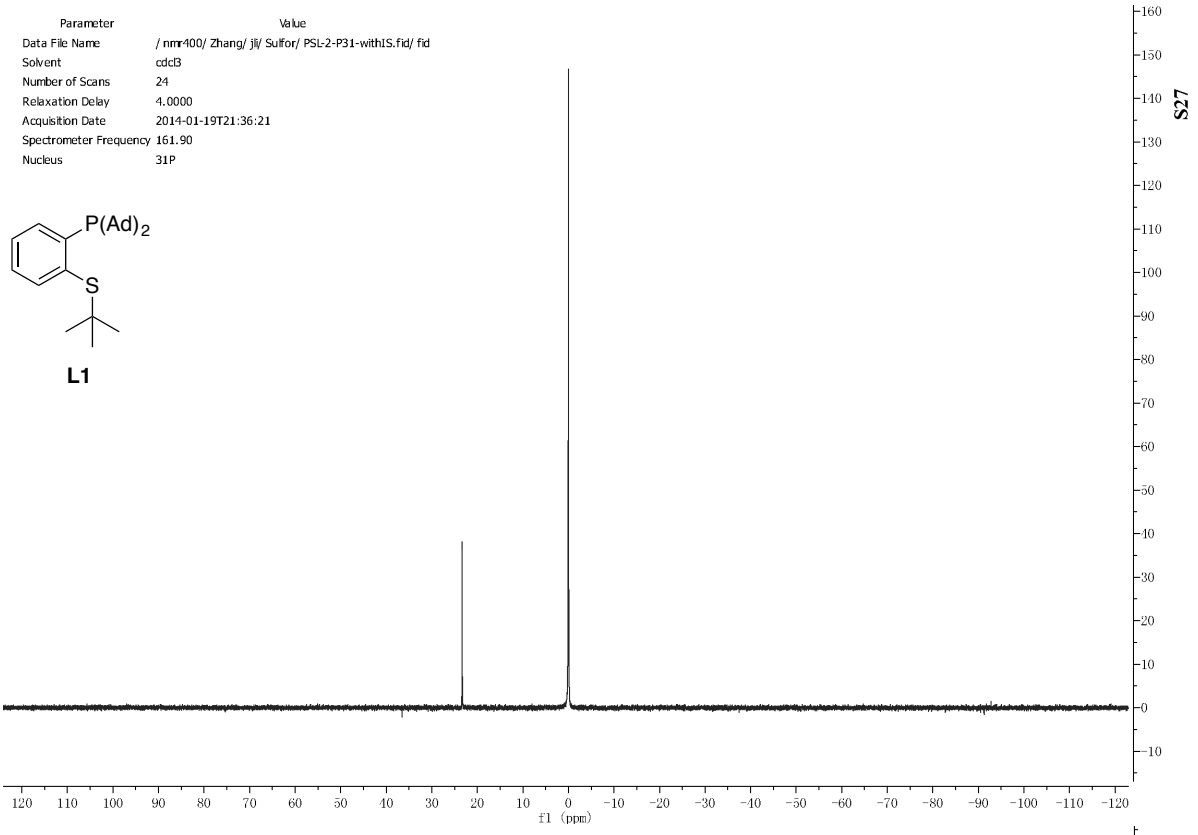
68. Salaun, J., PREPARATION AND SUBSTITUENT EFFECT IN SOLVOLYSIS OF 1-ETHYNYLCYCLOPROPYL TOSYLATES. *Journal of Organic Chemistry* **1976,** *41* (7), 1237-1240. DOI: 10.1021/jo00869a033.

69. Stork, G.; Takahashi, T.; Kawamoto, I.; Suzuki, T., Total synthesis of prostaglandin F2.alpha. by chirality transfer from D-glucose. *Journal of the American Chemical Society* **1978,** *100* (26), 8272-8273. DOI: 10.1021/ja00494a045.

8. Appendix: Selected NMR Spectra



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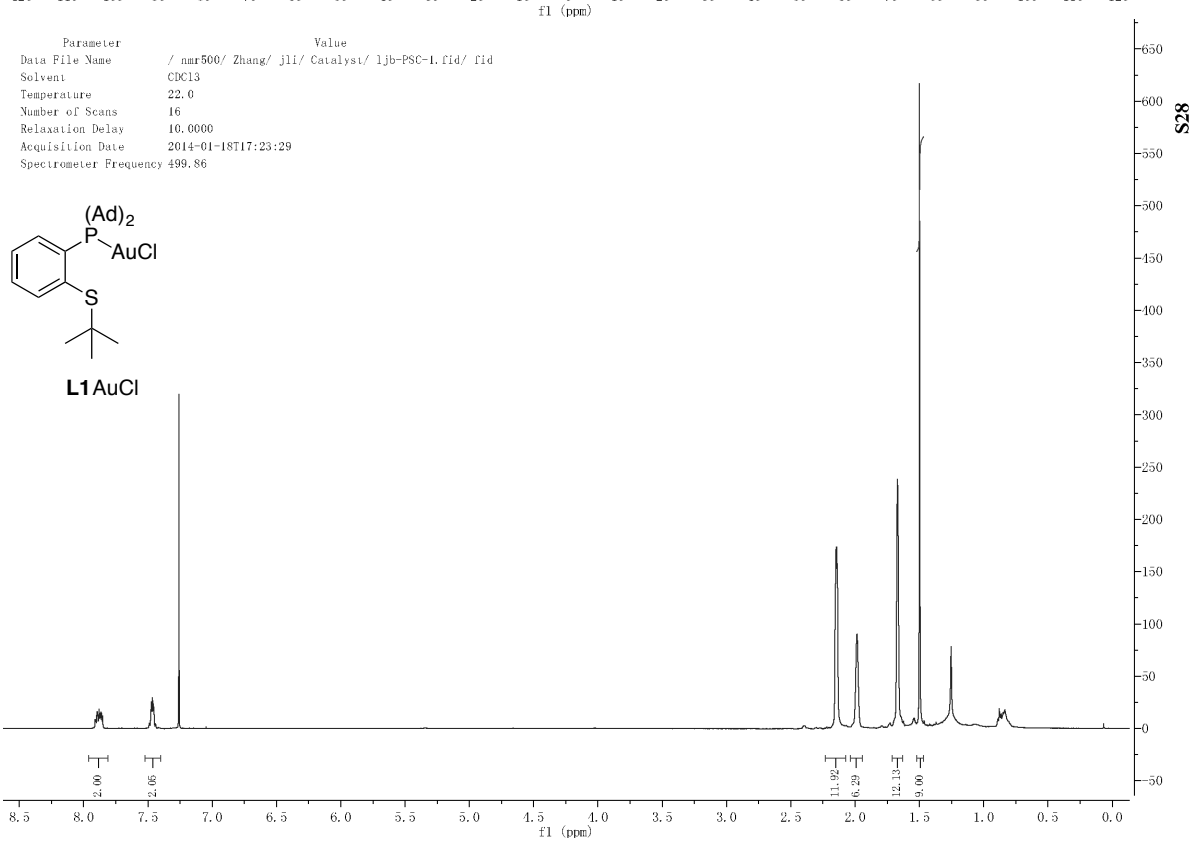
S
L1
f1 (ppm)

S27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Acquisition Date 2014-01-18T17:23:29
Spectrometer Frequency 499.86
(Ad)2
P
AuCl
S
L1AuCl
2.00
2.06
11.92
6.29
12.13
9.00
f1 (ppm)

S28

Parameter	Value
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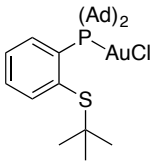

L1AuCl

S29

f1 (ppm)

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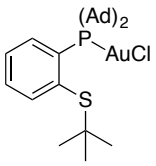
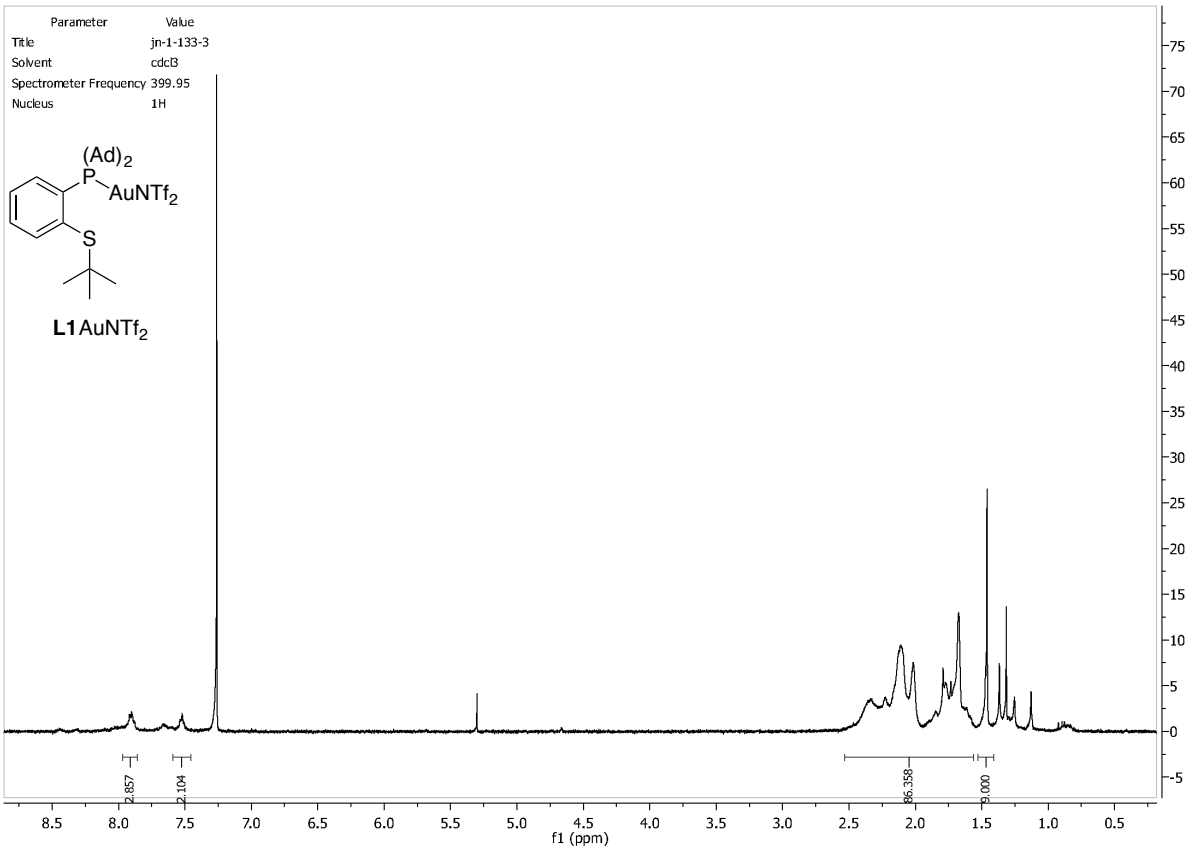
Nucleus	31P



L1AuCl

S30

f1 (ppm)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S
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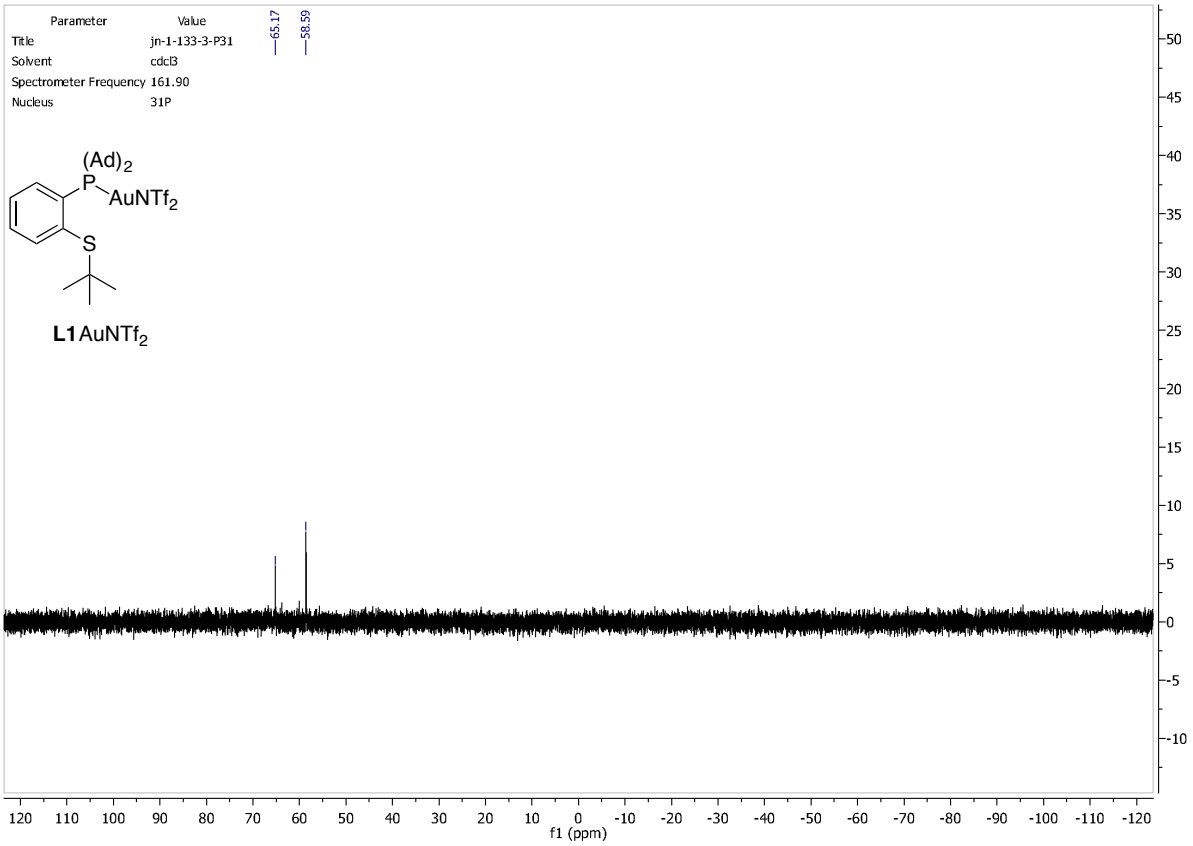
86.358
9.000
f1 (ppm)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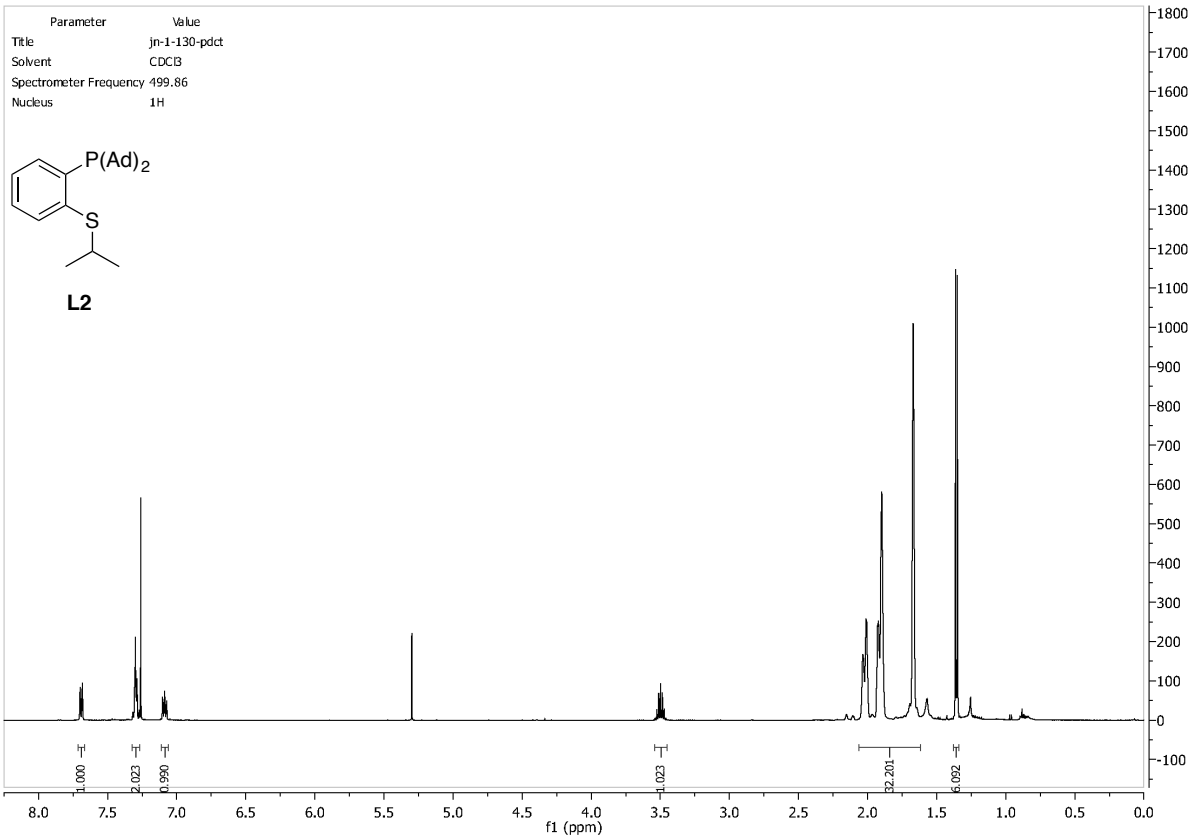
AuNTf2
S
L1AuNTf2
f1 (ppm)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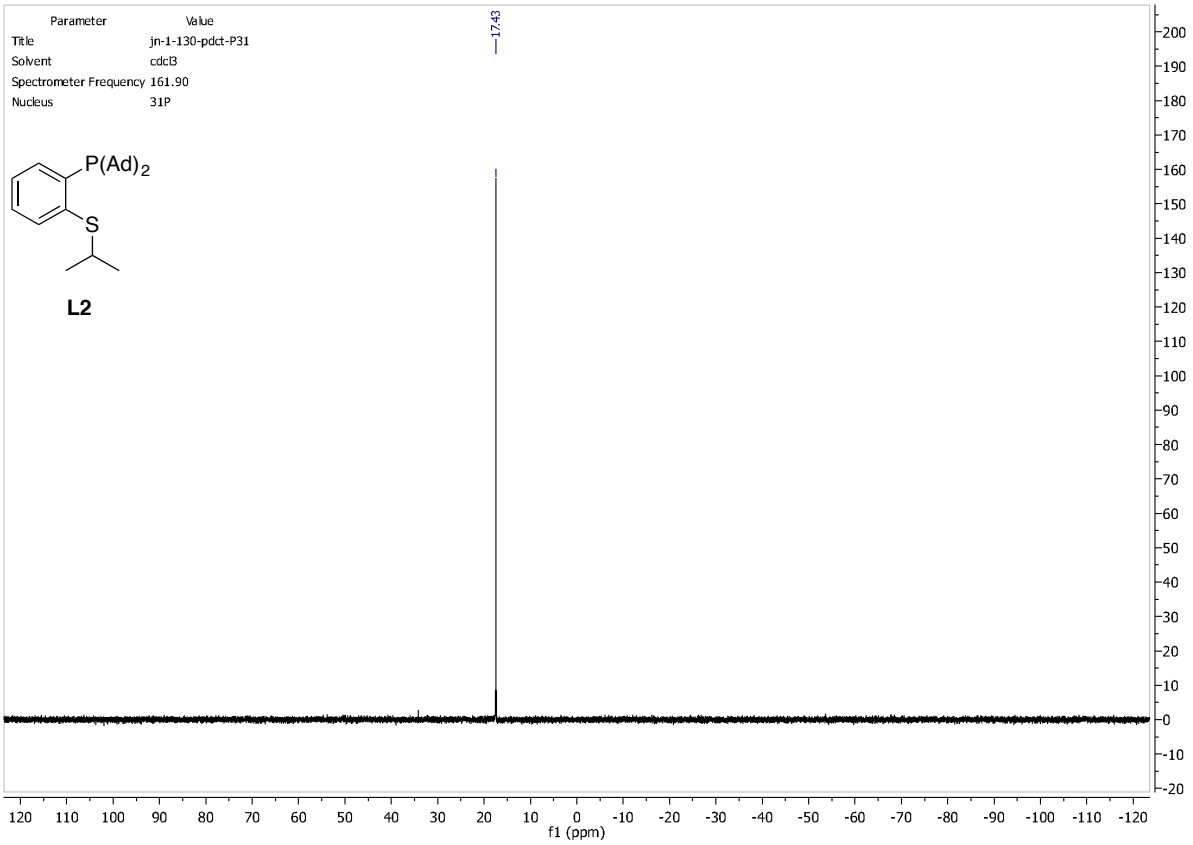
1.023
32.201
6.092
f1 (ppm)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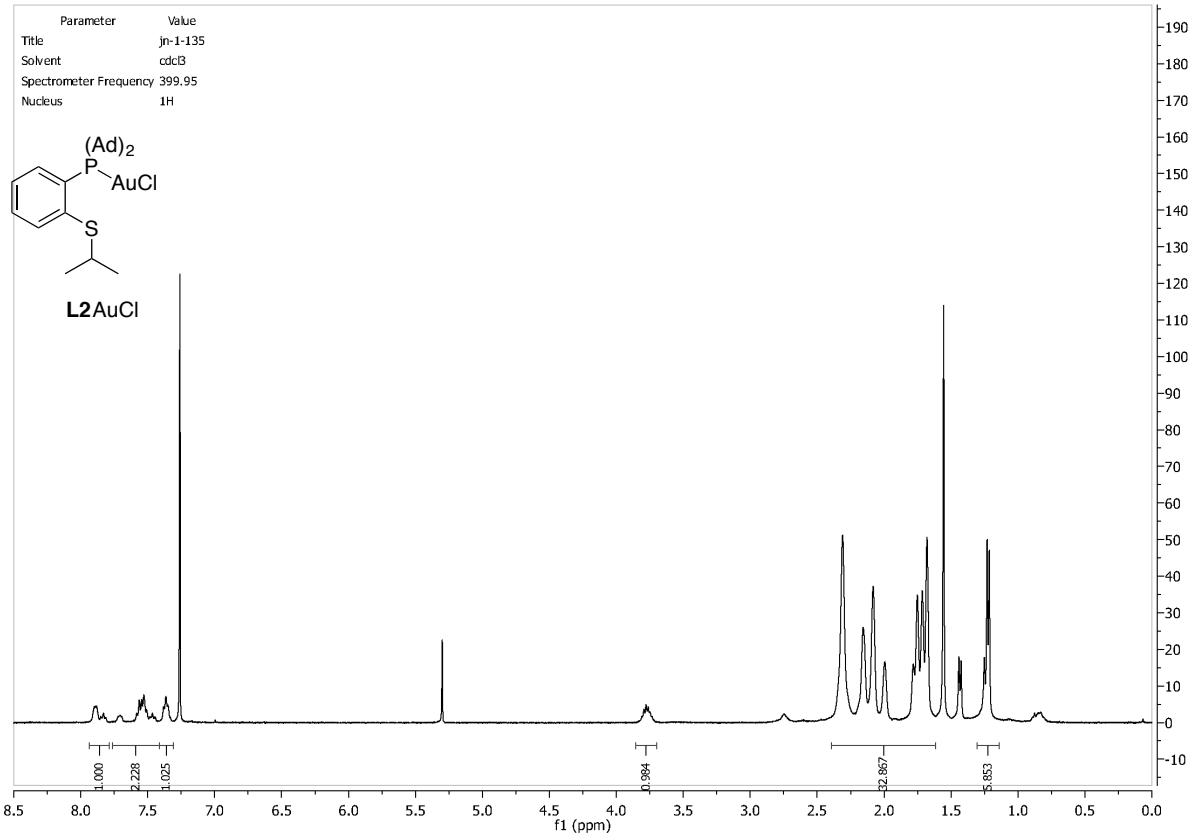
L2
f1 (ppm)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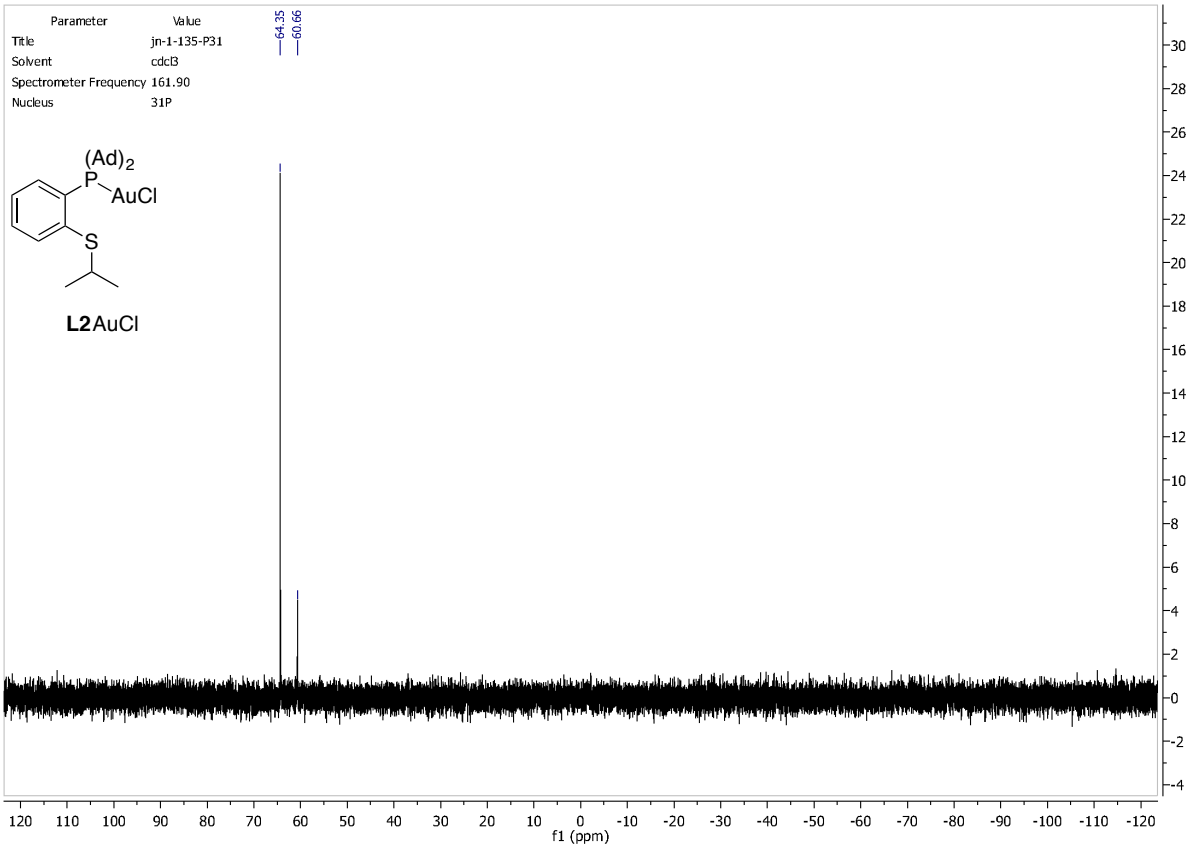
1.025
0.994
32.867
5.853
f1 (ppm)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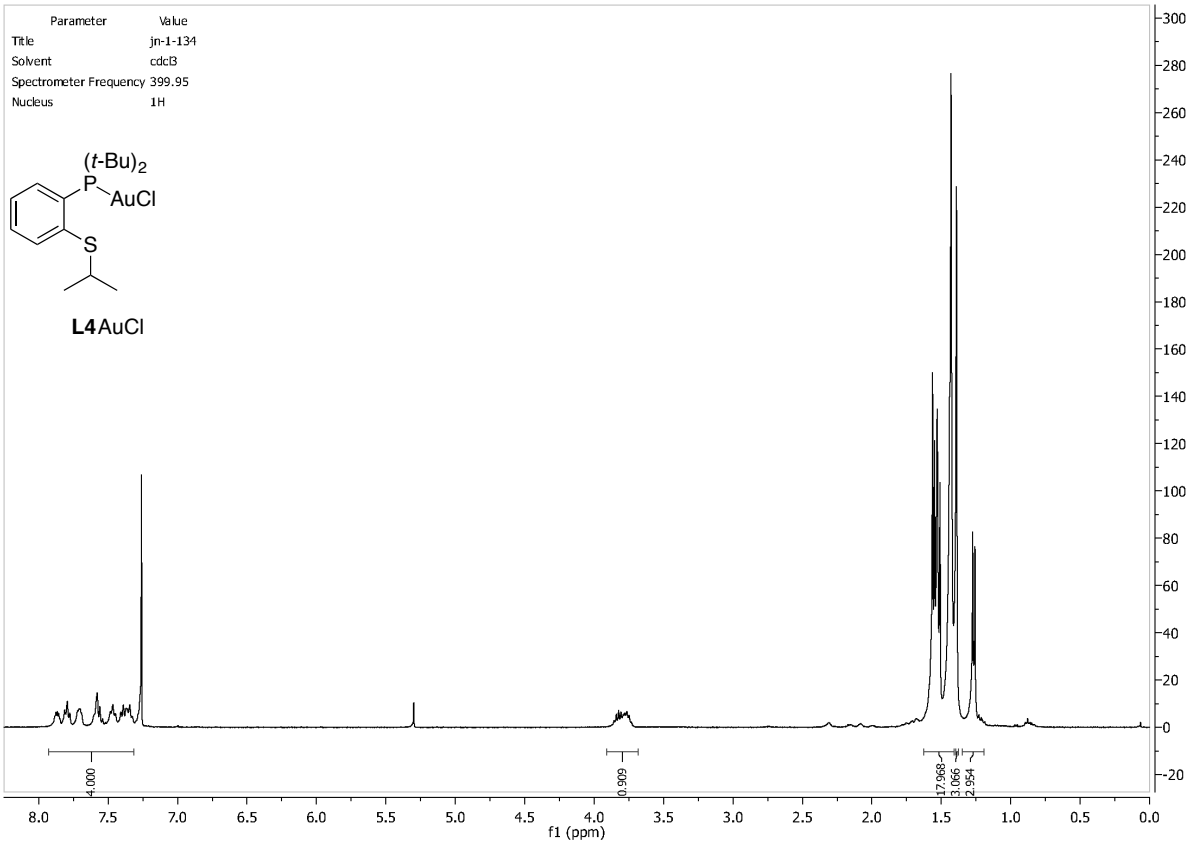
AuCl
S
L2AuCl
f1 (ppm)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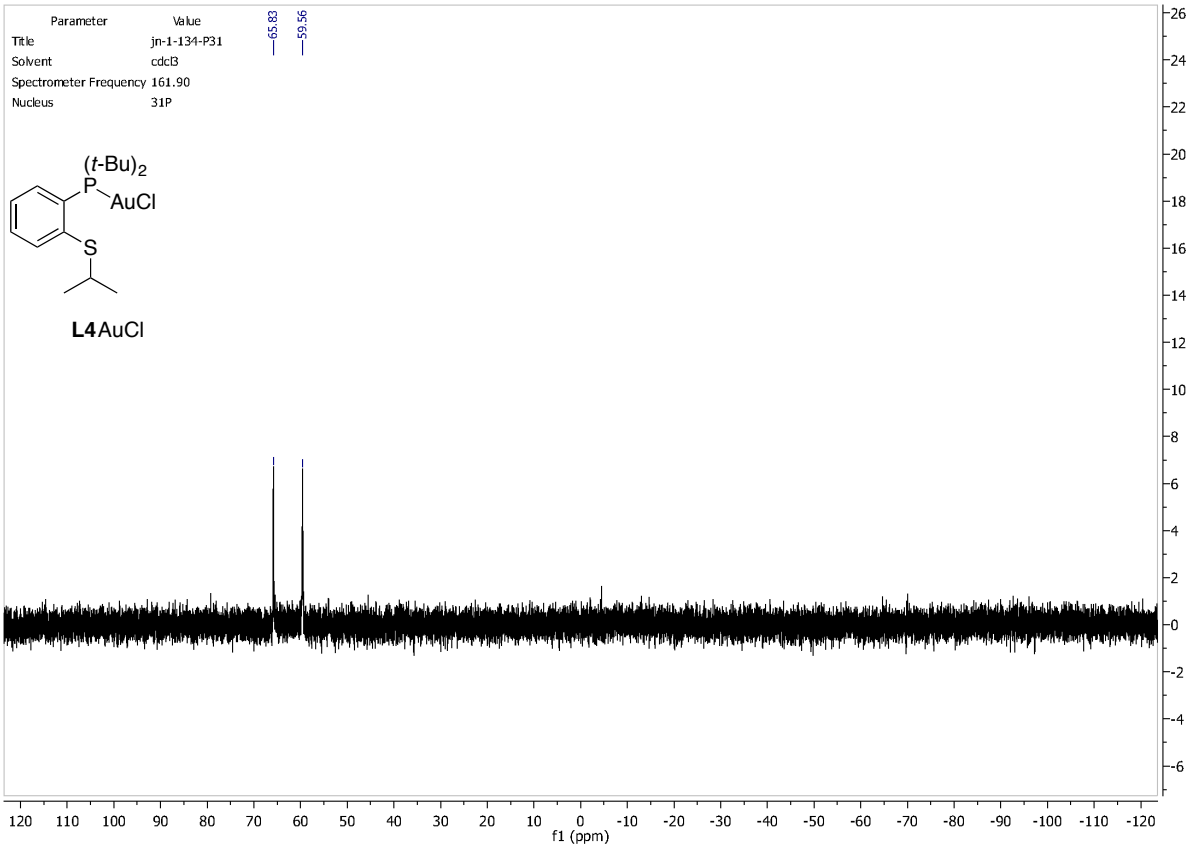
f1 (ppm)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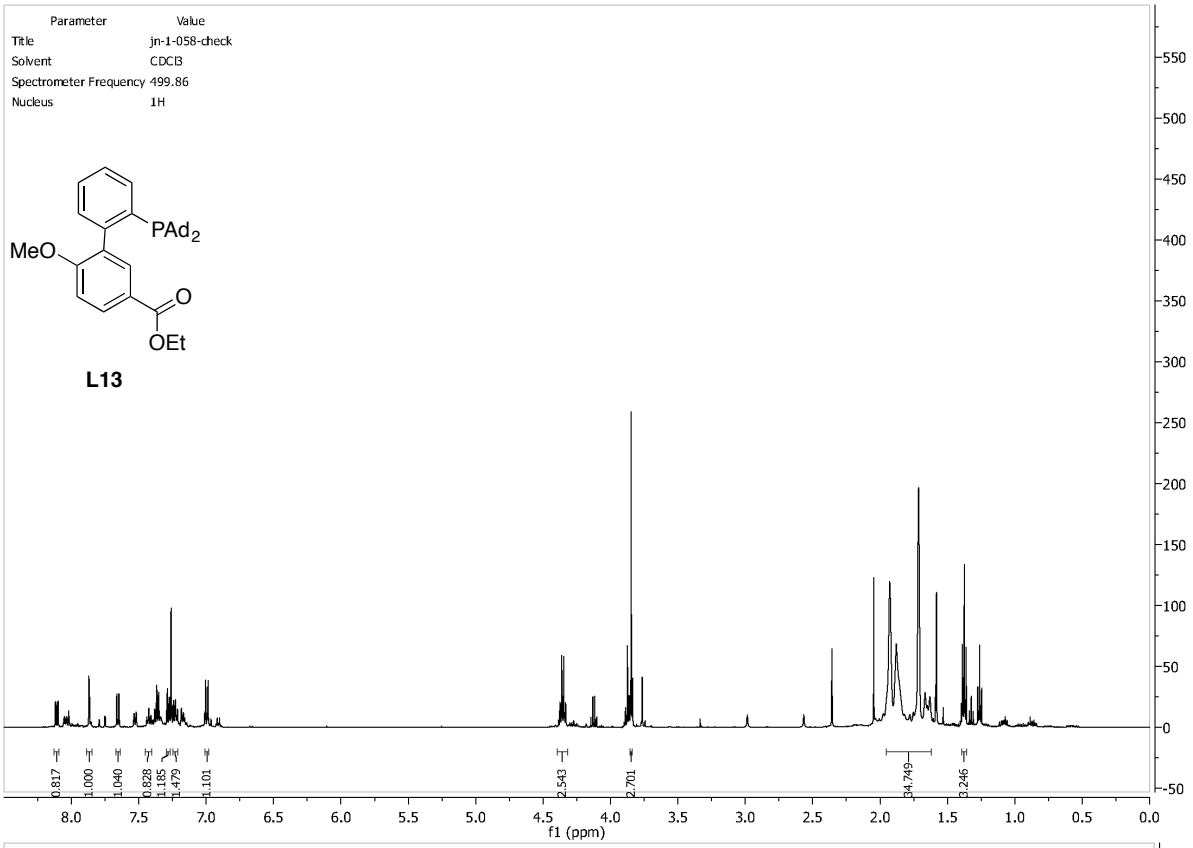
S
L4AuCl
f1 (ppm)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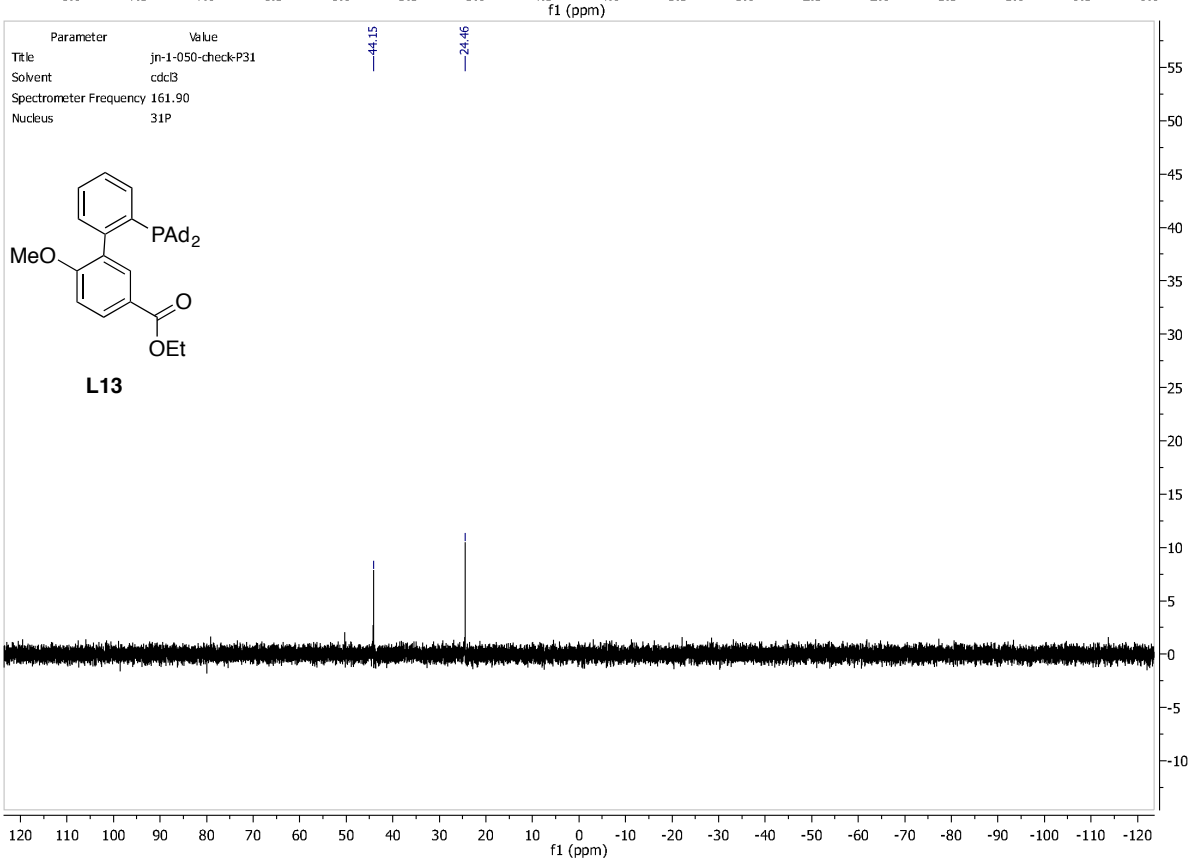
f1 (ppm)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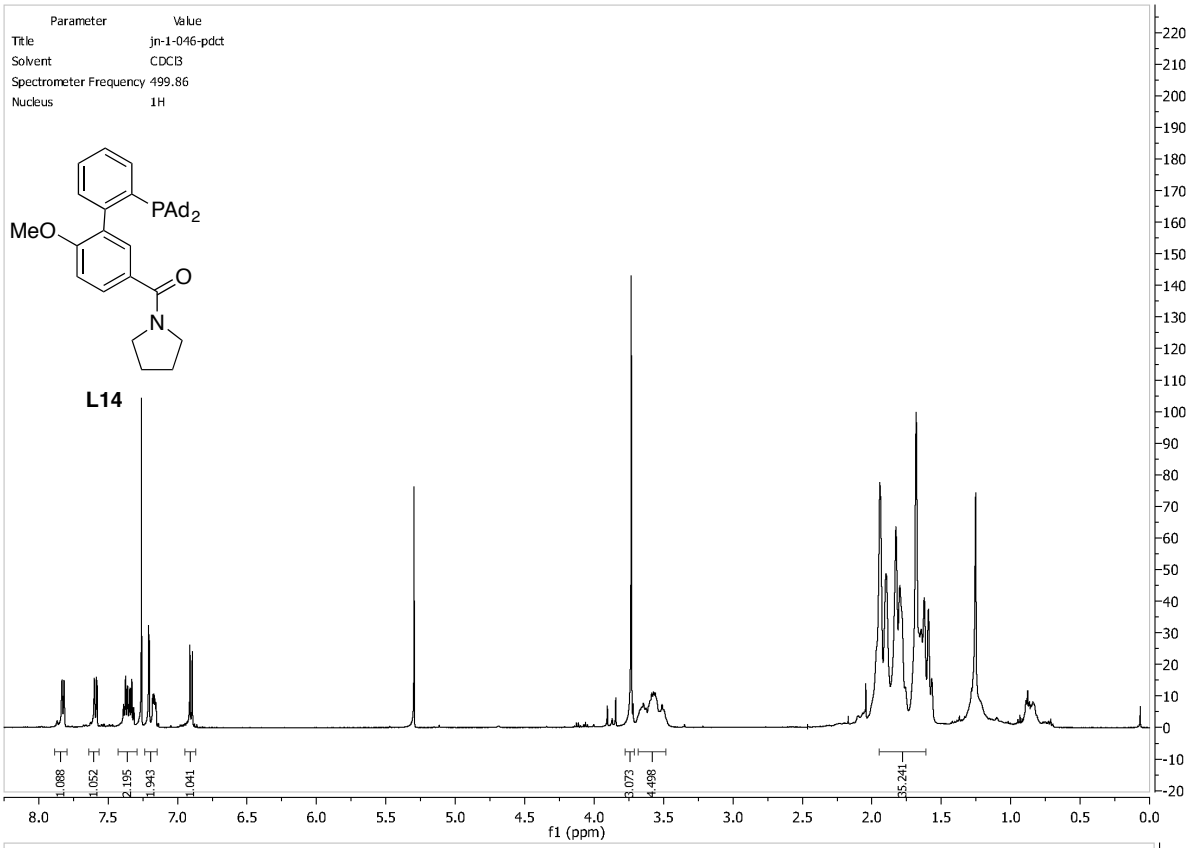
OEt
L13
f1 (ppm)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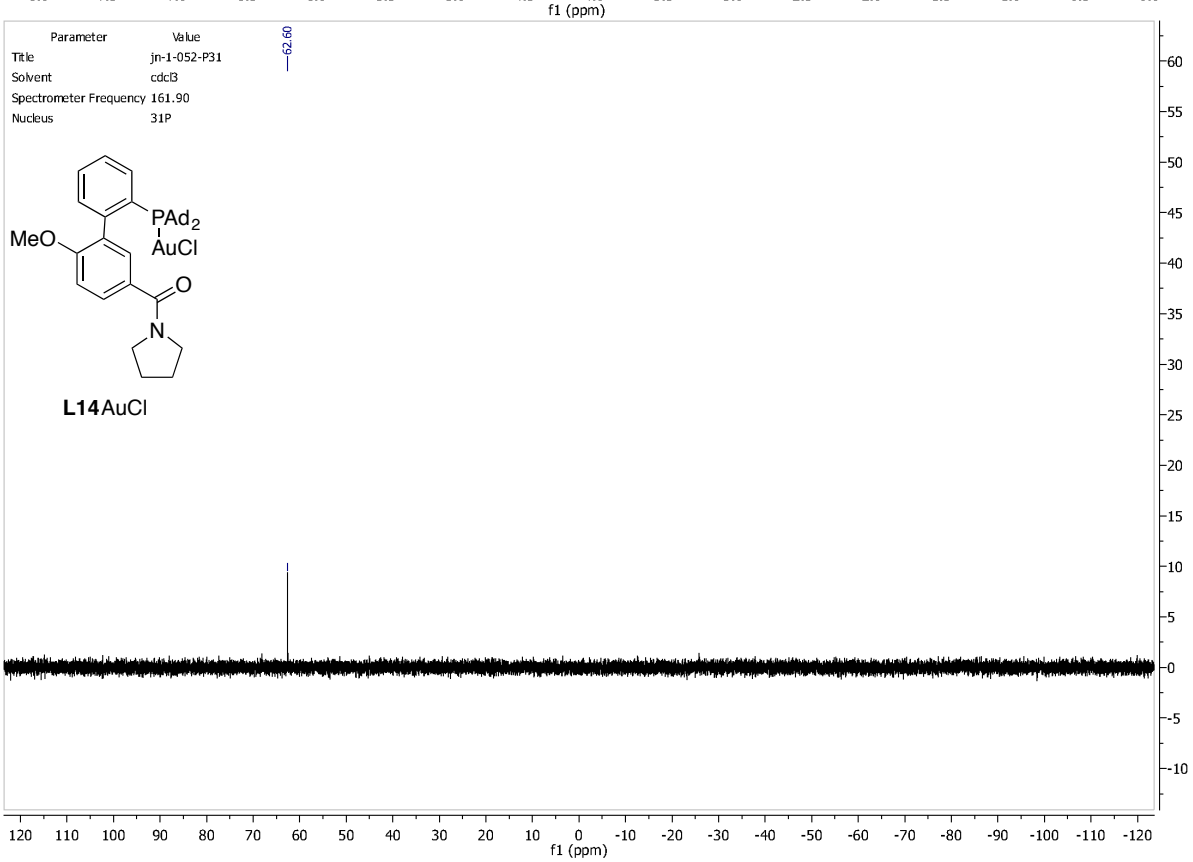
3.073
4.498
35.241
f1 (ppm)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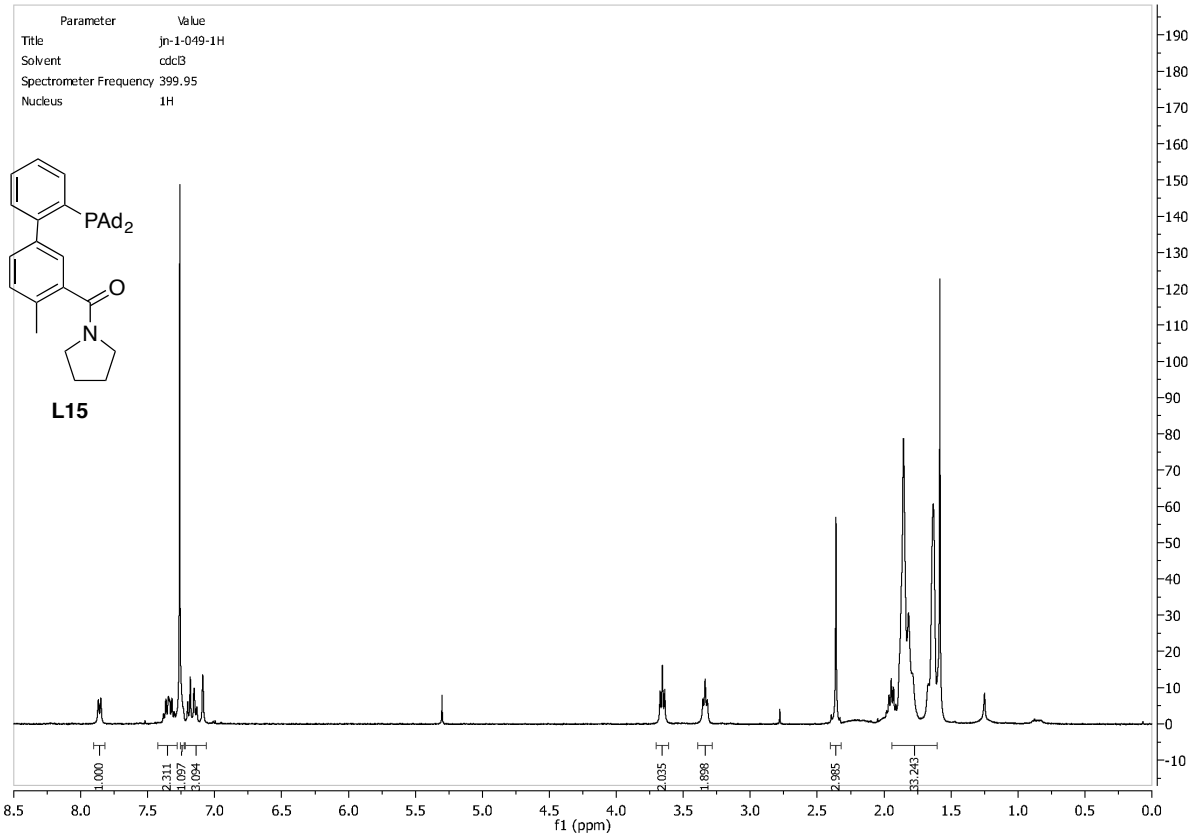
AuCl
MeO
O
N
L14AuCl
f1 (ppm)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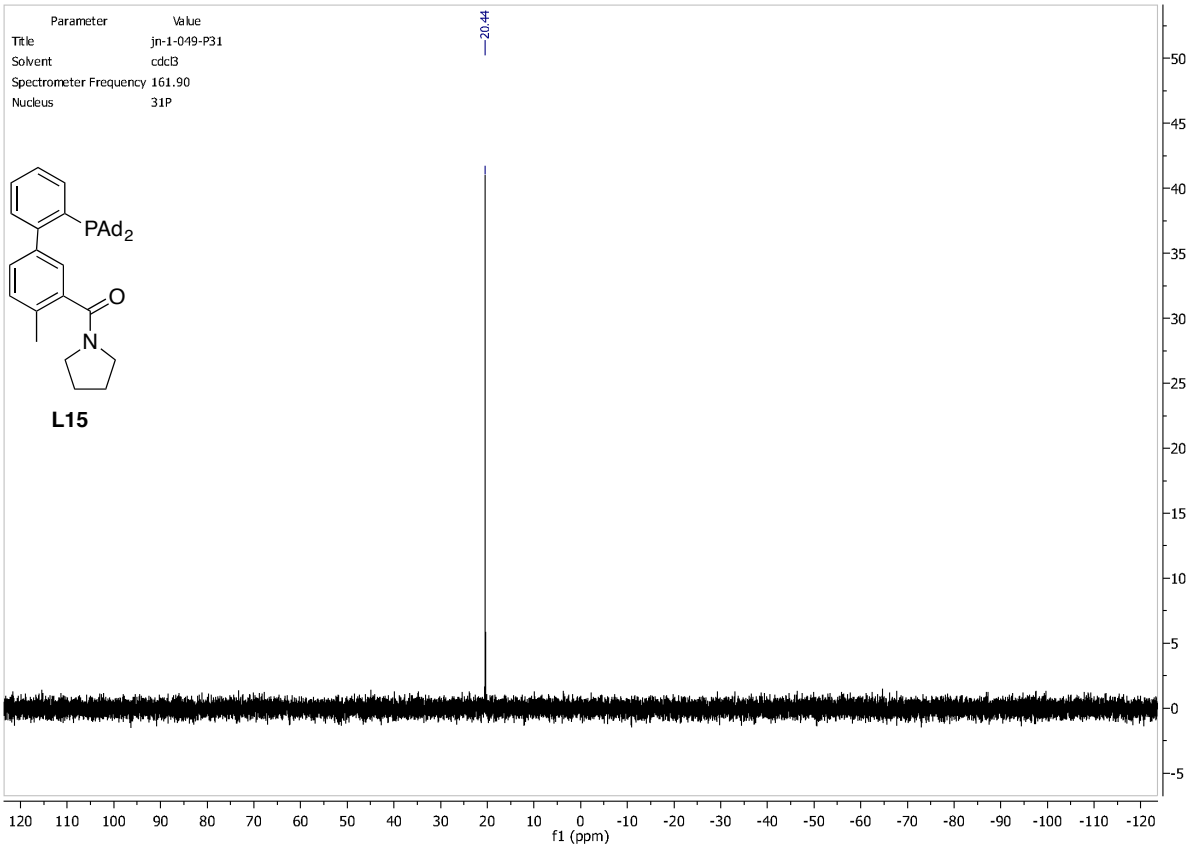
2.035
1.898
2.965
33.243
f1 (ppm)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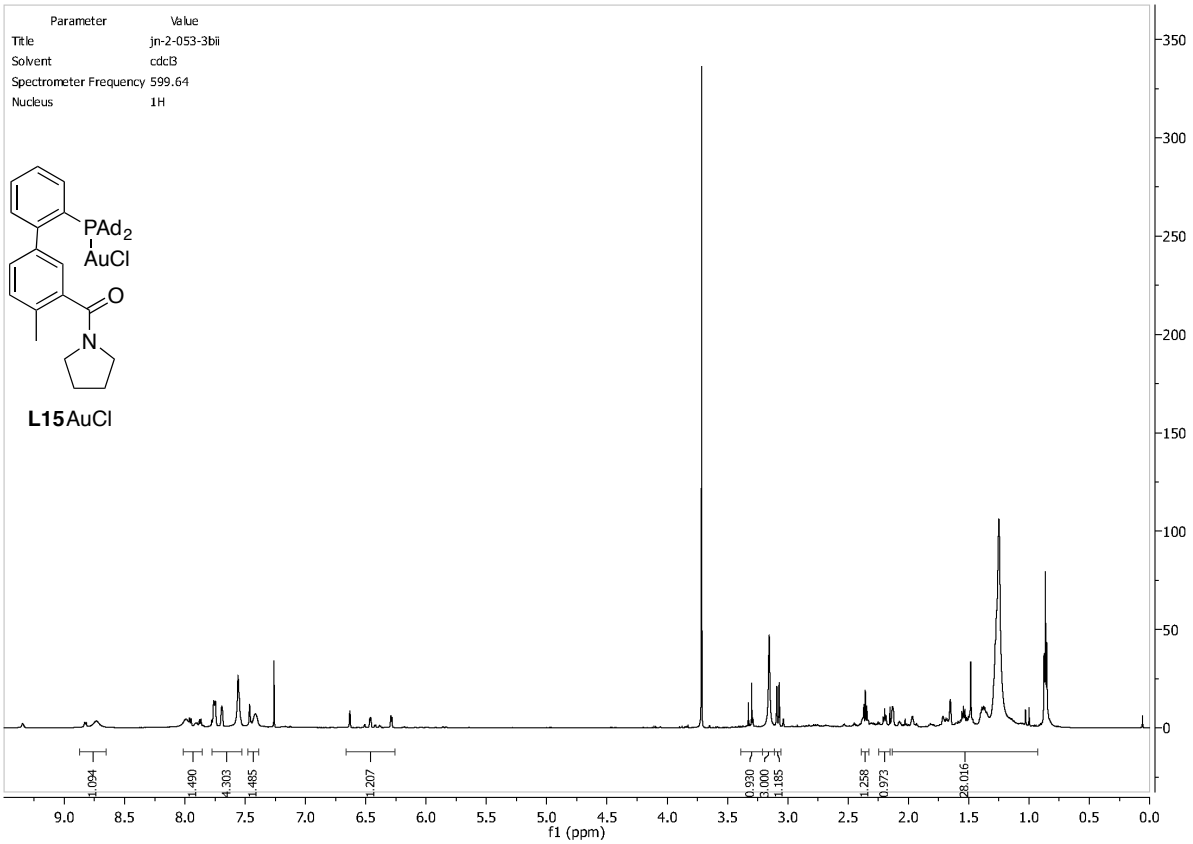
O
N
L15
f1 (ppm)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N
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1.485
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3.000
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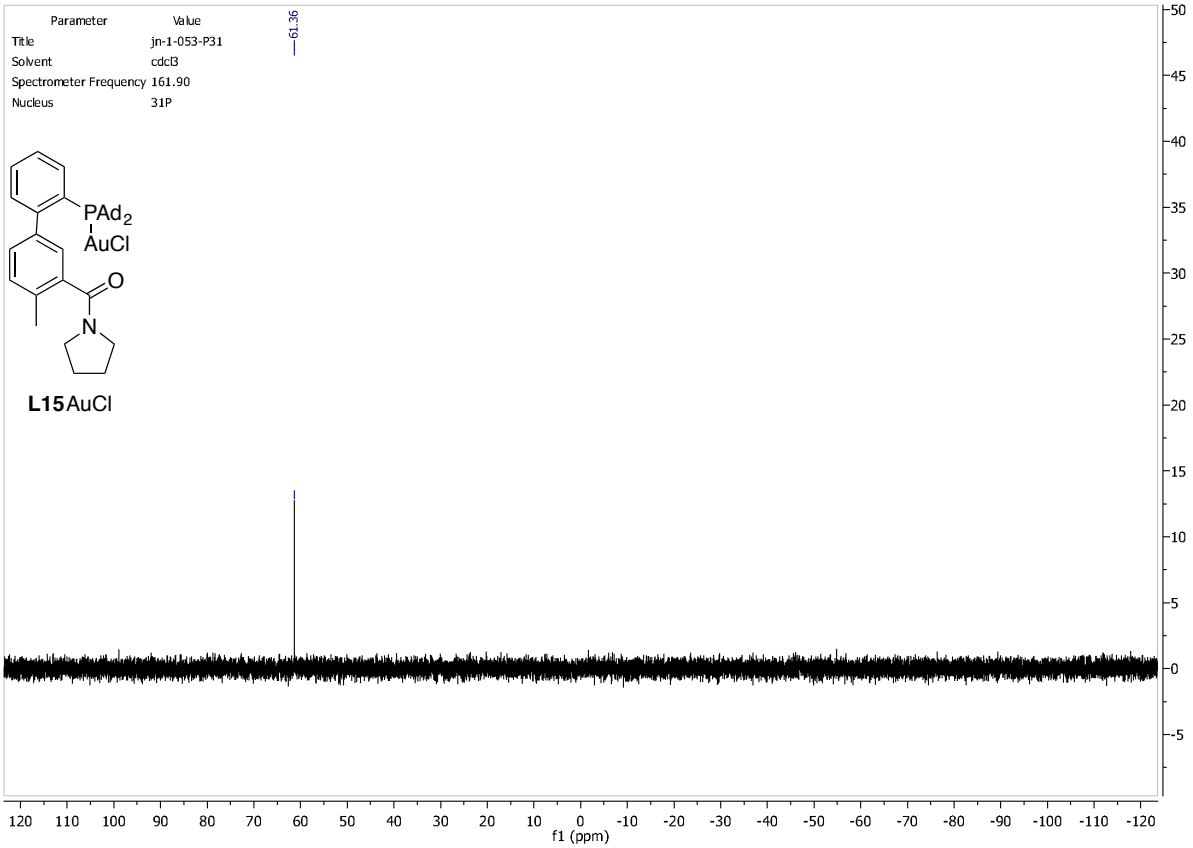
28.016
f1 (ppm)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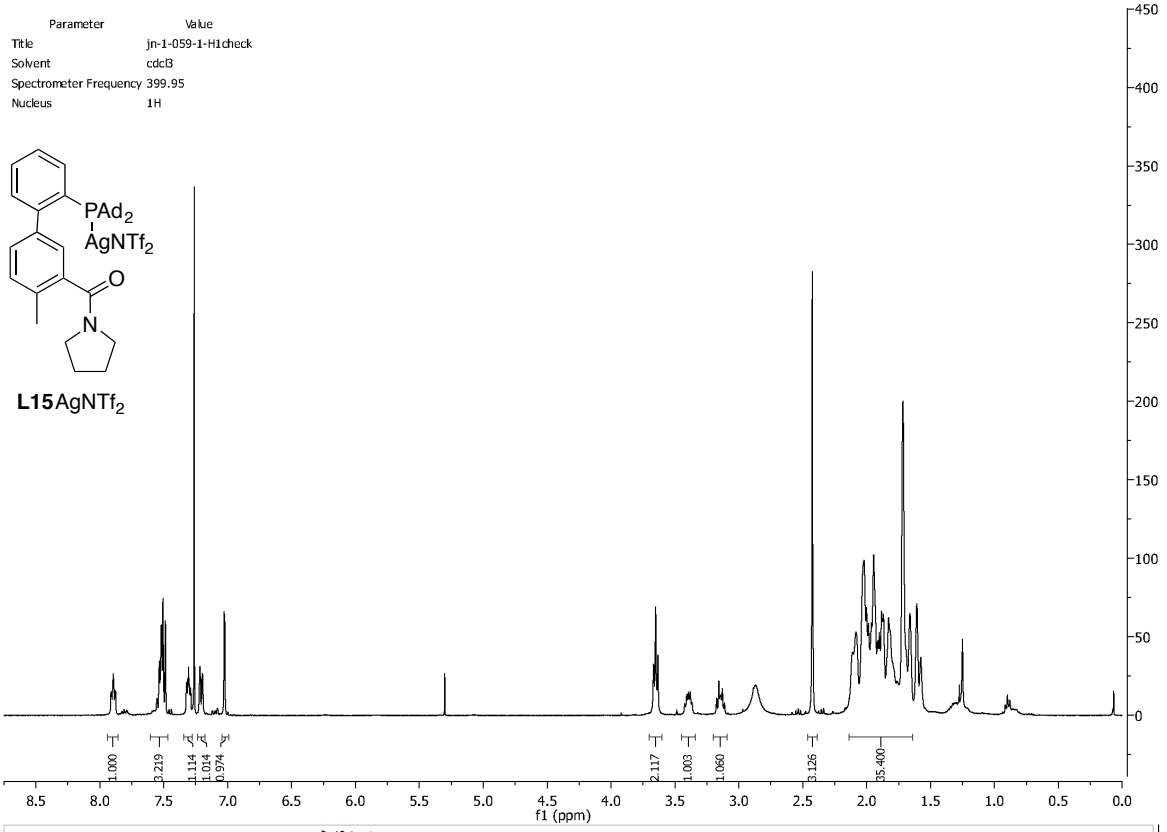
f1 (ppm)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O
N
L15AgNTf2
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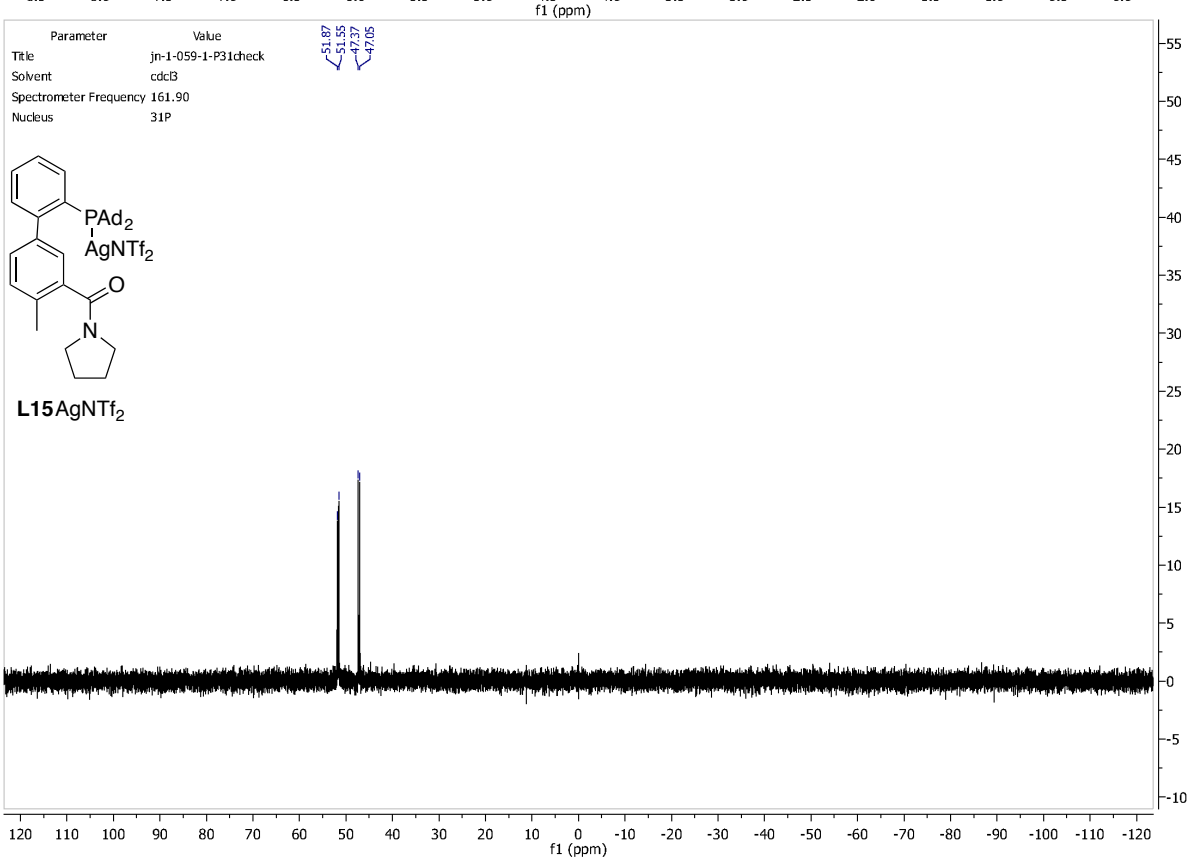
f1 (ppm)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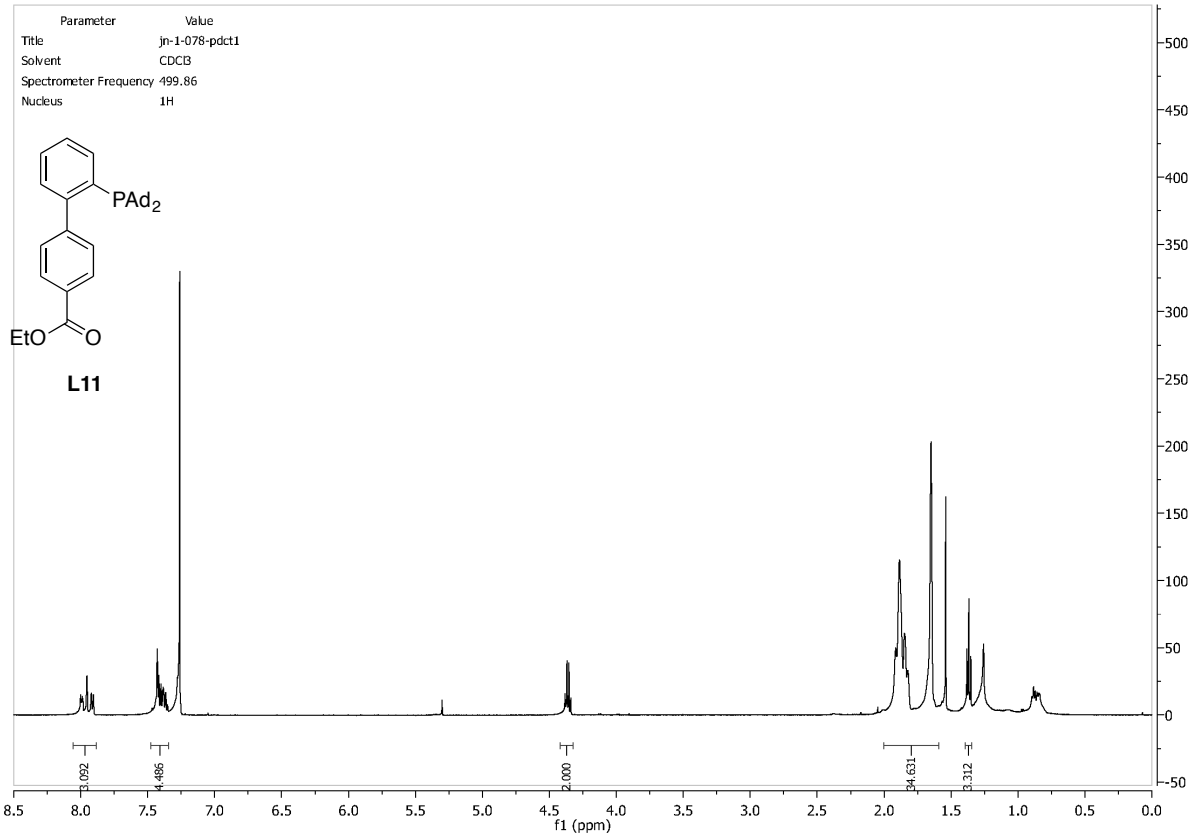
O
N
L15AgNTf2
f1 (ppm)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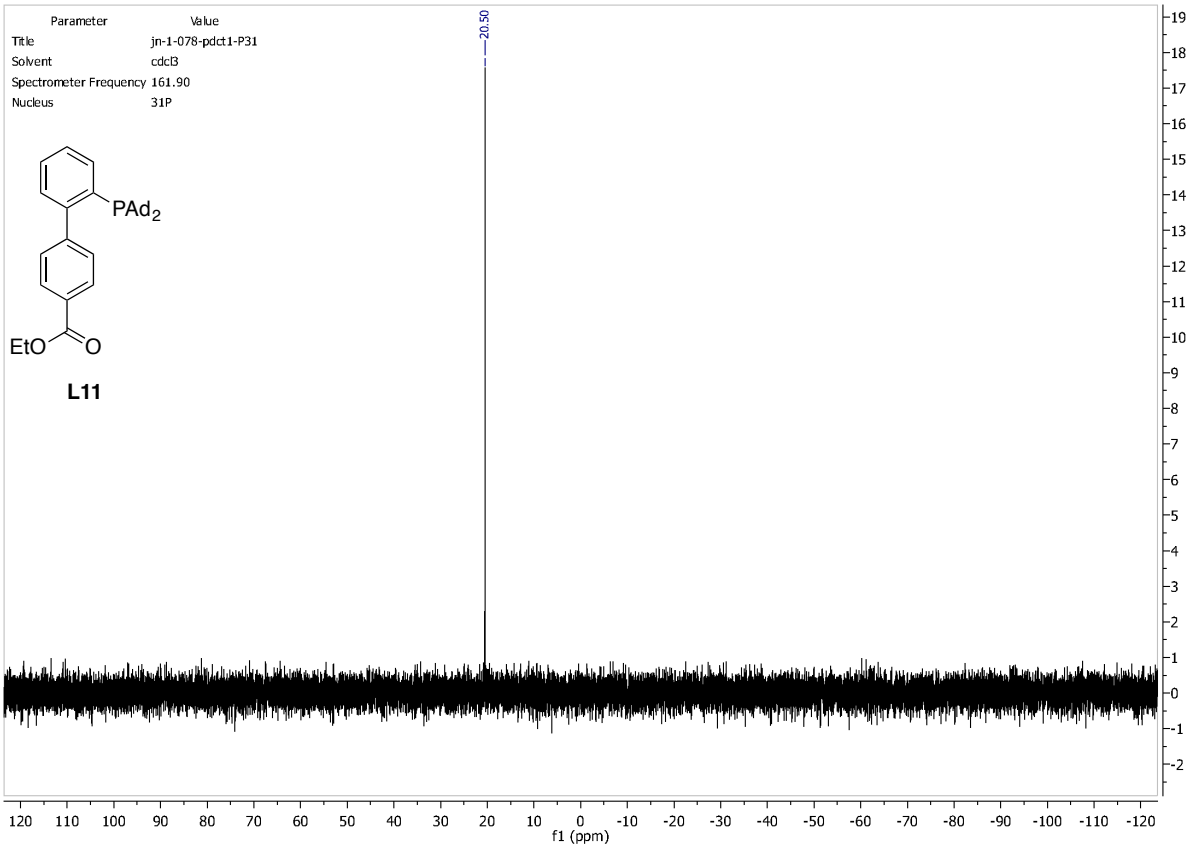
f1 (ppm)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O
L11
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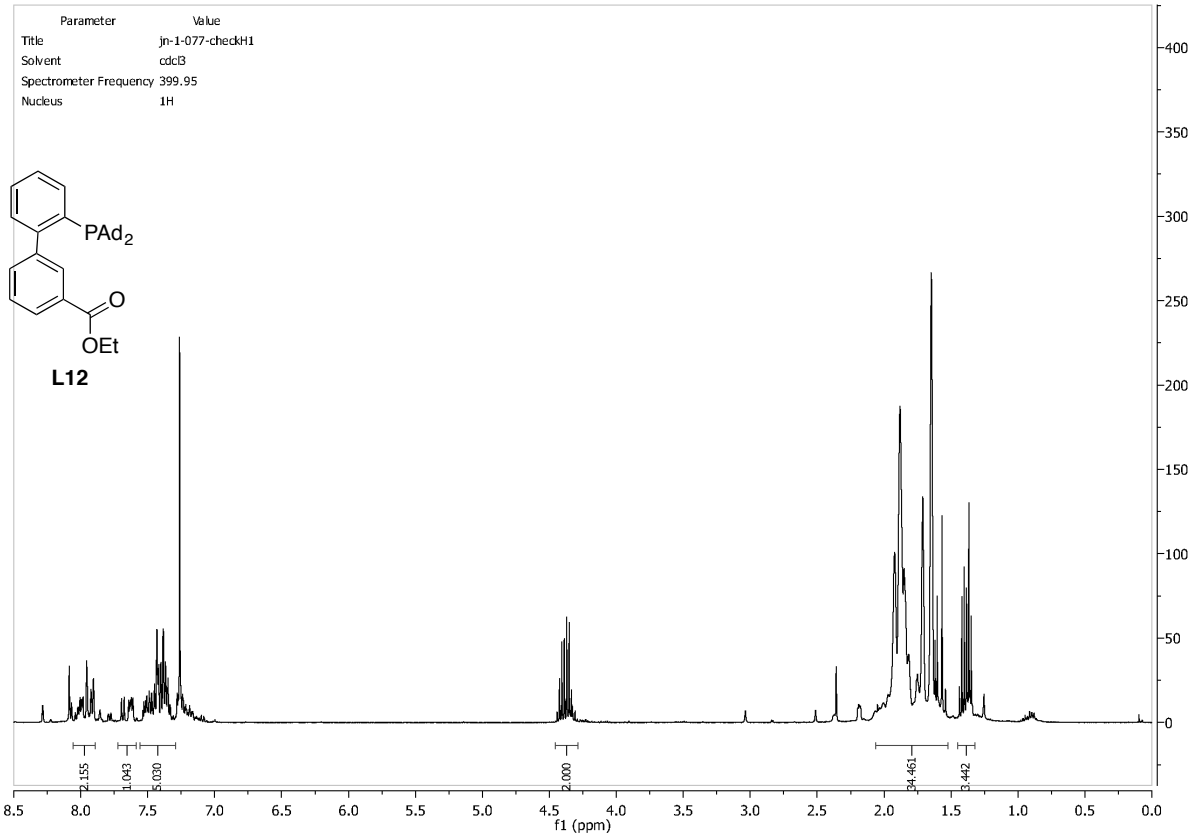
f1 (ppm)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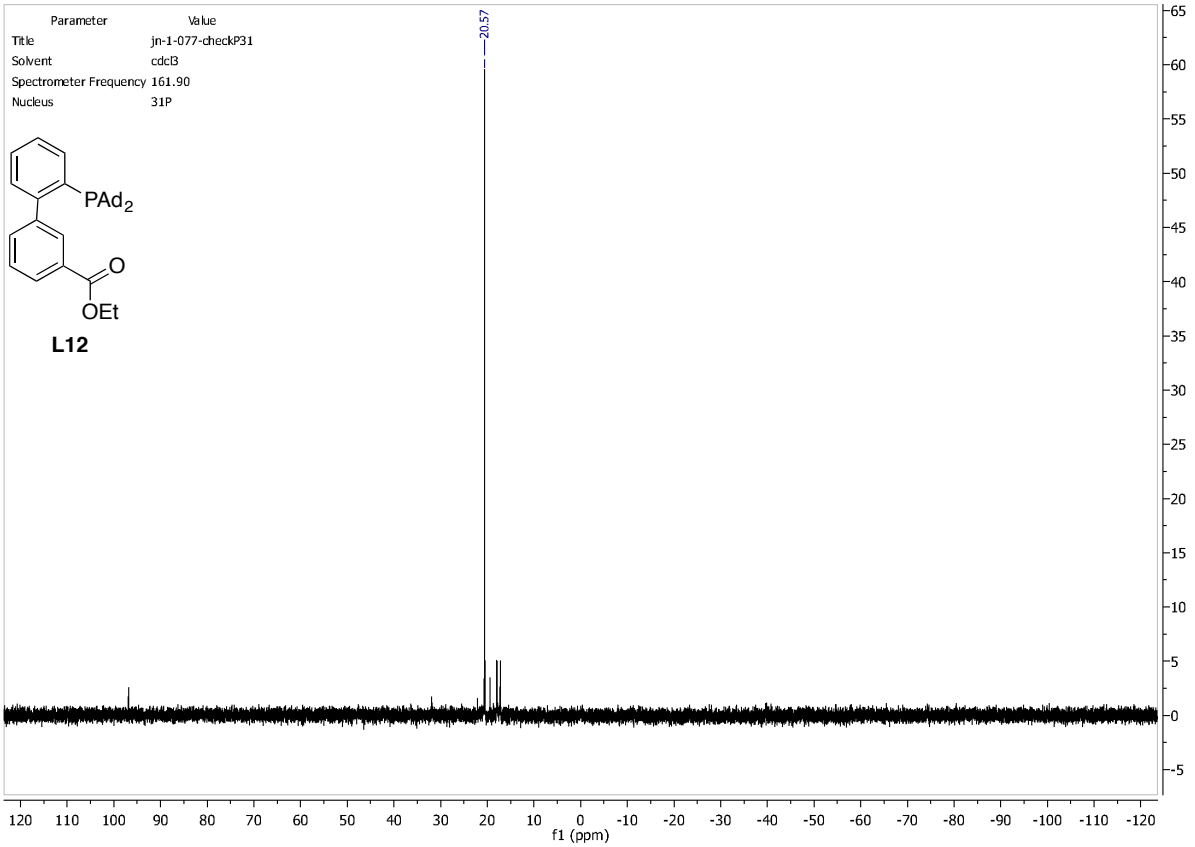
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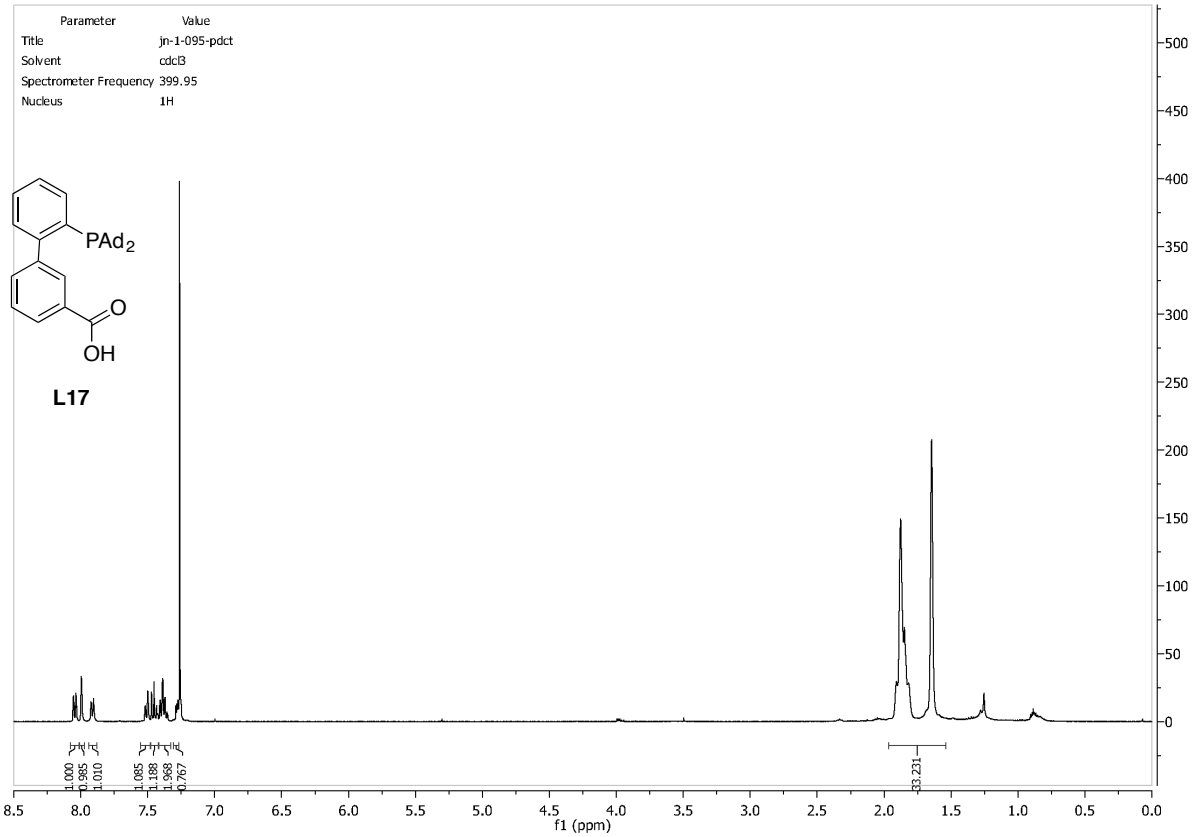
f1 (ppm)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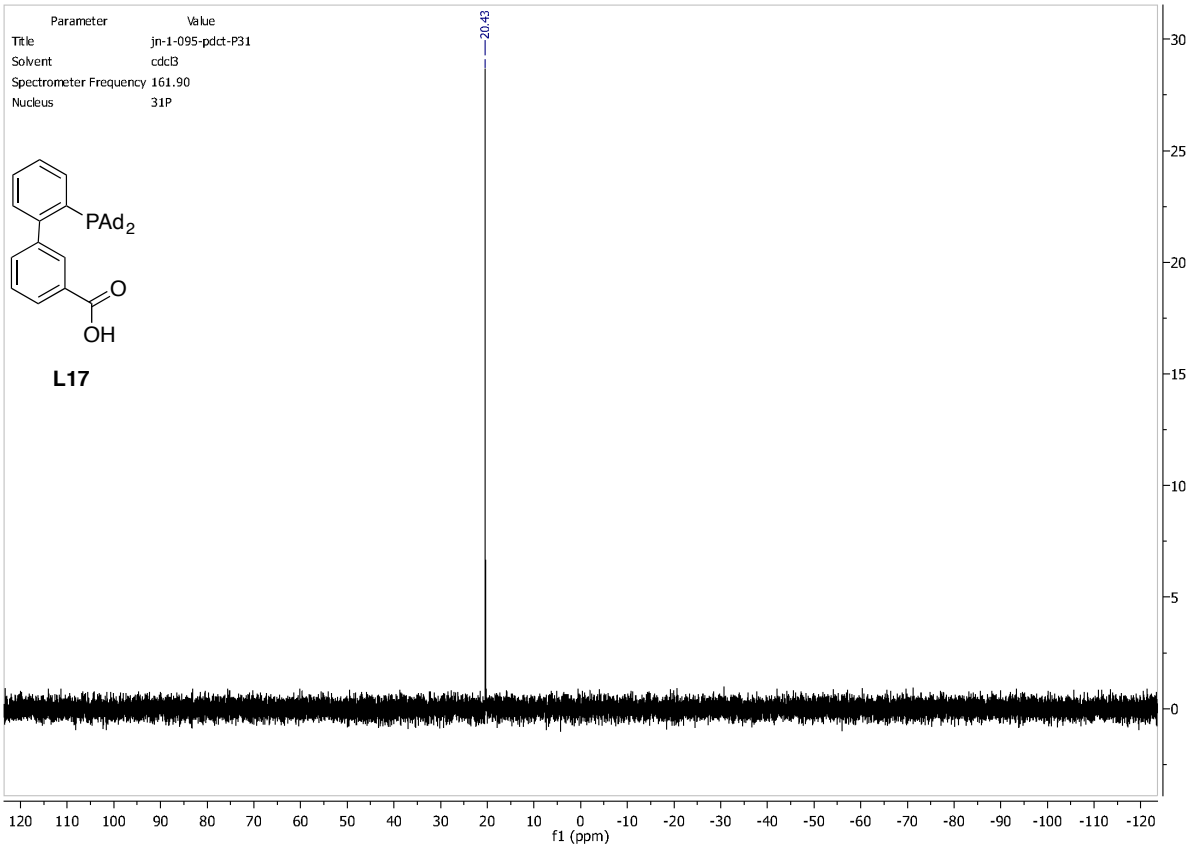
33.231
f1 (ppm)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OH
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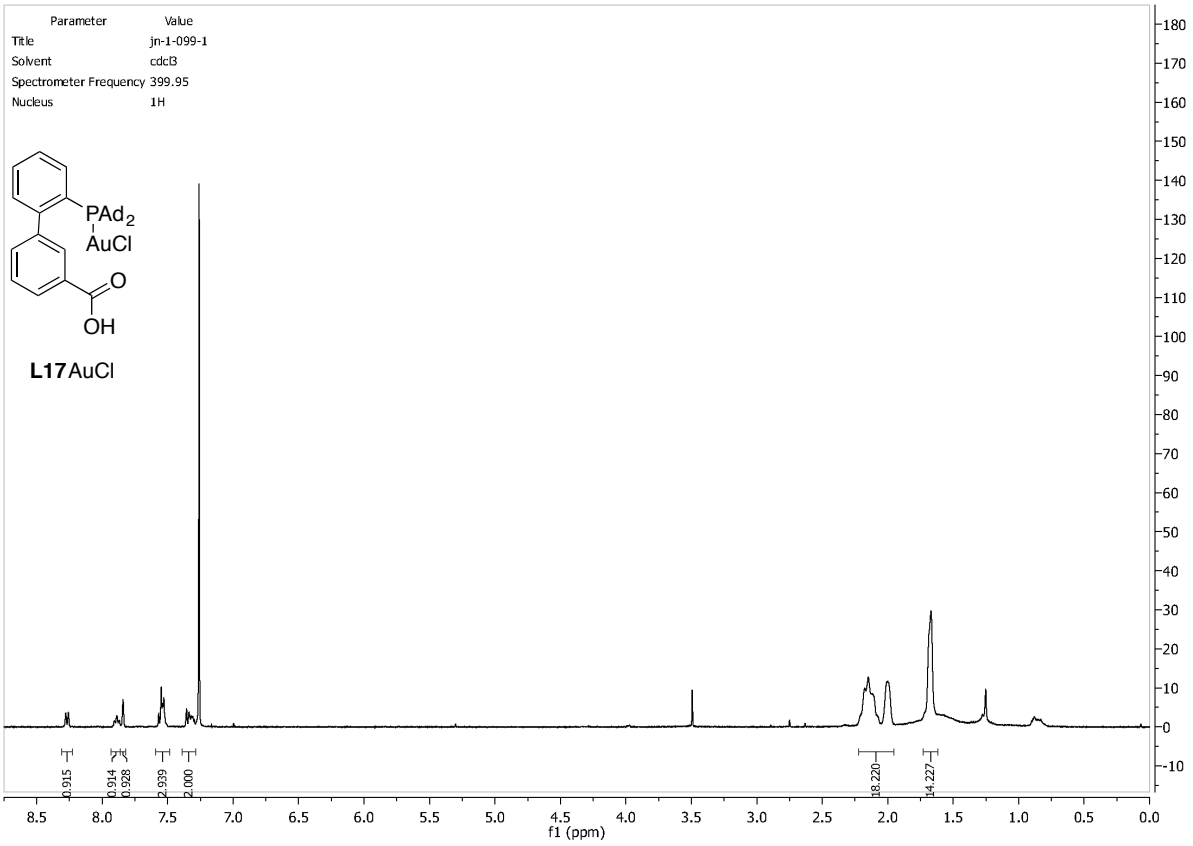
f1 (ppm)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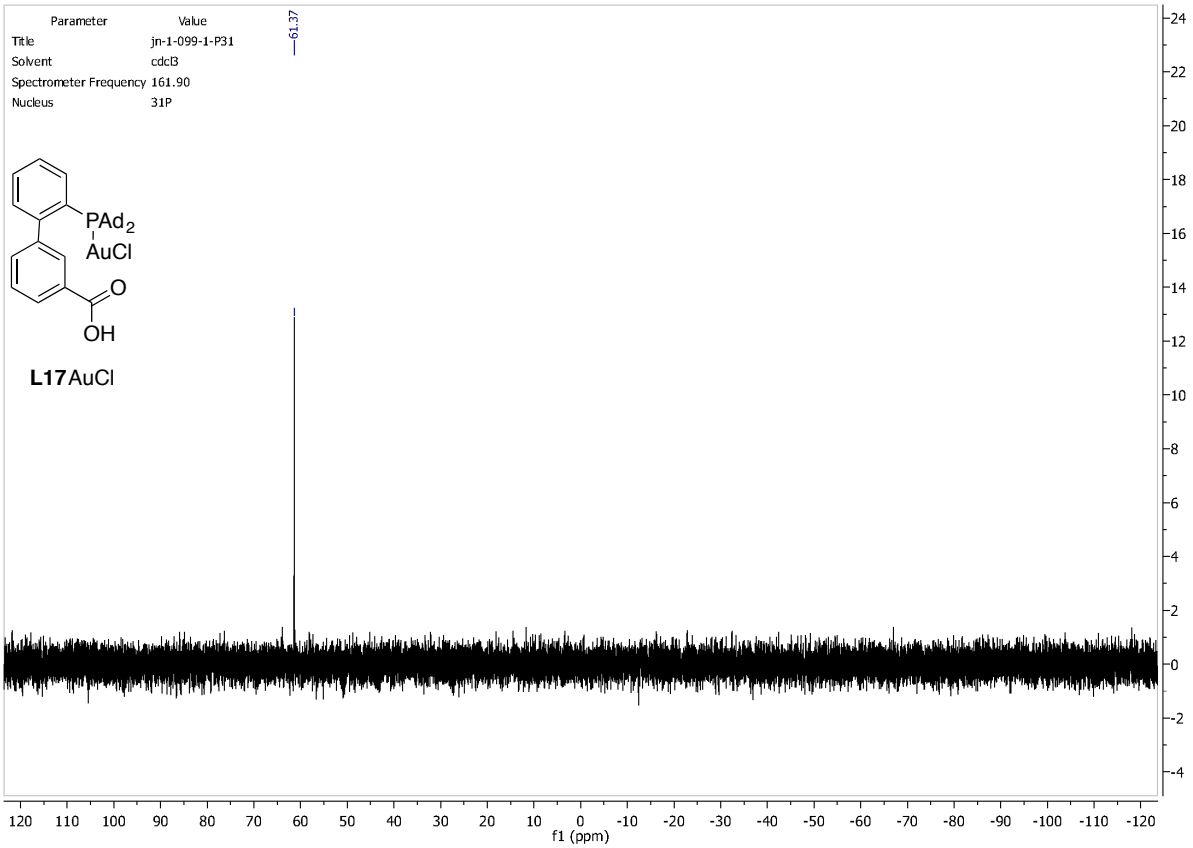
2.000
18.220
14.227
f1 (ppm)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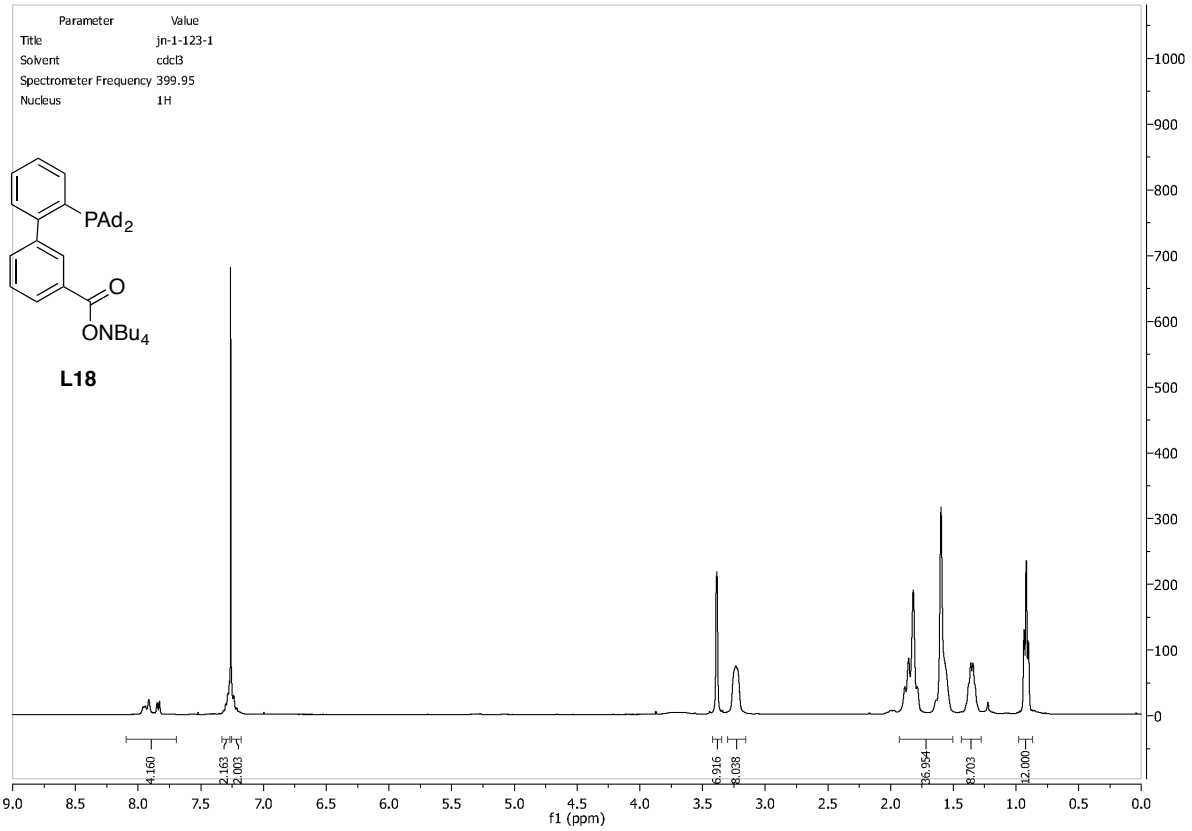
f1 (ppm)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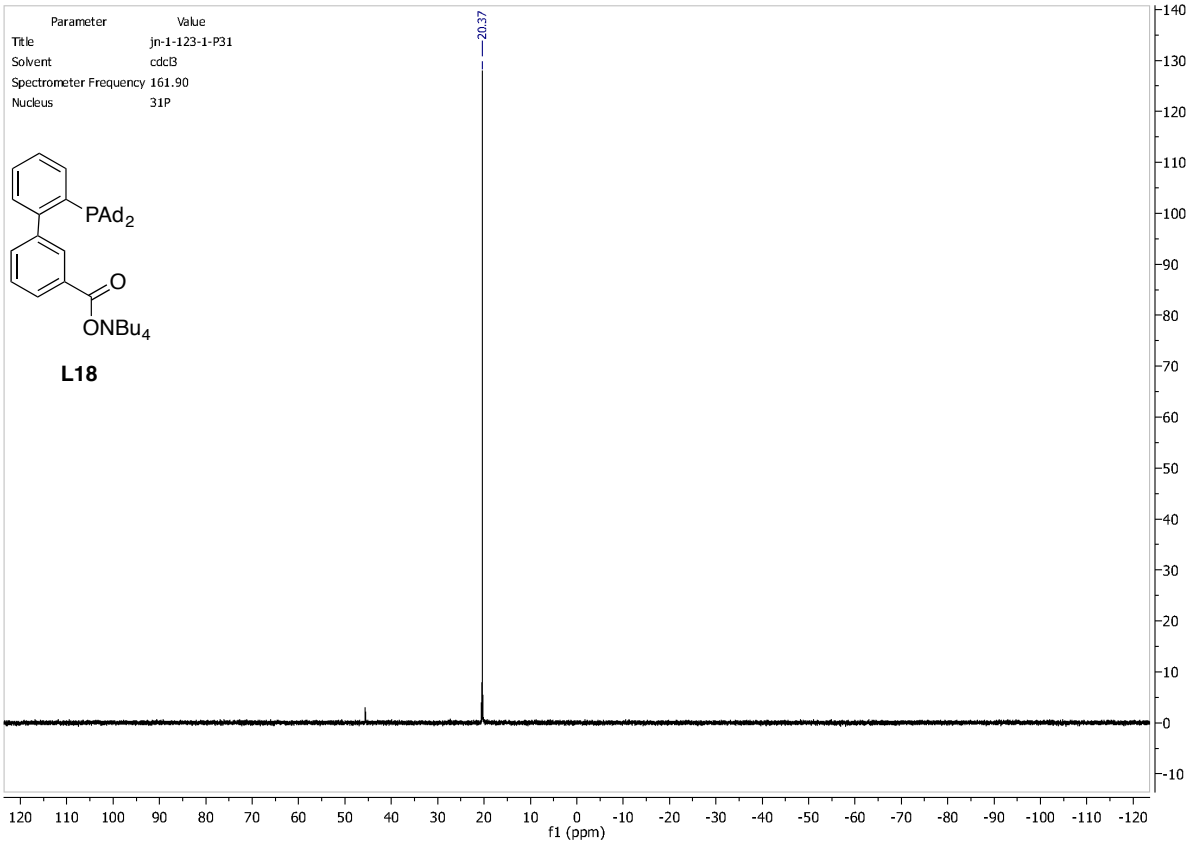
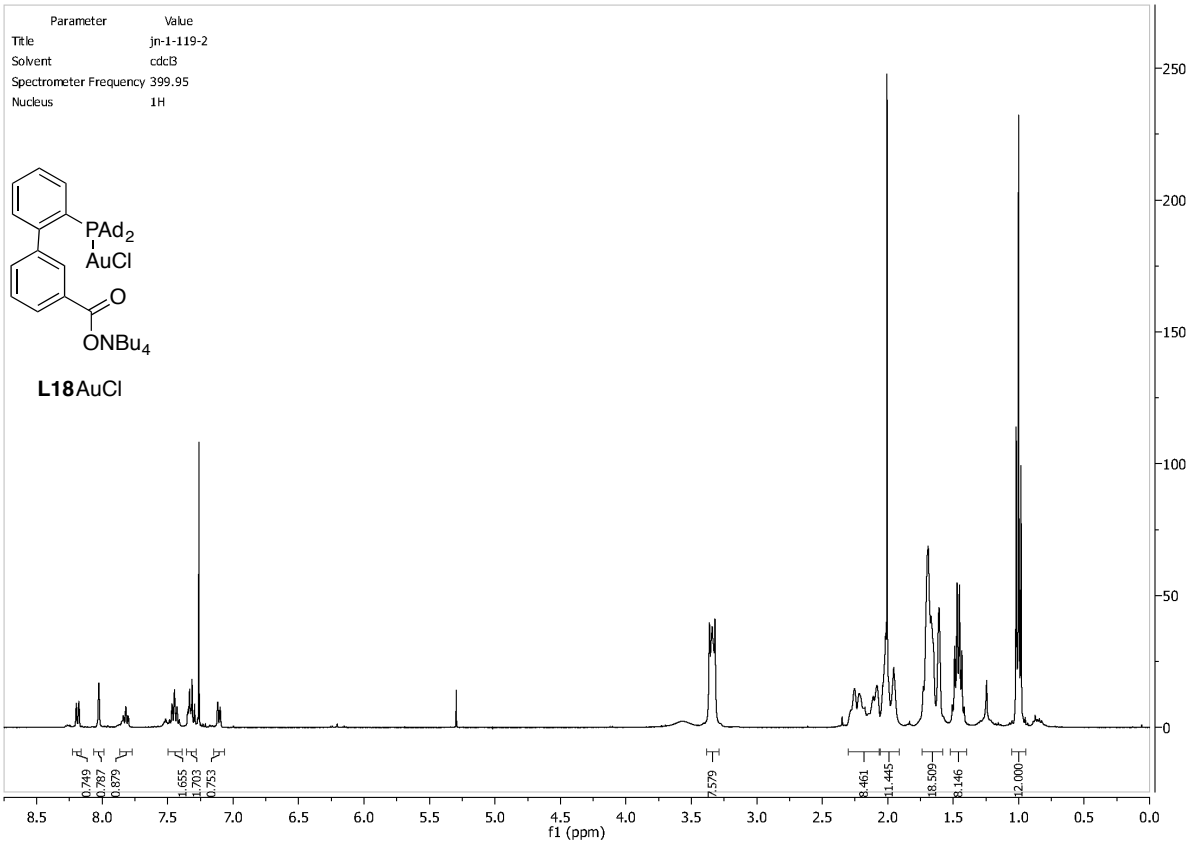
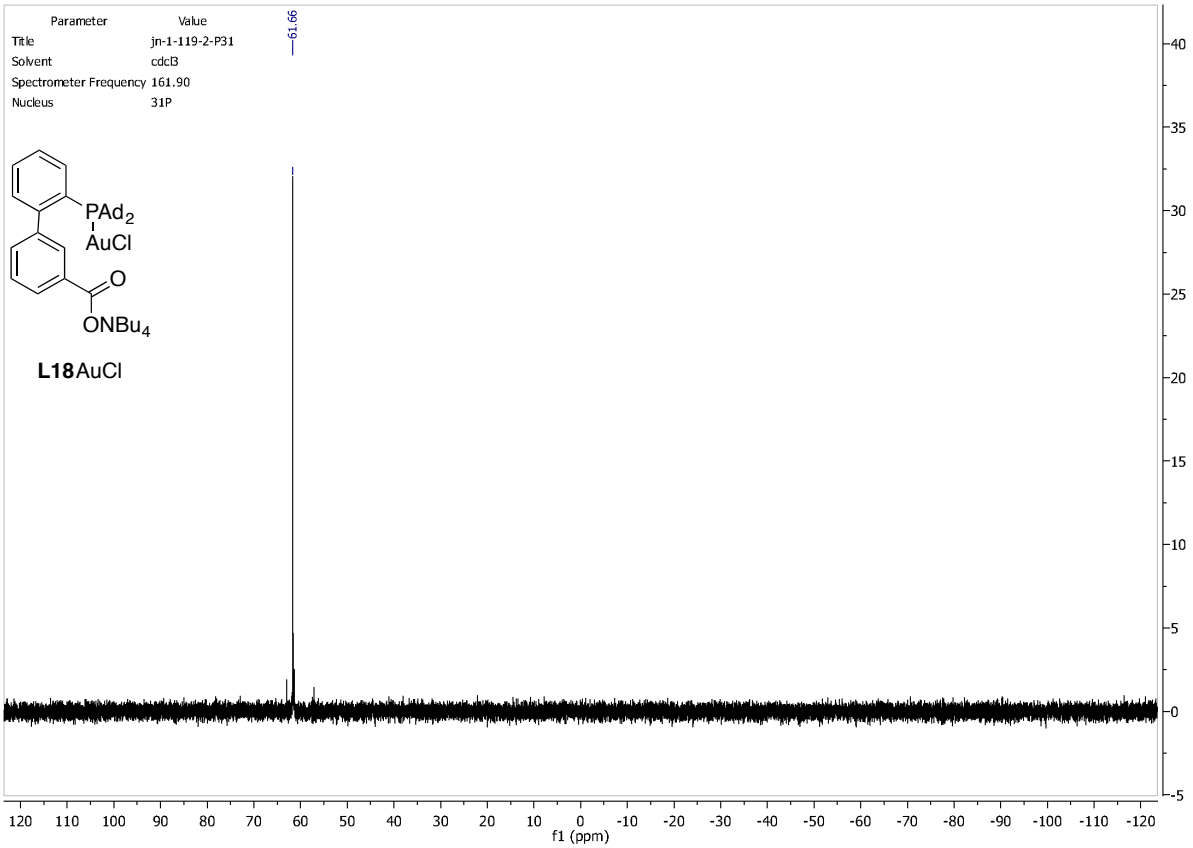
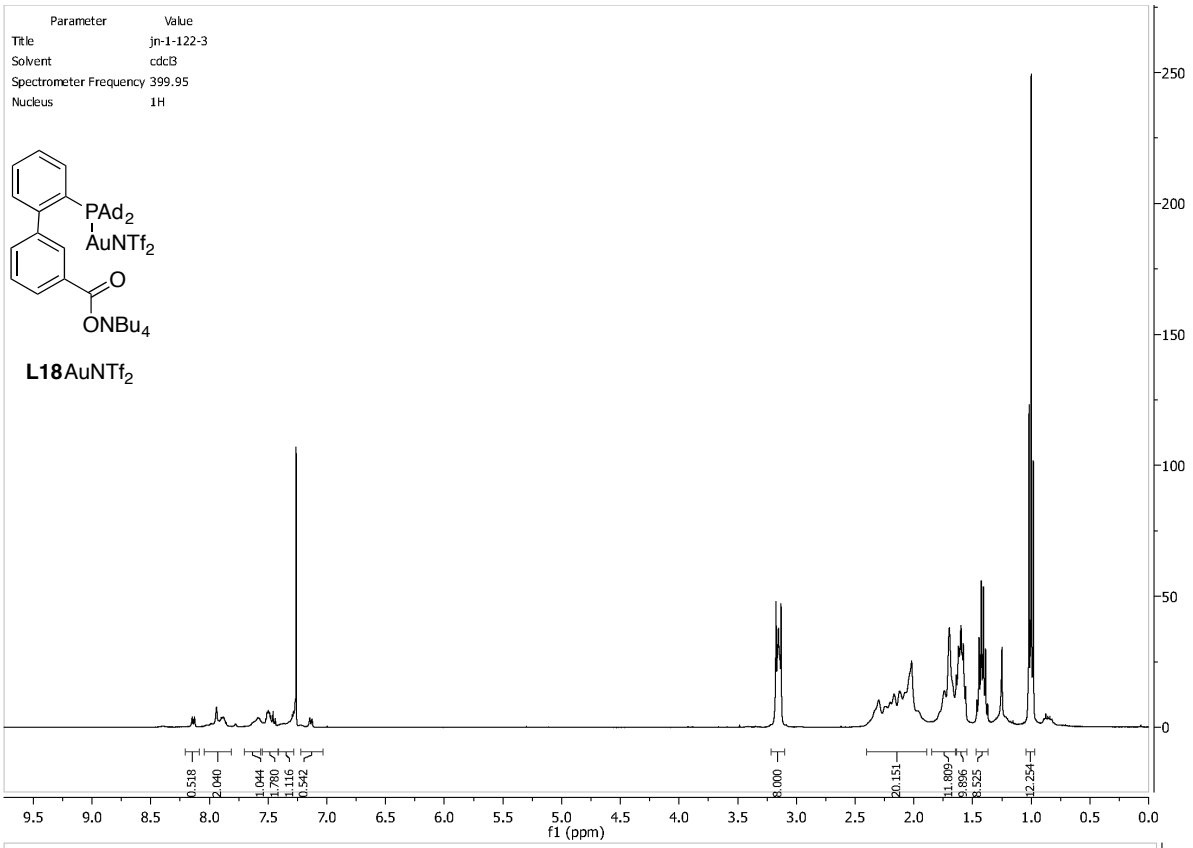
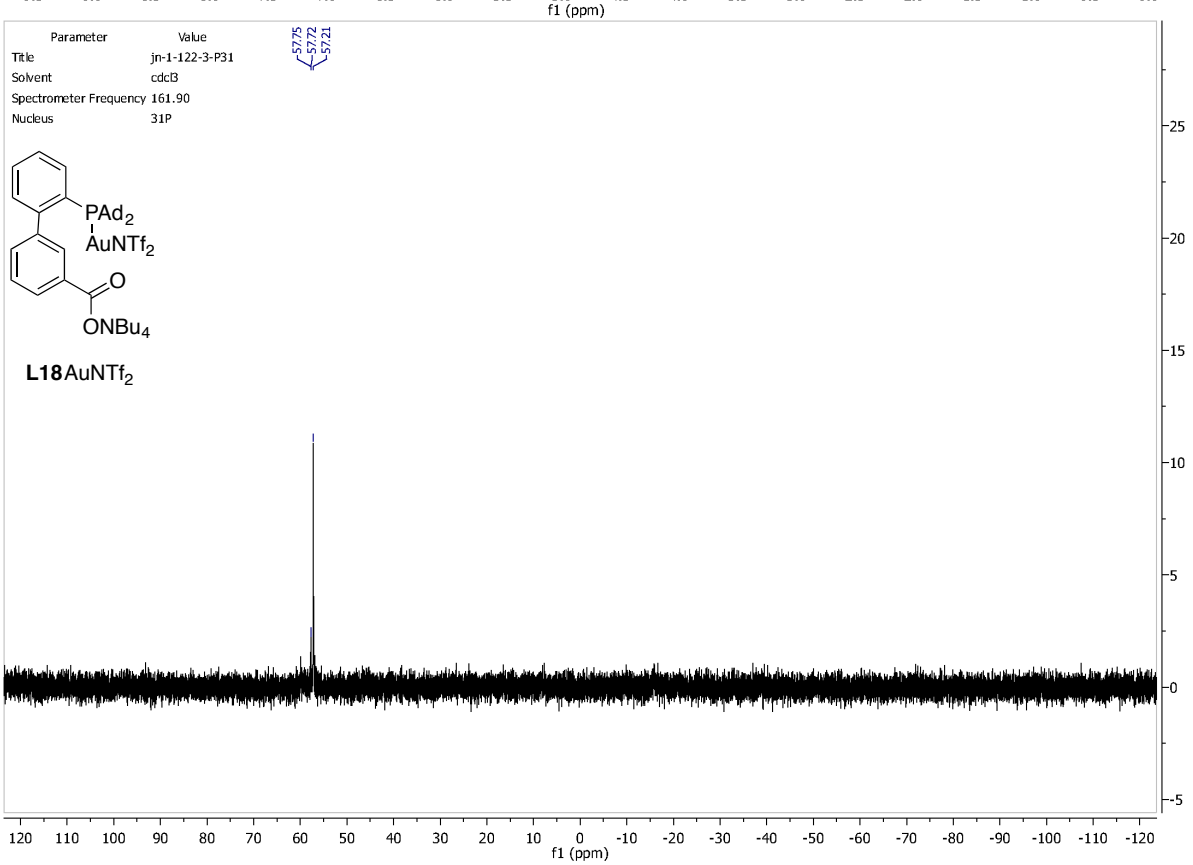
2.163
2.003
6.916
8.038
36.954
8.703
12.000
f1 (ppm)

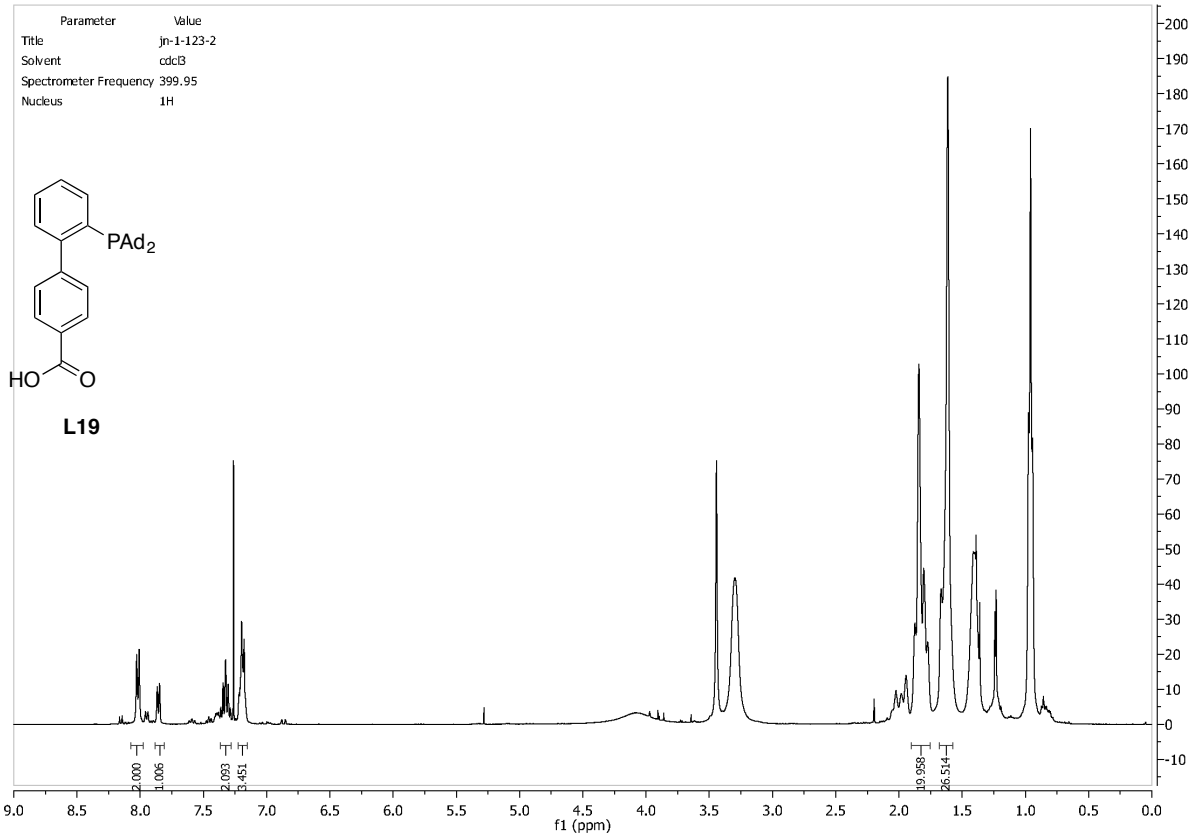

Parameter Value
Title jn-1-123-1-P31
Solvent cdcl3
Spectrometer Frequency 161.90
Nucleus 31P
20.37
PAd2
O
ONBu4
L18
f1 (ppm)

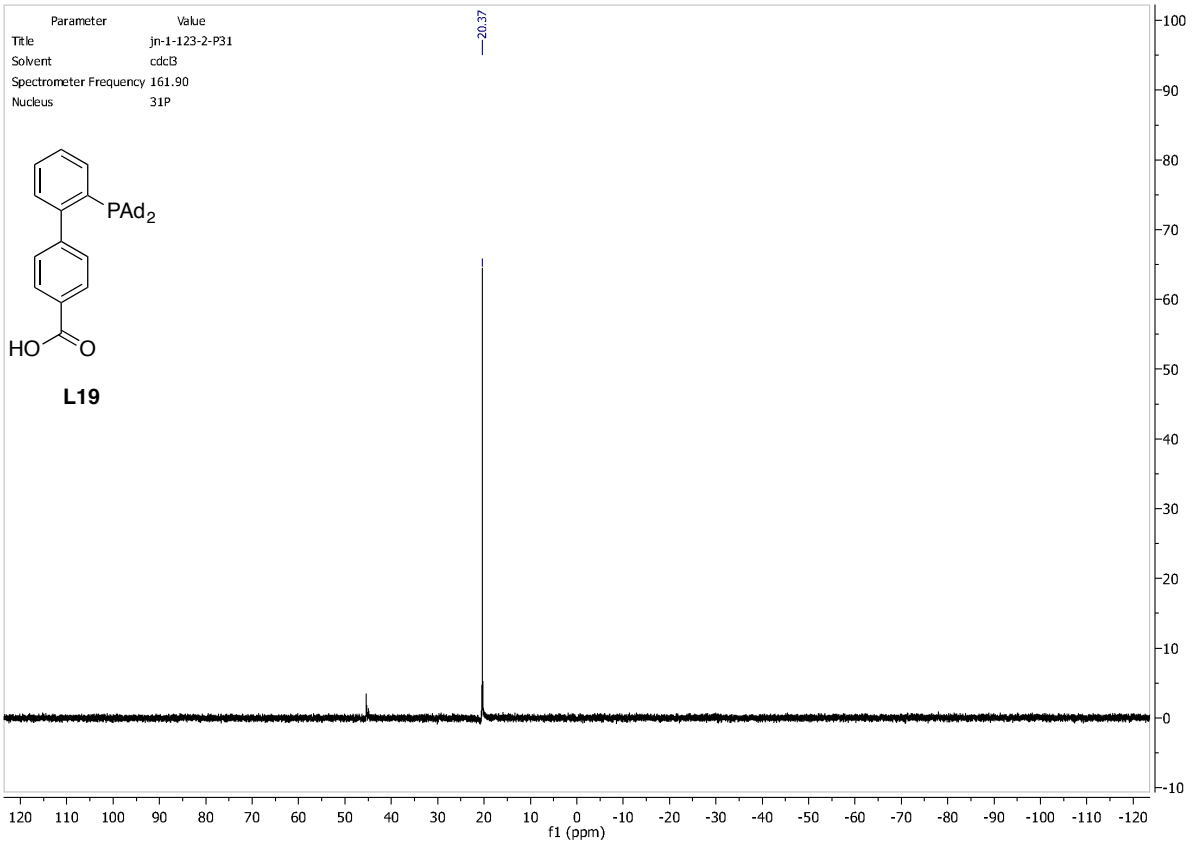

Parameter Value
Title jn-1-119-2
Solvent cdcl3
Spectrometer Frequency 399.95
Nucleus 1H
PAd2
AuCl
O
ONBu4
L18AuCl
0.749
0.787
0.879
1.655
1.703
0.753
7.579
8.461
11.445
18.509
8.146
12.000
f1 (ppm)

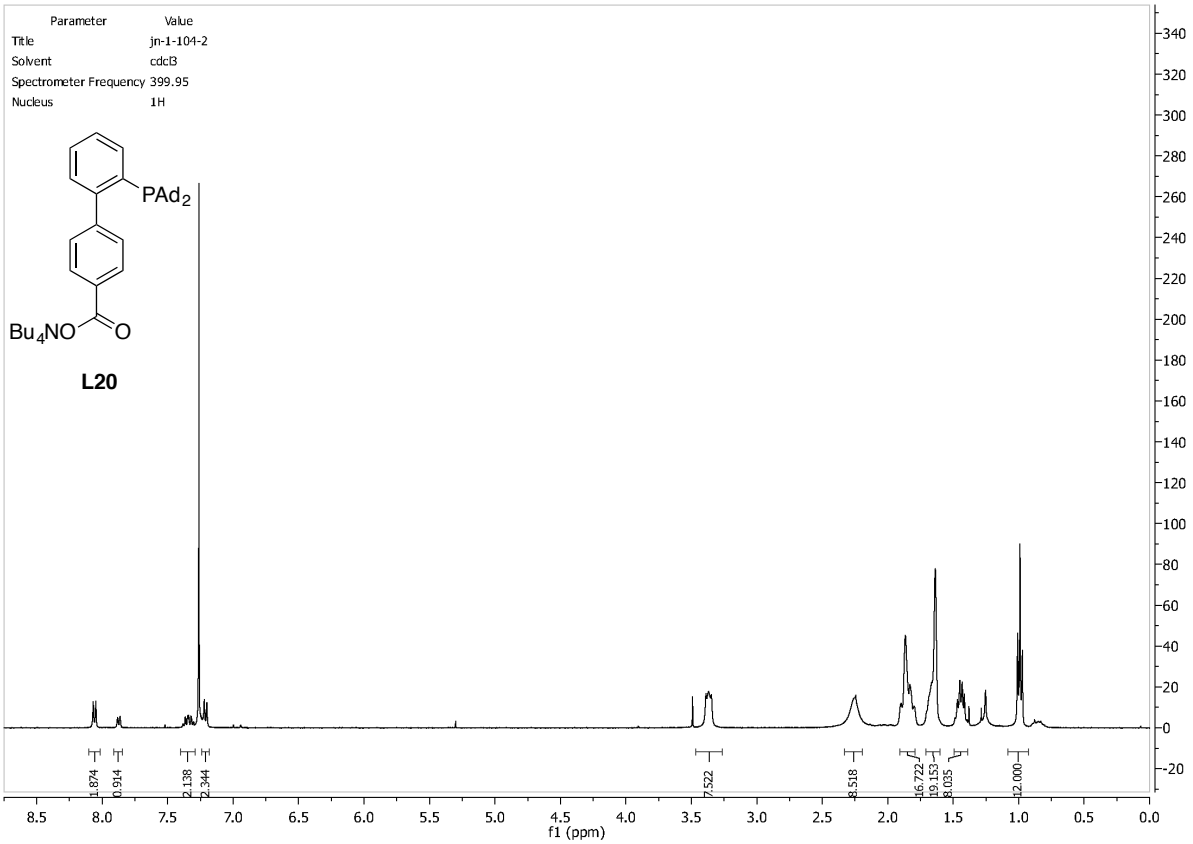

Parameter Value
Title jn-1-119-2-P31
Solvent cdcl3
Spectrometer Frequency 161.90
Nucleus 31P
61.66
PAd2
AuCl
O
ONBu4
L18AuCl
f1 (ppm)

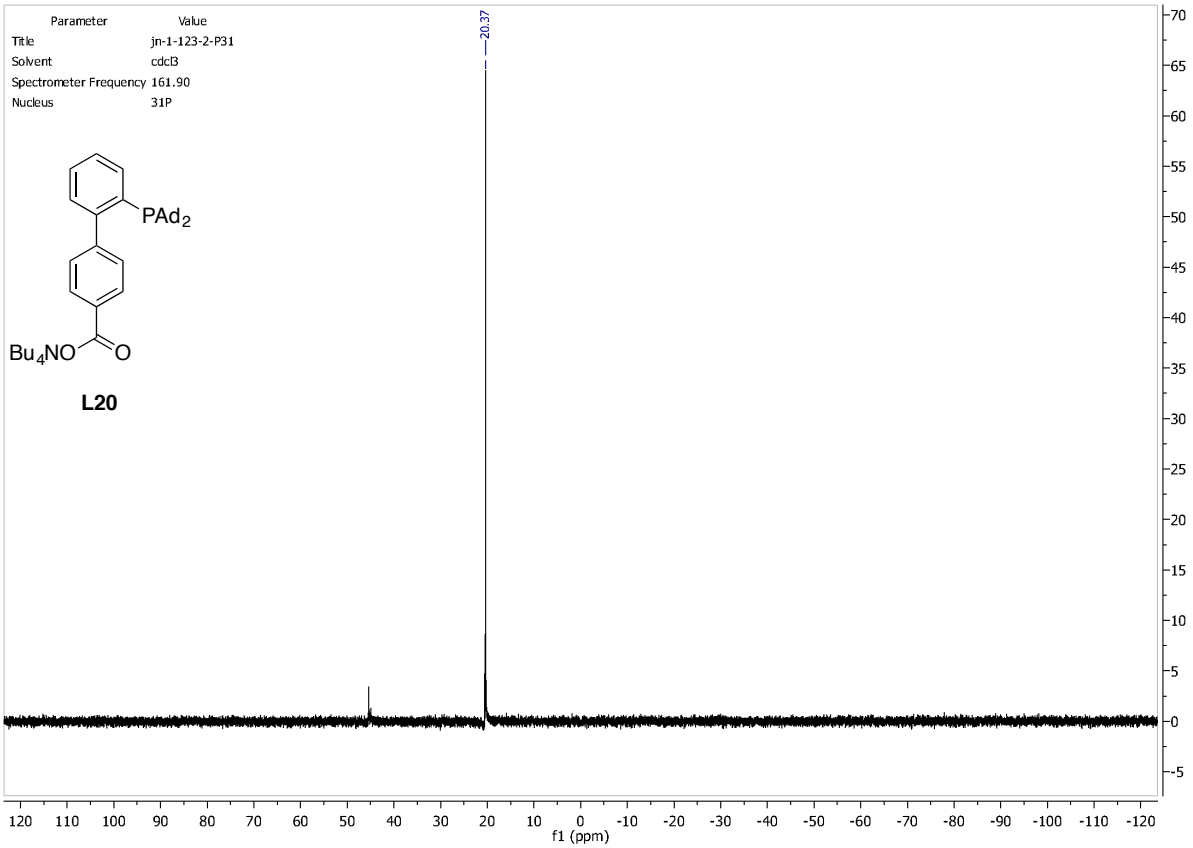

Parameter Value
Title jn-1-122-3
Solvent cdcl3
Spectrometer Frequency 399.95
Nucleus 1H
PAd2
AuNTf2
O
ONBu4
L18AuNTf2
0.518
2.040
1.044
1.780
1.116
0.542
8.000
20.151
11.809
9.896
8.525
12.254
f1 (ppm)

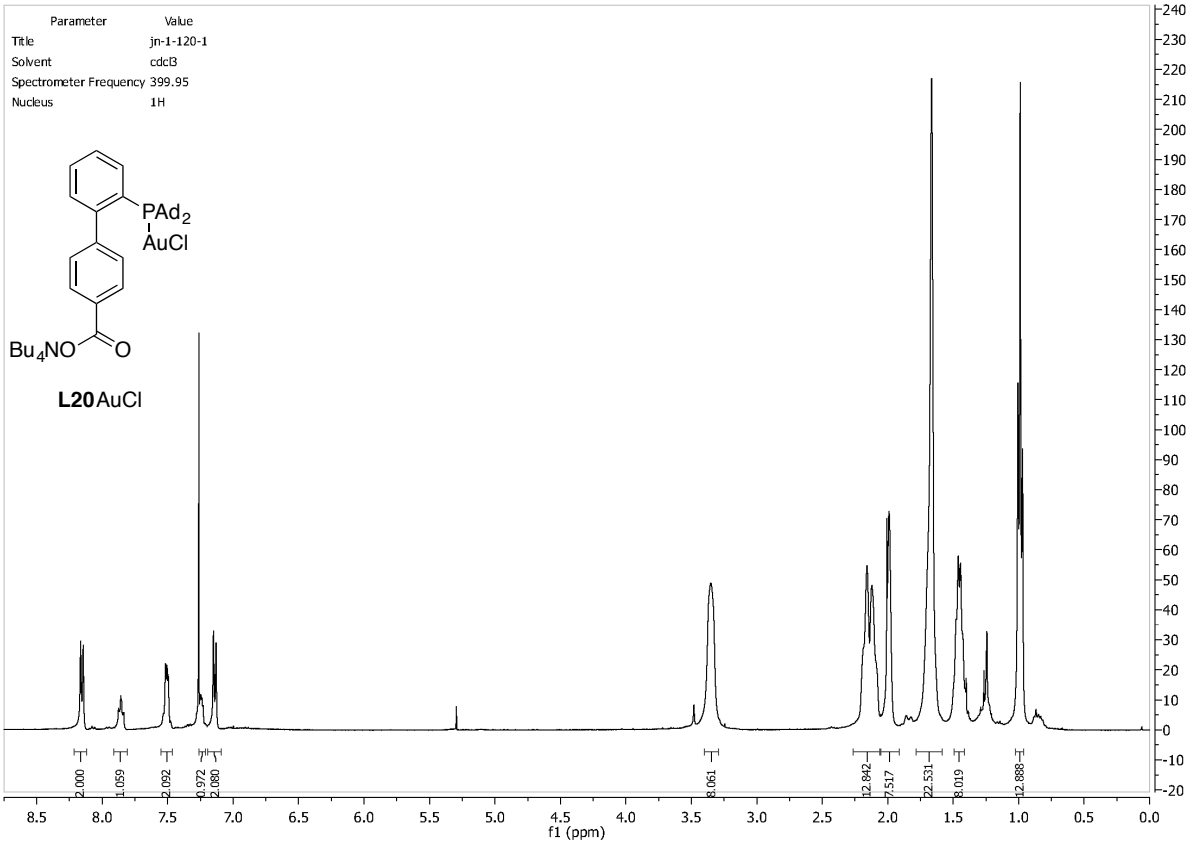

Parameter Value
Title jn-1-122-3-P31
Solvent cdcl3
Spectrometer Frequency 161.90
Nucleus 31P
57.75
57.72
57.21
PAd2
AuNTf2
O
ONBu4
L18AuNTf2
f1 (ppm)

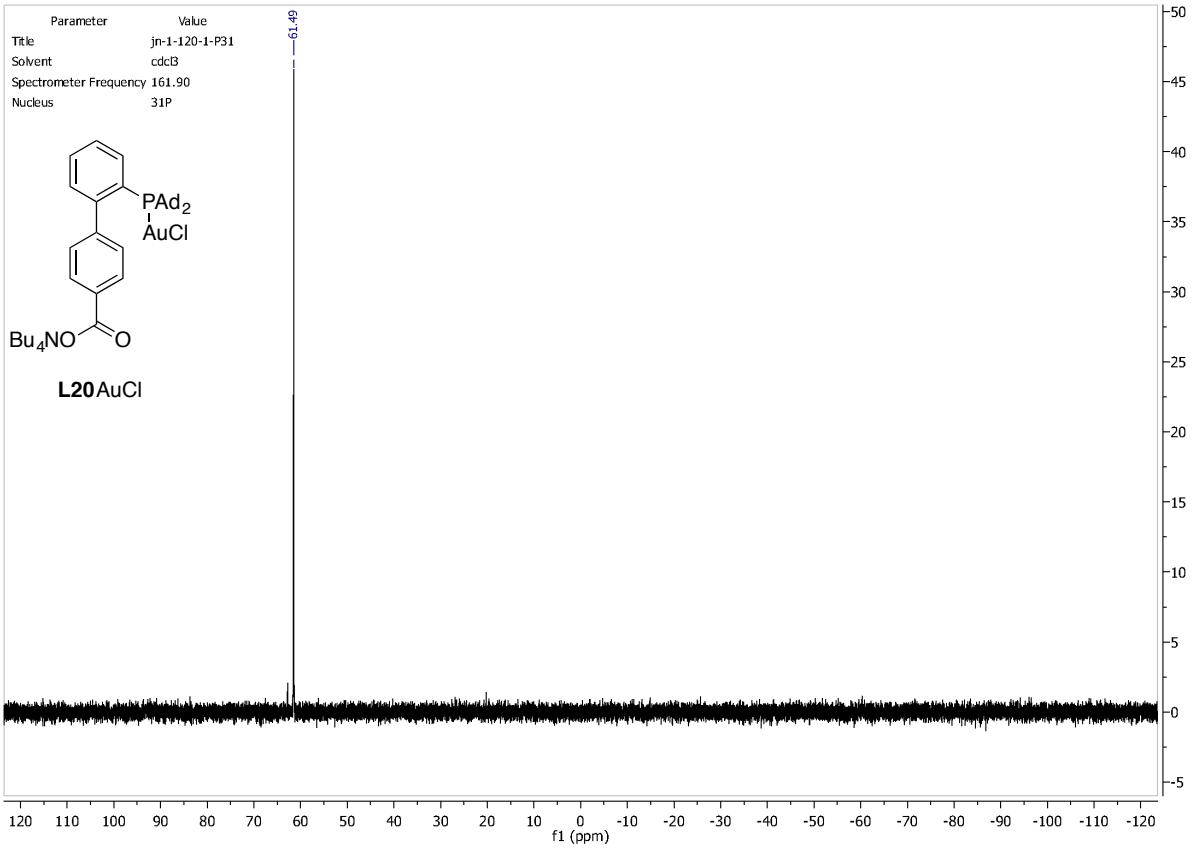

Parameter Value
Title jn-1-123-2
Solvent cdcl3
Spectrometer Frequency 399.95
Nucleus 1H
PAd2
HO
O
L19
2.000
1.006
2.093
3.451
19.958
26.514
f1 (ppm)

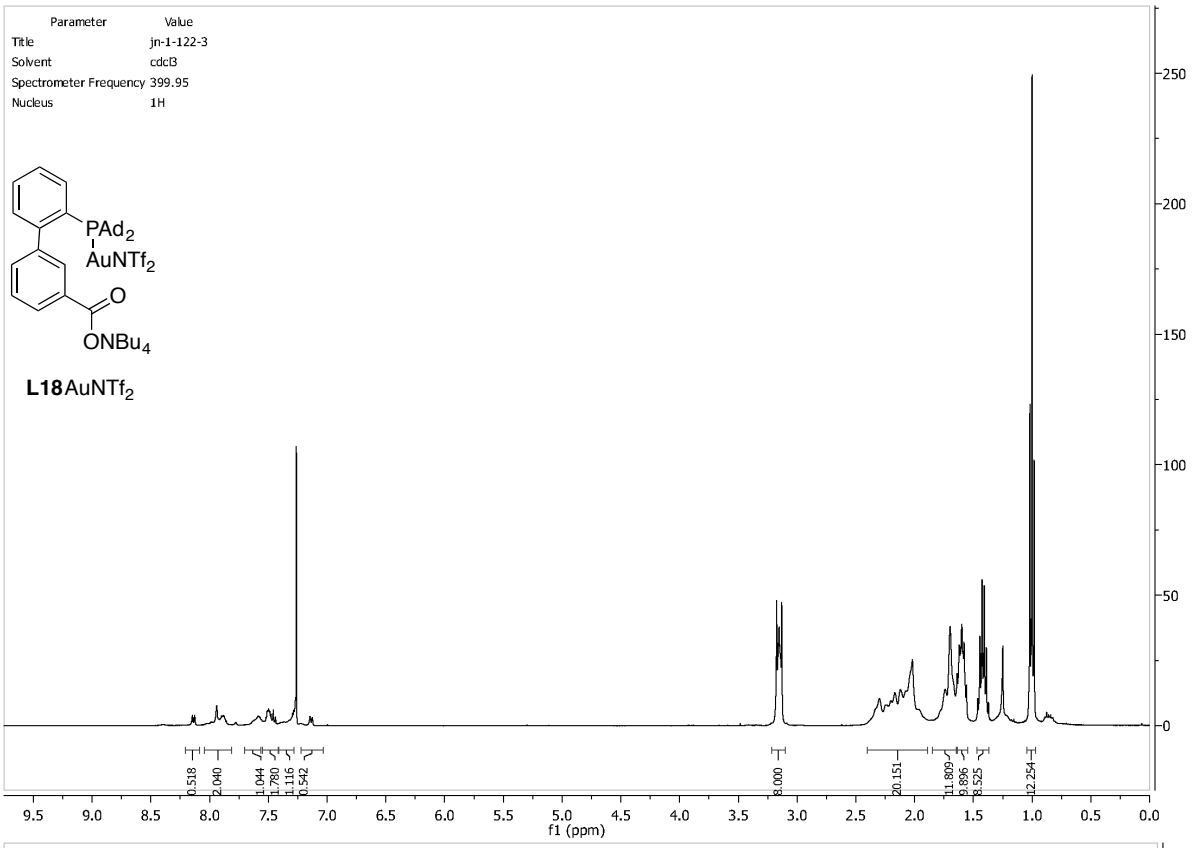

Parameter Value
Title jn-1-123-2-P31
Solvent cdcl3
Spectrometer Frequency 161.90
Nucleus 31P
20.37
PAd2
HO
O
L19
f1 (ppm)

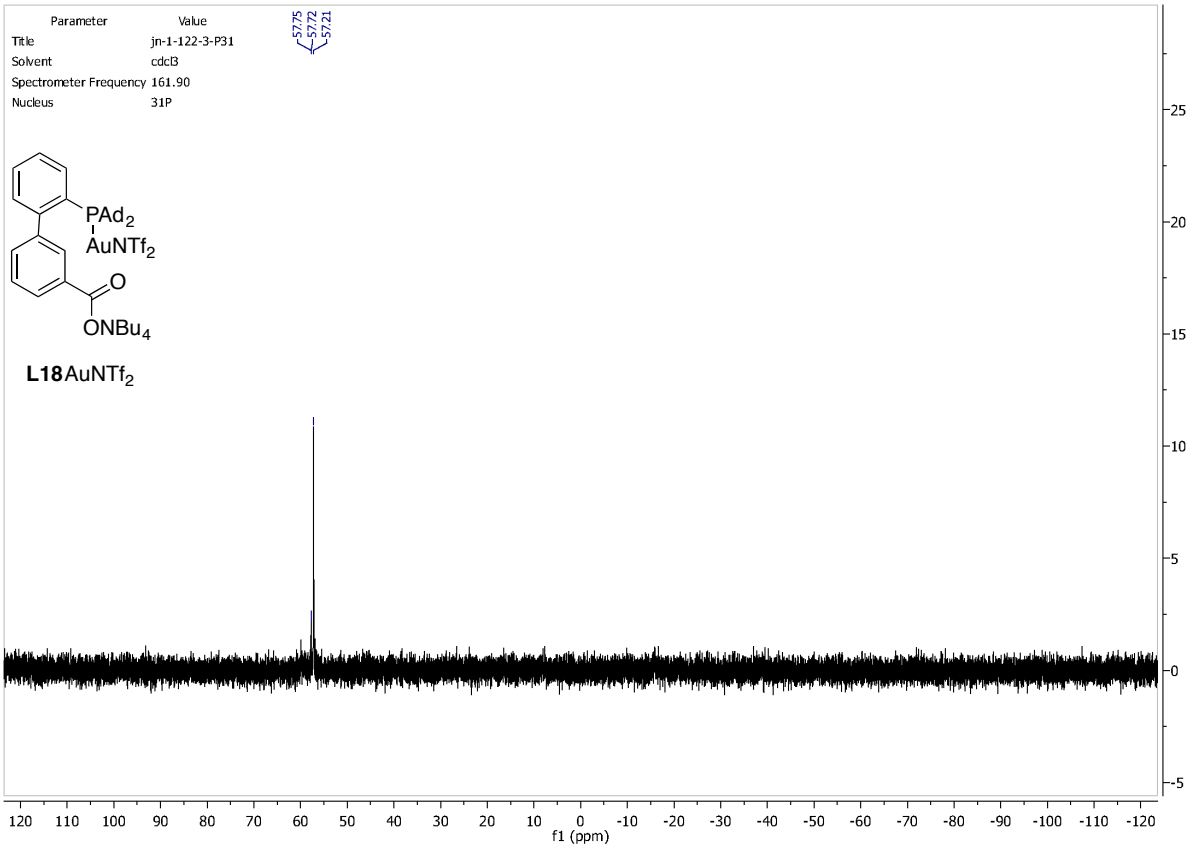

Parameter Value
Title jn-1-104-2
Solvent cdcl3
Spectrometer Frequency 399.95
Nucleus 1H
PAd2
Bu4NO
O
L20
1.874
0.914
2.138
2.344
7.522
8.518
16.722
19.153
8.035
12.000
f1 (ppm)


Parameter Value
Title jn-1-123-2-P31
Solvent cdcl3
Spectrometer Frequency 161.90
Nucleus 31P
20.37
PAd2
Bu4NO
O
L20
f1 (ppm)

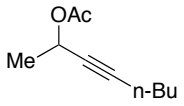

Parameter Value
Title jn-1-120-1
Solvent cdcl3
Spectrometer Frequency 399.95
Nucleus 1H
PAd2
AuCl
Bu4NO
O
L20AuCl
2.000
1.059
2.092
0.972
2.080
8.061
12.842
7.517
22.531
8.019
12.888
f1 (ppm)


Parameter Value
Title jn-1-120-1-P31
Solvent cdcl3
Spectrometer Frequency 161.90
Nucleus 31P
61.49
PAd2
AuCl
Bu4NO
O
L20AuCl
f1 (ppm)

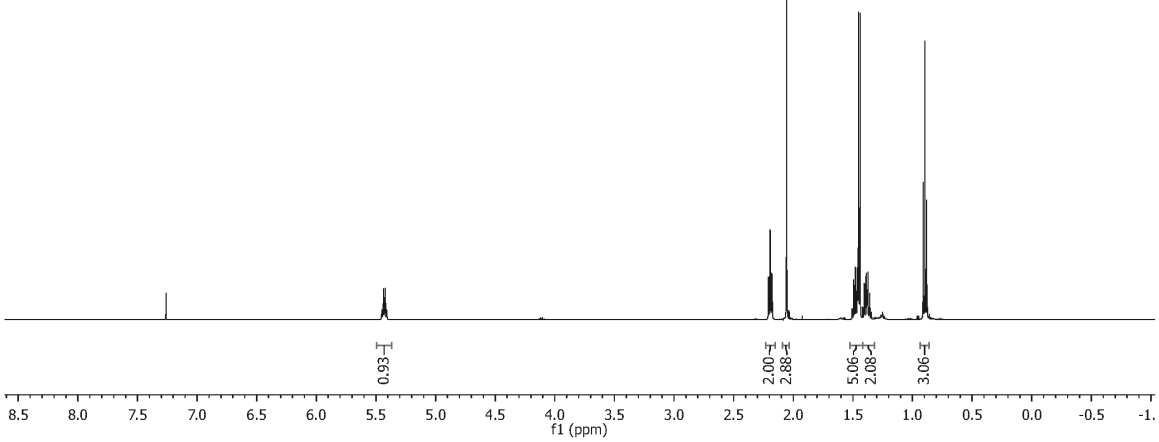

Parameter Value
Title jn-1-122-3
Solvent cdcl3
Spectrometer Frequency 399.95
Nucleus 1H
PAd2
AuNTf2
O
ONBu4
L18AuNTf2
0.518
2.040
1.044
1.780
1.116
0.542
8.000
20.151
11.809
9.896
8.525
12.254
f1 (ppm)


Parameter Value
Title jn-1-122-3-P31
Solvent cdcl3
Spectrometer Frequency 161.90
Nucleus 31P
57.75
57.72
57.21
PAd2
AuNTf2
O
ONBu4
L18AuNTf2
f1 (ppm)

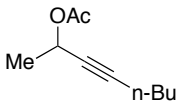
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ CASE-SM/ jkg-II-224B-P-H.fid/ fid
Title jkg-II-224B-P-H
Solvent CDCl3
Acquisition Date 2012-02-27T13:20:12
Spectrometer Frequency 499.86



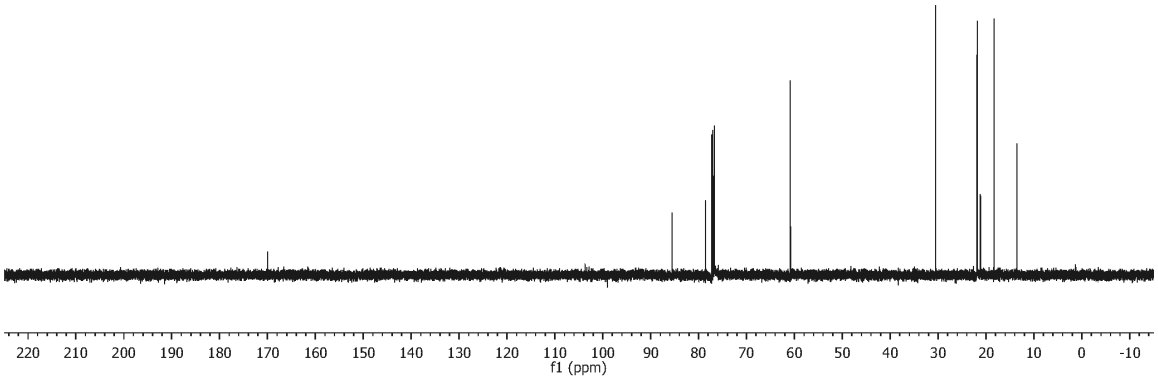
3-1



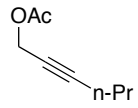
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ CASE-SM/ jkg-II-224B-P-C.fid/ fid
Title jkg-II-224B-P-C
Solvent CDCl3
Acquisition Date 2012-02-27T13:22:14
Spectrometer Frequency 125.70



3-1

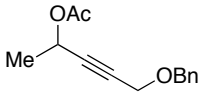


Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ CASE-SM/ jkg-II-226-SM-H.fid/ fid
Title jkg-II-226-SM-H
Solvent CDCl3
Acquisition Date 2012-02-27T17:10:33
Spectrometer Frequency 499.86

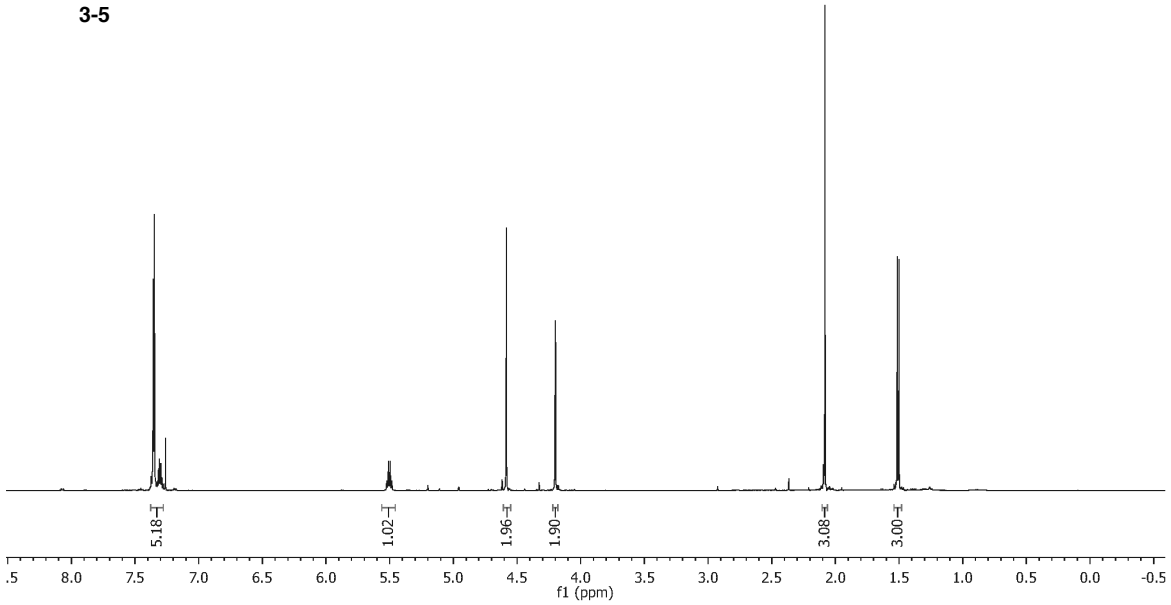


3-3

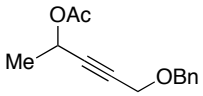
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ CASE-SM/ jkg-II-251-SM-H.fid/ fid
Title jkg-II-251-SM-H
Solvent CDCl3
Acquisition Date 2012-03-08T21:41:42
Spectrometer Frequency 499.86



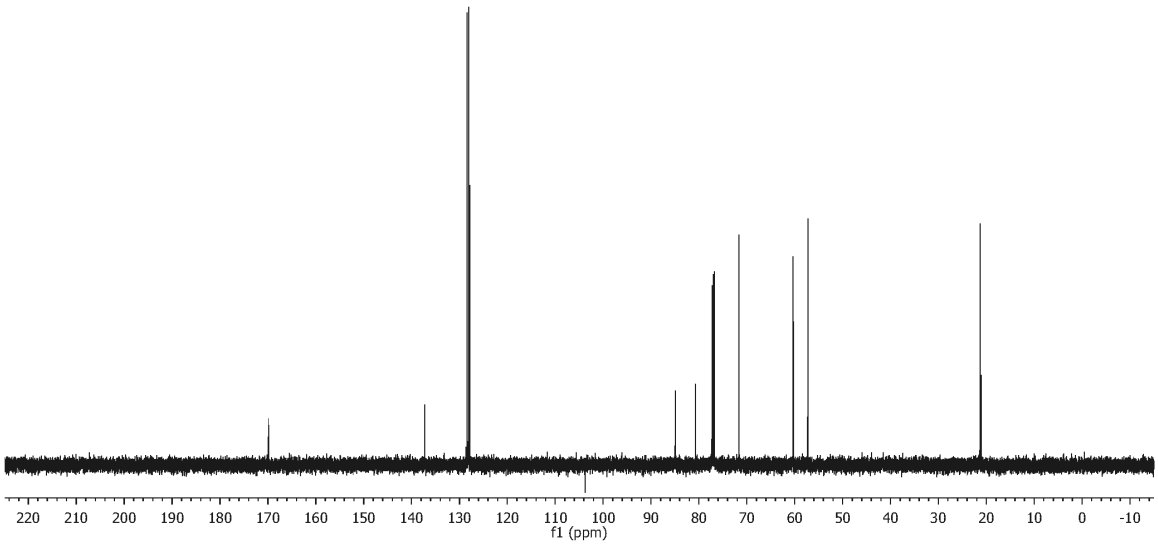
3-5



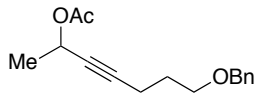
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ CASE-SM/ jkg-II-251-SM-C.fid/ fid
Title jkg-II-251-SM-C
Solvent CDCl3
Acquisition Date 2012-03-08T21:44:36
Spectrometer Frequency 125.70



3-5

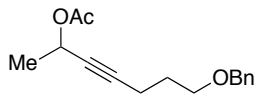


Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ CASE-SM/ jkg-ll-243-B-2-P-H.fid/ fid
Title jkg-ll-243-B-2-P-H
Solvent cdcl3
Acquisition Date 2012-03-05T22:20:56
Spectrometer Frequency 599.63

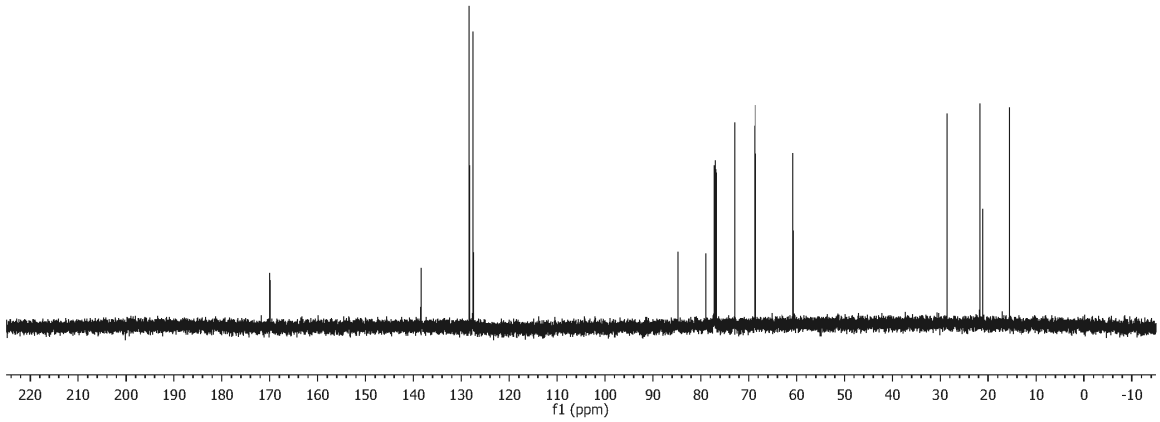


3-9

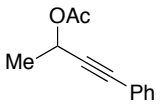
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ CASE-SM/ jkg-ll-243-B-2-P-C.fid/ fid
Title jkg-ll-243-B-2-P-C
Solvent cdcl3
Acquisition Date 2012-03-05T22:23:24
Spectrometer Frequency 150.79



3-9

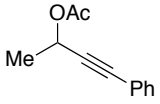


Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ CASE-SM/ jkg-ll-247B-SM-H.fid/ fid
Title jkg-ll-247B-SM-H
Solvent CDCl3
Acquisition Date 2012-03-07T14:32:25
Spectrometer Frequency 499.86

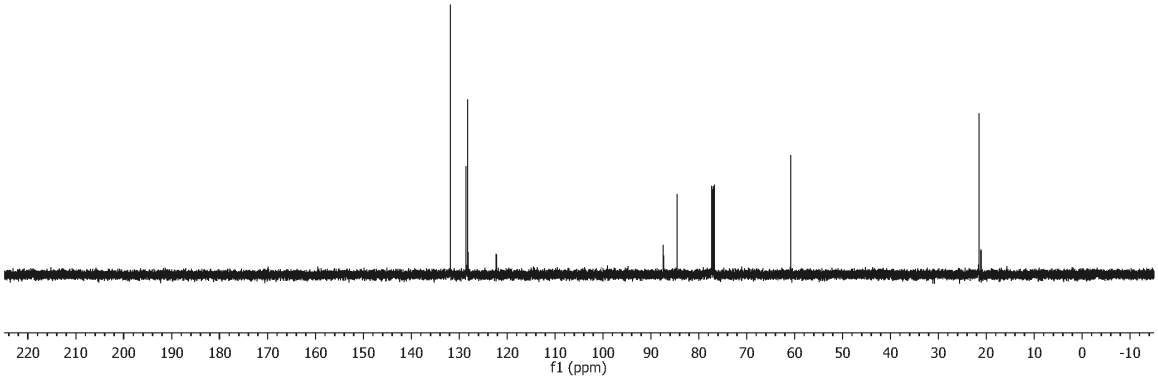


3-7

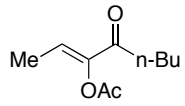
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ CASE-SM/ jkg-ll-247B-SM-C.fid/ fid
Title jkg-ll-247B-SM-C
Solvent CDCl3
Acquisition Date 2012-03-07T14:34:04
Spectrometer Frequency 125.70



3-7

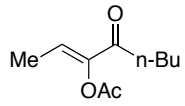


Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ product/ jkg-ll-246A-p-H.fid/ fid
Title jkg-ll-246A-p-H
Solvent CDCl3
Acquisition Date 2012-03-07T14:26:59
Spectrometer Frequency 499.86



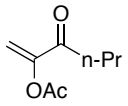
3-2b

Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ product/ jkg-ll-246A-p-C.fid/ fid
Title jkg-ll-246A-p-C
Solvent CDCl3
Acquisition Date 2012-03-07T14:28:26
Spectrometer Frequency 125.70



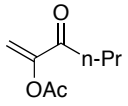
3-2b

Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ product/ jkg-ll-228-P-H.fid/ fid
Title jkg-ll-228-P-H
Solvent CDCl3
Acquisition Date 2012-02-27T22:26:10
Spectrometer Frequency 499.86

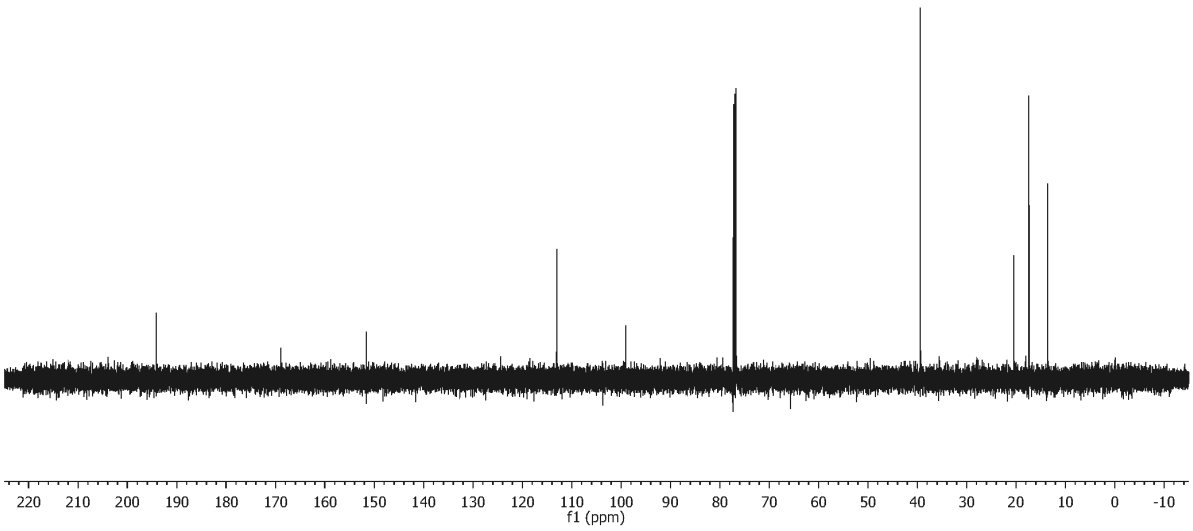


3-4

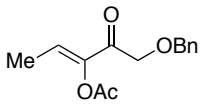
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ product/ jkg-ll-228-P-C.fid/ fid
Title jkg-ll-228-P-C
Solvent CDCl3
Acquisition Date 2012-02-27T22:27:39
Spectrometer Frequency 125.70



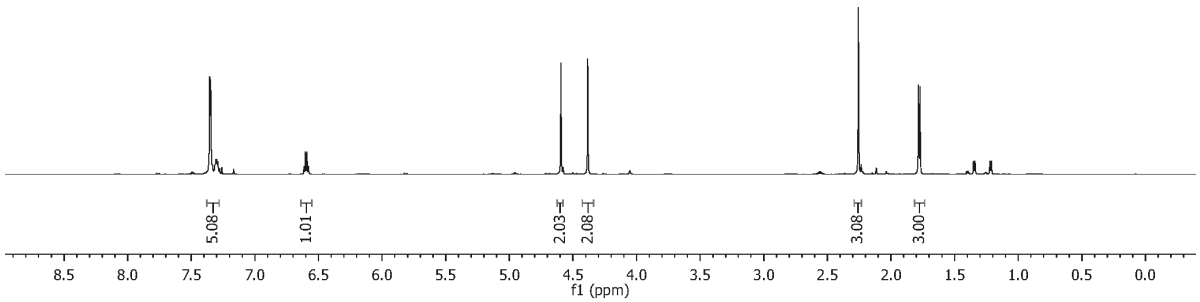
3-4



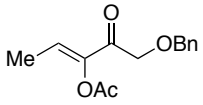
Data File Name	C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ product/ jkg-ll-251-P-H.fid/ fid
Title	jkg-ll-251-P-H
Solvent	cdcl3
Acquisition Date	2012-03-09T22:56:40
Spectrometer Frequency	599.63



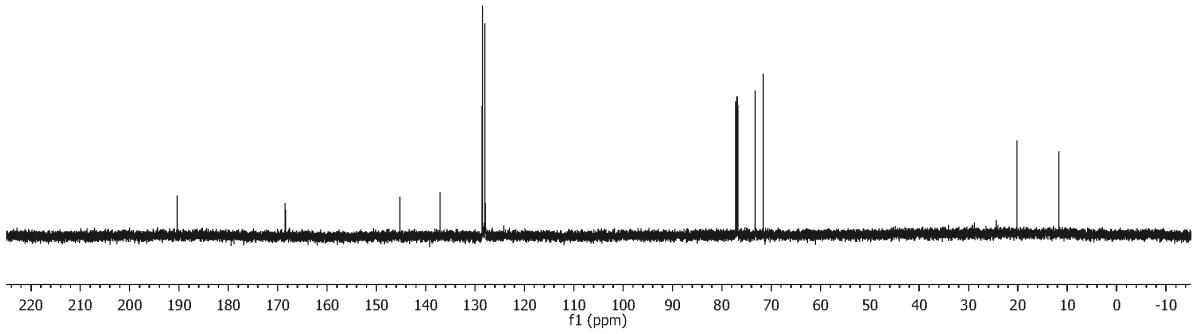
3-6



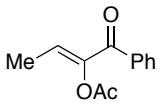
Data File Name	C:/ Users/ zhanglab1/ Desktop/ NMR/ jikg/ product/ jkg-ll-251-P-C.fid/ fid
Title	jkg-ll-251-P-C
Solvent	cdcl3
Acquisition Date	2012-03-11T17:09:20
Spectrometer Frequency	150.79



3-6



Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ product/ jkg-ll-248A-P-H.fid/ fid
Title jkg-ll-248A-P-H
Solvent cdcl3
Acquisition Date 2012-03-08T16:19:55
Spectrometer Frequency 599.63



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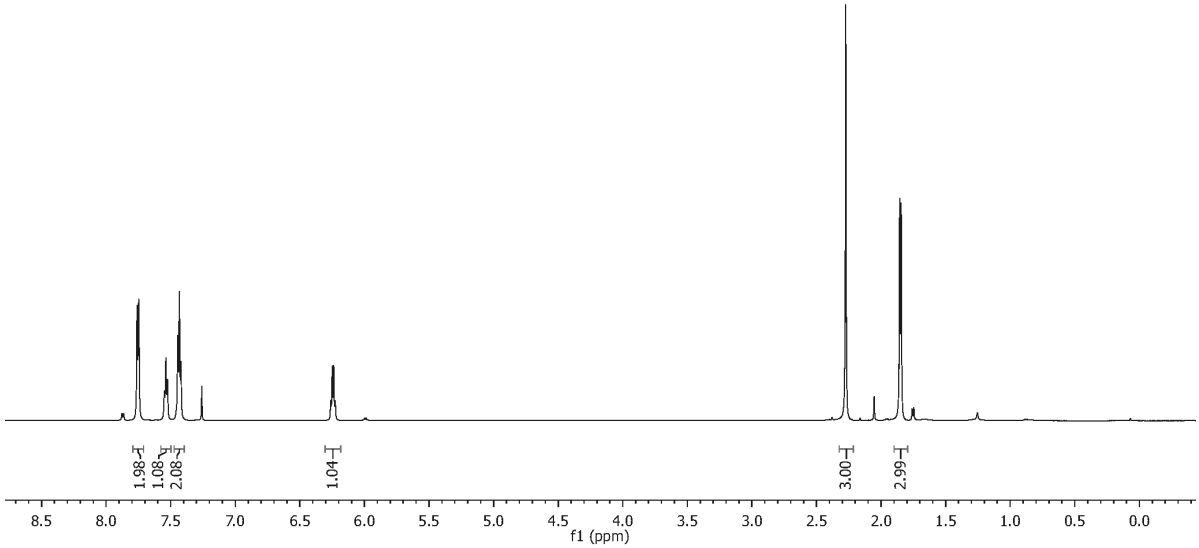
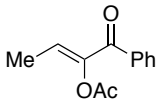
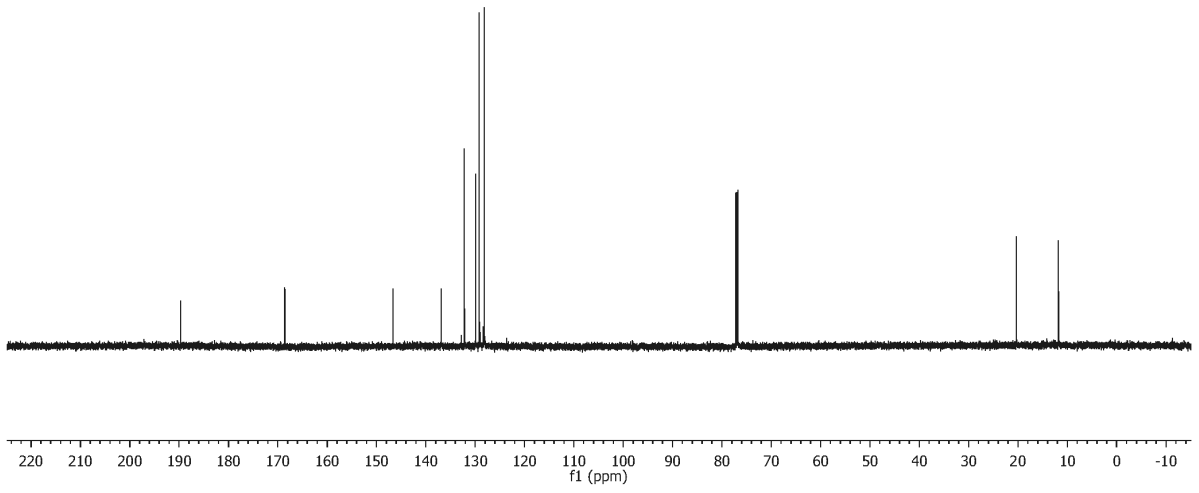


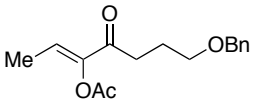
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ product/ jkg-ll-248A-P-C1.fid/ fid
Title jkg-ll-248A-P-C1
Solvent cdcl3
Acquisition Date 2012-03-08T15:05:54
Spectrometer Frequency 150.79



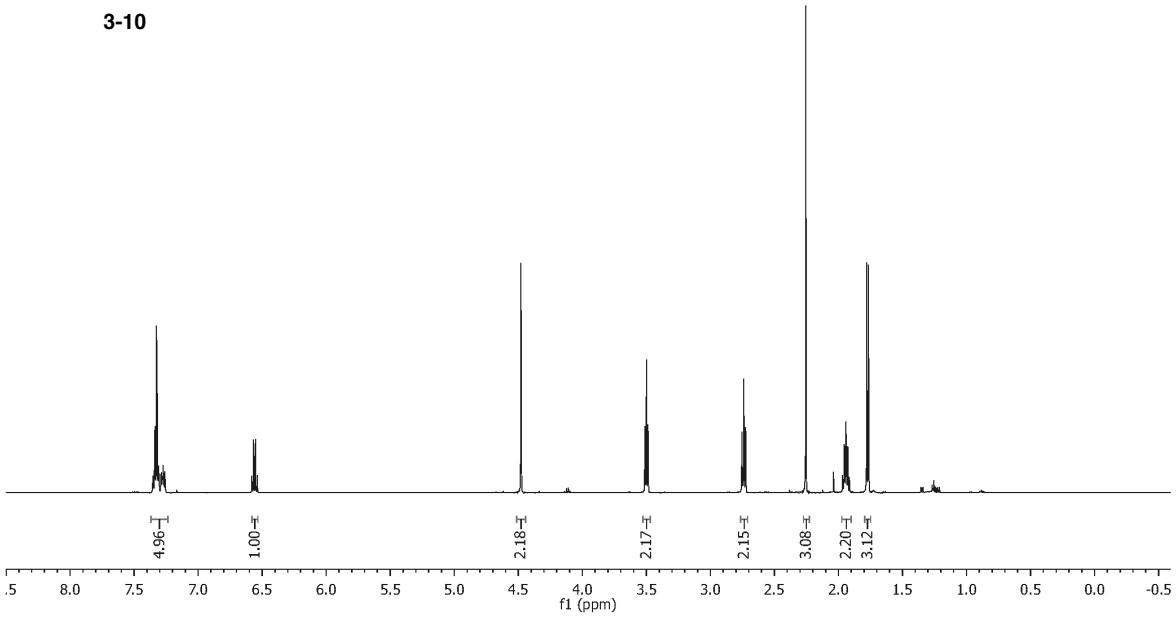
3-8



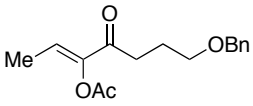
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ product/ jkg-ll-244-P-H.fid/ fid
Title jkg-ll-244-P-H
Solvent CDCl3
Acquisition Date 2012-03-06T16:23:19
Spectrometer Frequency 499.86



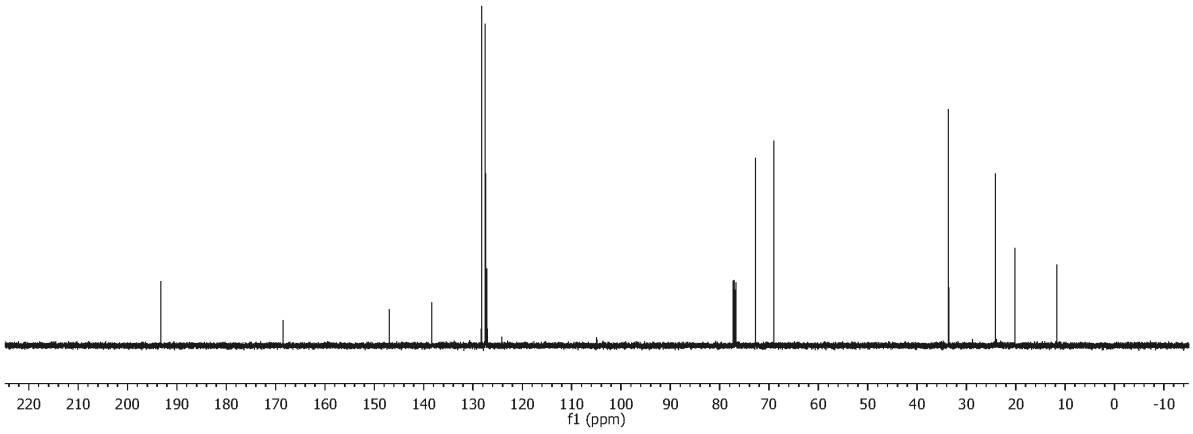
3-10

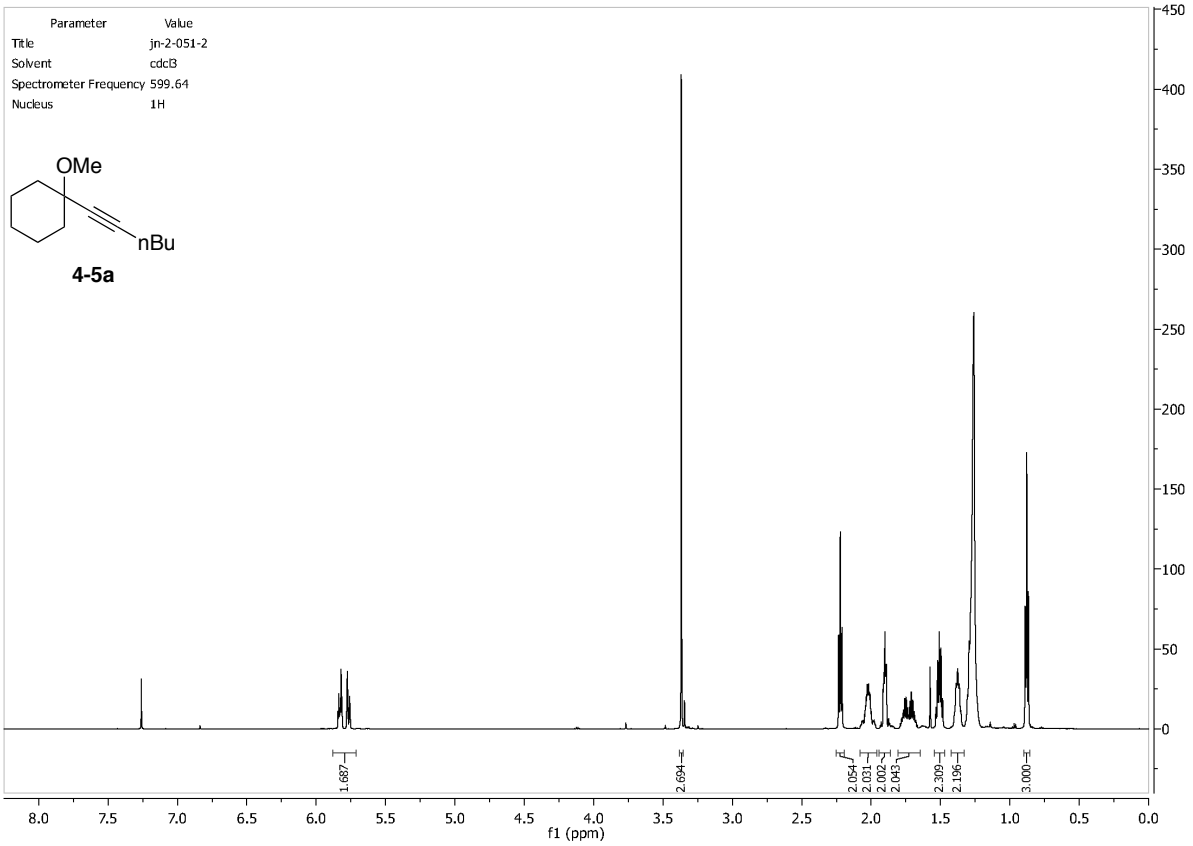


Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ product/ jkg-ll-244-P-C.fid/ fid
Title jkg-ll-244-P-C
Solvent CDCl3
Acquisition Date 2012-03-06T16:25:38
Spectrometer Frequency 125.70



3-10




Parameter Value
Title jn-2-051-2
Solvent cdcl3
Spectrometer Frequency 599.64
Nucleus 1H
OMe
nBu
4-5a
1.687
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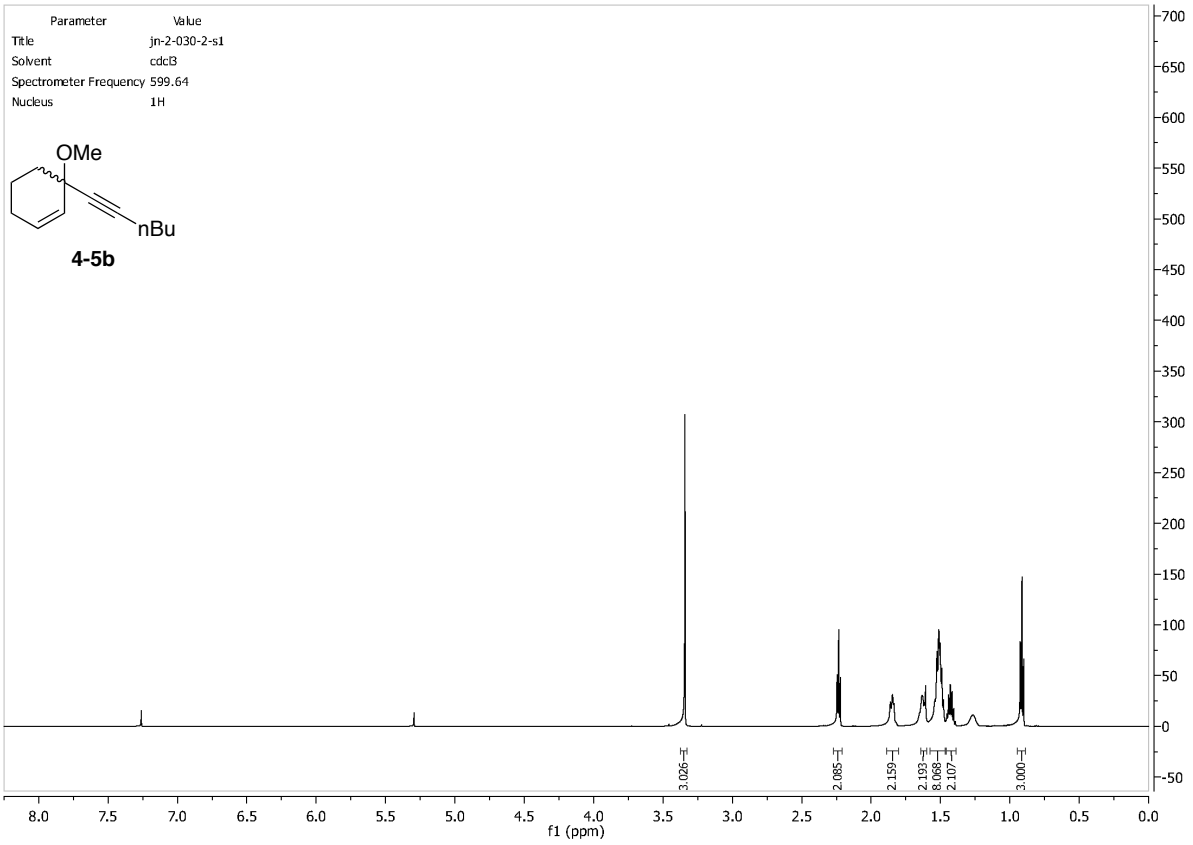
2.043
2.309
2.196
3.000
f1 (ppm)


Parameter Value
Title jn-2-030-2-s1
Solvent cdcl3
Spectrometer Frequency 599.64
Nucleus 1H
OMe
nBu
4-5b
3.026
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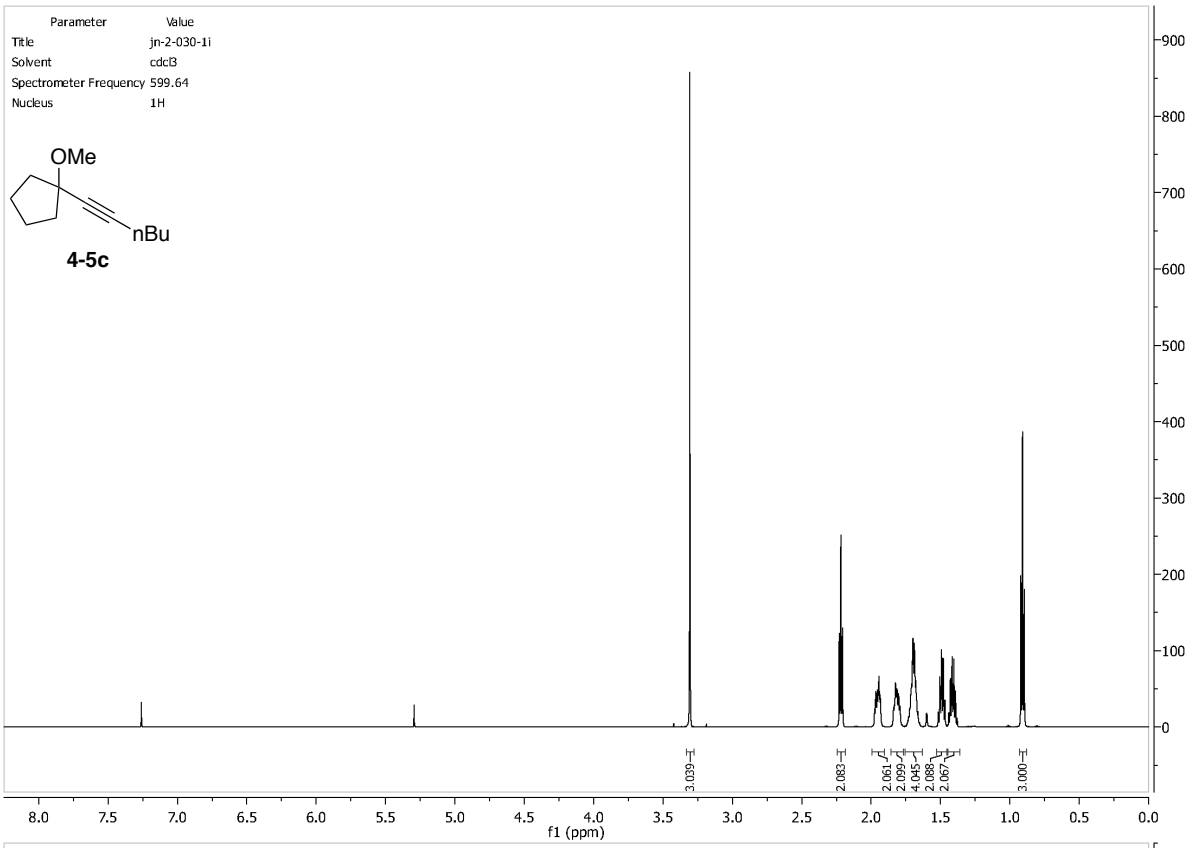
2.193
8.068
2.107
3.000
f1 (ppm)


Parameter Value
Title jn-2-030-1i
Solvent cdcl3
Spectrometer Frequency 599.64
Nucleus 1H
OMe
nBu
4-5c
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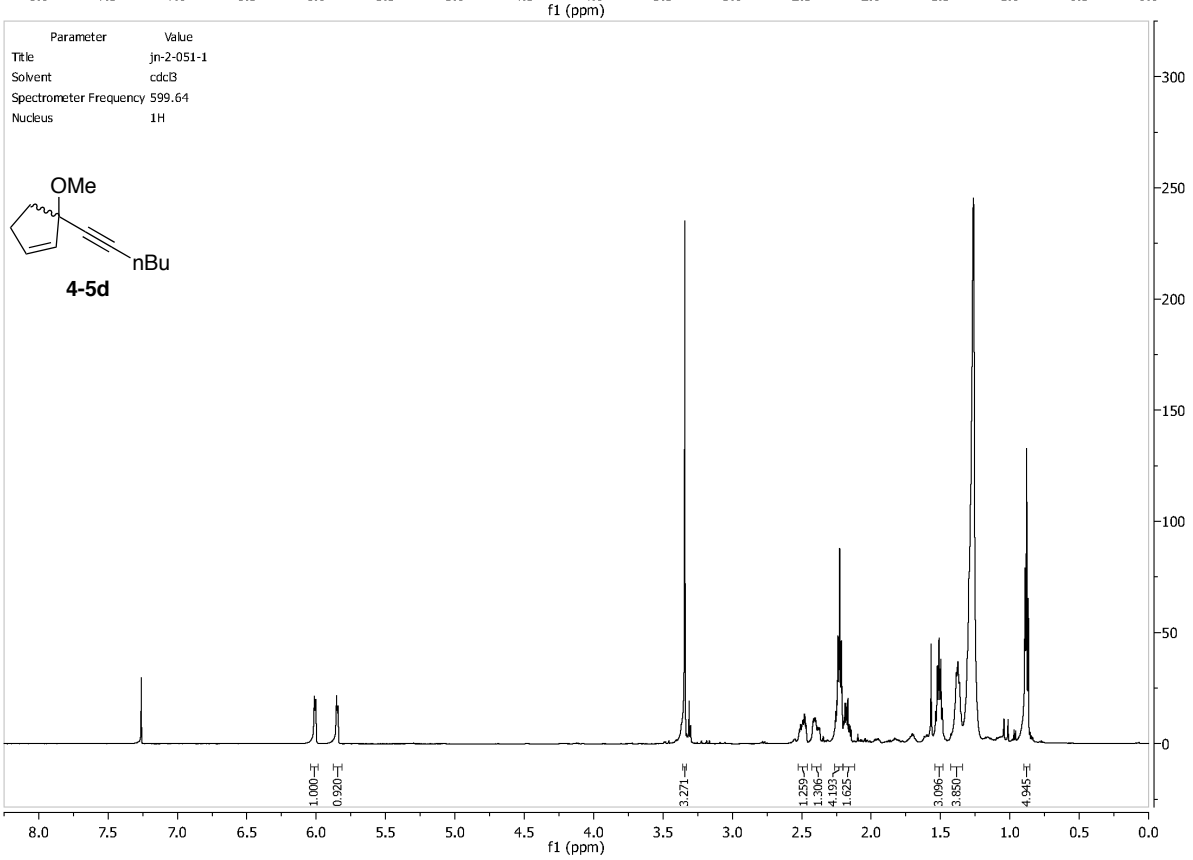
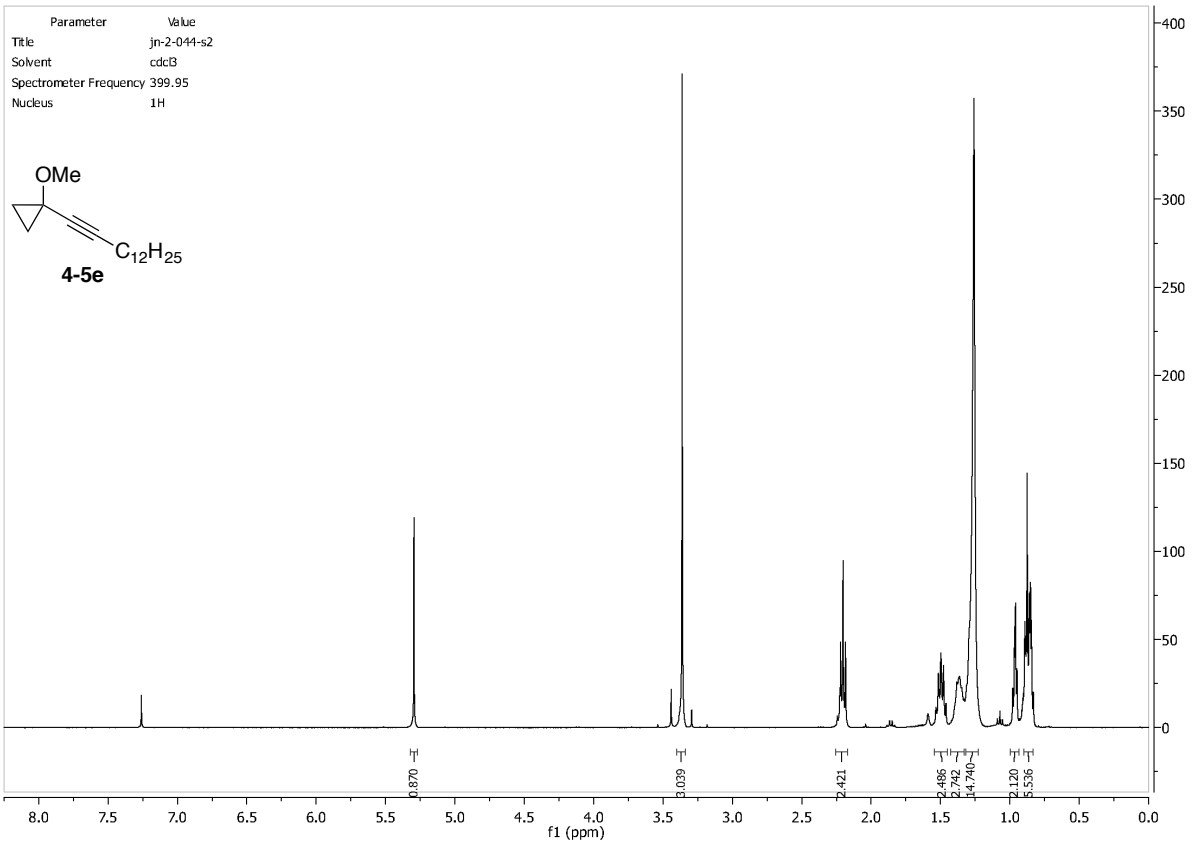
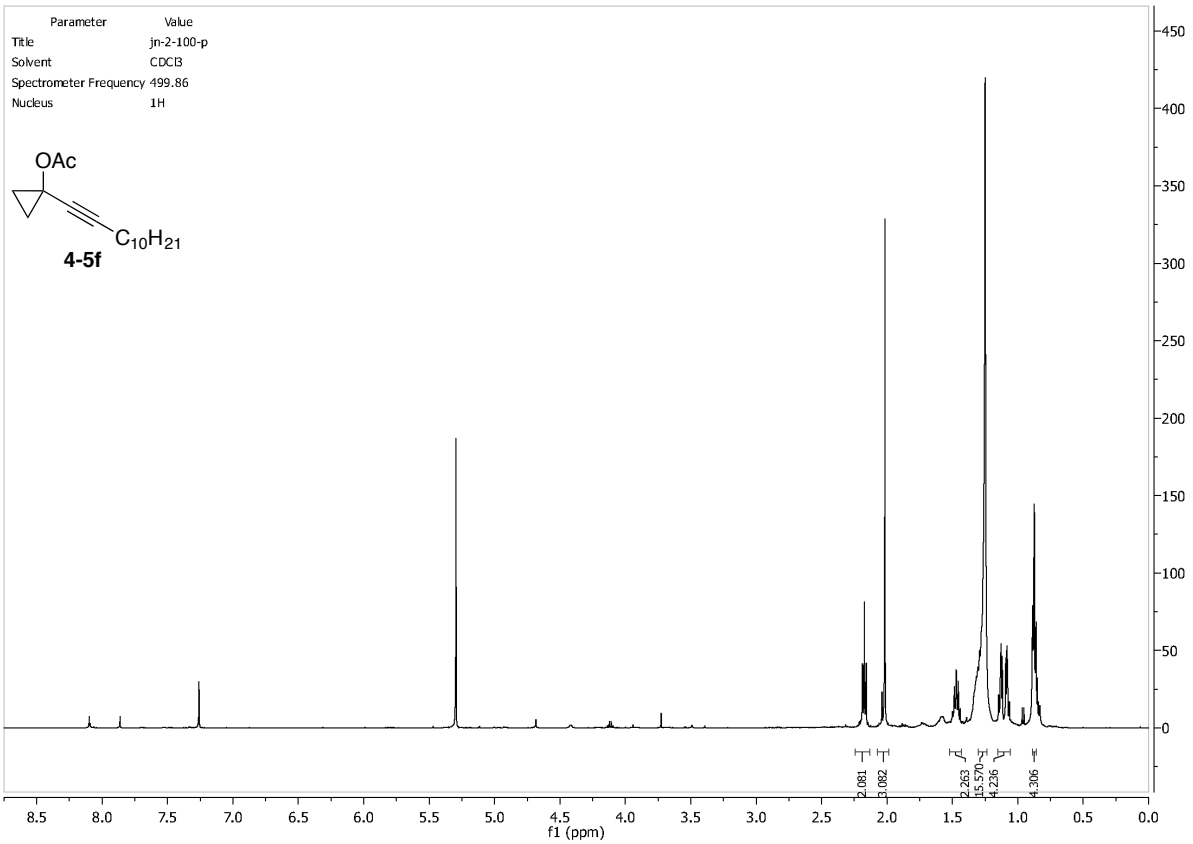
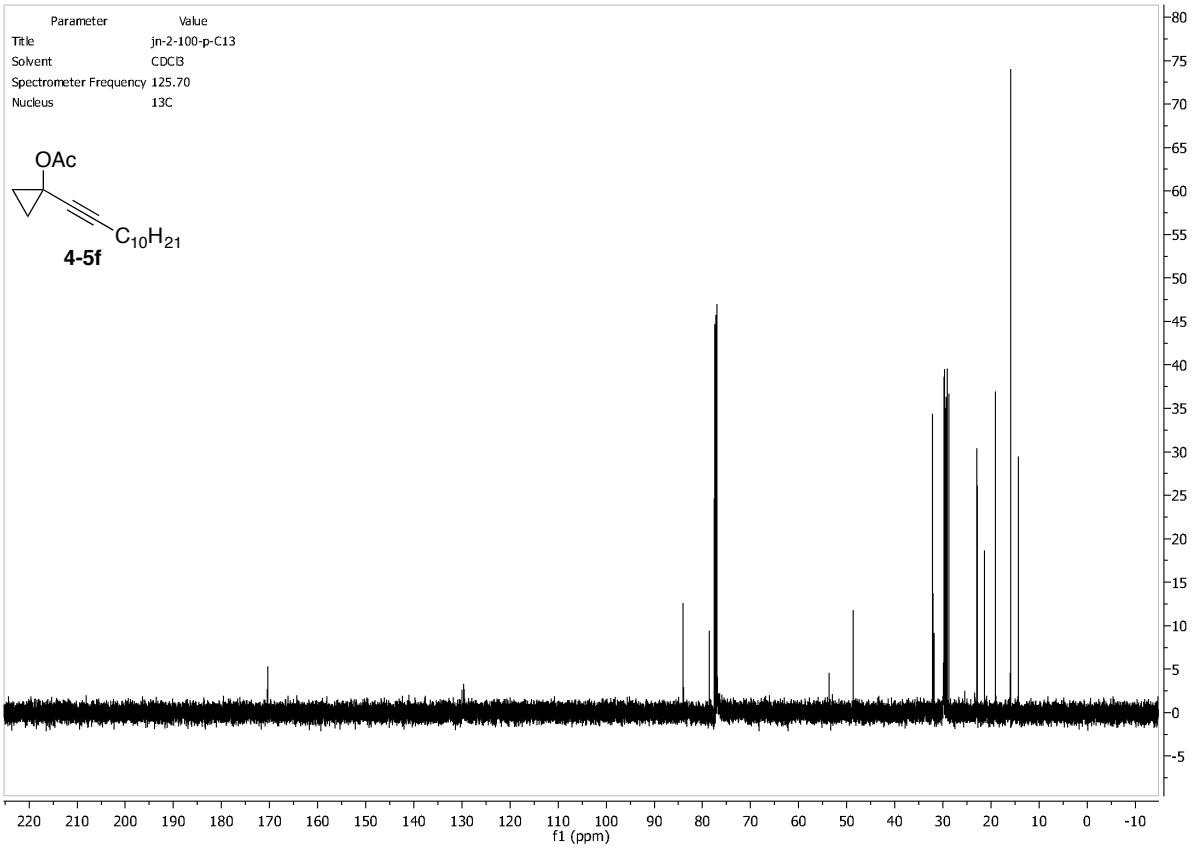
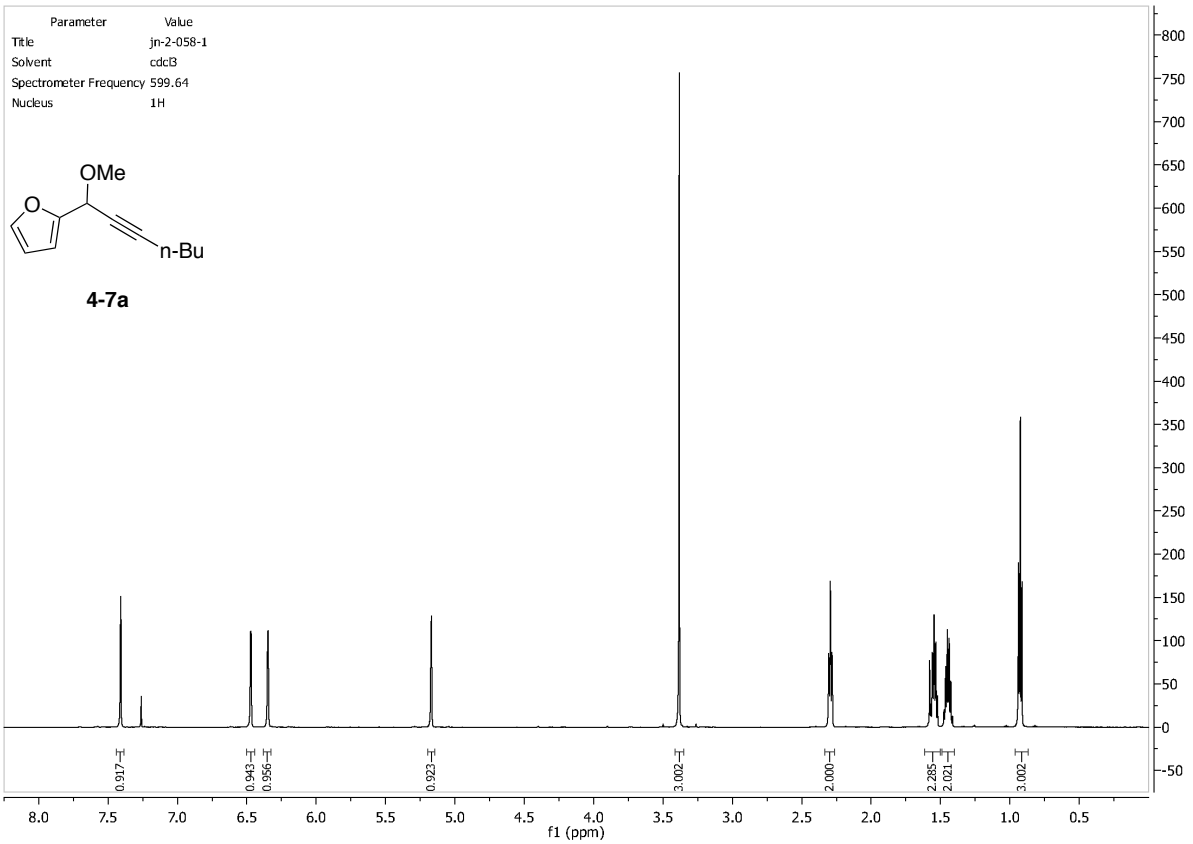
4.045
2.085
2.067
3.000
f1 (ppm)

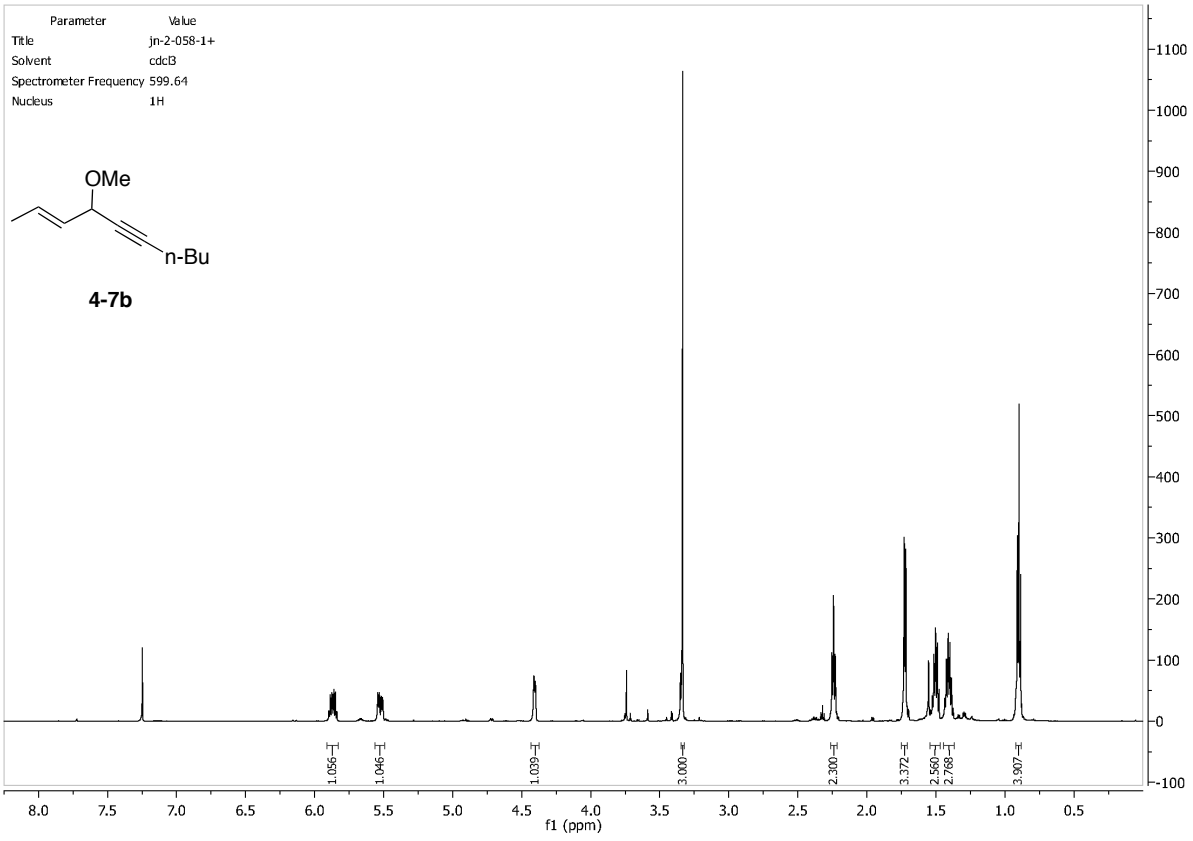

Parameter Value
Title jn-2-051-1
Solvent cdcl3
Spectrometer Frequency 599.64
Nucleus 1H
OMe
nBu
4-5d
1.000
0.920
3.271
1.259
1.306
4.193
1.625
3.096
3.850
4.945
f1 (ppm)


Parameter Value
Title jn-2-044-s2
Solvent cdcl3
Spectrometer Frequency 399.95
Nucleus 1H
OMe
$C_{12}H_{25}$
4-5e
0.870
3.039
2.421
2.486
2.742
14.740
2.120
5.536
f1 (ppm)

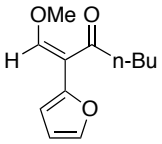

Parameter Value
Title jn-2-100-p
Solvent CDCl3
Spectrometer Frequency 499.86
Nucleus 1H
OAc
C10H21
4-5f
2.081
3.082
2.263
15.570
4.236
4.306
f1 (ppm)


Parameter Value
Title jn-2-100-p-C13
Solvent CDCl3
Spectrometer Frequency 125.70
Nucleus 13C
OAc
C10H21
4-5f
f1 (ppm)


Parameter Value
Title jn-2-058-1
Solvent cdcl3
Spectrometer Frequency 599.64
Nucleus 1H
OMe
O
n-Bu
4-7a
0.917
0.943
0.956
0.923
3.002
2.000
2.285
2.021
3.002
f1 (ppm)

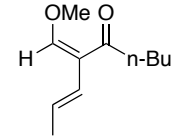

Parameter Value
Title jn-2-058-1+
Solvent cdcl3
Spectrometer Frequency 599.64
Nucleus 1H
OMe
n-Bu
4-7b
1.056
1.046
1.039
3.000
2.300
3.372
2.560
2.768
3.907
f1 (ppm)

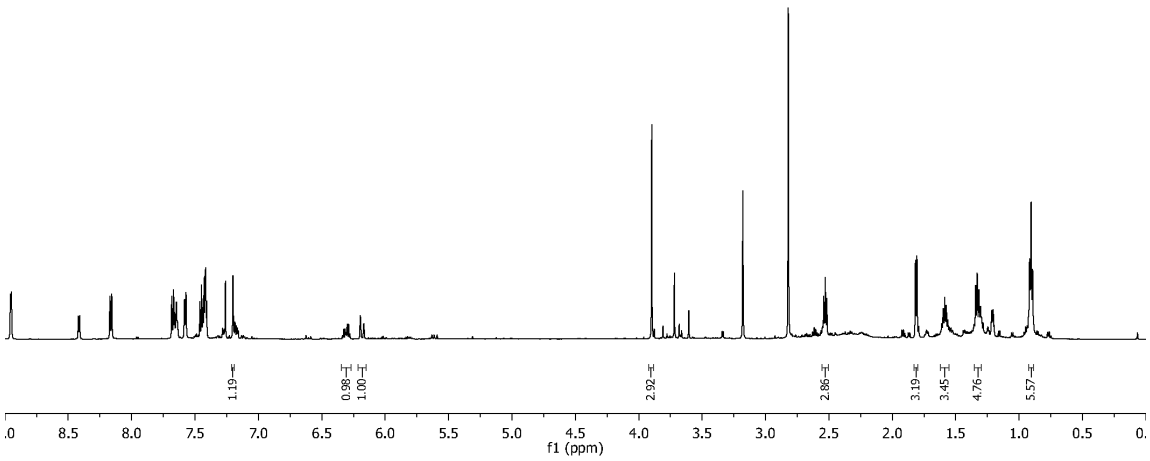
Parameter	Value
Title	jn-2-062-1b
Solvent	cdcl3
Spectrometer Frequency	599.64
Nucleus	1H



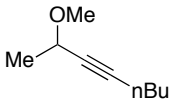
4-8a

Parameter	Value
Title	jn-2-062-2a
Solvent	cdcl3
Spectrometer Frequency	599.64
Nucleus	1H



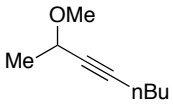


Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ CASE-SM/ jkg-II-224A-P-H.fid/ fid
Title jkg-II-224A-P-H
Solvent CDCl3
Acquisition Date 2012-02-27T13:11:45
Spectrometer Frequency 499.86

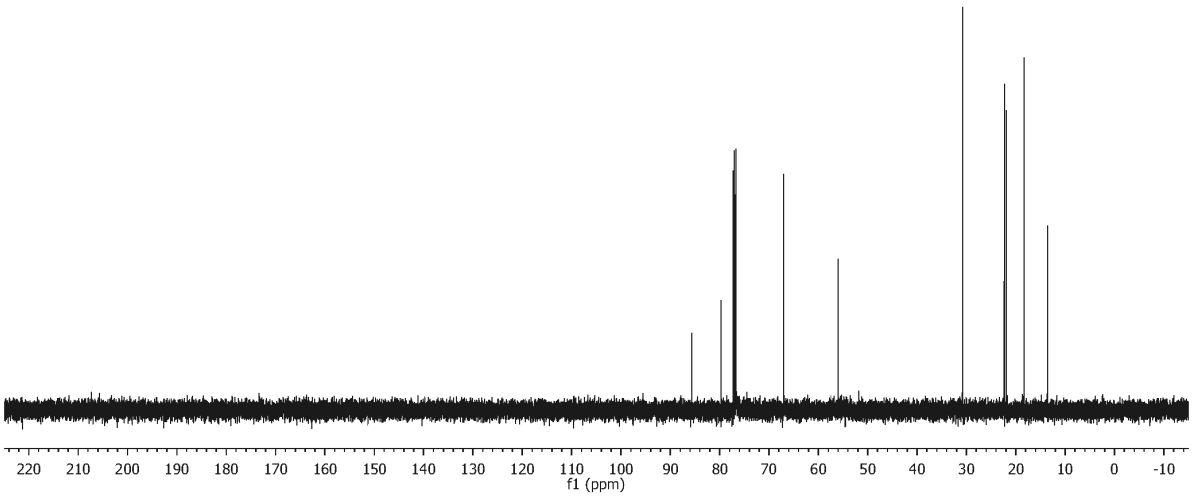


4-1

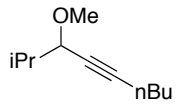
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ CASE-SM/ jkg-II-224A-P-C.fid/ fid
Title jkg-II-224A-P-C
Solvent CDCl3
Acquisition Date 2012-02-27T13:14:02
Spectrometer Frequency 125.70



4-1

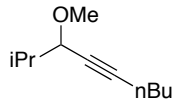


Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-114_H1_pure.fid/ fid
2 Title	BD-2-114_H1_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	599.63

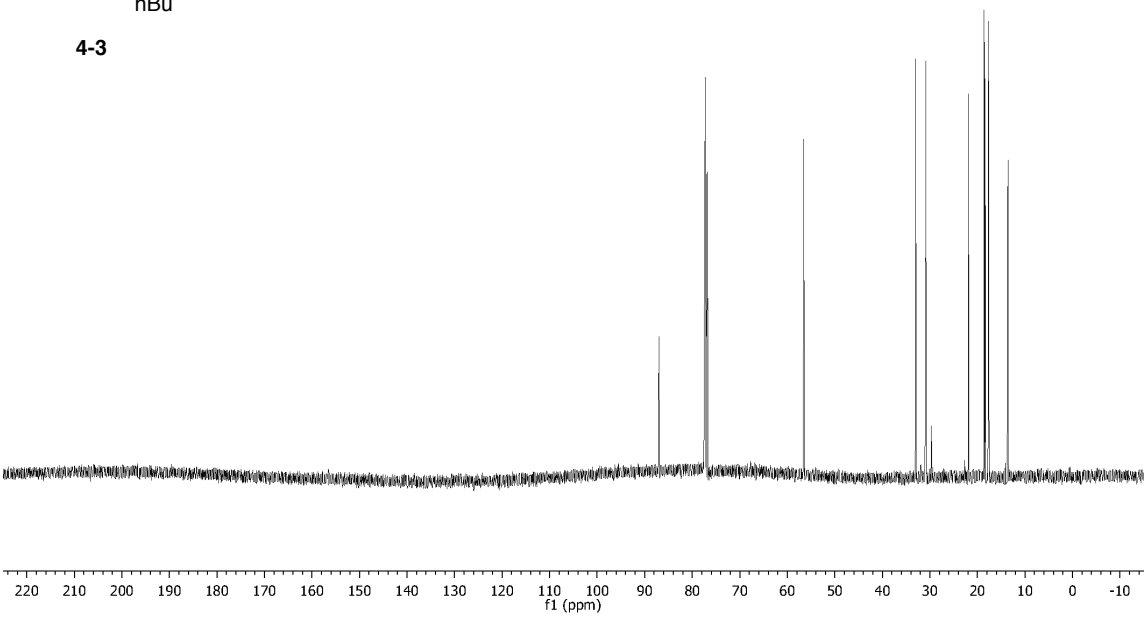


4-3

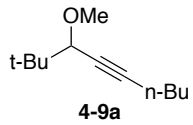
Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-114_C13_pure.fid/ fid
2 Title	BD-2-114_C13_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



4-3

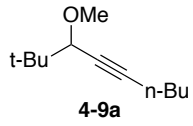


Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-154_H1_pure.fid/ fid
2 Title	BD-2-154_H1_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	599.63



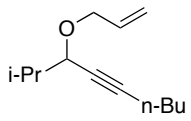
4-9a

Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-154_C13_pure.fid/ fid
2 Title	BD-2-154_C13_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



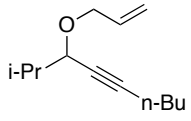
4-9a

Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-119_H1_pure.fid/ fid
2 Title	BD-2-119_H1_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	599.63

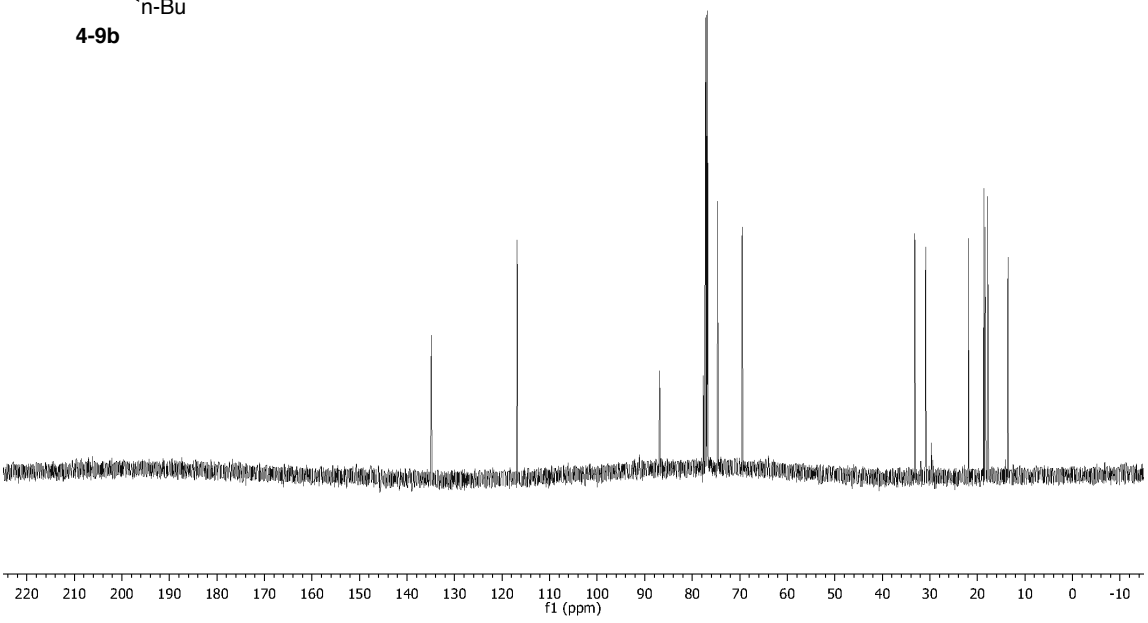


4-9b

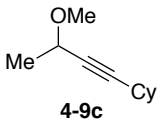
Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-119_C13_pure.fid/ fid
2 Title	BD-2-119_C13_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



4-9b

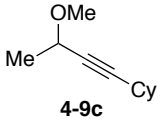


Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-129_H1_pure.fid/ fid
2 Title	BD-2-129_H1_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	599.63

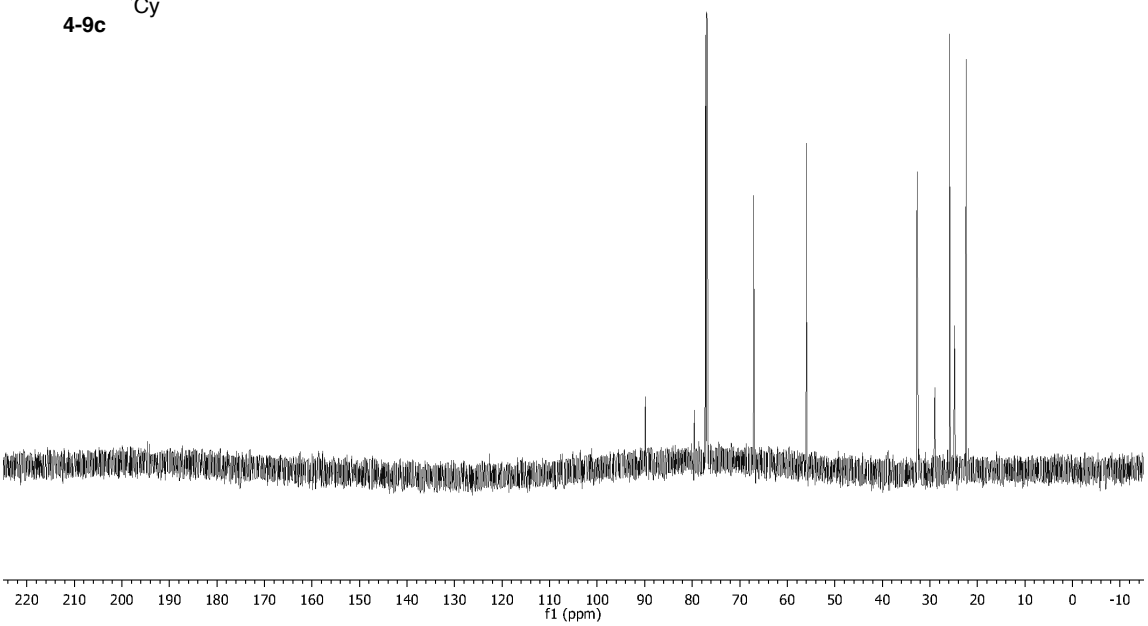


4-9c

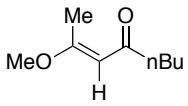
Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-129_C13_pure.fid/ fid
2 Title	BD-2-129_C13_pure
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



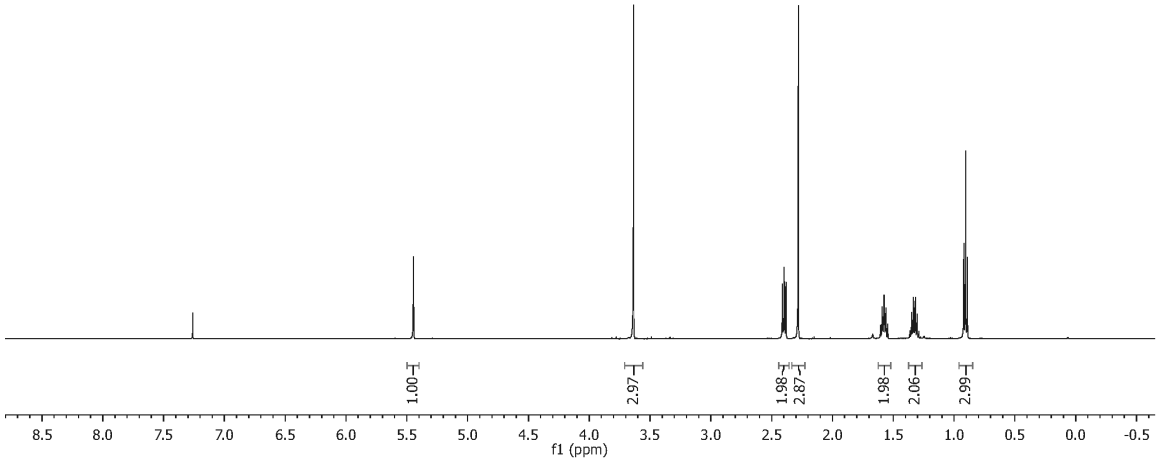
4-9c



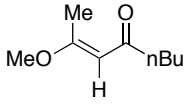
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ product/ jkg-II-229A-P-H.fid/ fid
Title jkg-II-229A-P-H
Solvent CDCl3
Acquisition Date 2012-02-28T21:17:49
Spectrometer Frequency 499.86



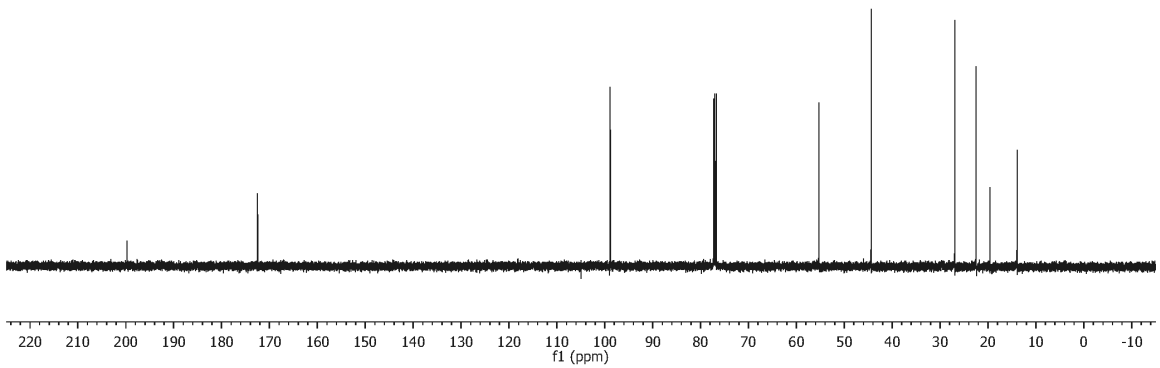
4-2b(*E*)



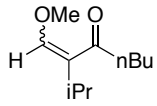
Data File Name C:/ Users/ zhanglab1/ Desktop/ NMR/ jkg/ product/ jkg-II-229A-P-C.fid/ fid
Title jkg-II-229A-P-C
Solvent CDCl3
Acquisition Date 2012-02-28T21:20:39
Spectrometer Frequency 125.70



4-2b(*E*)

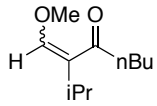


Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-139A_fr4-8.fid/ fid
2 Title	BD-2-139A_fr4-8
3 Solvent	cdcl3
4 Spectrometer Frequency	599.63

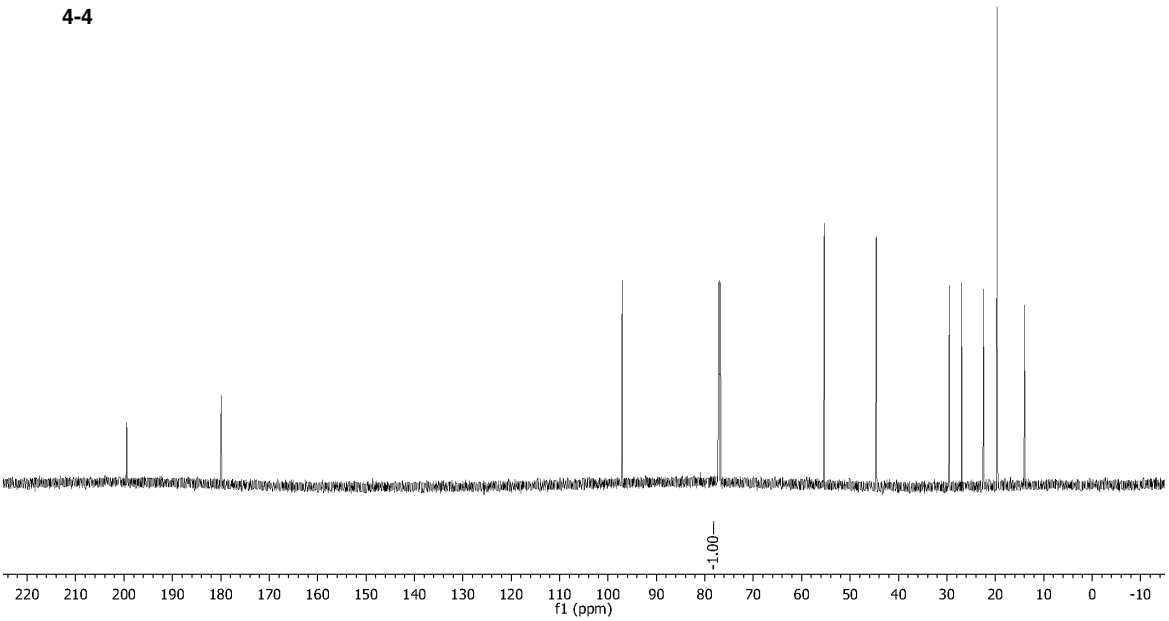


4-4

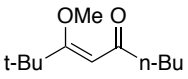
Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-139A_4-8_C13.fid/ fid
2 Title	BD-2-139A_4-8_C13
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



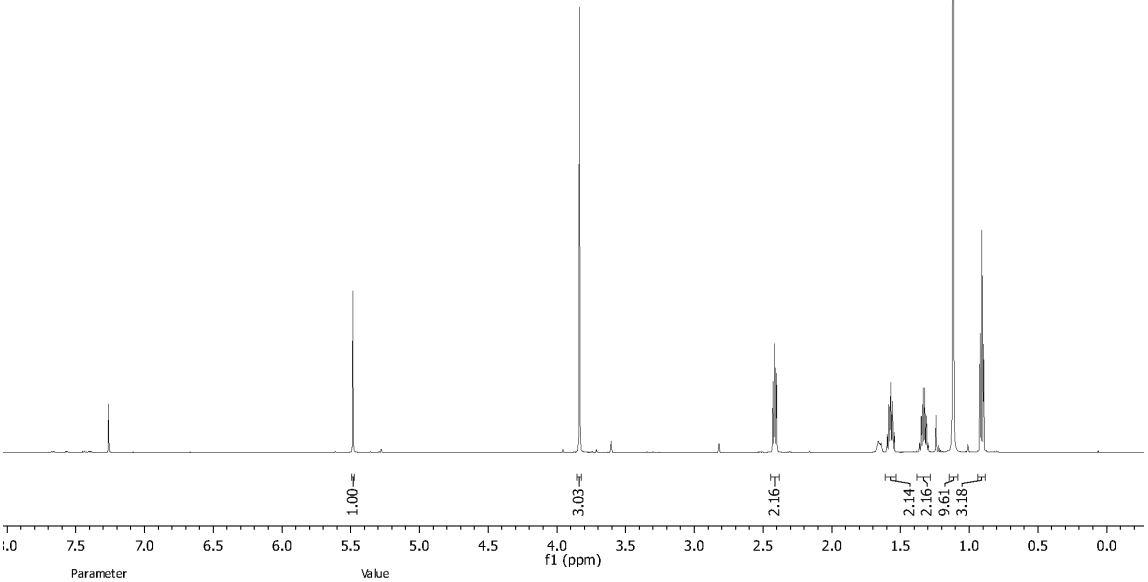
4-4



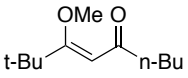
Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-161A_fr4_H1.fid/ fid
2 Title	BD-2-161A_fr4_H1
3 Solvent	cdcl3
4 Spectrometer Frequency	599.63



4-10a

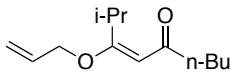


Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-161A_4_C13.fid/ fid
2 Title	BD-2-161A_4_C13
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



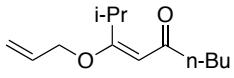
4-10a

Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-153A_4-7_H1.fid/ fid
2 Title	BD-2-153A_4-7_H1
3 Solvent	cdcl3
4 Spectrometer Frequency	599.63

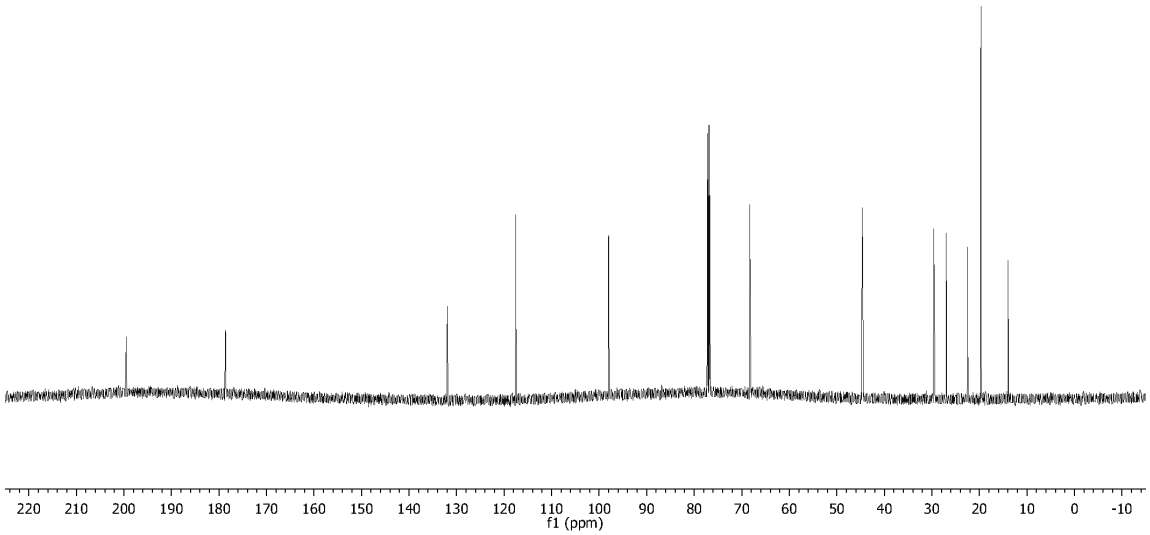


4-10b

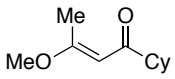
Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-153A_4-7_C13.fid/ fid
2 Title	BD-2-153A_4-7_C13
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



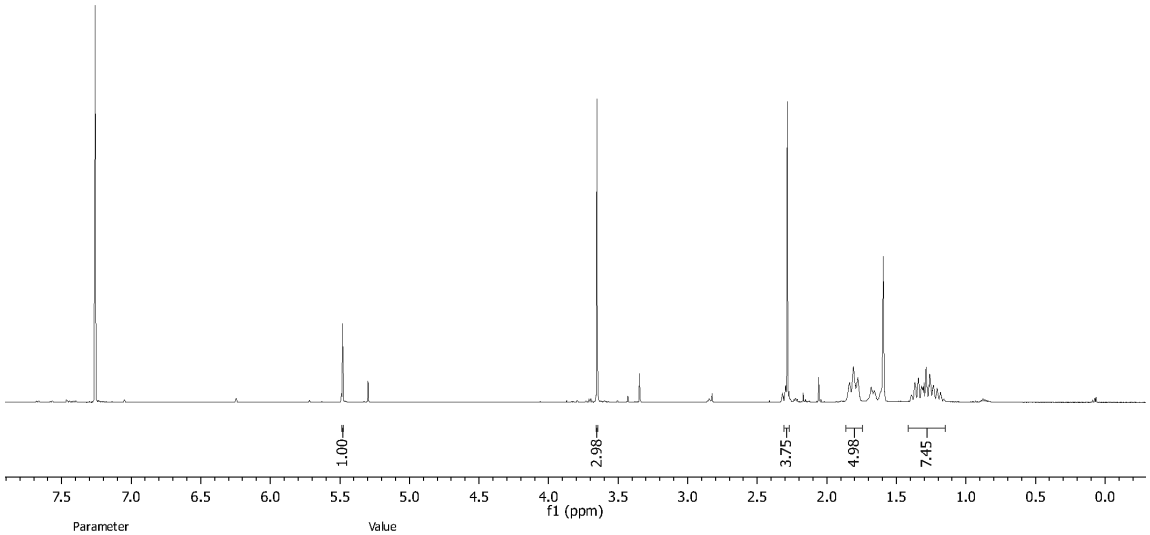
4-10b



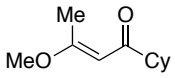
Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-137C_fr1-8.fid/ fid
2 Title	BD-2-137C_fr1-8
3 Solvent	CDCl3
4 Spectrometer Frequency	499.86



4-10c



Parameter	Value
1 Data File Name	C:/ Users/ zhang laptop/ Desktop/ NMR/ bdsouza/ BD-2-137C_1-7_C13.fid/ fid
2 Title	BD-2-137C_1-7_C13
3 Solvent	cdcl3
4 Spectrometer Frequency	150.79



4-10c