

(N-Heterocyclic-Carbene)Copper(I)-Catalyzed Carbon-Carbon
Bond Formation Using Carbon Dioxide

by Gergely Sirokman

B.S. Chemistry
Brandeis University, 2001

Submitted to the Department of Chemistry in Partial Fulfillment of the Requirements for
the Degree of

DOCTOR OF PHILOSOPHY IN
INORGANIC CHEMISTRY

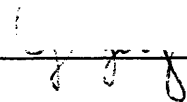
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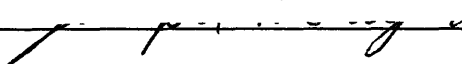
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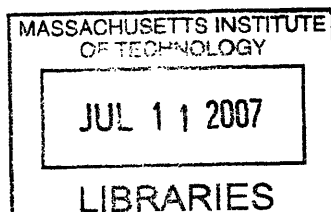


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ABSTRACT

This thesis presents work towards the development of a new catalytic C—C bond forming reaction. Alkynes and olefins insert into [(IPr)CuH]₂ (IPr = *N,N*-bis-(2,6-diisopropylphenyl)-1,3-imidazol-2-ylidene) to give copper vinyl and copper alkyl complexes. These copper complexes insert CO₂ into the Cu—C bond to form copper acrylate and copper carboxylate complexes. Acrylic and carboxylic acids can be isolated by hydrolysis.

A catalytic cycle based on (IPr)copper(I) was developed. Alkynes undergo reductive carboxylation to give acrylic acids in moderate yields. Unexpected interactions between several components of the catalytic system led to a number of side reaction, most importantly between [(IPr)CuH]₂ and the product silyl acrylate. The use of silylcarbonate salts to desylilate the product enhanced yield. In addition, silylcarbonates can also serve as a source of CO₂.

Thesis Supervisor: Joseph P. Sadighi
Title: Associate Professor of Chemistry

Victory needs no explanation.

Defeat allows none.

-Anon.

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List of Abbreviations

Anal. Calcd.	elemental analysis calculated
Ar	where part of a structure: aryl, alone: argon
Ar ^f	3,5-bis(trifluoromethyl)phenyl
bpy	2,2'-bipyridine
Bu	butyl
cat.	catalyst
Cy	cyclohexyl
D	deuterium
DFT	density functional theory
dbu	1,8-diazabicyclo[5.4.0]undec-7-ene
Et	ethyl
equiv	equivalent
<i>i</i> -	<i>iso</i> -
IAd	<i>N,N'</i> -bis-(1-adamantyl)-1,3-imidazol-2-ylidene
IMes	<i>N,N'</i> -bis-(2,4,6-trimethylphenyl)-1,3-imidazol-2-ylidene
IPr	<i>N,N'</i> -bis-(2,6-diisopropylphenyl)-1,3-imidazol-2-ylidene
ItBu	<i>N,N'</i> -bis-(<i>tert</i> -butyl)-1,3-imidazol-2-ylidene
Me	methyl
meIPr	4,5-dimethyl- <i>N,N'</i> -bis-(<i>iso</i> -propyl)-1,3-imidazol-2-ylidene
mmol	millimole
<i>n</i> -	normal (straight chain)
NHC	N-heterocyclic carbene
OAc	acetate
OTf	triflate
Ph	phenyl
pinB-Bpin	pinacolborane, 4,4,5,5-tetramethyl-1,3,2-dioxaborolane
Pr	propyl
salen	<i>N,N'</i> -bis-(salicylidene)-1,2-diaminoalkane
SIPr	<i>N,N'</i> -bis-(2,6-diisopropylphenyl)-1,3-imidazol-2-ylidene
SICy	<i>N,N'</i> -bis-(cyclohexyl)-1,3-imidazol-2-ylidene
<i>t</i> -	<i>tert</i> -
THF	tetrahydrofuran

Chapter 1
Introduction

Introduction

Carbon dioxide activation receives a great deal of attention as it is a readily available resource. Our current energy economy relies mostly on the burning of fossil fuels, which releases CO₂. Although industrial use of CO₂ is unlikely to have an impact on the environmental effects of carbon dioxide emissions, methods of activating CO₂ are of interest as new bond forming reactions could increase their synthetic utility. The transformation of carbon dioxide to useful products is a desirable goal, facing the hurdle of CO₂ activation.¹ Much has been accomplished in catalytic C—O²⁶ and C—H¹⁰ bond formation reactions with CO₂, but processes for the catalytic formation of C—C bonds with CO₂ are rare.

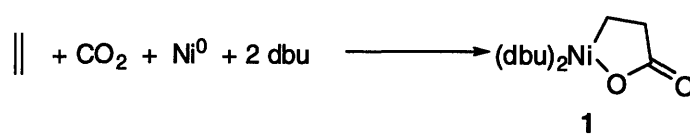
This thesis reports work using N-heterocyclic carbene (NHC) supported copper complexes to generate carbon—carbon bonds using CO₂. In this chapter a brief overview of carbon—carbon bond forming reactions involving CO₂ is given. The use of CO₂ as a substrate in catalysis is then presented. A discussion on the nature of NHCs and on NHC-supported complexes is presented.

Stoichiometric C—C Bond Formations Involving CO₂

Carbon—carbon formation has long been of interest to synthetic chemists, and a great wealth of chemistry, from the ubiquitous Grignard reaction on, has been developed to accomplish it. A great many of these transformations are summarized by Brown and Cooley in their review.⁷²

Reductive metal-assisted coupling of CO₂ to unsaturated organic substrates has been explored as a means of carbon-carbon bond formation. A broad range of products

have been generated from the addition of CO₂ to an olefin using a nickel complex.² When ethylene and CO₂ are added to Ni⁰ and 1,8-diazabicyclo[5.4.0]undec-7-ene (dbu) the complex formed, **1**, is a metallocycle with a carbon—carbon bond between the carbon of CO₂ and the ethylene.^{9b} This complex further reacts with unsaturated organic substrates to give a large range of organic carboxylic acid products. Examples of rhodium-,³ iridium-,⁴ and palladium-assisted⁵ couplings have also been reported.

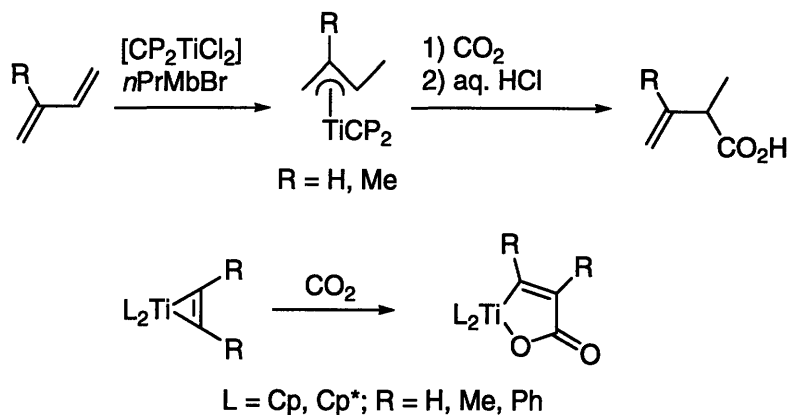


Scheme 1: Ni-mediated coupling of ethylene and CO₂. [Ref. 9b]

The electron-rich copper complex (Cy₃P)₃CuMe inserts CO₂ to give (Cy₃P)₃CuOAc.⁶ The titanium complex [Cp₂TiCl₂], after treatment with alkylmagnesium bromides, reacts with 1,3-dienes to generate allyl complexes, which afford β,γ-unsaturated carboxylic acids after addition of CO₂ and acidic workup.⁷ Titanium complexes can also facilitate the coupling of CO₂ into ethene, 2-butene, or stilbene to form cyclic titanofuranone complexes.⁸ When the nickel complex [NiBrPh(bpy)] is exposed to CO₂ in DMF solution and subsequently acidified the recovered product includes benzoic acid indicating the insertion of CO₂ into the Ni–aryl bond.⁹

Catalytic Conversions of CO₂

While it is important to understand stoichiometric CO₂ insertion chemistry, catalytic processes to integrate CO₂ into useful products are the ultimate goals of these lines of investigation.



Scheme 2: Reactions of titanium olefins complexes with CO₂. [Refs. 7, 8]

The insertion of CO₂ into M–H bonds, and the synthesis of formic acid from CO₂, in general, is of great industrial interest. Formic acid and its salts find uses in animal husbandry, leatherworking, food preservation, and as a reducing agent in a number of preparative scale industrial processes.¹⁰ Yearly industrial output of formic acid is 300,000 tons.¹¹ Achieving catalytic conversion to formic acid is one way to generate a commodity product from carbon dioxide. A great deal of progress has been made in this area of CO₂ research. The various avenues to this transformation include electrochemical and photochemical reductions, and transition—metal—catalyzed hydrogenation.¹⁵

Electrochemical reductions can be quite effective at generating formate. The complex [Co(terpy)₂](PF₆) converted CO₂ to formic acid with over 500 turn-overs in a four—hour reaction time.¹² Other electrochemical reductions, especially when run in an aqueous medium, encounter the problem of generating significant amounts of byproducts, mostly CO and H₂.¹³ Dubois has reported the efficient and selective electrochemical reduction of CO₂ assisted by palladium¹⁴, nickel¹⁵ and platinum¹⁴ catalyst.

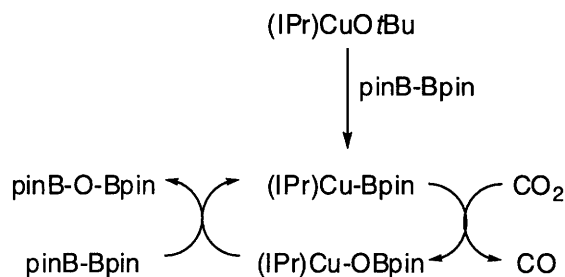
Photochemical systems with and without metal catalysts have been shown to reduce CO₂. Semiconductor materials as electrodes or colloids can reduce CO₂ such that

formate is the main product. A well studied system is one based on the $[\text{Ru}(\text{bpy})_3]^{+2}$ cation.^{16,17} This cation combined with $[\text{Ru}(\text{bpy})_2(\text{CO})(\text{L})]^{n+}$ ($\text{L}=\text{CO}$, $n=2$; $\text{L}=\text{H}\cdot\text{Cl}$, $n=1$), using triethylamine as a reducing agent, can generate 3700 equivalents of product.^{21b}

The metal-catalyzed hydrogenation of CO_2 has been explored extensively. In the earliest example, a catalyst generated from TiCl_4 and Mg generates magnesium formate when alternating equivalents of H_2 and CO_2 were added to the reaction.¹⁸ This method generated 15 equivalents of formate per Ti . A range of group 9 and 10 metal catalysts have been shown to catalytically hydrogenate CO_2 .¹⁹ A good example of such catalyst systems is $[(\text{cod})\text{Rh}(\mu\text{-Cl})_2]$ in the presence of $\text{Ph}_2\text{P}(\text{CH}_2)_4\text{PPh}_2$ which, at room temperature and 20 bar of H_2 and CO_2 each, turns over 1150 times.^{23d} A base must be used as a thermodynamic sink to drive the reactions forward.

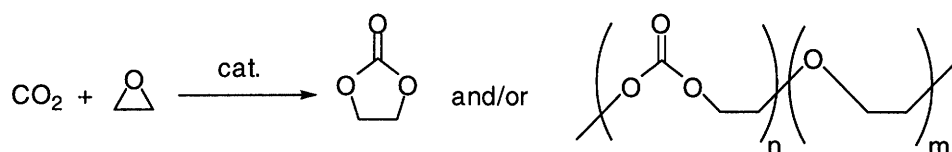
The hydrosilylation of CO_2 by ruthenium complexes was first reported in 1981. Koinuma reported the use of the catalyst $\text{RuCl}_2(\text{PPh}_3)_3$ to generate 14 equivalents of HCO_2SiR_3 per ruthenium from CO_2 and HSiR_3 .²⁰ Use of ruthenium clusters for the same transformation was reported the same year,²¹ and recent improvements on this reaction give high yields.²² Matsuo and Kawaguchi have reported a zirconium based catalyst that reduces CO_2 to methane with silanes as the hydrogen source.²³

The complex $(\text{IPr})\text{Cu}\text{-Bpin}$ reacts with CO_2 to generate CO and $(\text{IPr})\text{CuO}\text{-Bpin}$.²⁴ This reaction is of interest because CO is widely used in organic synthesis. The reaction proceeds catalytically in the presence of excess pinB-Bpin. The generation of CO from CO_2 can be done efficiently and rapidly. The mechanism of this reaction was investigated by DFT calculation.²⁵



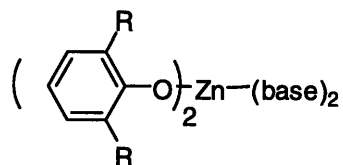
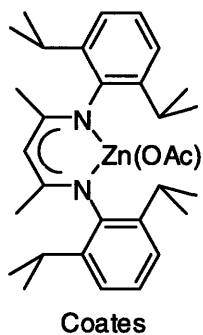
Scheme 3: Catalytic conversion of CO₂ to CO using an (NHC)copper catalyst. [Ref. 24]

Another approach to catalytic CO₂ fixation has been the reaction of CO₂ with epoxides to generate organic carbonates.²⁶ Formation of monomeric products from CO₂ and epoxides has been studied extensively. Quaternary ammonium and phosphonium halides are effective catalysts for the coupling of CO₂ and epoxides to generate cyclic carbonates.²⁷ Other catalysts have been developed for this transformation, such as triphenylstibine dibromide and tetraphenyl stibonium bromide.²⁸ Tin complexes such as Bu₃SnI are also very competent catalysts for cyclic carbonate formation.²⁹



Scheme 4: General types of carbonate formation from CO₂ and epoxide. [Ref 26]

The copolymerization of epoxides and CO₂ has been a widely explored field,²⁶ zinc catalysts showing early prominence.^{30,31,73} Recently improvements using salen supported metal catalyst (salen = N,N'-bis(salicylidene)-1,2-diaminoalkane) have been reported.^{32, 74} A range of other late transition metal catalysts exist for this transformation.³⁶



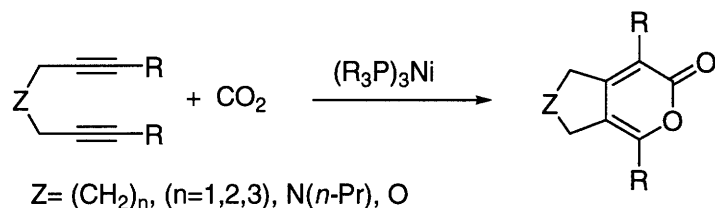
Darensbourg

R = Ph, *t*-Bu, *i*-Pr base = THF,
Et₂O, propylene carbonate

Scheme 5: Zinc catalysts for the copolymerization of CO₂ and epoxide. [Refs. 30, 31]

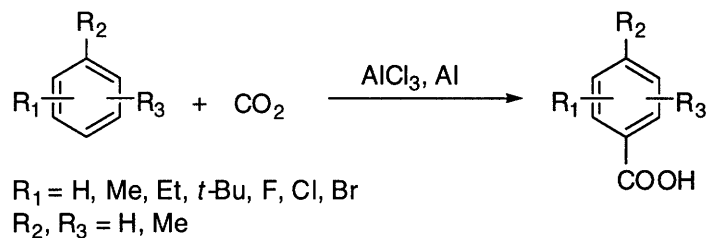
Furthermore, cyclic carbonates can be polymerized by a ring opening polymerization reaction. Five-membered rings are polymerized at higher temperatures and less efficiently than six-membered organic carbonates. A variety of catalysts, such as BF₃, TiCl₄, MeOTf, Bu₃SnOMe, are successful at propagating this reaction.^{36,33} Some of these, for example BF₃, lead to partial decarboxylation, the theory being that loss of gaseous CO₂ helps drive the polymerization thermodynamically.³⁴ Others, TiCl₄ and Bu₃SnOMe, lead to no decarboxylation.

In work by Tsuda, catalytic carbon-carbon bond formation using CO₂ was reported.³⁵ A tris(trialkylphosphine)nickel complex catalyzed the cycloaddition of CO₂ with alkynes. The reaction formed a bicyclic product (Scheme 6). Yields up to 85% were observed with catalyst loadings of 5 to 10%. Tsuda also reported the formation of 4,5-diethoxy- α -pyrone from CO₂ and ethoxyethyne using a phosphine supported Ni(0)catalyst. Louie expanded on this work using N-heterocyclic carbene (NHC) supported Ni(0) complexes to generate carbonates from CO₂ and diynes with yields similar to those in Tsuda's work.³⁶ Louie also studied the regioselectivity of these reactions by using asymmetric diynes, but saw no steric effect on insertion selectivity.



Scheme 6: Ni-catalyzed α -pyrone formation from diynes and CO_2 [Ref 35a].

Carbon dioxide insertion into aryl C–H bonds has been reported. Olah reported a system in which a mix of AlCl_3 and Al facilitates the insertion of CO_2 into benzene.³⁷ Although not catalytic, the system does provide yields as high as 111% based on AlCl_3 when large amounts of metallic Al additive are used to neutralize HCl generated during the reaction. Based on DFT calculations it is believed that AlCl_3 is responsible for superelectrophilic activation of CO_2 , allowing the subsequent reaction with aromatic substrates to take place.

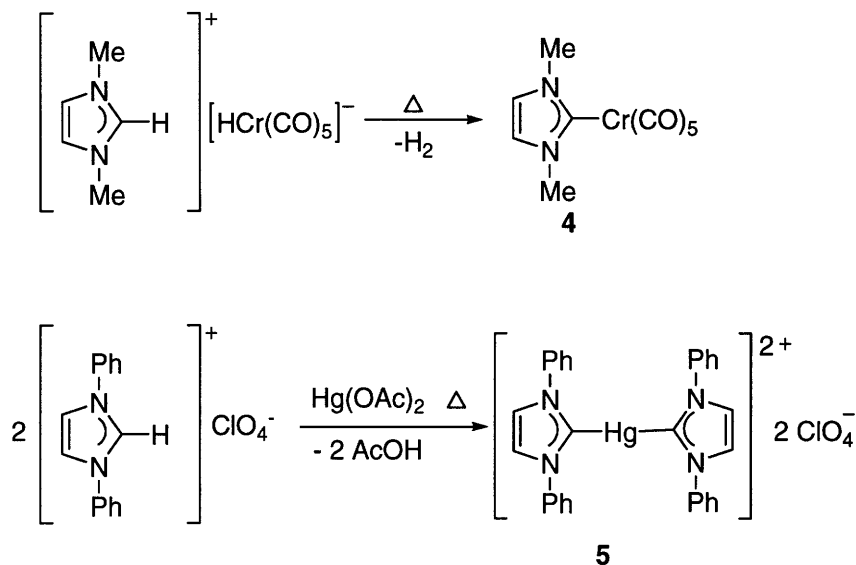


Scheme 7: AlCl_3/Al assisted CO_2 insertion into aromatic substrates. [Ref. 37]

NHC Chemistry

N-Heterocyclic carbenes (NHCs) are a class of supporting ligands for metal complexes. Metal complexes with NHC ligands were first reported in 1968 by Öfele³⁸ and Wanzlick³⁹. Complex **4** was prepared from $[\text{IMeH}][\text{HCr}(\text{CO})_5]^-$,³⁹ and **5** was prepared from the imidazolium salt and mercury acetate.⁴⁰ The use of NHCs as ligands

has proliferated greatly since Arduengo's isolation of the first stable free N-heterocyclic carbene, **6**.⁴⁰



Scheme 8: Complexes reported by Öfele, **4** [Ref 38], and Wanzlick, **5** [Ref 39], the first (NHC)M complexes.

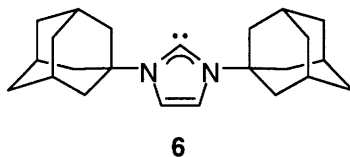


Figure 1: From work by Arduengo, the first reported stable free N- heterocyclic carbene. [Ref 40]

NHC Characteristics

N-Heterocyclic carbenes are unusually stable as free carbenes.⁴¹ Donation of electron density from the nitrogens stabilizes the carbene carbon. Structural data indicates that the C–N bonds between the carbene carbon and the nitrogens have some double bond character. N-Heterocyclic carbenes do not display aromatic character.⁷⁷ While NHCs are strong σ -donors, binding mostly through σ -donation to metal centers, they have significantly less ability to accept π -backdonation. Recent DFT work shows

that π -backbonding from a metal center to an NHC accounts for 15 to 20 percent of the covalent bond energy. It should be noted that the NHC-metal bond often involves a substantial ionic component as well.⁴²

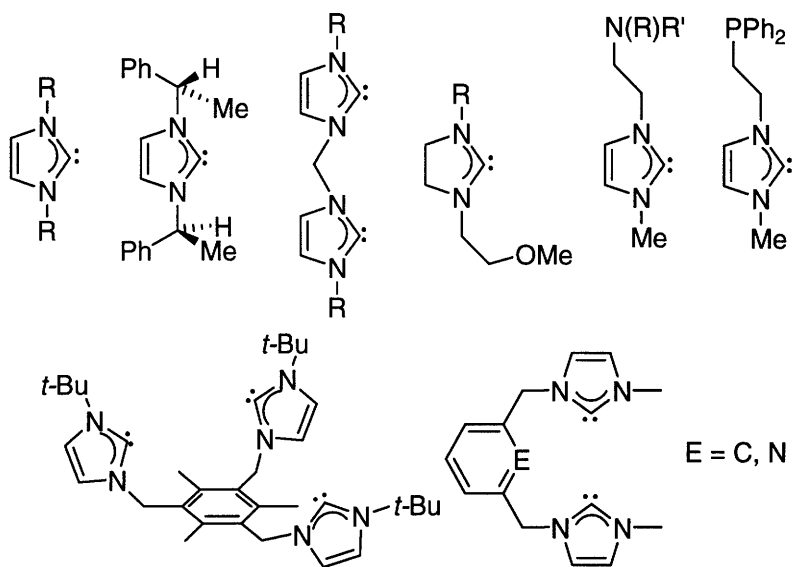


Figure 2: The range of NHC ligands is quite broad, as can be seen from the selection above. [Refs. 45, 46, 76]

The NHC ligand is frequently compared with phosphines.^{41,43} Both are strong σ -donor ligands, with the majority of NHCs displaying stronger electron-donating properties than the strongest phosphine donors. The π -acceptor character of phosphine ligands varies over a broad range, however, while NHCs tend to be poor π -acceptors. Phosphines are also relatively labile compared to NHCs, and NHC-supported complexes tend to display greater stability than phosphine-supported ones.

A wide variety of NHCs can be prepared.⁴⁴ Substituents on the N sites on the NHC can be alkyl or aryl, and can be further functionalized to have ethers, phosphines or amines. N-Heterocyclic carbenes with chiral N-substituents and backbones have also been prepared.⁷⁵ A range of bidentate carbenes has been reported with bridges of different length between the carbenes, and different N-substituents. Tridentate NHCs

have also been reported.^{45,46} Hahn reported the construction of a tetradentate NHC framework on a platinum center.⁴⁷

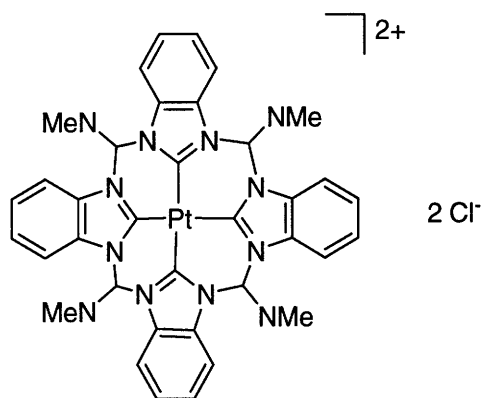


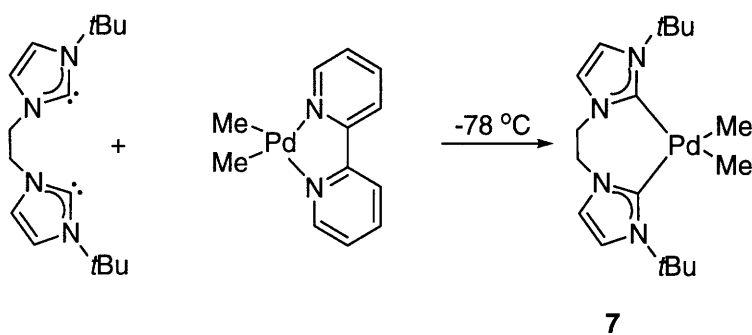
Figure 3: Tetradentate carbene ligand coordinated to Pt reported by Hahn. [Ref. 47]

Carbene pincers ligands with schemes such as NHC-N-NHC, NHC-P, and NHC-C-NHC, incorporating non-NHC binding sites, have also been prepared. The development of phosphine-tethered NHCs was prompted by the fact that for certain catalytic processes the use of both NHC and phosphine supporting ligands proved most effective.⁷⁶ Tridentate pincers have also been developed.⁴⁶

Metallation

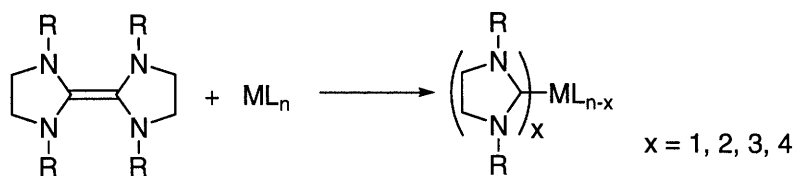
A range of methods to metallate carbenes has been developed. The technique Öfele used³⁹ to generate the first NHC complexes still sees broad applicability. In situ deprotonation of an imidazolium salt in the presence of a metal with labile ligands affords the NHC metal complex. This type of deprotonation can be accomplished with bases such NaOt-Bu,⁴⁸ or triethylamine.⁴⁹ For some syntheses, use of a metal complex with basic ligands, such as alkoxides or acetates, can accomplish the same goal.⁵⁰

Free carbenes being readily available can be used to displace other ligands in solution fairly easily. Metal complexes with labile two-electron donors such as THF, CO, or phosphines can undergo ligand displacement to generate NHC complexes.⁴¹ This technique can work for multidentate ligands as well: the synthesis of the palladium complex **7** proceeds by the displacement of bipyridine from a precursor complex.⁵¹



Scheme 9: Metallation of Pd with an NHC by displacement of more labile ligands. [Ref. 51]

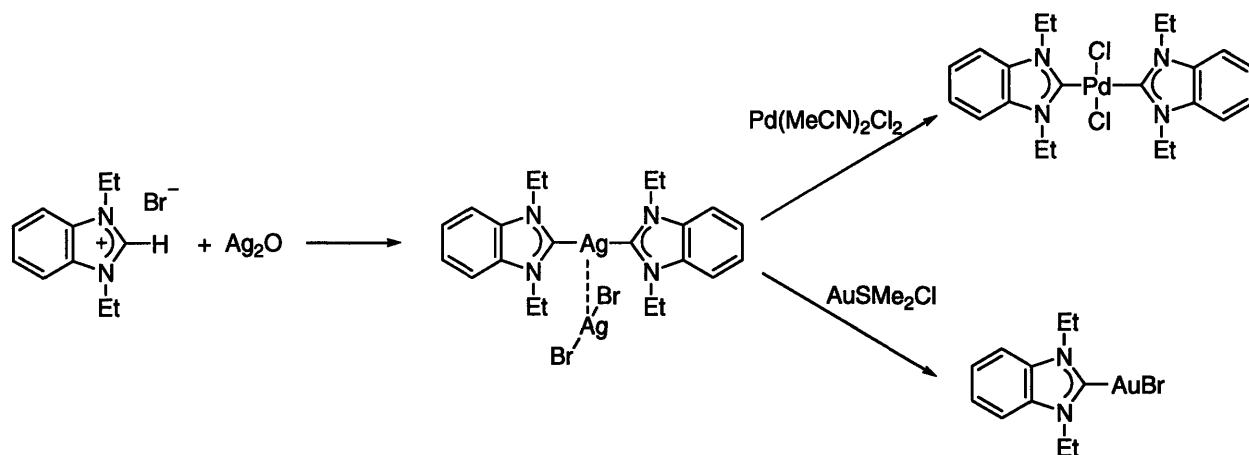
An electron-rich olefin derived from two imidazolylidene monomers can react with metal complexes to generate NHC-supported complexes. Mono, bis, tris, and tetrakis NHC complexes have been synthesized via this route.⁵²



Scheme 10: Reaction of olefinic dimer to generate (NHC)metal complexes. [Ref. 52]

More recently the transmetalation of NHCs has been used for the preparation of new (NHC)metal complexes. The use of group 6 metal carbene complexes to prepare group 9 and 10 carbene complexes was reported.⁵³ Silver NHC complexes are readily formed, most commonly from Ag_2O . Silver NHCs have proven to be excellent carbene

transfer agents, especially in cases where the target complex is unlikely to endure harsh synthetic conditions.⁵⁴



Scheme 11: Silver carbenes as transmetalation agents for the formation of other (NHC)M complexes. [Ref. 54a]

The metallation of *N,N'*-bis-*t*-butylimidazol-2-ylidene with nickel, palladium and platinum has been achieved by vapor condensation.⁵⁵ This process yields $(\text{NHC})_2\text{M}$ complexes in low to moderate yields, but its applicability is limited by the harsh conditions required.

Catalysis with NHC complexes

Because, NHCs are strong electron donors with important electronic differences from phosphines, and are readily tunable sterically and electronically, the exploration of catalysis by (NHC)metal complexes promised to be a rich field. The general stability of NHC complexes is an especially important property. Initial attempts to use NHCs in place of phosphines met with some success.⁵⁶ The advent of NHC supported Heck olefination catalysts,^{50b} reinvigorated the field.

Palladium complexes of the type $[PdL_2I_2]$ are used as Heck catalysts.^{50b} A great deal of stability is imparted to this class of catalysts by NHC ligands. Crabtree's tridentate carbene ligands allowed the catalyst to survive at high temperatures without decomposition over extended periods of time, reflecting far greater catalyst stability than that achieved using phosphine ligands, without loss of performance in conversion.⁴⁶

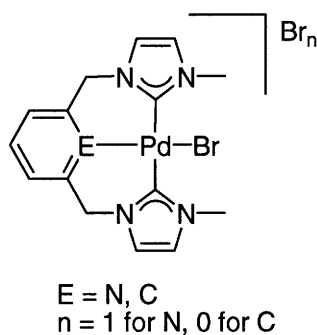
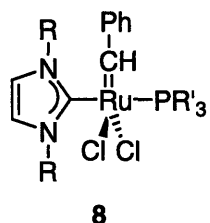


Figure 4: A thermally robust and highly active Heck coupling catalyst [Ref. 46].

Hydrosilylation of alkenes was effected by NHC-supported rhodium catalysts. A range of rhodium catalysts were investigated, including ones supported by both an NHC ligand and phosphines, $[RhCl(CO)(PPh_3)(NHC)]$.⁵⁶ Selective anti-Markovnikov hydrosilylation in up to 98% yield was attained. In comparison, $[RhCl(PPh_3)_3]$ gave lower yields. Rhodium catalysts also proved to be effective at hydrosilylation of alkynes, though selectivity was poor, yield was superior to catalysts supported exclusively by phosphines.

Hydrosilylation of ketones by rhodium catalysts has been established.⁵⁶ The complex $[RhCl(\eta^4\text{-}1,5\text{-cod})(NHC)]$ proved to be a superior catalyst, giving 98% conversion in 24 hours at room temperature. Of note is that increasing the number of carbene ligands led to a loss of efficiency. Enantioselective catalysis has been explored

for this conversion, though the rhodium catalyst described above with a chiral NHC generated only moderate enantiomeric excess.⁵⁷



R = *t*-Bu, Cy, Mes,
CHMePh, CHMeNaph
R' = Cy, Ph

Figure 5: NHC supported olefin metathesis catalyst [Ref 58]

Olefin metathesis with ruthenium carbene complexes has also been established.⁵⁸ Complexes such as **8** are very active for both ring opening and ring closing metathesis, and tuning of the complex with a combination of NHC and phosphine ligands proved beneficial. The steric effect of the R substituents is especially pronounced in the polymerization of cyclooctene, suggesting that greater control over catalytic efficiency can be achieved through changes in NHC ligands than in phosphine ligands.

Herrmann reported that chelating NHC supported complexes copolymerize ethylene and CO under mild conditions.⁵⁹ The polymer thus generated is of high molecular weight, and has alternating units of CO and C₂H₄.

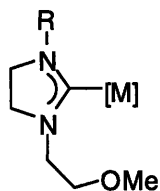


Figure 6: Metal complex with hemilabile ligand. Rhodium and ruthenium complexes of such ligands are reported to be efficient cyclopropanation catalysts. [Ref 61]

Polymerization of alkynes can be accomplished with an NHC-supported tungsten catalyst.⁶⁰ The yield of polymer based on alkyne consumed is 66%, with small amounts of oligomerization side product.

The cyclopropanation of olefins with NHC-supported complexes makes use of a system of hemilabile ligands.⁶¹ The N-substituents of a carbene ligand were functionalized with methoxy donor groups, which can coordinate to the NHC-bound the metal center but are relatively labile. This combination led to effective rhodium and ruthenium catalysts for the cyclopropanation of styrene with diazoalkanes.

Copper NHC chemistry

N-Heterocyclic-carbene-supported copper complexes were first reported in 1993.⁶² Their use in catalysis did not start until significantly later, with the preparation and of [(IPr)CuCl], and its use in the presence of sodium *tert*-butoxide as a precatalyst for the 1,4-hydrosilylation of α,β -unsaturated carbonyl compounds.⁶³ In related work, the 1,2-hydrosilylation of ketones was catalyzed by (NHC)copper(I) complexes.⁶⁴

The transfer of carbenes from diazo compounds to olefins, alcohols, amines and alkanes has been achieved using (IPr)CuCl as the precatalyst.⁶⁵ The use of this complex suppresses a significant side-reaction observed with other catalysts, the homocoupling of the diazo compound to form olefin. When a more weakly coordinating anion is used, as in [(IPr)Cu][B(Ar^f)₄] {Ar^f = 3,5-bis(trifluoromethyl)phenyl}, transfer of carbene from ethyl diazoacetate to unactivated alkanes is observed.⁶⁶

The monomeric, two coordinate (IPr)CuMe reacts smoothly with CO₂ to form the acetate (see Chapter 1)⁶⁷ and protonolysis of this complex affords copper anilide,

phenoxide and acetylide complexes.^{68a} The latter complexes are catalysts for Michael addition of N—H and O—H bonds to electron-poor olefins.^{68b}

Hoveyda reported the use of (NHC)copper complexes bearing chiral NHC ligands to catalytically alkylate allylic phosphonates with dialkyl zinc reagents in good yield and 92% enantiomeric excess.⁶⁹ The use of (NHC)copper complexes in conjunction with Grignard reagents to perform similar chemistry has been reported.⁷⁰

Research Goals

Development of processes for use of the incorporation of carbon monomers into organic compounds has received significant attention. Although processes for the use of CO₂ as a reagent have been developed, the field is still ripe for exploration. N-Heterocyclic carbene copper complexes were investigated for their potential as agents for carbon dioxide fixation. Previous work in (phosphine)copper chemistry established the potential for copper complexes supported by electron donating ligands to form alkyl complexes and insert CO₂. The goal of the work presented in this thesis was the reductive carboxylation of organic substrates via hydrometallation followed by CO₂ insertion. Ultimately, based on the established stoichiometric reactivity, a catalytic process for the formation of carbon—carbon bonds between CO₂ and unsaturated organic substrates is investigated.

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Chapter 2

Stoichiometric Reductive Carboxylation of Alkynes and Olefins

Using (NHC)copper(I) Complexes

Abstract

Alkynes and olefins insert into $[(\text{IPr})\text{CuH}]_2$ (IPr = *N,N*-bis-(2,6-diisopropylphenyl)-1,3-imidazol-2-ylidene) to give copper vinyl and copper alkyl complexes. These copper complexes insert CO_2 into the Cu—C bond to form copper acrylate and copper carboxylate complexes. Acrylic and carboxylic acids can be isolated by hydrolysis.

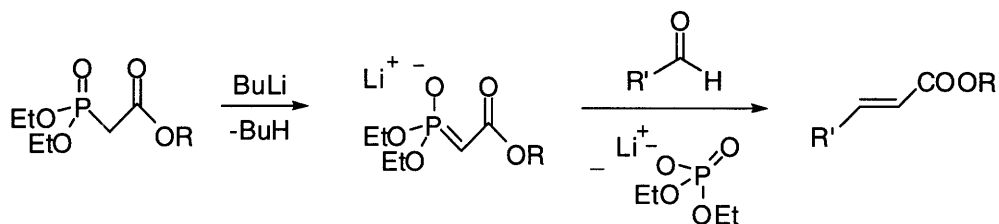
Introduction

The activation of CO_2 to form carbon-carbon bonds is of significant interest in organometallic chemistry.¹ Herein the development of new C—C bond forming reactions is reported. The synthetic approach examined was reductive carboxylation of alkynes to form acrylates via CO_2 insertion.

In addition to their widespread use as polymer precursors, acrylic acids have found application as pharmaceuticals. For example (E)-2-Propyl-2-pentenoic acid is a known antiepileptic drug.² A series of related acrylic acids, prepared by a multistep organic synthesis, also showed similar activity.³ As these compounds showed improved activity as pharmaceuticals, improved synthetic routes to them would have relevance to the medical community.

Acrylic acids can be synthesized from a number of organic precursors. The reaction of alkenes and phenyltrichloromethylselenide with subsequent reactions to dechlorinate, then deselenate in presence of H_2O generates acrylic acids in moderate yields with good regioselectivity.⁴ The synthesis of various 2-alkenoic acids by the Horner-Wadsworth-Emmons reaction (Scheme 1) is also established.⁵ The incorporation

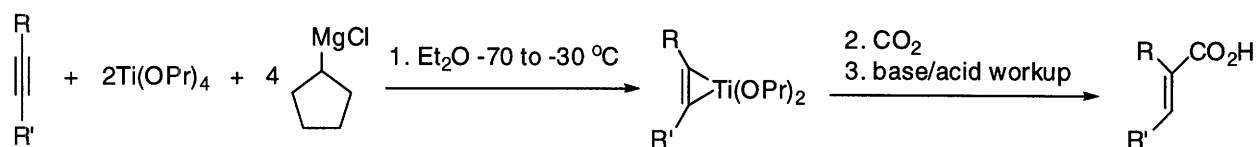
of CO into alkynes, catalyzed by Pd in the presence of formic acid, also produces acrylic acids.⁶



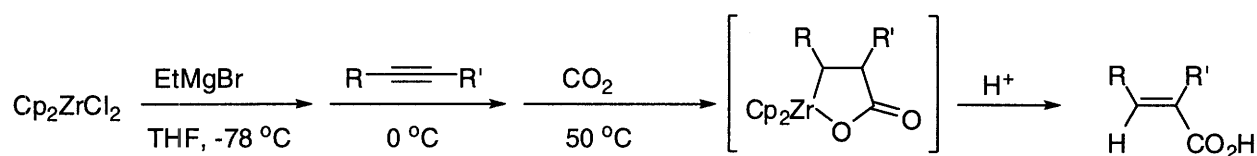
Scheme 1: General route for Horner-Wadsworth-Emmons reaction for the preparation of acrylic acids.

The incorporation of CO₂ into organic substrates to generate acrylic acids, often mediated by transition metal complexes, has been investigated by a number of researchers. The fixation of CO₂ by early transition metals generates acrylate products stoichiometrically. When Ti(Oi-Pr)₄ is treated with Grignard reagents in the presence of internal alkynes, titanacyclopropenes were formed (Scheme 2a).⁷ After exposure to CO₂ and subsequent hydrolysis titanacyclopropenes afforded acrylic acids. In this system, insertion of CO₂ into an alkyne bearing both a phenyl and alkyl substituent leads preferentially to the α -alkylcinnamic acid regioisomer. In a similar sequence, reaction of Cp₂ZrCl₂ with EtMgBr, followed by sequential addition of alkyne and CO₂ generates an unsaturated zirconacycle (Scheme 2b).⁸ Acrylic acids can be isolated in roughly 70 % yield after treatment of this complex with HCl. In this system, insertion of CO₂ into the bond between Zr and the phenyl-substituted carbon is preferred, with a selectivity of 2:1 over the alternative regioisomer for the substrate 1-phenyl-1-butyne. The terminal alkyne substrate, 1-phenylacetylene, gives *trans*-cinnamic acid as the predominant product, with only a small amount of 2-phenylacrylic acid. Nickel catalyts have been used in the catalytic reductive electrocarboxylation of alkynes (Scheme 2c),⁹ allenes (Scheme 2d)¹⁰

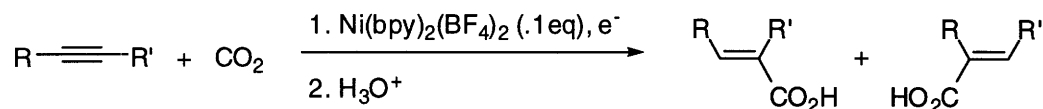
and 1,3-enynes.¹¹ Selectivity in the case of allenes favored insertion geminal to aromatic substituents in case of a phenyl functionality, although the carboxylic functionality did not always end up on an unsaturated carbon. For 1-ethynylcyclohexene insertion geminal to the cycle was the predominant pathway. The electrochemistry involved, however, required a sacrificial magnesium anode and led to solvent degradation.



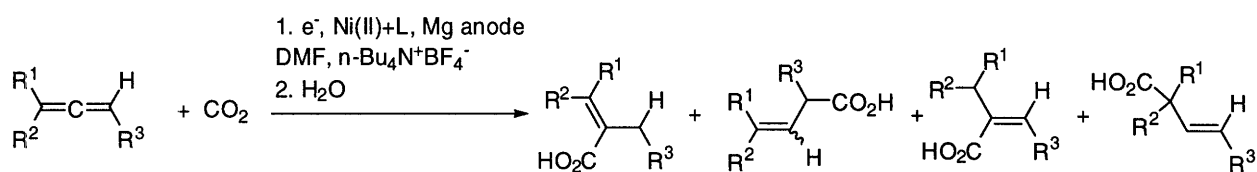
Scheme 2a: Titanium assisted formation of acrylic acids [Ref. 7]



Scheme 2b: Zirconium assisted formation of acrylates from alkynes and CO₂. [Ref. 8]



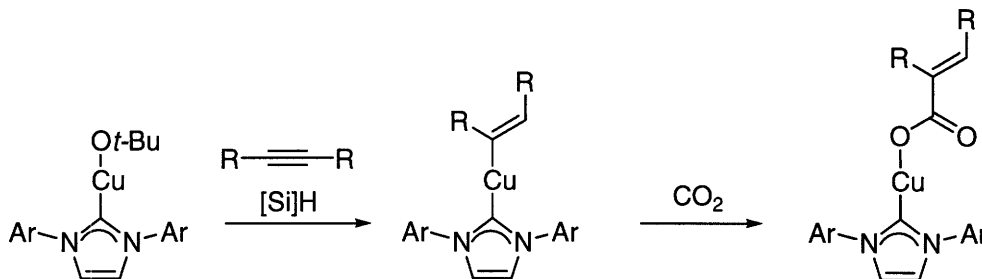
Scheme 2c: Electrocarboxylation of alkyne. [Ref. 9]



Scheme 2d: Electrocarboxylation of allenes. Note, under all conditions reported significant amounts of at least three if not all four regioisomers were formed in significant quantities, depending on the nickel catalyst used. [Ref. 10]

The sequence we envisioned for the transformation of alkynes and CO₂ to acrylates is presented in Scheme 3. A copper hydride complex would insert an alkyne to

forming a copper vinyl complex. The copper vinyl complex might then insert CO₂ to generate a copper acrylate.

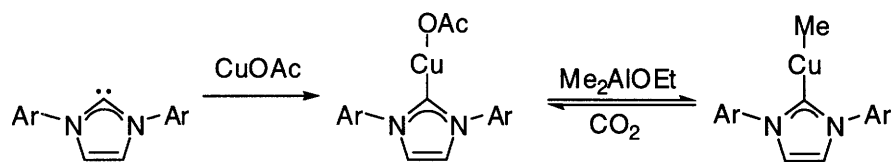


Scheme 3: Proposed pathway for formation of acrylates from CO₂ and alkynes.

Hydrocupration of alkynes can be inferred from the work of Stryker.¹² The copper hydride hexamer [(Ph₃P)₃CuH]₆ readily hydrogenates 3-hexyne to *cis*-3-hexene. Although no copper vinyl complex was isolated, the hydrocupration of an alkyne to form a copper vinyl intermediate and further reaction with additional copper hydride was indicated by labeling experiments. The hexameric nature of the copper hydride may have made isolation of a vinyl complex impossible by presenting a second copper hydride close to the copper vinyl, leading to rapid hydrogenation. We hoped that a sterically encumbering supporting ligand might support a monomeric copper hydride, allowing the undesired second C-H bond formation to be avoided.

Alkylcopper complexes require the support of donor ligands to be stable. The complex [CuMe]₄ is known to be explosive.¹³ Copper(0) species have been identified as sources of decomposition in copper alkyl chemistry.¹⁴ Several other (phosphine)copper alkyl complexes have been reported including MeCu(PMePh₂)₃¹⁵ and MeCu(PPh₃)₃.¹⁶ The electron-rich MeCu(PCy₃) reacts with CO₂ in ethereal solution at 0 °C to form the corresponding copper acetate.¹⁷

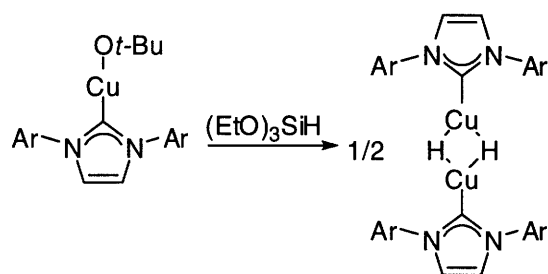
Initial studies on the synthesis of an N-heterocyclic-carbene-supported copper hydride, and on the insertion of CO₂ into (NHC)copper alkyls, were carried out by Neal Mankad.²² The first target complex was (IPr)CuMe (IPr = *N,N*-bis-(2,6-diisopropylphenyl)-1,3-imidazol-2-ylidene).¹⁸ Initial attempts to prepare this complex by reaction of (IPr)CuCl with MeLi or MeMgBr did not yield the desired product, so a carboxylate was examined as the precursor to the copper methyl complex. The reaction of free IPr with copper(I) acetate formed (IPr)CuOAc (Scheme 4). The X-ray crystal structure of the acetate complex indicated monodentate acetate coordination in the solid state. In DFT calculations on a related model complex, the energy difference between the κ^1 and κ^2 binding modes was found to be very small. Treatment of the acetate with Me₂AlOEt afforded the methyl complex (IPr)CuMe, which is sufficiently stable to permit isolation and structural characterization. Insertion of CO₂ to reform (IPr)CuOAc occurs over a period of two hours, in benzene solution under 1 atm CO₂.



Scheme 4: Preparation of (IPr)CuOAc, its transformation to (IPr)CuMe, and its regeneration by addition of CO₂ to the methyl complex.

A copper hydride complex could be prepared readily from (IPr)CuO*t*-Bu by reaction with triethoxysilane in benzene solution.¹⁹ The crystal structure of the copper hydride showed that it is a dimer, [(IPr)CuH]₂. The [(IPr)CuH]₂ complex is heat- and light-sensitive, but sufficiently stable at room temperature to allow characterization by NMR spectroscopy. Notably, [(IPr)CuH]₂ has the shortest copper—copper distance found in the Cambridge Crystallographic Database.

In this work¹⁹ it was also established that 3-hexyne readily inserts into $[(\text{IPr})\text{CuH}]_2$, affording the vinyl complex in near-quantitative yield. In contrast to the reaction of alkynes with $[(\text{Ph}_3\text{P})_3\text{CuH}]_6$ no hydrogenation is observed. The insertion of CO_2 into the vinylic $\text{Cu}-\text{C}$ bond occurs rapidly, within minutes rather than the hours required for carboxylation of the copper methyl. This establishes a stepwise stoichiometric method for copper acrylate synthesis.



Scheme 5: Synthesis of $[(\text{IPr})\text{CuH}]_2$ [Ref. 19]

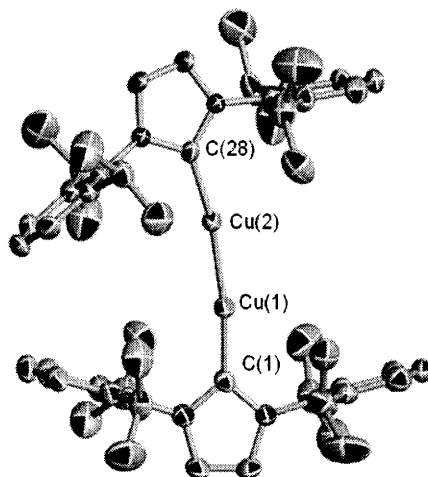


Figure 1: Crystal structure of $[(\text{IPr})\text{CuH}]_2$. Selected bond angles and distances: $\text{Cu}(1) - \text{C}(1)$: 1.878(6) Å, $\text{Cu}(1) - \text{Cu}(2)$: 2.3059(11) Å, $\text{Cu}(2) - \text{C}(28)$: 1.882(6) Å, $\text{C}(1) - \text{Cu}(1) - \text{Cu}(2)$: 169.4(2) °, $\text{Cu}(1) - \text{Cu}(2) - \text{C}(28)$: 170.33(19) ° [Ref. 19]

Other copper hydrides have been reported. Although most contain several copper centers, one other dimeric complex $[\kappa^2\text{-CH}_3\text{C}(\text{CH}_2\text{PPh}_2)_3]_2\text{Cu}_2(\mu\text{-H})_2$ was described.²⁰ Its reported reactivity is limited to the hydrogenation of CO_2 to give

$[\text{CH}_3\text{C}(\text{CH}_2\text{PPh}_2)_3]\text{Cu}(\eta^1\text{-O}_2\text{CH})_2$. The new $[(\text{IPr})\text{CuH}]_2$ complex is relatively stable, well characterized, and low nuclearity copper hydride complex amenable to study.

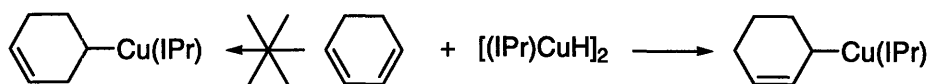
Results and Discussion

With the reactivity of 3-hexyne established, a broader substrate range was of interest. Alkynes were likely substrates for carboxylation. It was expected that olefins, especially strained or otherwise activated ones would also be suitable candidates for functionalization. The results for the synthesis of (IPr)-copper acrylates and (IPr)-copper carboxylates is summarized in Table 1. All products were isolated from a benzene slurry by precipitation with pentane. The ratios of the different regioisomers were determined by integration of their ^1H NMR signals.

The generality with respect to alkynes was first investigated by testing the carboxylation of a range of alkynes. As an initial variation on 3-hexyne, the asymmetric alkyne 2-pentyne was investigated. This alkyne gave a 3:1 distribution between insertion at the 2- versus the 3- position. As expected there is a steric directing effect from the ethyl group versus the methyl group on the acetylene.

Investigation of phenyl-substituted alkynes led to some interesting revelations. The substrates used were 1-phenyl-1-propyne, 1-phenyl-1-butyne, and diphenylacetylene. All three substrates readily inserted into the copper hydride, and the resulting vinyl complexes subsequently inserted CO_2 as expected. In the reactions with the two phenyl/alkyl-substituted alkynes, the rapid disappearance of the characteristic yellow color of the copper hydride suggests that insertion occurs faster than for dialkyl substituted alkynes. In the case of both 1-phenyl-1-propyne and 1-phenyl-1-butyne the

insertion was regioselective, favoring the α -phenylvinyl insertion product. The ratios of observed regioisomers are unchanged between hydrocupration and carboxylation. In the case of 1-phenyl-1-propyne this resulted in a 3 to 1 mixture of (IPr)Cu-2-phenylbutenoate and (IPr)Cu(2-methyl-3-phenylprop-2-enoate). For 1-phenyl-1-butyne the product ratio was 5 to 1 in favor of (IPr)Cu-2-phenylpent-2-enoate over (IPr)Cu-2-ethyl-3-phenylprop-2-enoate. Given these observations, it is likely that the phenyl group stabilizes the buildup of electron density on the adjacent carbon atom during the hydrocupration step, leading to regioselective insertion.



Scheme 6: Regioselectivity of 1,3-hexadiene insertion into copper hydride.

An investigation into the reactivity of [LCuH]₂ with olefins was also conducted. No reaction was observed between [LCuH]₂ and *cis*-3-hexene. The strained olefin norbornene, however, reacted with [LCuH]₂ over several hours to generate an alkyl copper complex as observed in solution by ¹H NMR spectroscopy. The carboxylation of these secondary alkyl complexes was slower than that of the vinyl complexes, and comparable in rate to that of the (IPr)CuMe, taking three hours to run to completion. The reaction of 1,3-cyclohexadiene with [LCuH]₂ forms an η^1 -allylcopper complex, identified by ¹H NMR spectroscopy. This allyl copper reacts with CO₂ over the course of two hours. Insertion occurred exclusively across the 1- and 2- positions, with the copper always adding at the 2- position.

Styrene, and a number of *para*-substituted styrenes also react with [LCuH]₂. The presence of electron-withdrawing substituents such Cl, F, and Br as well as CF₃ led to

very rapid insertion of the alkene into the copper hydride, leading exclusively to benzylic products. The complexes derived from chloro- and bromo- substituted styrene insertion, however, decompose after an initial clean insertion, the bromo- substituted product within minutes, and the chloro- over 12 hours. Styrene reacts cleanly with $[\text{LCuH}]_2$ over a half-hour. 4-Dimethylamino-, and 4-methoxystyrene react with $[\text{LCuH}]_2$ over several hours; decomposition of the $[\text{LCuH}]_2$ is a significant competing reaction over this timescale. The resulting copper alkyl complexes, stable in solution at ambient temperatures, inserted CO_2 over two to three hours, a reaction time similar to that required for LCuMe .

The acrylic acids can be prepared and isolated cleanly from the copper(I) acrylates. Due to the relatively high water-solubility of some acids, isolated yields were not always representative of conversion, but the mixture of 2-methyl-3-phenylprop-2-enoic acid and 2-phenyl-butenoic acid derived from 1-phenyl-1-propyne was recovered in near-quantitative yield.

Conclusion

The insertion of a range of alkynes and olefins into an (NHC)copper hydride to form stable copper vinyl complexes was demonstrated. Subsequent insertion of carbon dioxide into the $\text{Cu}-\text{C}$ bond of the copper vinyl complex was shown. For dialkyl functionalized acetylenes, regioselectivity favoring the formation of a copper-carbon bond geminal to the less sterically demanding alkyl substituent was observed. Interestingly when a phenyl/alkyl-substituted acetylene inserts into the copper hydride,

copper—carbon bond formation geminal to the aryl group is favored. This chapter has shown stoichiometric reductive carboxylation of alkynes using CO₂.

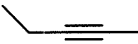
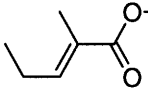
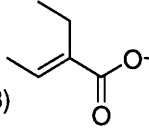
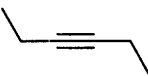
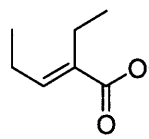
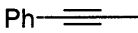
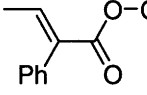
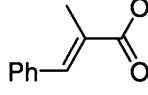
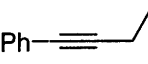
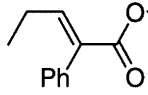
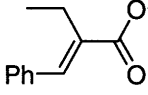
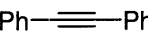
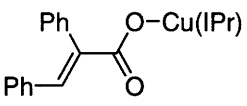
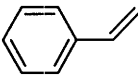
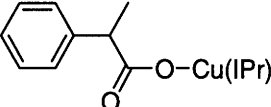

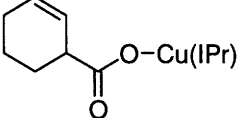

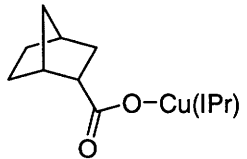
Substrate	Product (Distribution)	Yield
1. 	 -Cu(IPr) (1 : 3)  -Cu(IPr)	71 %
2. 	 -Cu(IPr)	90 %
3. 	 -Cu(IPr) (4 : 1)  -Cu(IPr)	76 %
4. 	 -Cu(IPr) (5 : 1)  -Cu(IPr)	85 %
5. 	 -Cu(IPr)	98 %
6. 	 -Cu(IPr)	60 %
7. 	 -Cu(IPr)	85 %
8. 	 -Cu(IPr)	92 %

Table 1: Yields for preparation of carboxylate copper complexes. Product distribution is noted for asymmetric substrates.

Experimental

General Procedures: All procedures performed in a glovebox under nitrogen atmosphere or using standard Schlenk techniques under argon. Benzene and pentane were purchased anhydrous from Aldrich and dried over molecular sieves. Alkynes and 1,3-cyclohexadiene were purchased from Aldrich, stirred over sodium borohydride for 24 hours, degassed, and distilled before use. Norbornene and styrene were purchased from Aldrich and used as received. (IPr)CuO*t*-Bu was prepared according to published methods.¹⁹ Triethoxysilane from Aldrich was degassed before use. NMR data was collected on a Varian Mercury 300 or Varian 500. Elemental analyses were performed by Desert Analytics.

General method for preparation of (IPr)copper acrylates: In a 10 mL pear Schlenk (IPr)CuO*t*-Bu (0.150 g, 0.29 mmol) of and alkyne were dissolved in 4 mL benzene. Triethoxysilane (0.053 mL, 0.29 mmol) was added and the solution was stirred for 20 minutes in the dark, until the yellow color faded. On a Schlenk line carrying CO₂ gas, the reaction was put under 1 atm of CO₂ by opening the vessel to vacuum briefly, to minimize evaporation of volatiles, then backfilling with CO₂. The reaction mixture was stirred for 3 hours, and then the volatiles were removed under vacuum. In the box a slurry of the crude reaction mixture was formed in benzene (aprox. 1 mL). The product was precipitated by the addition of 8 mL dry pentane and collected by filtration.

Preparation of (IPr)copper(2-ethylpent-2-enoate): Prepared according to the general method using 3-hexyne (0.28 mL, 2.7 mmol). The product complex was isolated: 0.150 g (0.257 mmol, 90%). ^1H NMR (C_6D_6): δ 7.16 (t, $J = 7.8$ Hz, 2 H, *para*-CH), 7.04 (d, $J = 7.5$ Hz, 4 H, *meta*-CH), 6.83 (t, $J = 7.5$ Hz, 1 H, C=CH), 6.26(s, 2 H, NCH), 2.61 (sept, $J = 6.9$ Hz, 4 H), 2.45 (quart, $J = 7.4$ Hz, 2 H, CCH₂), 1.88 (quint, $J = 7.5$ Hz, 2 H, C=CCH₂), 1.45 (d, $J = 6.8$ Hz, 12 H), 1.07(m, 15H), 0.73 (t, $J = 7.5$ Hz, 3 H). ^{13}C (C_6D_6): δ 182.6, 174.7, 146.0, 138.7, 137.8, 135.3, 131.1, 124.6, 123.2, 29.4, 25.4, 24.3, 22.1, 21.7, 15.2, 14.4. Anal. Calcd. for $\text{C}_{34}\text{H}_{48}\text{CuN}_2\text{O}_2$: C, 70.37; H, 8.34. Found: C, 70.46; H, 7.92

Preparation of (IPr)copper(2-ethylbut-2-enoate) / (IPr)copper(2-methylpent-2-enoate): Prepared according to the general method using 2-pentyne (0.28 mL, 2.7 mmol). The mixture of product complexes was isolated: 0.116 g (0.201, 71%). mmol ^1H NMR (C_6D_6): δ 7.16 (t, $J = 7.8$ Hz, 2 H, *para*-CH), 7.03 (d, $J = 7.8$ Hz, 4 H, *meta*-CH), 6.77 (m, 1 H), 6.38 (s, 2 H, NCH), 2.59 (m, 4 H), 2.35 (quart, $J = 7.4$ Hz, 0.75 H), 1.81 (d, $J = 1.3$ Hz, 1.5 H), 1.77 (m, 1.5H) 1.36 (m, 14 H), 1.04 (d, 14 H), 0.64 (t, $J = 7.5$ Hz, 1.5 H). ^{13}C (C_6D_6): δ 182.4, 175.2, 174.5, 146.1, 140.3, 138.2, 135.4, 124.6, 123.3, 29.4, 29.3, 25.4, 24.3, 22.4, 21.4, 14.7, 14.2, 14.0, 13.9. Anal. Calcd. for $\text{C}_{33}\text{H}_{46}\text{CuN}_2\text{O}_2$: C, 69.99; H, 8.19. Found: C, 69.75; H, 7.82.

Preparation of (IPr)copper(2-phenylbut-2-enoate) / (IPr)copper(α -methylcinnamate): Prepared according to the general method using 1-phenyl-1-propyne (0.080 mL, 0.64 mmol). A mixture of the product complexes was isolated: 0.135 g

(0.220mmol, 76 %). ^1H NMR (C_6D_6): δ 7.98 (s), 7.1-7.2 (m, 6H), 7.1-6.8 (m, 8H), 6.24 (s, 2H), 2.59 (m, 4H), 2.16 (d, $J = 1.5$ Hz, 0.5 H), 1.41 (m, 15 H), 1.06 (d, $J = 6.9$ Hz, 13 H). ^{13}C NMR (C_6D_6): δ 182.4, 175.2, 173.4, 146.0, 140.6, 139.9, 139.2, 135.3, 135.1, 134.7, 133.8, 131.1, 131.1, 130.0, 127.6, 126.9, 126.1, 124.7, 123.2, 29.5, 29.4, 25.4, 24.2, 16.1, 15.4. Anal. Calcd. for $\text{C}_{37}\text{H}_{46}\text{CuN}_2\text{O}_2$: C, 72.46; H, 7.55. Found: C, 72.11; H, 7.16.

Preparation of (IPr)copper(2-phenylpent-2-enoate) / (IPr)copper(α -ethylcinnamate): Prepared according to the general method using 1-phenyl-1-butyne (0.080 mL, 0.62 mmol). A mixture of the product complexes was isolated: 0.154 g (0.246 mmol, 85 %) ^1H NMR (C_6D_6): δ 7.83 (s), 7.1-7.2 (m, 4 H), 7.0-7.06 (m, 7 H), 6.90 (m, 1 H), 6.26 (s, 1 H), 2.55 (m, 4 H), 1.81 (quint, $J = 7.5$ Hz, 2 H), 1.36 (d, $J = 6.6$ Hz), 1.02 (d, $J = 6.6$ Hz), 0.59 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (C_6D_6): δ 182.3, 173.6, 146.0, 140.9, 139.0, 135.3, 131.1, 130.9, 129.6, 127.6, 126.1, 124.7, 123.2, 29.4, 25.4, 24.2, 23.3, 14.9, 14.3. Anal. Calcd. for $\text{C}_{38}\text{H}_{48}\text{CuN}_2\text{O}_2$: C, 72.64; H, 7.70. Found: C, 72.52; H, 7.42.

Preparation of (IPr)copper(2,3-diphenylprop-2-enoate): Prepared according to the general method using diphenylacetylene (0.200 g, 1.1 mmol). The product complex was isolated: 0.194 g (0.28 mmol, 98 %) ^1H NMR (C_6D_6): δ 8.04 (s, 1 H), 7.18 (m, 2 H), 7.14 (t, $J = 7.8$ Hz, 4 H), 7.01 (d, $J = 7.8$ Hz, 5 H), 6.92 (m, 2 H), 6.87 (m, 3 H), 6.71 (m, 3 H), 6.22 (s, 2 H), 2.56 (sept, $J = 6.8$ Hz, 4 H), 1.39 (d, $J = 6.9$ Hz, 12 H), 1.02 (d, $J = 6.9$ Hz, 12 H). ^{13}C (C_6D_6): δ 182.4, 173.8, 146.1, 140.4, 139.8, 137.9, 136.4, 135.3, 132.3, 131.1,

131.0, 130.7, 129.0, 128.8, 128.2, 127.4, 126.6, 124.7, 123.1, 31.9, 29.4, 25.4, 24.2.

Anal. Calcd. for $C_{42}H_{48}CuN_2O_2$: C, 74.69; H, 7.01. Found: C, 75.11; H, 7.16.

Preparation of (IPr)copper(cyclohex-2-enoate): Prepared according to the general method with 1,3-cyclohexadiene (0.30 mL, 2.6 mmol). The product complex was isolated: 0.143 g (0.248 g, 85%). 1H NMR (C_6D_6): δ 7.19 (m, 2 H), 7.06 (d, $J = 7.8$ Hz, 3 H), 6.36 (s, 2 H), 6.20 (m, 1 H), 5.52 (m, 1 H), 3.02 (m, 1H), 2.60 (sept, $J = 6.8$ Hz, 4 H), 1.99 (m, 1 H), 1.86 (m, 1 H), 1.72 (m, 2 H), 1.63 (m, 1 H), 1.42 (d, $J = 6.9$ Hz, 12H), 1.32 (m, 1 H), 1.08 (d, $J = 6.9$ Hz, 12 H). ^{13}C NMR (C_6D_6): δ 183.4, 180.1, 146.0, 135.3, 131.5, 130.7, 130.6, 126.0, 124.6, 123.3, 123.2, 43.9, 29.4, 24.2, 25.7, 25.3, 24.2, 22.4. Anal. Calcd. for $C_{34}H_{46}CuN_2O_2$: C, 70.74; H, 7.86. Found: C, 70.72; H, 7.61.

Preparation of (IPr)copper(bicyclo[2.2.1]-2-heptanoate): The general method was modified as follows: Norbornene (141 mg, 1.5 mmol) was added to the reaction vessel before transfer to the glovebox. The product complex was isolated: 0.157 g (0.266 mmol, 92 %). 1H NMR (C_6D_6): δ 7.13 (t, $J = 7.8$ Hz, 2 H), 7.03 (d, 7.8 Hz, 3 H), 6.28 (s, 2 H), 2.63 (m, 1 H), 2.58 (sept, $J = 6.9$ Hz, 4 H), 2.24 (m, 1 H), 2.14 (m, 1 H), 2.03 (s, 1 H), 1.65 (m, 1 H), 1.39 (d, $J = 6.9$ Hz, 12 H), 1.24 (m, 3 H), 1.15 (m, 1 H), 1.03 (d, $J = 6.9$ Hz, 12 H), 0.95 (m, 1 H), 0.89 (m, 1 H). ^{13}C NMR (C_6D_6): δ 182.3, 146.1, 135.3, 131.0, 124.6, 123.1, 123.1, 123.1, 49.4, 42.1, 37.2, 37.0, 36.0, 30.3, 29.9, 29.4, 25.3, 24.2. See 1H and ^{13}C spectra in appendix.

Preparation of (IPr)copper(2-phenylethanoate): The general method was modified as follows: Styrene (0.20 mL, 1.7 mmol) was added to the reaction flask before transferring the vessel into the glovebox. The product complex was isolated: 0.104 g (0.170 mmol, 60 %). ^1H NMR (C_6D_6): δ 7.30 (pseudo-d, 1 H), 7.13 (t, $J = 7.8$ Hz, 2 H), 7.03 (t, $J = 5$ Hz, 1H), 7.00 (d, $J = 7.8$ Hz, 3 H), 6.96 (m, 1 H), 6.28 (s, 2H), 3.66 (quart, 7.2 Hz, 1 H), 2.52 (sept, $J = 6.8$ Hz, 4 H), 1.41 (d, $J = 7$ Hz, 3 H), 1.32 (d, $J = 6.8$ Hz, 12 H), 1.01 (d, $J = 6.8$ Hz, 12 H). See ^1H and ^{13}C spectra in appendix

Preparation of 2-phenylbut-2-enoic acid / α -methylcinnamic acid: The general method was used to prepare the copper acrylate complex with the following modifications: (IPr)CuOt-Bu (0.250 g, 0.47 mmol), 1-phenyl-1-propyne (0.070 mL, 0.56 mmol) and $(\text{EtO})_3\text{SiH}$ (0.092 mL, 0.47 mmol) were used. After completion of reaction, solvent was removed *in vacuo*. The reaction vessel was then opened to air. Diethyl ether (10 mL) was added to dissolve the remaining solid copper complex, then hydrochloric acid (2mL, 1M) was added. The reaction was stirred vigorously for 2 hours forming a thick precipitate. The biphasic mixture was passed through a frit to remove particulates. The ether layer was set aside, and the aqueous layer was extracted with Et_2O (2 x 5 mL). The ether layers were combined, and extracted with aqueous sodium bicarbonate solution (3 x 20 mL). The aqueous layer was then acidified to pH 2, as tested by pH paper by dropwise addition of hydrochloric acid (12 M). The aqueous layer became cloudy, and then extracted with Et_2O (6 x 40 mL). The combined ether portions were dried over magnesium sulfate, filtered, and concentrated *in vacuo*, affording the product as a mixture of 2-phenylbutenoic acid and 2-methyl-3phenyl-prop-2-enoic acid 0.075g (.46

mmol; 98% based on silane). The ^1H NMR spectrum is consistent with published spectra.²¹ ^1H NMR (acetone- d_6): δ 10.43 (broad s, 1 H), 6.76 (t, $J = 7.5$ Hz, $\text{CH}=\text{CCOOH}$), 2.30 (quart, $J = 7.5$ Hz, 2 H), 2.21 (quint, $J = 7.6$ Hz, 2H), 1.04 (t, $J = 7.6$ Hz, 3 H), 0.99 (t, $J = 7.6$, 3 H). ^{13}C NMR (acetone- d_6): δ 170.0, 144.8, 133.9, 22.1, 20.2, 14.3, 13.6.

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Chapter 3

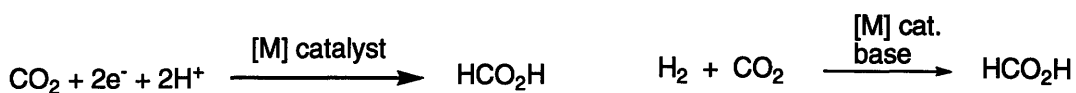
Catalytic Reductive Carboxylation of Alkynes

Abstract

A catalytic cycle for the reductive carboxylation of alkynes based on a (IPr)copper(I) catalyst was developed. Acrylic acids can be isolated in moderate yields. Unexpected interactions between several components of the catalytic system led to a number of side reaction, most importantly between [(IPr)CuH]₂ and the product silyl acrylate. The use of silylcarbonate salts to desilylate the product enhanced yield. In addition, silylcarbonates can also serve as a source of CO₂.

Introduction

Use of monocarbon feedstocks to build or functionalize larger organic molecules has been applied broadly in industry and academia, and continues to be of interest as an area of research. Carbon dioxide would be an ideal source of carbon building blocks.¹ Methane,² phosgene,³ and CO³⁵ are all potential monocarbon sources, which have either been explored or are already exploited for this purpose. Methane is highly flammable, and its activation continues to be a challenge. Phosgene, while highly reactive, is also highly toxic. Carbon monoxide is both toxic and flammable. In contrast, carbon dioxide has low toxicity and is not flammable.



Other Products: H₂, CO

Scheme 1: General approaches to reduction of CO₂ to formic acid.

The processing of CO₂ to useful products is a field that has been explored by a number of researchers. In his review,¹ Leitner points out that reducing CO₂ to formic

acid is an excellent way to generate an industrially useful precursor. In a number of studies,⁴ a metal catalyst is used to catalyze the electrochemical reduction of CO₂ to formic acid in the presence of a proton source. Chemical hydrogenation using a metal catalyst and a base has also been achieved.⁵

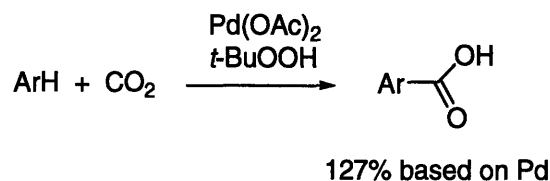
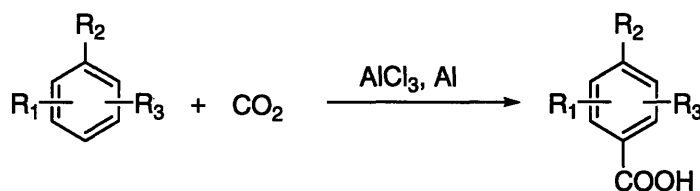
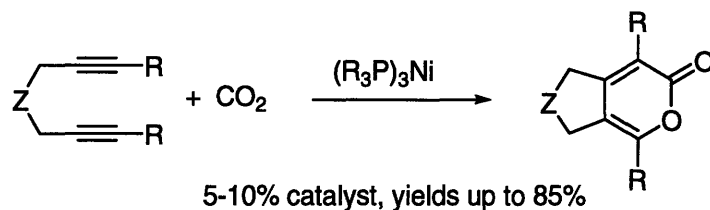
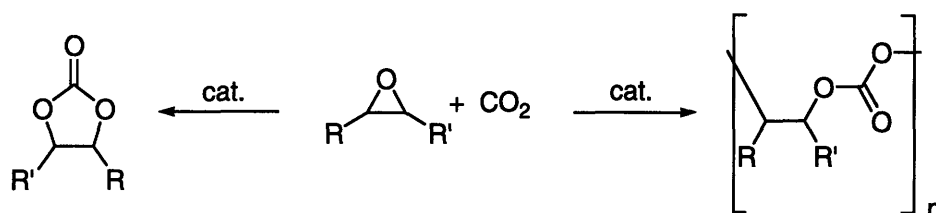


Figure 1: Schemes for methods of CO₂ fixation previously reported. [Refs. 6, 11, 12, 13]

Another approach has been the reaction of CO₂ with epoxides to generate organic carbonates.⁶ Notable contributions to this field have been made by Darensbourg⁷ and Coates⁸. Highly competent zinc catalysts were independently developed in their

laboratories, and improvements to these systems continue to be made.^{9,36} Quaternary ammonium and phosphonium salts catalyze for the generation of cyclic organic carbonates from CO₂ and epoxides.⁶

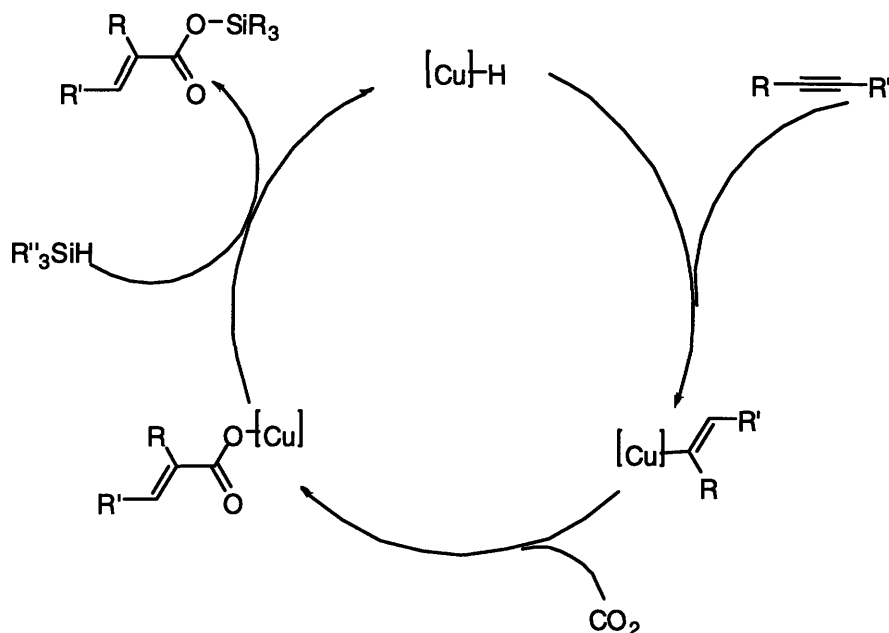
Catalytic carbon—carbon bond formation between CO₂ and two alkynes, either linked or unlinked, using a tris(trialkylphosphine)nickel complex proceeds by the formation of a carbon—carbon bond and a carbon—oxygen bond.¹⁰ These reactions gave yields up to 85% with catalyst loadings of 5 to 10%. NHC supported Ni(0) complexes have been used to produce similar results, and have been used to study the regioselectivity of the insertion process.¹¹

Olah reported a system where a mix of AlCl₃ and Al facilitates the insertion of CO₂ into aryl C-H bonds.¹² In research by Fujiwara, palladium acetate, in the presence of CO₂ and *tert*-butyl hydroperoxide, generated benzoic acid from benzene in 127 % yield.¹³ It was not, however, confirmed that the carboxylate carbon originated from CO₂.

Although many stoichiometric CO₂ insertions into metal-carbon σ -bonds have been reported,¹⁴ these reactions tend to form stable complexes and do not generate C-C bonds catalytically. A key to catalytic turnover would be complexes in which the metal-carbon bond is sufficiently basic to insert CO₂, yet the resulting carboxylate is labile enough to permit catalytic turnover. Late transition metal centers, as soft Lewis acids, should form weaker and more labile bonds to carboxylate than early transition metals. One strategy to achieve catalytic turnover would be to couple metal-oxygen bond cleavage with silicon-oxygen bond formation.

The catalytic cycle envisioned would proceed as follows (Scheme 2). A copper hydride would react with alkyne to generate a copper vinyl species. The copper vinyl

species would insert CO_2 to form a copper acrylate complex. The cycle would be completed through the reaction of the copper acrylate with silane to form a silylacrylate and regenerate the copper hydride.



Scheme 2: Envisioned catalytic cycle.

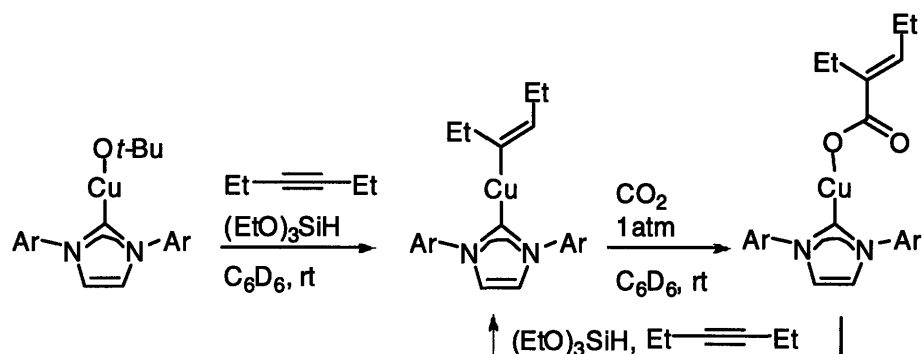
Some precedent exists for each key step in the proposed cycle. Copper–oxygen bonds are known to turn over to form copper hydrides. Ketones can be reduced to alcohols via hydrosilylation using phosphine–supported copper catalysts.¹⁵ An N-heterocyclic carbene supported copper complex has been used in the 1,4-reduction of α,β -unsaturated carbonyl compounds.¹⁶ The 1,2-reduction of ketones to silyl-protected alcohols using N-heterocyclic–carbene–supported copper complex has been accomplished.¹⁷ Remarkably, $(\text{CuO}t\text{-Bu})_4$ reacts with H_2 in the presence of triarylphosphine, forming $[(\text{Ar}_3\text{P})\text{CuH}]_6$ and $t\text{-BuOH}$.¹⁸

The proposed catalytic cycle relies on the formation of a copper–carbon bond through insertion of alkyne into a copper(I) hydride. Hydrocupration of alkynes to form

vinylcopper complexes was unknown, however, it can be inferred from the hydrogenation of alkynes by $[(\text{Ph}_3\text{P})\text{CuH}]_6$.¹⁹ A vinylcopper intermediate was proposed but never directly observed. Using $[(\text{Ph}_3\text{P})\text{CuD}]_6$ in the presence of H_2O gave rise to some doubly deuterated product. This outcome is consistent with the reaction of a vinylcopper intermediate, formed via insertion into a copper-deuterium bond, with a nearby copper deuteride. If alkyne insertion could lead to a mononuclear vinylcopper species, the absence of a neighboring hydride should allow the rapid formation of a second C–H bond to be avoided. Monomeric copper(I) hydrides had not been reported. Such a complex would not present a hydride close to the copper vinyl bond. Thus it was hoped the copper vinyl complex could be isolated. We set about exploring whether the right ligand could support a monomeric copper(I) hydride.

The chemistry of metal complexes supported by N-heterocyclic carbenes (NHCs) began to be explored in 1968, when Öfele²⁰ and Wanzlick²¹ reported (NHC)metal complexes for the first time. Since the isolation of a stable, free NHC by Arduengo in 1990,²² NHCs have been widely used as supporting ligands for metal complexes.²³ The use of NHCs as an alternative to phosphine ligands has been of special interest. Phosphines and NHCs are both strong electron–donors.²⁴ The two compounds differ, however, in that phosphines tend to be labile ligands, while NHCs are more apt to form strong bonds to metal centers. Steric and electronic variations are easily achieved by variation of the substituents on the nitrogens, and electronic changes can also be achieved through variation of a saturated versus unsaturated backbone on the heterocycle ring. N-Heterocyclic carbenes, being strong–field ligands, can promote low coordination numbers.²⁵

Chapter 1 describes stoichiometric examples, from previous work by Neal Mankad, of each step in the proposed catalytic cycle.²⁶ The generation of $[(\text{IPr})\text{CuH}]_2$ in the presence of 3-hexyne led to the insertion of alkyne into the copper hydride to give a stable copper vinyl complex quantitatively. Subsequent addition of CO_2 led to the formation of a copper acrylate by CO_2 insertion into the copper vinyl complex. The cycle was closed stepwise by addition of triethoxysilane to the copper acrylate in the presence of 3-hexyne to regenerate the copper vinyl complex. Observation of *cis*-3-hexene as a byproduct of this turnover step indicated an important side reaction, which will be addressed later in this chapter.



Scheme 3: Establishing viability of catalytic cycle step by step.

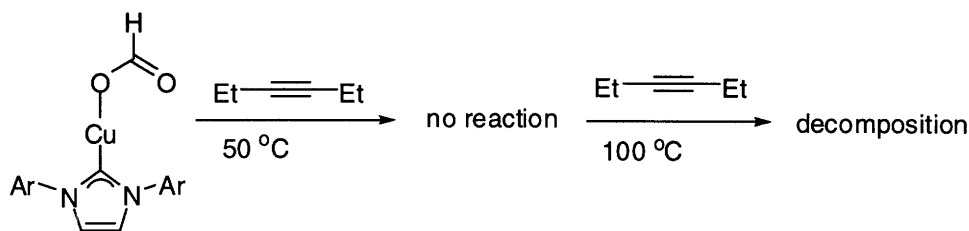
Control of CO_2 addition is crucial to the selective formation of acrylate. Generation of $[(\text{IPr})\text{CuH}]_2$ in the presence of alkyne and under a CO_2 atmosphere led to exclusive formation of copper formate.³⁴ When CO_2 was added as a 1% mixture with argon the copper acrylate formed in a ratio of 1 to 2.5 relative to copper formate. This result suggested that under the right conditions unproductive carbon—hydrogen bond formation could be limited, and carbon-carbon bond formation from CO_2 could be achieved. The key challenge in the development of efficient catalysis would be to keep

the concentration of CO₂ low, allowing the insertion of alkyne into the copper hydride to be favored over the insertion of CO₂.

Results and Discussion

Although the rapid reaction between CO₂ and [(IPr)CuH]₂ has been established, further attempts were made to assess the relative reactivity of CO₂ and alkyne toward the hydride. In preparing one of these attempts we noticed that CO₂ reacts very rapidly even with solid [(IPr)CuH]₂, the yellow color of the hydride disappearing instantly on exposure to the gas. Although unidentified byproducts formed, analysis of the product by ¹H NMR in solution showed the presence of (IPr)CuOCHO.

The reversibility of CO₂ insertion into a copper hydride was of interest. If the process were reversible, alkyne carboxylation could be achieved by deinsertion of CO₂ from the formate followed by insertion of alkyne and reinsertion of CO₂ into the resulting copper vinyl. This could potentially eliminate problems with the sensitivity of [(IPr)CuH]₂. The formate complex (IPr)CuOCHO was prepared by generating [(IPr)CuH]₂ under a CO₂ atmosphere, and under N₂ was combined with 3-hexyne in benzene-*d*₆ solution. No reaction was observed at room temperature, so the NMR tube was heated. After 16 hours at 50 °C no change was observed in the NMR spectrum. After an additional 16 hours at 100 °C, decomposition of the copper formate was observed, but no sign of copper vinyl or copper acrylate was seen. These results suggest that CO₂ insertion is not a reversible process for this complex.



Scheme 4: Insertion of CO₂ into [(IPr)CuH]₂ proved irreversible.

To examine the turnover of copper carboxylate by excess silane, the catalytic reduction of CO₂ to silyl formate was examined. A solution of (IPr)CuO*t*-Bu in benzene-*d*₆ was put under a CO₂ atmosphere and triethoxysilane (20 equiv) was added. As observed by ¹H NMR spectroscopy roughly 10 equivalents of silyl formate per copper were generated.

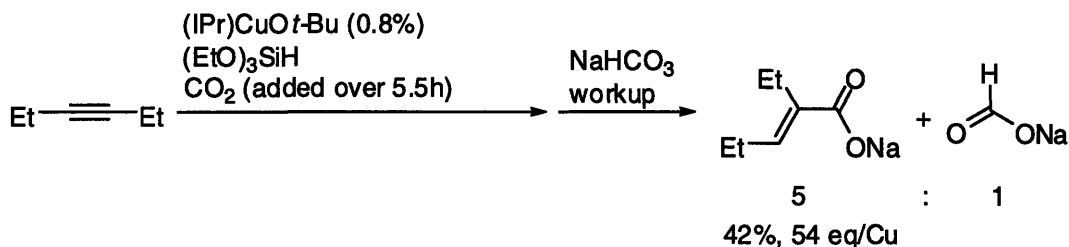
Next, the production of multiple equivalents of silyl acrylate ester from the copper precatalyst (IPr)CuO*t*-Bu was attempted. Initially, control of CO₂ concentration was solved by alternating addition of 1 equivalent per copper of CO₂ and silane via syringe (Figure 5, Exptl. section). This method afforded a little over one equivalent of acrylate per copper. Because the copper hydride and copper vinyl intermediates are very air- and moisture-sensitive, the entry of air through the pierced septum could have led to catalyst decomposition. Slight stoichiometric errors could also have led to catalyst degradation by pathways discussed below.

Catalytic activity was initially achieved by slow diffusion of carbon dioxide into a reaction vessel. The reaction was set up using triethoxysilane, 3-hexyne (5 equiv), and (IPr)CuO*t*-Bu (5 mol%). A glass transfer bridge was used to connect the reaction vessel with a CO₂ reservoir containing frozen CO₂ (Figure 2, Exptl. section). This reservoir was allowed to warm gradually, leading to slow sublimation of CO₂ into the reaction mixture.

This method generated 3.6 equivalents of acrylate per copper, with 1 equivalent per copper of formate side product.

Improved control of CO₂ addition was clearly necessary. Use of 1% CO₂ in argon was investigated. The reaction was run in a large vessel necessitated by the low CO₂ concentration (Figure 3, Exptl. section), using triethoxysilane, 3-hexyne (5 equiv), (IPr)CuOt-Bu (4 mol%) in a solution of benzene. These conditions led to improved catalytic efficiency, with 9 equivalents of acrylate generated per copper, and an acrylate to formate ratio of 5:1.

The use of a syringe pump to control the rate of CO₂ delivery gave further improvements in efficiency (Figure 4, Exptl. section). Carbon dioxide (50 mL) was delivered to the reaction vessel over a 6 hour period. Low catalyst loading (0.8%) proved ideal. Excess substrate (5–10 equiv.) was necessary to produce reasonable yields and acrylate to formate ratios. In some cases, running the reaction without cosolvent led to greatly improved results.



Scheme 5: Catalytic conversion of 3-hexyne to 2-ethyl-2-pentenoic acid with addition of CO₂ via a syringe pump.

Having established the conversion of one substrate, we examined a range of other alkyne substrates. The lighter alkynes 2-pentyne and 2-butyne reacted productively, but yields were low. It is possible that the volatility of these substrates lowered their concentrations to the point that they could not compete effectively against formate

formation. Though *tert*-butylacetylene inserts very rapidly into the copper hydride, it also proved to be a poor substrate for catalytic reductive carboxylation.

Aryl-substituted alkynes proved to be superior substrates for carboxylation. Diphenylacetylene required higher catalyst loading than 3-hexyne, but gave a similar yield. Two phenyl/alkyl-substituted substrates, 1-phenyl-1-propyne and 1-phenyl-1-butyne gave better yields than 3-hexyne with the same low catalyst loading. With all three of these substrates an improvement in acrylate versus formate selectivity was also observed.

Isolation of the acrylic acid product was accomplished by multiple extractions. The reaction mixture was acidified to digest the silyl acrylate, then filtered to remove precipitated copper complex and silicon oxide. The acrylic acid was extracted into an ether layer. To separate the acrylic acid product from other organics it was extracted from the ether layer with a concentrated solution of sodium bicarbonate in water, as sodium acrylate. Reacidification and extraction with ether gave pure acrylic acids.

Attempts were made to produce the carboxylic acid derivatives from norbornene, but no catalytic turnover was observed. Given the relatively slow insertion of CO₂ into *sec*-phenethylcopper complex (see Chapter 1), the reductive carboxylation of styrene was not attempted.

Investigation of the side reactions was undertaken in order to minimize them. As mentioned, (IPr)copper hydride readily inserts CO₂ to make (IPr)copper formate. While this side reaction does not remove copper from the catalytic system, it does decrease yield based on silane. Slow addition of CO₂, over six hours, was the key to achieving a reasonable ratio of acrylate to formate formation. A large excess of substrate, five to ten

equivalents, was still required for reasonable yields. To establish other potential decomposition pathways the stability of the various complexes formed during the catalytic cycle to the catalytic conditions was investigated.

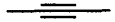
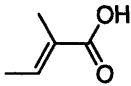

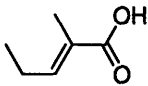
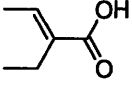
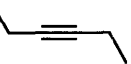
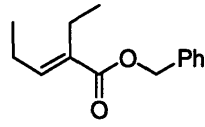
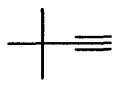
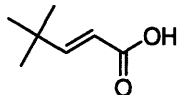
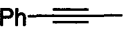
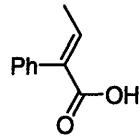
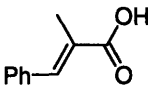
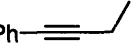
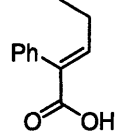
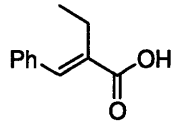
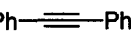
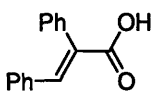
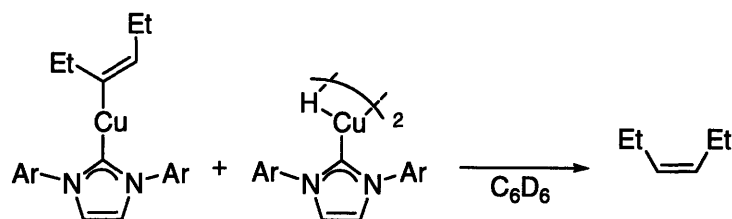
	Alkyne	Substrate Load (eq/Si)	Product (Distribution)	Yield based on Si	Yield of Formate (based on Si)
1		13		16%, 4.1eq/Cu	2%
2		10	 (3 : 1) 	18%, 4.7eq/Cu	2%
3		10		42%, 54eq/Cu	8%
4		10		28%, 7eq/Cu	1%
5		2	 (3 : 1) 	65%, 84eq/Cu	1.6%
6		2	 (5 : 1) 	55%, 70eq/Cu	1%
7		6		47%, 12eq/Cu	<1%

Table 1: Catalytic results for the conversion of alkynes to acrylic acids. Ratios of regioisomers and quantities of formate formed were determined by NMR integration.

Because alkene had been observed as a side product of the carboxylation reaction, the reactivity of a copper vinyl complex with [IPrCuH]₂ was examined. The reaction was set up in benzene-*d*₆, with two equivalents of (IPr)copper(1-ethyl-1-butenyl) per [IPrCuH]₂. Their interaction was monitored by ¹H NMR spectroscopy. After 20 minutes

a small peak corresponding to 3-hexene appeared in the spectrum. Integration of the methylene protons of 3-hexyne and the vinylic proton of the copper complex indicated a 1:20 ratio of 3-hexyne to vinylcopper complex. After 16 hours there had been significant further reaction, giving a 2:1 ratio of 3-hexene to vinylcopper complex.

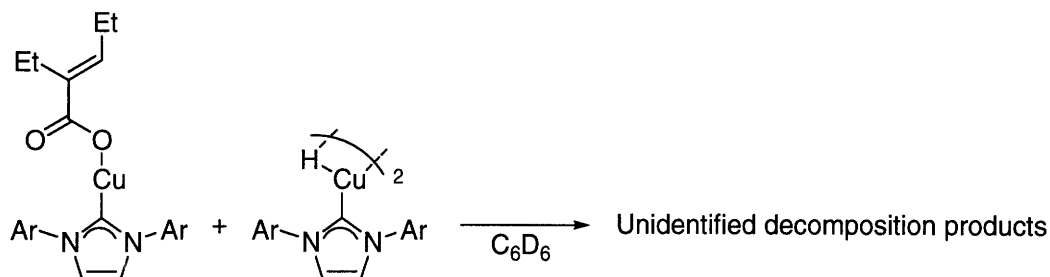


Scheme 6: Alkene formation from copper vinyl complex and copper hydride.

Other copper hydrides are known to react with alkynes to generate *cis*-alkenes.¹⁹ This process is believed to occur through the insertion of alkyne into a copper hydride, followed by rapid reaction of the resulting copper vinyl with a neighboring copper hydride. We suspect that [(IPr)CuH]₂ dissociates in solution and may react as a monomer, allowing formation of the copper vinyl complex. When equal amounts of [(IPr)CuH]₂ and [(IPr)CuD]₂ are combined in THF-*d*₈, a new broad singlet resonance appears at δ 2.11 ppm in the ¹H NMR spectrum, 0.04 ppm upfield of the parent hydride resonance. The new resonance is assigned to the isotopomer (μ -D)(μ -H)[(IPr)Cu]₂ which could form via dissociation of the dimers and recombination of (IPr)CuH and (IPr)CuD.

The interaction between (IPr)Cu(2-ethyl-2-pentenoate) and [(IPr)CuH]₂ was investigated. Independently prepared copper acrylate and copper hydride were combined, two equivalents of copper acrylate per copper hydride dimer, in benzene-*d*₆. After 20 minutes the ¹H NMR spectrum of the reaction mixture indicates degradation of

the copper acrylate complex. The characteristic triplet signal of the acrylate proton is broadened. After 16 hours, the acrylate signal is no longer observable, and the other peaks in the spectrum are significantly broadened.



Scheme 7: Decomposition of copper acrylate by copper hydride.

These experiments suggest that side reactions between the copper hydride and other key intermediates can lead to deactivation of the catalytic system. These results also suggest that lower catalyst concentration might help to avoid deactivation, consistent with the higher yields noted earlier (Table 1, entries 3, 5 and 6). According to ¹H NMR spectra of the crude reaction mixtures of catalytic runs, silane was completely consumed. This suggested that other side-reactions must be occurring, given that the yields of acrylates were well short of quantitative.

In light of the complete consumption of silane, it was unlikely that catalyst decomposition alone could account for the observed modest yields of acrylate. Other decomposition pathways, consuming either product, silane, or both were considered likely. The interaction of the silane with expected intermediates in the reaction cycle was then investigated.

First, (IPr)Cu(1-ethyl-1-butenyl) and 10 equivalents of triethoxysilane were combined in benzene-*d*₆. After 16 hours, there was a trace amount of a new signal in the ¹H NMR spectrum, but most of the copper complex and the silane remained unreacted.

The new signals did not grow in intensity over time, suggesting that they originated from some impurity. These observations lead us to believe no chemical interaction takes place between the copper vinyl complex and silane.

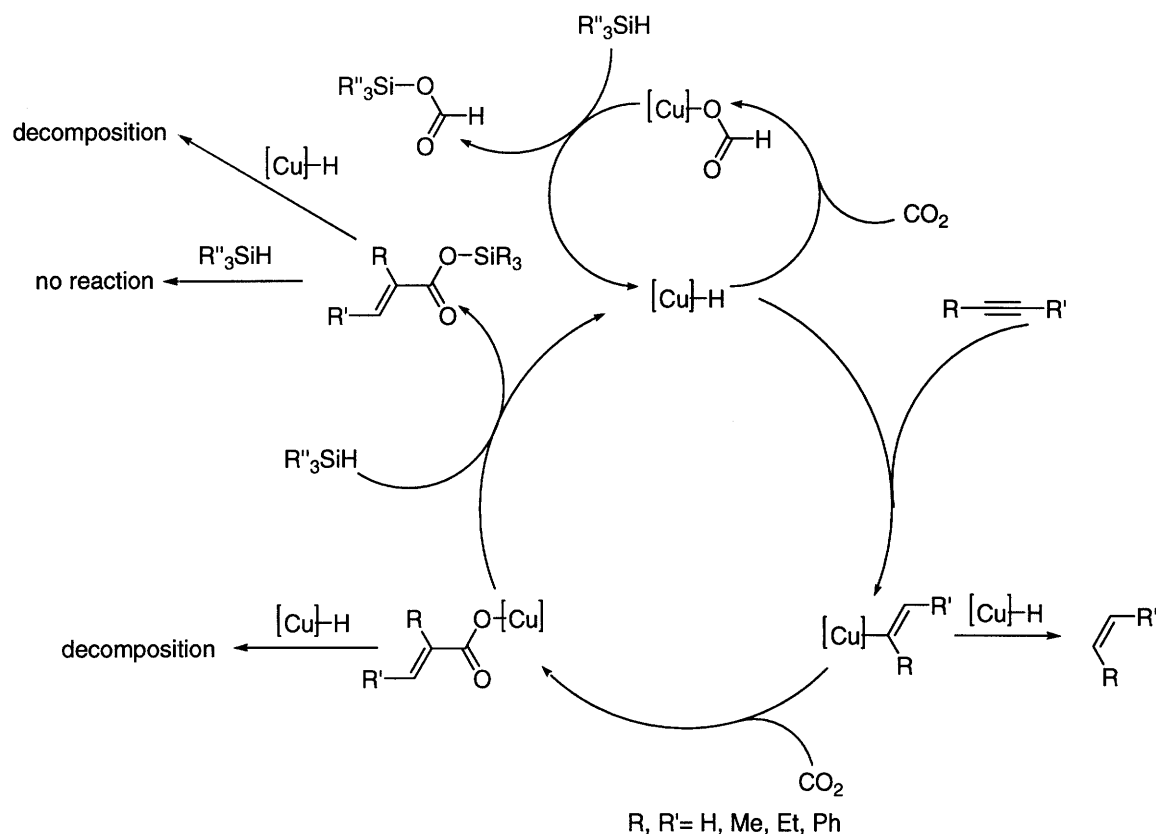
The interaction of triethoxysilane with the product silyl acrylate was investigated by treating (IPr)Cu(2-ethyl-2-pentenoate) with triethoxysilane (10 equiv) in the presence of *tert*-butylacetylene (10 equiv) in benzene-*d*₆. The *tert*-butylacetylene reacts rapidly with the copper hydride as it is generated to form a stable copper vinyl complex, leaving the triethoxysilyl-2-ethyl-2-pentenoate in the presence of 9 equivalents of silane. After 16 hours no decomposition of the silyl acrylate is observed by ¹H NMR.

Next, the interaction between [(IPr)CuH]₂ and the silyl acrylate product was examined. The copper hydride had shown undesired reactivity towards other components of the catalytic system, it was considered a likely culprit for product decomposition as well.

Triethoxysilane and (IPr)copper(2-ethyl-2-pentenoate) were combined in a 1:1 ratio in benzene-*d*₆ and their reaction was monitored by ¹H NMR. This reaction generates [IPrCuH]₂ and silyl acrylate. After 2.5 hours no silyl acrylate was observed. Although the resulting decomposition products remain unidentified, this decomposition pathway has proven to be the most rapid, and likely the most damaging to the productivity of the catalytic cycle.

Protection of the product from reaction with [IPrCuH]₂ was expected to enhance the productivity of the catalytic process. It was hoped that sufficient steric encumbrance of the silyl acrylate product could prevent this side-reaction. Several silanes were investigated as reducing agents. Triphenylsilane generates copper hydride too slowly, on

the order of days, to be an effective reducing agent. The use of triisopropoxysilane and pentamethyldisiloxane heavily favored the production of formate observed in a 2:1 ratio relative to acrylate. The desired product was formed in only 10% yield. The inexpensive and safe polymethylhydrosiloxane, unfortunately, showed decreased activity: No catalytic carboxylation of 3-hexyne was observed, and 1-phenyl-1-propyne gave rise to 38% yield of desired product, compared to the 65% yield obtained with triethoxysilane.



Scheme 8: Summary of known side reactions from main catalytic cycle.

Silane	Results
Ph ₃ SiH	No reaction, copper hydride forms very slowly
(<i>i</i> -PrO) ₃ SiH	Favors formate formation 2:1 over acrylate, yield only 10%
H(Me) ₂ SiOSiMe ₃	Favors formate formation 2:1 over acrylate, yield lowered
polymethylhydrosiloxane	No reaction with 3-hexyne, lowered (38%) yield with 1-phenyl-1-propyne

Table 2: Summary of results of silane variation in catalytic runs.

An increase in the size of the ligand might also prevent the hydride from interacting with other intermediates in the catalytic cycle. Copper complexes supported

by IMes, SIMes, and IAd were examined, but attempts at catalysis failed. The (IMes)CuOt-Bu and (SIMes)CuOt-Bu catalyst decomposed rapidly, within a minute after the addition of silane to the reaction mixture, and no acrylate product was observed. No reaction was evident between (IAd)CuOt-Bu and silane. On the theory that reduced ligand size could facilitate alkyne insertion, allowing the rapidity of that insertion to dominate other decomposition pathways, less sterically demanding ligands were tried. Use of SICy, *It*-Bu, and *meIPr* as ligands all gave results similar to IMes and SIMes, with rapid decomposition of the copper complex upon addition of silane, and no generation of acrylate product.⁴⁰

The initial choice of ligand and silane proved to be optimal. High alkyne concentration had proved critical for good catalytic yield and selectivity; thus, cosolvents were avoided where possible. As the relative concentration of alkyne was decreased, formate formation and copper hydride decomposition pathways became more favorable. Manipulation of sterics, either those of the ligand or the silane, proved to be ineffective at minimizing side reactions. The main decomposition pathway was the reaction of the product silyl acrylate with copper hydride.

An alternative strategy for protecting the acrylate, by removing it from solution as the reaction progresses, was investigated.⁴⁰ The formation of a silicon—fluoride bond is thermodynamically highly favorable. Acrylate salts should be insoluble in the organic media in which the catalytic reactions take place. The in-situ desilylation of the silyl acrylate product was thus attempted by addition of cesium fluoride or potassium fluoride to the catalytic reactions. The metal fluoride would react with the silyl acrylate to generate a metal acrylate salt and silyl fluoride. Although the overreduction of acrylate

by copper hydride was shut down, the reaction now heavily favored the formation of formate over acrylate.

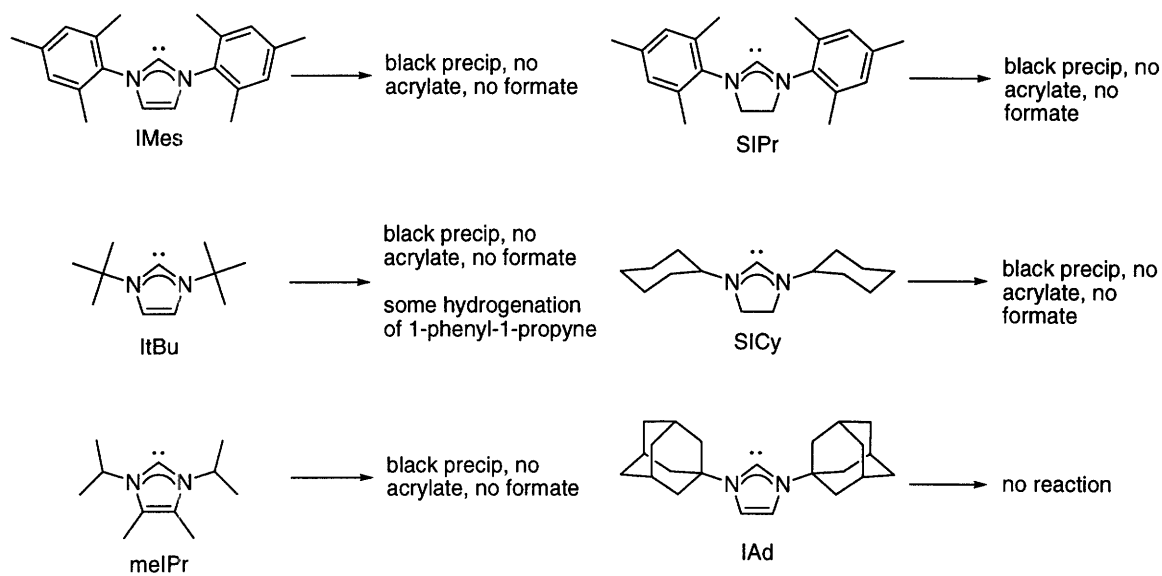


Table 3: Ligands used to generate (NHC)CuO*t*-Bu complexes as precatalysts, and the corresponding reactivity.

The carbonate salts of sodium, potassium, and cesium were also examined as desilylating agents; however, their addition to the catalytic system lead to lowered yield. It was theorized that these carbonates may form silyl carbonates, which are known to decompose to silyl ethers releasing CO₂.³⁷ Carbonates were tested as potential CO₂ sources, in reactions run without the addition of gaseous CO₂, but no reactivity was observed.

Organic carbonates were tried in place of carbonate salts. When sodium *tert*-butoxycarbonate, generated from sodium *tert*-butoxide in diethyl ether by placing under a CO₂ atmosphere, was used as an additive to the catalytic reaction, a decrease in activity was observed relative to the parent system. Attempts to use sodium *tert*-butoxycarbonate as a CO₂ source led to no catalytic activity.

Silyl carbonate salts are significantly less stable than either carbonate or alkyl carbonate salts. At room temperature silyl carbonate salts decompose releasing CO₂.³⁷ Silylcarbonate salts were an excellent candidate for a desilylating agent that could serve as a source of CO₂. Silyl carbonates can be readily prepared from silanolates. Sodium trimethylsilanolate, commercially available, was converted to the carbonate by dissolving in diethyl ether and stirring under a CO₂ atmosphere for 16 hours. The catalytic reaction was run using triethoxysilane, IPrCuOt-Bu (5 mol%), 3-hexyne (5 equiv.), and sodium trimethylsilylcarbonate (1.1 equiv.), giving a 20% yield of sodium 2-ethyl-2-pentenoate.

Initial improvements in yield were achieved using thermal control. In the absence of cooling, interaction of sodium trimethylsilyl carbonate and triethoxysilane caused the reaction vessel to become warm to the touch. Cooling the reaction vessel to 0 °C during silane addition gave significantly improved yields, up to 47% 2-ethyl-2-pentenoic acid.

Solvent effects were then investigated. Initial reactions were run in benzene, which was replaced by THF when the need for cooling became evident. Diethyl ether, hexanes, and toluene were then screened. Lower yields were obtained in hexanes, but diethyl ether and especially toluene both led to improvements (Table 4, entry 6).

Entry	Silane	Silyl Carbonate	Temp.	Solvent	Yield of 2-ethyl-2-pentenoic acid
1	(EtO) ₃ SiH	KOCO ₂ SiMe ₃	RT	THF	17%, 5eq/Cu
2	(EtO) ₃ SiH	NaOCO ₂ SiMe ₃	RT	THF	47%, 12eq/Cu
3	(EtO) ₃ SiH	NaOCO ₂ SiMe ₃	0 °C	THF	34%, 9eq/Cu
4	(<i>i</i> -PrO) ₃ SiH	NaOCO ₂ SiMe ₃	0 °C	THF	50%, 13eq/Cu
5	(<i>i</i> -PrO) ₃ SiH	NaOCO ₂ Si(<i>i</i> -Pr) ₃	RT	toluene	18%, 5eq/Cu
6	(<i>i</i> -PrO) ₃ SiH	NaOCO ₂ SiMe ₂ (<i>t</i> -Bu)	RT	toluene	65%, 27 eq/Cu
7	(<i>i</i> -PrO) ₃ SiH	KOCO ₂ SiMe ₂ (<i>t</i> -Bu)	RT	toluene	68%, 28 eq/Cu

Table 4: Selected conditions for catalytic reductive carboxylation of alkynes using sodium trialkylsilylcarbonates as the CO₂ source and trapping agent.

The effect of steric variation in silyl carbonates was investigated. Sodium triethylsilylcarbonate, sodium triisopropylsilylcarbonate, and sodium *tert*-butyldimethylsilylcarbonate were prepared from the silanols. The silanol in diethyl ether solution was stirred for 12 hours over sodium. Exposure of the filtered silanolate solutions to a CO₂ atmosphere led to precipitation of the silylcarbonate salts.

Sodium triisopropylsilylcarbonate did not form a gel with triethoxysilane, but gave rise to lower catalytic yield than did the trimethylsilylcarbonate. Oddly, the use of sodium triethylsilyl carbonate yielded no product. Given the results with trimethylsilyl- and triisopropylsilyl-carbonate, a silyl group with steric demand intermediate between that of trimethylsilyl and triisopropylsilyl was sought. Sodium *tert*-butyldimethylsilyl carbonate gave no apparent exotherm on treatment with triethoxysilane, and catalytic yields improved significantly, increasing to 65% for 2-ethyl-2-pentenoic acid.

The effect of a cation other than sodium on catalytic efficiency was examined next. Potassium trimethylsilylcarbonate and potassium *tert*-butyldimethylsilylcarbonate were prepared by the procedure used for sodium salts. Reductive carboxylation reactions using potassium trimethylsilylcarbonate gave significantly lower yields (Table 4, entries 1 and 2, 17% as opposed to 47%) than those using the sodium salt. The potassium and sodium salts of *tert*-butyldimethylsilylcarbonate gave very similar results (Table 4, entries 6 and 7, 65% and 68% respectively). Further variations in counteranion were not pursued.

The effect of using different silanes as the reducing agent in these reactions was also of interest. Pentamethyldisiloxane, polymethylhydrosiloxane and trimethoxysilane led to decreased yield and increased formation of formate. Triisopropoxysilane,

however, gave improved yields for most substrates. In the isolated case of *tert*-butylacetylene, the use of triethoxysilane gave the highest catalytic efficiency.

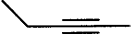
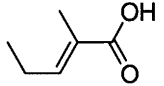
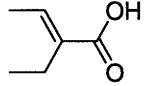
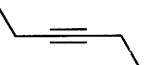
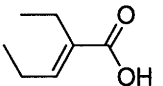
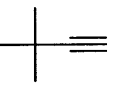
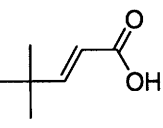
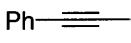
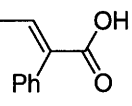
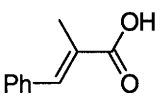
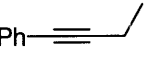
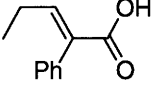
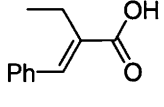

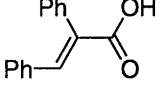
Alkyne	Load (eq/Silane)	Product (Distribution)	Yield (based on silane)	Formate (based on silane)
1 	2	 (2 : 1) 	44%, 19 eq/Cu	14%
2 	2		64%, 27 eq/Cu	5%
3 	2		34%, 14 eq/Cu	11%
4 	2	 (3 : 1) 	72%, 30 eq/Cu	4%
5 	2	 (7 : 1) 	45%, 19 eq/Cu	2%
6 	1		64%, 27 eq/Cu	7%

Table 5: Catalytic results for the reductive carboxylation of alkynes using sodium *tert*-butyldimethylsilylcarbonate as a CO₂ source and protecting agent.

To confirm that our strategy was having the desired effect, a catalytic reaction was run in toluene-*d*₈ with one equivalent of substrate. The quantity of unreacted substrate and *cis*-3-hexene, as measured by ¹H NMR, and the isolated product accounted for 99% of the starting material. This result indicates that the side reaction of silyl acrylate and [(IPr)CuH]₂ has been successfully mitigated.

Conclusion

A new catalytic C—C bond forming reaction for the reductive carboxylation of alkynes with CO₂ using an (NHC)copper(I) catalyst has been established. The details of the catalytic system were studied to understand the nature of side reactions. Based on the information from these investigations, several strategies were explored to enhance catalytic performance. The use of sodium silylcarbonates as trapping agents for the product acrylates proved fruitful, mitigating overreduction of the acrylate. In addition, silylcarbonates can also serve as a CO₂ source.

Experimental

General Procedures: All procedures were performed in a glovebox under nitrogen atmosphere, or using standard Schlenk techniques under argon. Tetrahydrofuran (THF) was purchased anhydrous from Aldrich and passed under argon pressure through columns of alumina and molecular sieves before use. Benzene and pentane were purchased anhydrous from Aldrich and dried over molecular sieves. Alkynes were purchased from Aldrich, stirred over sodium borohydride for 24 hours, degassed with three to five freeze-pump-thaw cycles, and distilled before use. The complexes IPrCuOt-Bu,²⁶ and (IPr)copper(1-ethyl-1-butenyl)²⁶ and (IPr)CuF⁴¹ were prepared according to published methods. Sodium *tert*-butyldimethylsilylcarbonate was prepared according to literature methods³⁷ from sodium *tert*-butyldimethylsiloxide prepared according to literature methods.³⁸ Polymethylhydrosiloxane, triethoxysilane and pentamethyldisiloxane were purchased from Aldrich and degassed before use. It is important to note that while silanes can be degassed by freeze-pump-thaw techniques, they have a tendency to crack glassware on thawing. Sparging is strongly recommended

for degassing silanes. Triisopropoxysilane was synthesized according to literature methods.³⁹ CO₂ was purchased from AirGas at 'bone dry' grade, and passed through a filter of P₂O₅. NMR data was collected on a Varian Mercury 300 or Varian 500. Elemental analyses were performed by Desert Analytics

Catalytic run for the preparation of sodium 2-ethylpent-2-enoate by CO₂ sublimation and diffusion: In the glovebox a 25 mL resealable Schlenk tube, A, was charged with (IPr)CuO*t*-Bu (0.10 g, 0.019 mmol), 3-hexyne (0.250 mL, 2.2 mmol), and triethoxysilane (0.050 mL, .27 mmol) in THF (1 mL). The tube was sealed with a Teflon screwcap and removed from the glovebox. A 25 mL resealable Schlenk tube, B, was put under an atmosphere of CO₂ and sealed. The two Schlenk tubes were connected by a glass vacuum transfer bridge, and the bridge put under Ar atmosphere. All joints were secured with elastic bands and Keck clamps against pressure buildup within the system. Schlenk flask B, still sealed, was cooled with liquid N₂ to condense the CO₂. The liquid N₂ bath was quickly replaced with a dry ice/isopropanol bath. See Figure 2 for diagram of apparatus. Flask B was opened to Ar from the glass transfer bridge, then the bridge was sealed off from Ar pressure. Flask A was then opened to the glass transfer bridge. The dry ice/isopropanol bath was allowed to come to room temperature over 12 hours, allowing slow diffusion of CO₂ from the cold reservoir to the reaction vessel. The reaction mixture was extracted with aqueous sodium bicarbonate, the water was removed in vacuo. The product was prepared for analysis by washing it from the residue with methanol-*d*₄ (0.7 mL), filtering, and adding 1,4-dimethoxybenzene (2.7 mg) as an internal standard. Ratio of acrylate to formate formation and yield were established by ¹H NMR

spectroscopy. The acrylate to formate ratio was 3.6:1. Yield based on the integration of ^1H NMR signals was 0.06 mmol, 21 %.

Catalytic run for the preparation of sodium 2-ethylpent-2-enoate using 1% CO_2 in

Ar: To accommodate the required volume of gas, a 1L glass vessel (depicted in Figure 3) with a 10 mL bulb at the bottom was manufactured. The reaction vessel, with a Teflon stir bar in the bulb, was oven dried. In the glovebox, in a vial (IPr)CuOt-Bu (0.015 g, 0.029 mmol), 3-hexyne (0.500 mL, 4.8 mmol) and triethoxysilane (0.89 mL, 0.49 mmol) were dissolved in 0.5 mL THF. In the glovebox, the reaction mixture was then transferred to the bulb of the reaction vessel, and the vessel was sealed with a 24/40 ground glass joint to rubber hose adapter. The reaction vessel was removed from the glovebox and connected to a Schlenk line. The bulb was immersed in a dry ice/isopropanol bath. The reaction vessel was then put under partial vacuum (~ 0.1 torr) and then backfilled with 1% CO_2 in argon. The reaction was stirred in the dark for 16 hours. The plug of the reaction vessel was then tightly tied to the reaction vessel with copper wire, and the vessel returned to the glovebox. An NMR sample was prepared in benzene- d_6 , and analyzed by ^1H NMR to ascertain acrylate to formate ratio. The product was isolated by extracting the reaction mixture with aqueous sodium bicarbonate, removing the water in vacuo, and triturating the remaining residue with methanol. Yield of sodium 2-ethylpent-2-enoate was 0.026 g (36% based on silane).

Method A: In the glovebox a Schlenk flask was charged with (IPr)CuOt-Bu, alkyne and, in some cases, solvent, followed by triethoxysilane (0.45 mL, 2.4 mmol). The flask was

sealed with a rubber septum and taken outside the box. The flask was wrapped in aluminum foil, then set on a stir plate and the contents were stirred. A 50 mL Norm-Ject syringe, with a 4" long 22 gauge needle, was charged with 50 mL CO₂. The syringe was connected to the reaction flask with the needle piercing the septum. A small amount of grease was used to improve the seal. The syringe was operated by a syringe pump set to deliver the full volume in 6.5 hours. See figure 4 for diagram of apparatus. The reaction mixture was stirred an additional hour after CO₂ addition was complete. The reaction vessel was returned to the box, and 1,4-dimethoxybenzene (0.030 g) was added as internal standard. The ¹H NMR was taken of an aliquot of the reaction mixture in benzene-*d*₆ to establish quantity of formate formed. The reaction mixture and NMR sample were recombined under air, and the solution was then diluted with Et₂O (10 mL). The solution was extracted with aqueous sodium bicarbonate (3 x 14 mL) by stirring the two phases vigorously for several hours. The water layers were combined and filtered then acidified and extracted with Et₂O (6 x 40 mL). The ether phases were combined and concentrated in vacuo.

Synthesis of 2-methylbut-2-enoic acid: The synthesis was performed according to general method A using (IPr)CuO*t*-Bu (0.050 g, 0.095 mmol), 2-butyne (2.5 mL, 30 mmol) and 2.5 mL THF. Isolation of product gave 2-methylbut-2-enoic acid, 0.038 g (0.38 mmol, 16 % based on silane). ¹H and ¹³C NMR spectra are consistent with published spectra.²⁷ ¹H NMR (CDCl₃): δ 11.94 (broad s, 1 H), 7.00 (m, 1 H), 1.82 (m, 6H). ¹³C NMR (CDCl₃): δ 174.1, 140.3, 128.3, 14.9, 11.9. Anal. Calcd. for C₅H₈O₂: C, 59.98; H 8.05. Found: C, 59.61; H, 7.97.

Synthesis of 2-ethylpent-2-enoic acid: The synthesis was performed according to general method A using (IPr)CuOt-Bu (0.010 g, 0.019 mmol), using 3-hexyne (2.5 mL, 24 mmol). Isolation of product gave 2-ethylpent-2-enoic acid 0.128 g (1.00 mmol, 42 %). The ^1H NMR spectrum is consistent with published spectra.²⁸ ^1H NMR (acetone- d_6): δ 10.43 (broad s, 1 H), 6.76 (t, $J = 7.5$ Hz, $\text{CH}=\text{CCOOH}$), 2.30 (quart, $J = 7.5$ Hz, 2 H), 2.21 (quint, $J = 7.6$ Hz, 2H), 1.04 (t, $J = 7.6$ Hz, 3 H), 0.99 (t, $J = 7.6$, 3 H). ^{13}C NMR (acetone- d_6): δ 170.0, 144.8, 133.9, 22.1, 20.2, 14.3, 13.6. Anal. Calcd. for $\text{C}_7\text{H}_{12}\text{O}_2$: C, 65.60; H, 9.44. Found: C, 65.90; H, 9.39.

Synthesis of 2-phenylbut-2-enoic acid and α -methylcinnamic acid: The synthesis was performed according to general method A using (IPr)CuOt-Bu (0.010 g, 0.019 mmol), 1-phenyl-1-propyne (0.63 mL, 24 mmol). Isolation of product gave a mixture of 2-phenylbut-2-enoic acid and α -methylcinnamic acid 0.295 g (1.56 mmol, 65 %). ^1H and ^{13}C NMR are consistent with published spectra.^{29,30} ^1H NMR (CDCl_3): δ 12.2 (broad s, 1H), 7.83 (d, $J = 1.4$ Hz, 0.25 H), 7.32-7.46 (m, 4H), 7.20-7.31 (m, 2H), 2.14 (d, $J = 1.4$ Hz, .8 H), 1.79 (d, $J = 7.3$ Hz, 2.4 H). ^{13}C NMR (CDCl_3): δ 175.4, 173.7, 143.7, 141.9, 136.3, 135.2, 135.0, 130.7, 130.6, 129.5, 129.2, 129.1, 129.0, 128.8, 128.7, 128.5, 128.4, 128.3, 16.6, 14.5. Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{O}_2$: C, 74.06; H, 6.21. Found: C, 73.65; H, 6.00.

Synthesis of 3,3-dimethylpent-2-enoic acid: The synthesis was performed according to general method A using (IPr)CuOt-Bu (0.050 g, 0.095 mmol), *tert*-butylacetylene (3 mL,

24 mmol) and 2.5 mL dry THF. Isolation of product gave 3,3-dimethylpent-2-enoic acid 0.86 g (.67 mmol, 28 %). ^1H and ^{13}C NMR are consistent with published spectra.³¹ ^1H NMR (CDCl_3): δ 12.28 (s, 1 H), 7.08 (d, $J = 5.7$ Hz, 1 H), 5.74 (d, $J = 5.7$ Hz, 1 H), 1.08 (s, 9 H). ^{13}C NMR (CDCl_3): δ 173.8, 162.5, 116.9, 34.6, 29.2. Anal. Calcd. for $\text{C}_7\text{H}_{11}\text{O}_2$: C, 65.60; H, 9.44. Found: C, 65.90; H, 9.39.

Synthesis of 2-ethylbut-2-enoic acid and 2-methylpent-2-enoic acid: The synthesis was performed according to general method A using (IPr)CuOt-Bu (0.050 g, 0.095 mmol), 2-pentyne (2.3 mL, 24 mmol). Isolation of product gave a mixture of 2-ethylbut-2-enoic acid and 2-methylpent-2-enoic acid 0.049 g (0.43 mmol, 18 %). ^1H and ^{13}C NMR are consistent with published spectra.²⁸ ^1H NMR (acetone- d_6): δ 10.27 (broad s, 1 H), 6.83 (quart, $J = 7.2$ Hz, 0.3 H), 6.77 (dt, $J = 1.5, 7.6$ Hz 1 H), 2.31 (quart, $J = 7.5$ Hz, 0.6 H), 2.20 (d quint, $J = 0.9, 7.5$ Hz 1 H), 1.79 (m, 2 H) 1.00 (m, 3 H). ^{13}C NMR (CDCl_3): δ 168.9, 168.4, 144.0, 136.9, 134.9, 127.2, 21.8, 19.4, 13.4, 13.2, 12.6, 11.6.

Synthesis of 2-phenylpent-2-enoic acid and α -ethylcinnamic acid: The synthesis was performed according to general method A using (IPr)CuOt-Bu (0.010 g, 0.019 mmol), 1-phenyl-1-butyne (0.700 mL, 5 mmol). Isolation of products gave a mixture of 2-phenylpent-2-enoic acid and α -ethylcinnamic acid 0.232 g (1.32 mmol, 55 %). ^1H and ^{13}C NMR are consistent with published spectra.³² ^1H NMR (CDCl_3): δ 11.18 (broad s, 1 H), 8.06-8.18 (m, 0.2 H), 7.28-7.45 (m, 3 H), 7.17-7.26 (m, 2 H), 2.57 (quart, $J = 7.4$ Hz, .2 H), 2.14 (m, 1 H), 1.22 (t, $J = 7.5$ Hz, .3H) 1.042 (m, 2 H). ^{13}C NMR (CDCl_3): δ 182.4,

173.6, 146.0, 140.9, 140.2, 139.0, 135.3, 131.1, 129.6, 127.6, 126.1, 124.7, 123.2, 29.4, 25.4, 24.3, 23.3, 14.3

Synthesis of 2,3-diphenylprop-2-enoic acid: The synthesis was performed according to general method A using (IPr)CuOt-Bu (0.050 g, 0.095 mmol), diphenylacetylene (2.4g, 14 mmol), and 2 mL THF. Isolation of product gave 2,3-diphenylprop-2-enoic acid 0.224 g (1.12 mmol, 47 %). ¹H and ¹³C NMR are consistent with published spectra.³³ ¹H NMR (CDCl₃): δ 11.96 (broad s, 1 H), 7.98 (s, 1 H), 7.40 (m, 3 H), 7.27 (m, 2 H), 7.24 (m, 1 H), 7.19 (m, 2 H), 7.09 (m, 2 H). ¹³C NMR (CDCl₃): 174.1, 143.2, 136.0, 135.0, 132.4, 131.6, 130.5, 130.2, 129.4, 129.0, 128.8.

Reaction of (IPr)copper(2-ethylpent-2-enoate) with [(IPr)CuH]₂: In the glovebox a J. Young NMR tube was charged with (IPr)copper(2-ethylpent-2-enoate) (26.7 g, 0.046 mmol) in benzene-*d*₆ (0.4 mL). In the glovebox, in a vial, [(IPr)CuH]₂ was generated from (IPr)CuOt-Bu (0.024 g, 0.046 mmol) and triethoxysilane (0.0089 mL, .046 mmol) in benzene-*d*₆ (0.4 mL). The reaction was monitored by ¹H NMR spectroscopy. After 20 minutes, partial decomposition of (IPr)copper(2-ethylpent-2-enoate) was observed. After 16 hours decomposition to unidentified products of all species was observed

Reaction of (IPr)copper(1-ethyl-1-butenyl) with [(IPr)CuH]₂: In the glovebox a J. Young NMR tube was charged with (IPr)copper(1-ethyl-1-butenyl) (24.6 g, 0.046 mmol) in benzene-*d*₆ (0.4 mL). In the glovebox, in a vial, [(IPr)CuH]₂ was generated from (IPr)CuOt-Bu (0.024 g, 0.046 mmol) and triethoxysilane (0.0089 mL, .046 mmol) in

benzene- d_6 (0.4 mL). The reaction was monitored by ^1H NMR spectroscopy. After 20 minutes, *cis*-3-hexene was observed in a 1:20 ratio with (IPr)copper(1-ethyl-1-butenyl). After 16 hours, the ratio of *cis*-3-hexene to (IPr)copper(1-ethyl-1-butenyl) was 2:1.

Reaction of triethoxysilyl-2-ethylpent-2-enoate with [(IPr)CuH] $_2$: In the glovebox a J. Young NMR tube was charged with (IPr)copper(2-ethylpent-2-enoate) (26.7 g, 0.046 mmol) and dissolved in benzene- d_6 (0.8 mL). Triethoxysilane (.0089 mL, .046 mmol) was added to generate triethoxysilyl-2-ethylpent-2-enoate (0.046 mmol) and [(IPr)CuH] $_2$ (0.023 mmol). The reaction was monitored by ^1H NMR spectroscopy. After 2.5 hours no triethoxysilyl-2-ethylpent-2-enoate was observed in solution, having yielded unidentified decomposition products.

Reaction of triethoxysilyl-2-ethylpent-2-enoate with (EtO) $_3$ SiH: In the glovebox a J. Young NMR tube was charged with (IPr)copper(2-ethylpent-2-enoate) (26.7 g, 0.046 mmol) and *tert*-butylacetylene (0.01 mL, .09 mmol) and dissolved in benzene- d_6 (0.8 mL). Triethoxysilane (0.08 mL, .46 mmol) was added to generate triethoxysilyl-2-ethylpent-2-enoate (0.046 mmol) and [(IPr)CuH] $_2$ (0.023 mmol). The [(IPr)CuH] $_2$ reacted with *tert*-butylacetylene near instantaneously, preventing reaction between [(IPr)CuH] $_2$ and triethoxysilyl-2-ethylpent-2-enoate, and leaving triethoxysilyl-2-ethylpent-2-enoate in the presence of 9 equivalents of triethoxysilane. The reaction was monitored by ^1H NMR spectroscopy. A trace of a new ^1H NMR signal was observed after 16 hours, which did not continue to increase in intensity with additional time.

Two methods (B and C) were used for the synthesis of acrylates with the use of a silyl carbonate as a CO₂ source and as a trapping agent.

Method B: In the box a resealable Schlenk tube was charged with IPrCuOt-Bu (0.015 g, 0.029 mmol), alkyne, NaOCO₂SiMe₂*t*-Bu (0.260 g, 1.3 mmol) and toluene. To the slurry (*i*-PrO)₃SiH (0.265 mL, 1.22 mmol) was added and the tube was sealed using a Teflon screwcap. The reaction vessel was taken from the box, wrapped in aluminum foil and set stirring for 4 hours. The darkened slurry was diluted with Et₂O (5 mL) which forced a white precipitate out of solution. The resultant suspension was extracted with H₂O (3 x 4 mL), and the water extracts were combined and filtered. Sodium acetate (0.020 g, 0.246 mmol) was added as internal standard and the water removed by rotary evaporation. The ¹H NMR was taken in D₂O to establish a rough yield and ratio of acrylate to formate formation. The entire sample was recombined, acidified, and extracted into diethyl ether. The product was isolated by evaporation of volatiles (solvent plus accompanying acetic acid) in vacuo.

Method C: In the box a resealable Schlenk tube was charged with IPrCuOt-Bu (0.015 g, 0.029 mmol), NaOCO₂SiMe₂*t*-Bu (0.260 g, 1.3 mmol), alkyne and toluene. A 500 μL syringe was charged with (*i*-PrO)₃SiH (0.265 mL, 1.22 mmol) and the needle was plugged with a rubber septum. The syringe and sealed Schlenk tube were taken from the box. The Schlenk tube was connected to a Schlenk line and cooled to 0°C, and the Teflon screwcap was replaced under a flow of argon with a rubber septum. Silane was added via syringe to the reaction slurry, and the septum was replaced by the Teflon

screwcap, and the tube was resealed. The reaction mixture was stirred for 4 hours. The darkened slurry was diluted with Et₂O (5 mL) which forced a white precipitate out of solution. The resultant suspension was extracted with H₂O (3 x 4 mL), and the water extracts were combined, and filtered. Sodium acetate (0.020 g, 0.246 mmol) was added as internal standard and the water was removed by rotary evaporation. The ¹H NMR was taken in D₂O to establish a rough yield and ratio of acrylate to formate formation. The entire sample was recombined, acidified, and extracted into diethyl ether. The product was isolated by evaporation of volatiles (solvent plus accompanying acetic acid) in vacuo.

Synthesis of 2-ethylpent-2-enoic acid: The synthesis was performed according to general method B using 3-hexyne (0.250 mL, 2.4 mmol) and 0.5 mL toluene. Isolation of product gave 2-ethyl-pent-2-enoic acid .100 g (.78 mmol, 64 %). The ¹H NMR spectrum is consistent with published spectra.²⁸ (See above for spectral details.)

Synthesis of 2-phenylbut-2-enoic acid and α -methylcinnamic acid: The synthesis was performed according to general method B using 1-phenyl-1-propyne (310 mL, 2.4 mmol) and 0.5 mL toluene. Isolation of products gave a mixture of 2-phenylbut-2-enoic acid and α -methylcinnamic acid 0.143 g (0.88 mmol, 72 %) ¹H and ¹³C NMR are consistent with published spectra.^{29,30} (See above for spectral details.)

Synthesis of 3,3-dimethylpent-2-enoic acid: The synthesis was performed according to general method B using *tert*-butylacetylene (0.280 mL, 2.3 mmol) and 0.5 mL toluene. Isolation of product gave 3,3-dimethylpent-2-enoic acid 0.053 g (0.41 mmol, 34 %) Instead of (*i*-PrO)₃SiH, (EtO)₃SiH (0.225 mL, 1.22 mmol) was used. ¹H and ¹³C NMR are consistent with published spectra.³³ (See above for spectral details)

Synthesis of 2-ethylbut-2-enoic acid and 2-methylpentenoic acid: The synthesis was performed according to general method C using 2-pentyne (0.280 mL, 2.9 mmol) and 0.5 mL toluene. Isolation of product gave a mixture of 2-ethylbut-2-enoic acid and 2-methylpentenoic acid .062 g (0.54 mmol, 44 %) ¹H and ¹³C NMR are consistent with published spectra.²⁸ (See above for spectral details.)

Synthesis of 2-phenylpent-2-enoic acid and α -ethylcinnamic acid: The synthesis was performed according to general method B using 1-phenyl-1-butyne (0.350 mL 2.4 mmol) and 0.5 mL toluene. Isolation of products gave 2-phenylpent-2-enoic acid and α -ethylcinnamic acid 0.097 g (0.55mmol, 45 %) ¹H and ¹³C NMR are consistent with published spectra.³² (See above for spectral details.)

Synthesis of 2,3-diphenylprop-2-enoic acid: The synthesis was performed according to general method C using diphenylacetylene (0.220 g, 1.2 mmol) and 1.0 mL toluene. Isolation of product gave 2,3-diphenylprop-2-enoic acid .175g (0.78 mmol, 64 %) ¹H and ¹³C NMR are consistent with published spectra.³³ (See above for spectral details.)

Complete conversion of 1-phenyl-1-propyne to 2-phenylbut-2-enoic acid and α -methylcinnamic acid: Method B was used with the following modifications. 1-Phenyl-1-propyne (0.070 mL, 0.55 mmol) was used with a 12 hour reaction time. Isolation of product gave a mixture of 2-phenylbut-2-enoic acid and α -methylcinnamic acid 0.082 g (0.51 mmol, 93%). ^1H and ^{13}C NMR are consistent with published spectra.^{29,30} (See above for spectral details.)

Reaction for determining efficacy of sodium *tert*-butyldimethylsilanolate as trapping agent in the reductive carboxylation of 3-hexyne: The synthesis was performed according to general method B using 3-hexyne (0.250 mL, 2.4 mmol) and 0.5 mL toluene- d_8 with the following modifications. The reaction slurry had 1,4-dimethoxybenzene (0.020 g) added and a ^1H NMR of an aliquot was taken in toluene- d_8 . *cis*-3-Hexene (2% compared to starting alkyne) and 3-hexyne (40% compared of starting material) were observed in solution. The product 2-ethylpent-2-enoic acid was isolated as the sodium salt, sodium acetate (0.020 g, 0.25 mmol) was added as internal standard and the yield confirmed by ^1H NMR in D_2O (57%).

Observation of dissociation of $[(\text{IPr})\text{CuH}]_2$ using deuterium labeling: The reaction was performed in the glovebox under nitrogen atmosphere. Vial A was charged with $(\text{IPr})\text{CuOt-Bu}$ (0.020 g, 0.039mmol). Vial B was charged with $(\text{IPr})\text{CuF}$ (0.018 g, 0.039 mmol). To each vial $\text{THF-}d_8$ (0.4 mL) was added. Silane was added to the copper complexes, to vial A $(\text{EtO})_3\text{SiH}$ (7 μL), and to vial B Et_3SiD to $(\text{IPr})\text{CuF}$. The contents of the vials were mixed and then transferred to a J. Young NMR tube. The ^1H NMR

spectrum of the sample was then recorded. Two signals for a copper-bound hydrogen were observed, and assigned to $[(\text{IPr})\text{CuH}]_2$ and $(\mu\text{-D})(\mu\text{-H})[(\text{IPr})\text{Cu}]_2$.

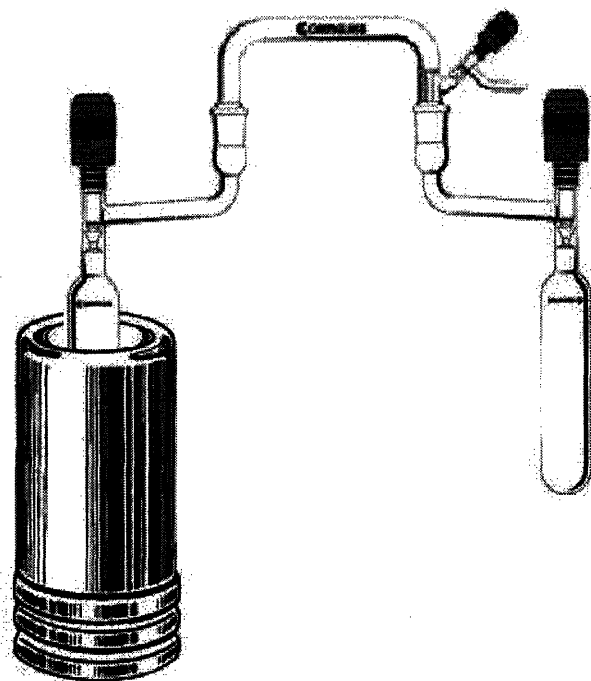


Figure 2: Apparatus for addition of CO_2 through sublimation. reactions

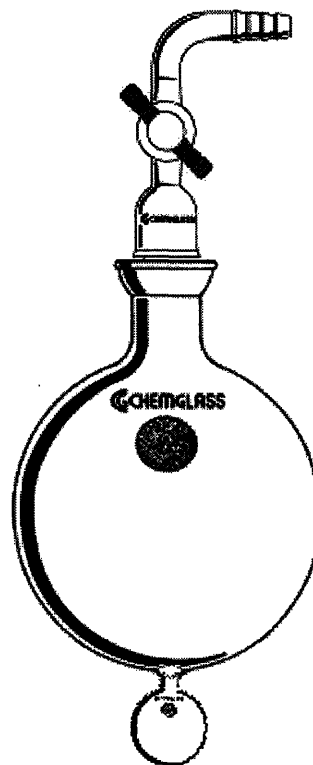


Figure 3: Apparatus used for 1% CO_2 reactions

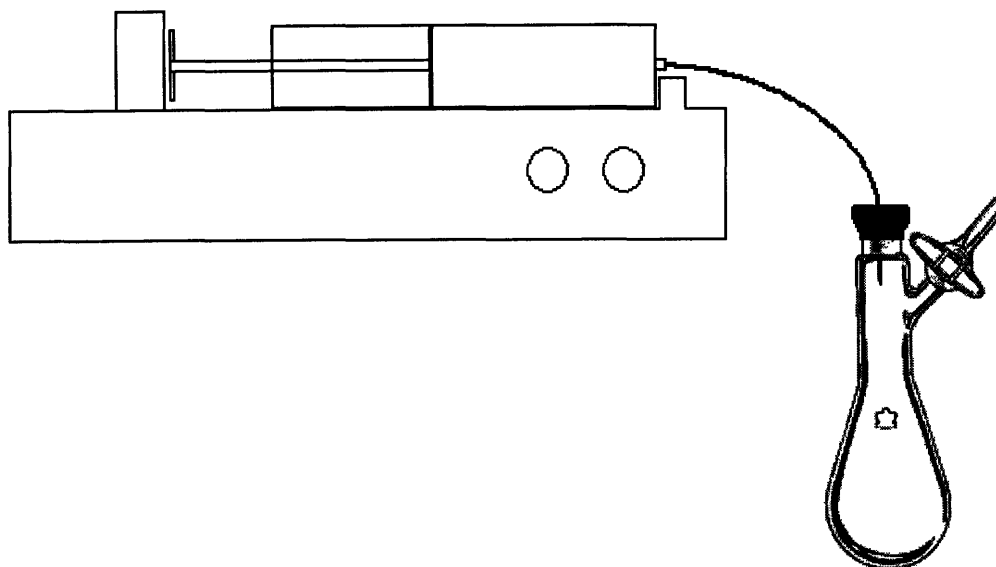


Figure 4: Setup for addition of CO₂ to reaction vessel using a syringe pump.

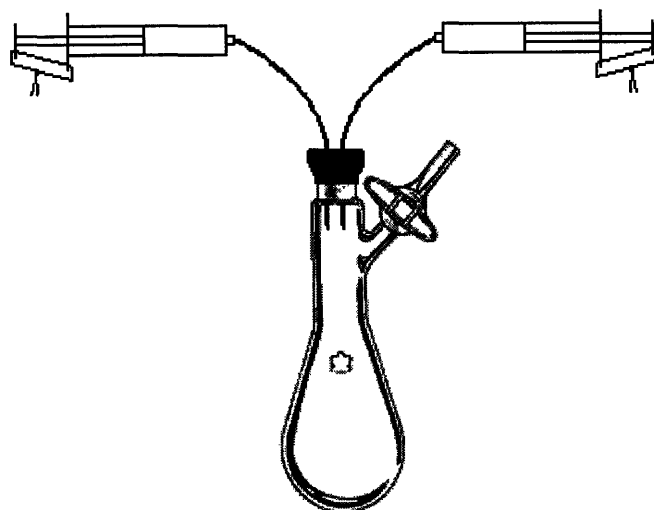


Figure 5: Setup for addition of silane and CO₂ one equivalent at a time. Copper wire threaded through plunger was used for fine control of plunger movement through barrel.

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40. The complexes (IMes)CuOt-Bu, (SIMes)CuOt-Bu, (SICy)CuOt-Bu, (It-Bu)CuOt-Bu, and (meIPr)CuOt-Bu were provided by David S. Laitar. The suggestion

for desilylation as a route to protect the desired product was given by David S. Laitar, I thank him for these contributions.

41. a) Laitar, D.S. "Synthetic and Catalytic Studies of Group 11 N-Heterocyclic Carbene Complexes" Ph.D. Thesis, MIT, Cambridge, MA 2006 b) (IPr)CuF used for this thesis was prepared by Ms. Koyel X. Bhattacharyya.

Appendix

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Figure A1: ^1H NMR of (IPr)copper(2-phenylethanoate) in benzene- d_6 .

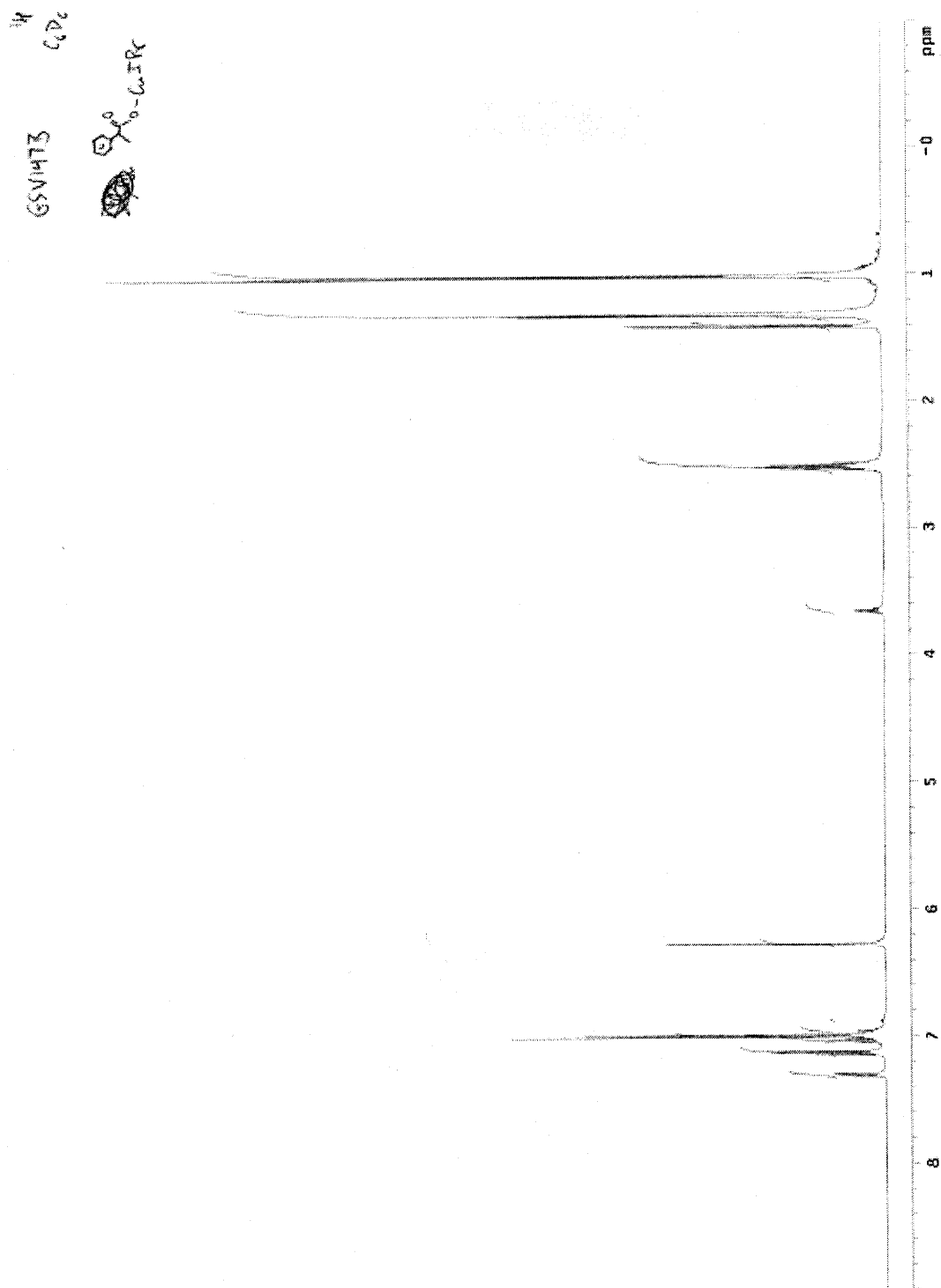


Figure A2: ^{13}C NMR of (IPr)copper(2-phenylethanoate) in benzene- d_6

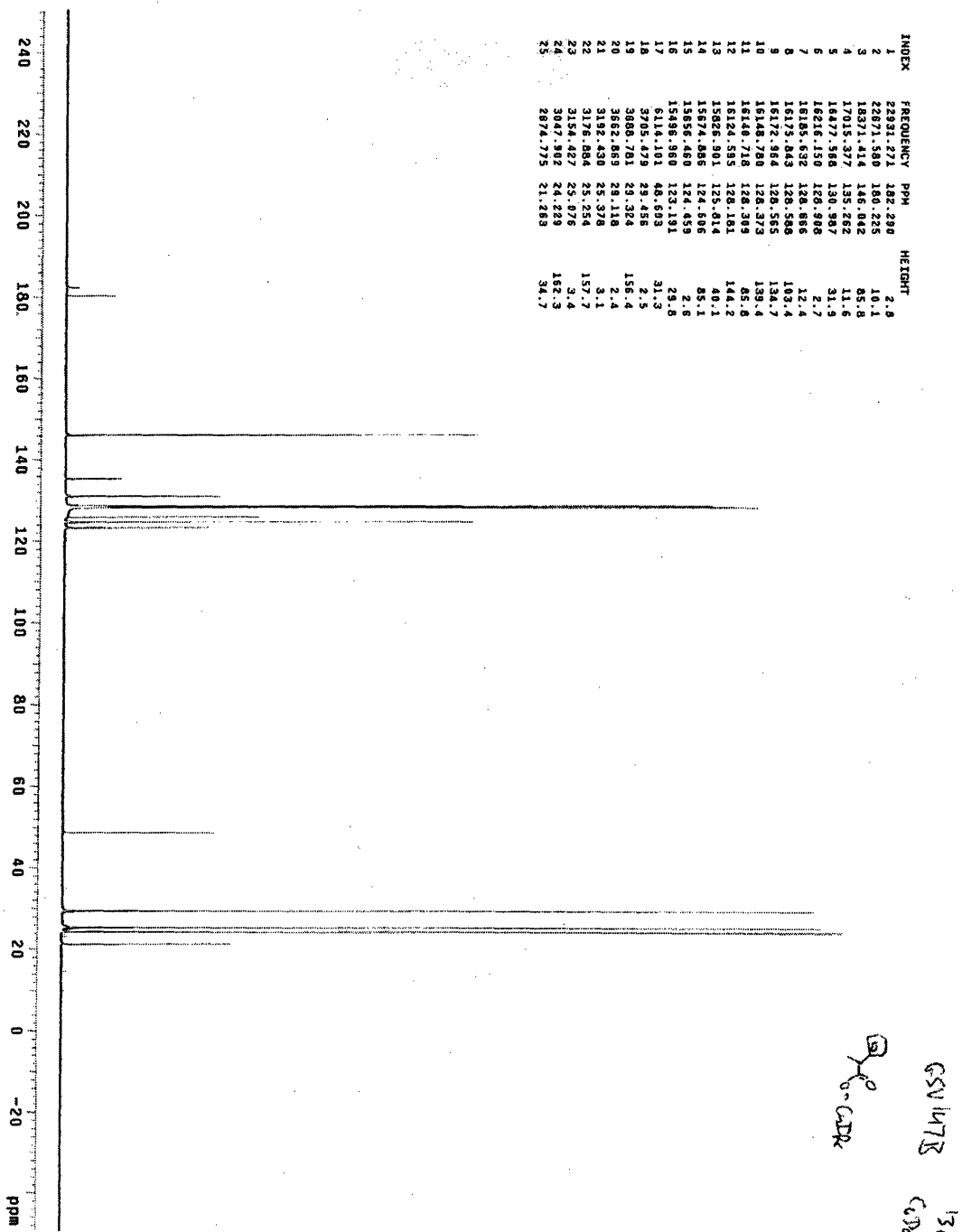


Figure A3: ^1H NMR of (IPr)copper(bicyclo[2.2.1]-2-heptanoate) in benzene- d_6 .

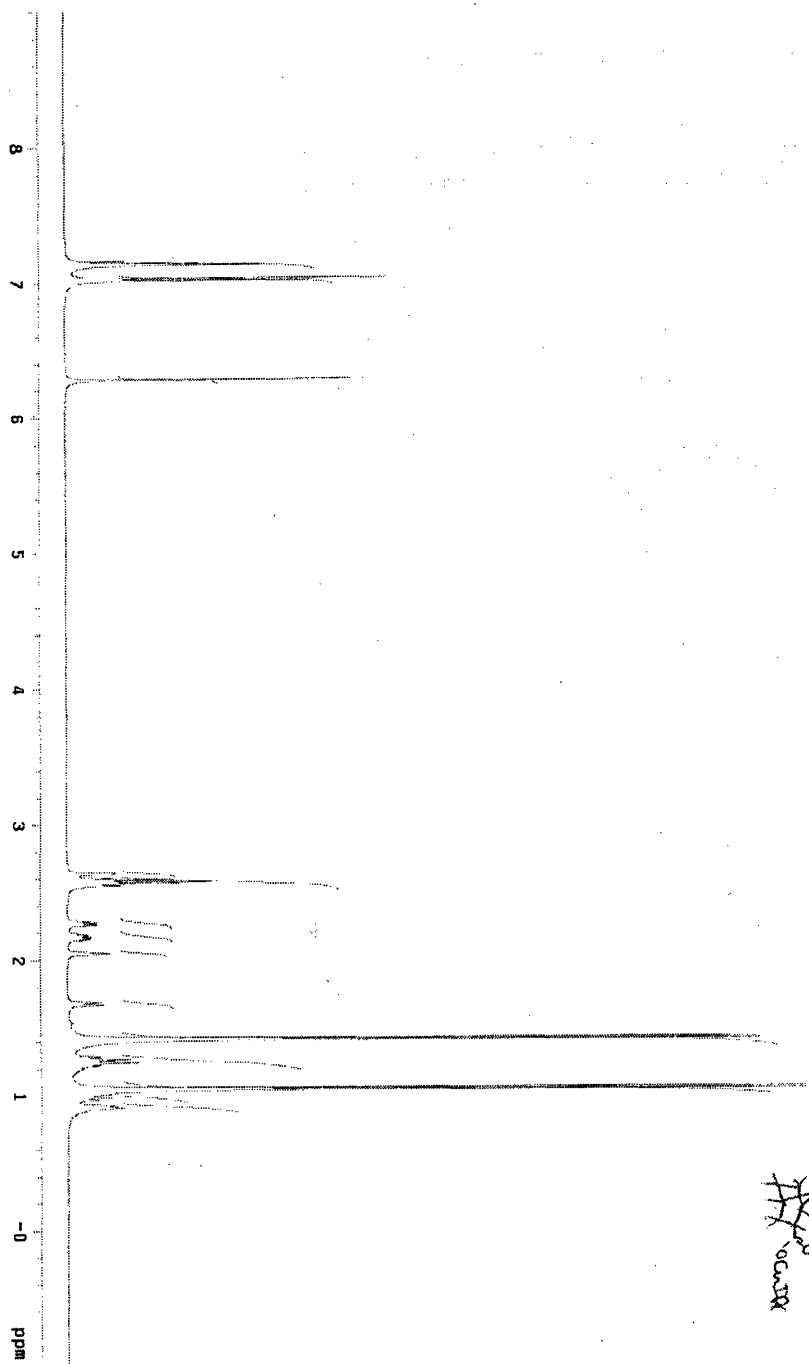
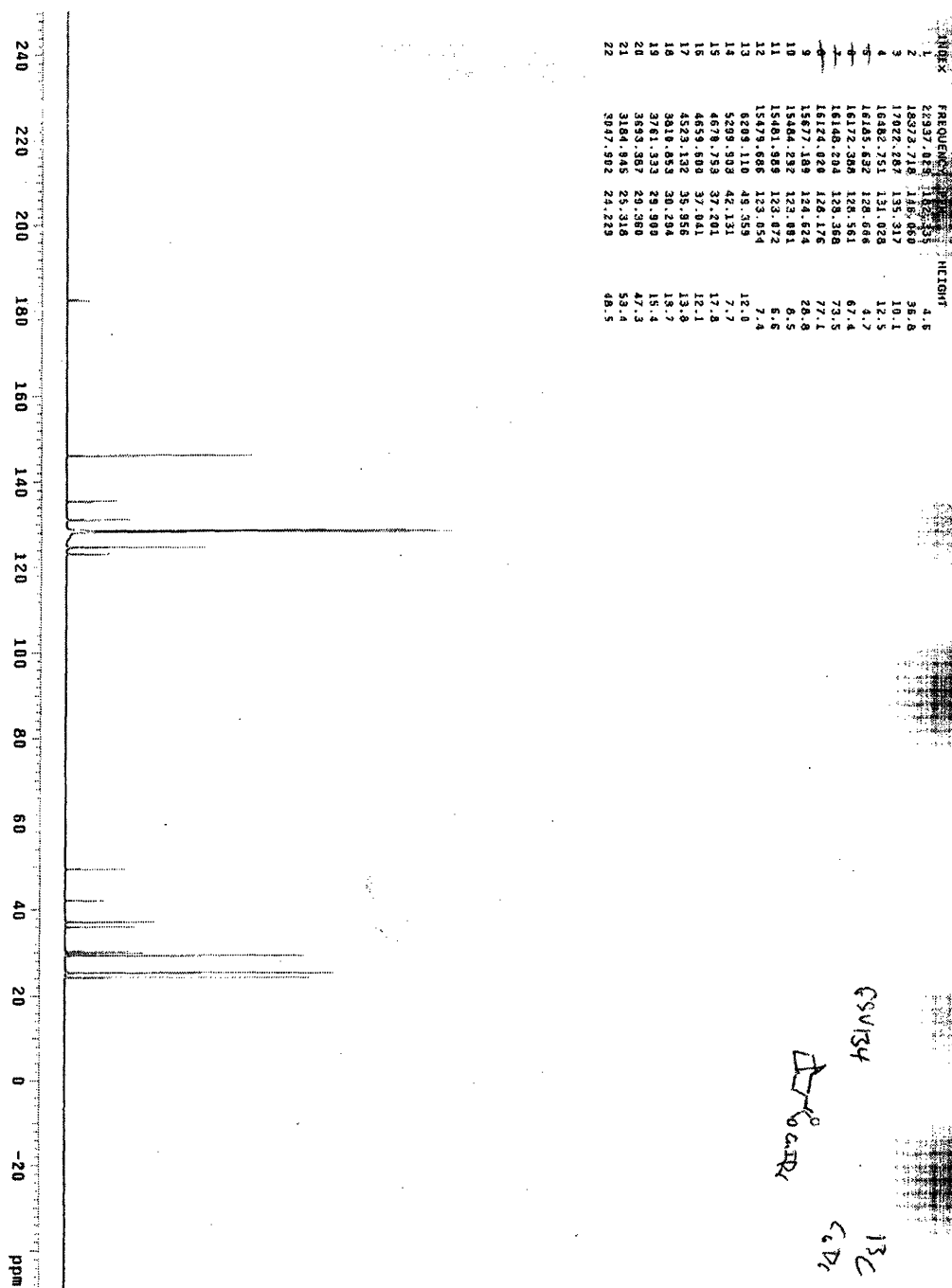


Figure A4: ^{13}C NMR of (IPr)copper(bicyclo[2.2.1]-2-heptanoate) in benzene- d_6 .



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Curriculum Vitae

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Objective: To acquire employment in the field of chemistry where my skills can be put to use in a research or educational setting.

Education:

2001 – 2007

MASSACHUSETTS INSTITUTE OF TECHNOLOGY Cambridge, MA

Candidate for Ph.D. in Chemistry (Inorganic)

- Thesis: (NHC)Copper(I) Catalyzed Carbon-Carbon Bond Formation Using CO₂ as a Carbon Source
- Developed and perfected a catalytic system to form carbon-carbon bonds between a desirable mono carbon source and organic substrates

1997 – 2001

BRANDEIS UNIVERSITY

Waltham, MA

BS in Chemistry, Magna Cum Laude

- Thesis: Rational Synthesis of Chiral Nanoporous Materials and Crystal Engineering of a Metal-Ligand Coordination Polymers for NLO Applications

Experience:

2001 – 2007

MASSACHUSETTS INSTITUTE OF TECHNOLOGY Cambridge, MA

RESEARCH ASSISTANT. Department of Chemistry

- Prepared a range of organometallic complexes.
- Investigated potential catalysts for the fixation of carbon dioxide
- Developed a catalytic system based on NHC supported copper complexes for the fixation of carbon dioxide.
- Applied a range of analytical methods for characterizing small molecules and complexes including NMR spectroscopy, GC/MS, and IR spectroscopy.
- Taught sections for introductory chemistry laboratory course

1999 – 2001

BRANDEIS UNIVERSITY

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UNDERGRADUATE RESEARCHER. Department of Chemistry

- Extensive work with hydrothermal synthesis of metal-ligand coordination polymers

Skills:

Laboratory Skills: Schlenk line techniques, glovebox techniques, general organic synthesis and workup

Analytical Instrumentation: Varian NMR for acquisition and analysis of 1D signals, GC/MS, IR spectroscopy.

Computer: familiarity with Microsoft Office, spreadsheet programs, ChemDraw.

Awards:

Grunwald Fellowship (2000), Schiff Undergraduate Program (2000 – 2001), MIT Department of Chemistry Award for Outstanding Teaching (2004 – 2005)

Publications:

Ponnaiyan Ayyappan, Gergely Sirokman, Owen R. Evans, Timothy H. Warren, Wenbin Lin. *Inorganica Chimica Acta*. **2004**, *357*, 3999–4004