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Palladium-Catalyzed Carbonylation of Alkynes

by

Davit Zargarian

A thesis

submitted to the School of Graduate Studies

in fulfillment of the

thesis requirement for the degree of

Doctor of Philosophy

in

Chemistry

Department of Chemistry

University of Ottawa

Ottawa, Ontario, Canada

Research Supervisor

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Howard Alper (Professor of Chemistry)

Davit Zargarian



Davit Zargarian, Ottawa, Canada, 1992



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To Angela

Abstract

This thesis describes the palladium-catalyzed carbonylation of alkynes with formic acid. Terminal alkynes react with formic acid in the presence of catalytic amounts of $\text{Pd}(\text{OAc})_2$ and suitable phosphine ligands (120 psi of CO gas pressure, 100-110 °C) to produce the unsaturated carboxylic acids $\text{CR}(\text{COOH})=\text{CH}_2$, **1**, and (*E*)- $\text{CHR}=\text{CH}(\text{COOH})$, **2**. The combined yields of **1** and **2** for various R's range from 60 to 90%. The regioselectivity is approximately 90:10 in favour of **1** when R is a phenyl or a straight chain alkyl group; **2** is the favoured product when R is *t*-Bu and the exclusive one when R is SiMe_3 . Under similar conditions, internal alkynes react with formic acid to produce the unsaturated carboxylic acids (*E*)- $\text{CR}(\text{COOH})=\text{CHR}'$, **3**, and (*E*)- $\text{CHR}=\text{CR}'(\text{COOH})$, **4**, also in 60-90% combined yields. The regioselectivity of this reaction, however, is not as high as for terminal alkynes. Oxalic acid can be used instead of formic acid in both of these reactions.

The most suitable phosphine ligands for alkyne hydrocarboxylation in the present system are PPh_3 and dppb (1,4-bis(diphenylphosphino)butane). In some cases, using a mixture of these two ligands remarkably improves the reaction yields; the implications of such ligand synergism are discussed. On the basis of deuterium labelling studies and other experimental results, a reaction mechanism has been proposed which involves the addition of the O-H bond of formic acid to form a cationic hydrido(alkyne) intermediate. This intermediate is thought to undergo a sequence of reactions, including hydride and CO insertions, to give the acid product and regenerate the active catalyst.

Terminal alkynes undergo dicarbonylation upon reacting with formic acid and/or water in a catalytic system consisting of $\text{PdCl}_2/\text{CuCl}_2/\text{O}_2/\text{CO}$ (room temperature, atmospheric pressure); the products are monosubstituted maleic anhydrides and the corresponding maleic and fumaric acids in 30-75% combined yields. The product distribution is influenced

by both the steric bulk of the alkyne substituent and the amount of water present in the reaction medium. Internal alkynes are unreactive in this system. Among the solvents tested, THF is the most suitable one. Phosphines and phosphites completely inhibit the reaction.

In contrast to most systems in which CuCl_2 acts as the principal oxidant for converting $\text{Pd}(0)$ to $\text{Pd}(\text{II})$, the role of CuCl_2 in the present system seems to be secondary to that of oxygen. For instance, modest catalytic turnovers are observed in the absence of CuCl_2 , whereas no catalysis occurs if oxygen is excluded from the system, even in the presence of excess CuCl_2 . These and other observations are rationalized by invoking various oxidation schemes involving oxygen as the main oxidant. The role of CuCl_2 is thought to be one of facilitating the catalysis by forming a heterometallic Cu/Pd complex.

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Dr. Howard Alper is credited with supervising my research efforts, for supporting me in many ways, and for encouraging me in undertaking new ideas and initiatives. Thank you very much, Dr. Alper.

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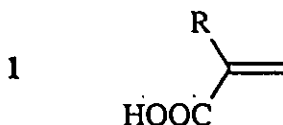
Abbreviations

Å	Ångstrom, unit of length (10^{-8} m)
acac	acetylacetonate, $[\text{CH}_3\text{COCHCOCH}_3]^-$
atm	atmosphere, unit of pressure (101325 Pa)
br	broad
n-Bu	n-butyl group, $\text{CH}_3(\text{CH}_2)_3-$
t-Bu	t-butyl group, $(\text{CH}_3)_3\text{C}-$
cod	1,5-cyclooctadiene
δ	chemical shift, in ppm
d	doublet
dba	dibenzylidene acetone, $(\text{PhCH}=\text{CH})_2\text{CO}$
dd	doublet of doublets
dmpe	bis(dimethylphosphino)ethane, $(\text{CH}_3)_2\text{PCH}_2\text{CH}_2\text{P}(\text{CH}_3)_2$
DMSO	dimethyl sulfoxide, $(\text{CH}_3)_2\text{SO}$
dppb	1,4-bis(diphenylphosphino)butane, $(\text{C}_6\text{H}_5)_2\text{P}(\text{CH}_2)_4\text{P}(\text{C}_6\text{H}_5)_2$
dppe	1,4-bis(diphenylphosphino)ethane, $(\text{C}_6\text{H}_5)_2\text{P}(\text{CH}_2)_2\text{P}(\text{C}_6\text{H}_5)_2$
dppp	1,3-bis(diphenylphosphino)propane, $(\text{C}_6\text{H}_5)_2\text{P}(\text{CH}_2)_3\text{P}(\text{C}_6\text{H}_5)_2$
dq	doublet of quartets
dquin	doublet of quintets
dt	doublet of triplets
DTBP	di- <i>t</i> -butyl peroxide, $((\text{CH}_3)_3\text{CO})_2$

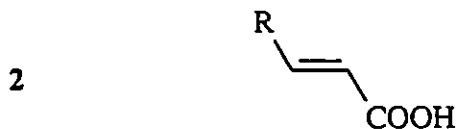
Et	ethyl group, $\text{CH}_3\text{CH}_2\text{-}$
h	hour, unit of time (3600 s)
Hz	Hertz, cycles per second
IR	infrared
J	coupling constant, in Hertz
m	medium
Me	methyl group, $\text{CH}_3\text{-}$
MHz	megaHertz, 10^6 Hz
min	minute, unit of time (60 s)
mL	milliliter, unit of volume (10^{-6} m ³)
NMR	nuclear magnetic resonance
OAc	acetate anion, CH_3CO_2^-
Ph	phenyl group, $\text{C}_6\text{H}_5\text{-}$
pH	measure of solution acidity ($-\log [\text{H}^+]$)
$\text{p}K_{\text{a}}$	measure of acid strength ($-\log K_{\text{a}}$)
i-Pr	isopropyl group, $(\text{CH}_3)_2\text{CH-}$
q	quartet
quin	quintet
s	singlet
sh	shoulder, a weak band on the side of a strong one
t	triplet
THF	tetrahydrofuran, $\text{C}_4\text{H}_8\text{O}$
vs	very strong
vw	very weak
w	weak

Glossary of Compounds

The following compounds were prepared during the course of this study, and have been referred to in this thesis by the indicated Arabic numerals.

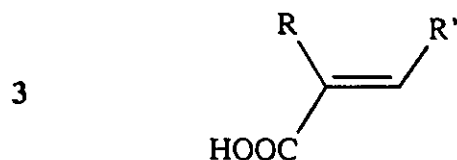


1a	R= Ph	α -Methylenebenzeneacetic acid (Atropic acid)
1b	R= PhCH ₂ CH ₂	2-Methylene-4-phenylbutanoic acid
1c	R= CH ₃ (CH ₂) ₅	2-Methyleneoctanoic acid
1d	R= CN(CH ₂) ₃	5-Cyano-2-methylenepentanoic acid
1e	R= Cl(CH ₂) ₃	5-Chloro-2-methylenepentanoic acid
1f	R= <i>sec</i> -Bu	3-Methyl-2-methylenepentanoic acid
1g	R= <i>t</i> -Bu	3,3-Dimethyl-2-methylenebutanoic acid

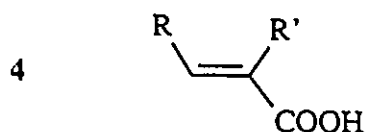


2a	R= Ph	(<i>E</i>)-3-Phenyl-2-propenoic acid (Cinnamic acid)
2b	R= PhCH ₂ CH ₂	(<i>E</i>)-5-Phenyl-2-pentenoic acid
2c	R= CH ₃ (CH ₂) ₅	(<i>E</i>)-2-Nonenoic acid
2d	R= CN(CH ₂) ₃	(<i>E</i>)-6-Cyano-2-hexenoic acid

2e	R = Cl(CH ₂) ₃	(<i>E</i>)-6-Chloro-2-hexenoic acid
2f	R = <i>sec</i> -Bu	(<i>E</i>)-4-Methyl-2-hexenoic acid
2g	R = <i>t</i> -Bu	(<i>E</i>)-4,4-Dimethylpentenoic acid
2h	R = SiMe ₃	(<i>E</i>)-3-Trimethylsilyl-2-propenoic acid

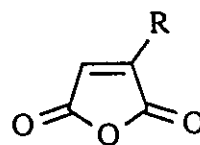


3a	R = Bu	R' = Me	(<i>E</i>)-2-Ethylidene-hexanoic acid
3b	R = <i>i</i> -Pr	R' = Me	(<i>E</i>)-2-(1-Methylethyl)-2-butenic acid
3c	R = Ph	R' = Me	(<i>E</i>)- α -Ethylidene-benzeneacetic acid
3d	R = Ph	R' = Et	(<i>E</i>)- α -Propylidene-benzeneacetic acid
3e	R = R' = Ph		(<i>E</i>)-2,3-Diphenyl-2-propenoic acid



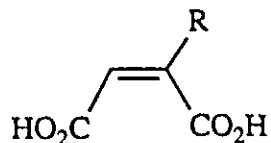
4a	R = Bu	R' = Me	(<i>E</i>)-2-Methyl-2-heptenoic acid
4b	R = <i>i</i> -Pr	R' = Me	(<i>E</i>)-2,4-Dimethyl-2-pentenoic acid
4c	R = Ph	R' = Me	(<i>E</i>)-2-Methyl-3-phenylpropenoic acid (<i>E</i>)- α -Methylcinnamic acid)
4d	R = Ph	R' = Et	(<i>E</i>)-2-Phenylmethylene-butanoic acid

5



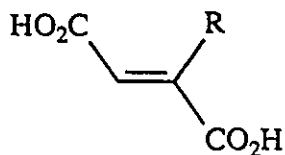
5a	R=Ph	3-Phenyl-2,5-furandione (Phenylmaleic anhydride)
5b	R=<i>t</i>-Bu	<i>tert</i>-Butylmaleic anhydride
5c	R=<i>i</i>-Pr	1-(Methylpropyl)maleic anhydride
5d	R=PhCH₂CH₂	3-(2-Phenylethyl)-2,5-furandione ((2-Phenylethyl)maleic anhdride)
5e	R=Ph(CH₂)₃	3-(3-Phenylpropyl)-2,5-furandione ((3-Phenylpropyl)maleic anhydride)
5f	R=Cl(CH₂)₃	3-Chloropropyl-2,5-furandione ((3-Chloropropyl)maleic anhydride)
5g	R=CN(CH₂)₃	3-Cyanopropyl-2,5-furandione ((3-Cyanopropyl)maleic anhydride)
5h	R=<i>n</i>-Bu	Butylmaleic anhydride
5i	R=CH₃(CH₂)₅	Hexylmaleic anhdride

6



6b	R= <i>t</i> -Bu	<i>tert</i> -Butylmaleic acid
6c	R= <i>i</i> -Pr	(<i>Z</i>)-2-(1-Methylpropyl)-2-butenedioic acid
6f	R=Cl(CH ₂) ₃	(<i>Z</i>)-2-(3-Chloropropyl)-2-butenedioic acid
6g	R=CN(CH ₂) ₃	(<i>Z</i>)-2-(3-Cyanopropyl)-2-butenedioic acid
6h	R= <i>n</i> -Bu	(<i>Z</i>)-2-Butyl-2-butenedioic acid
6i	R=CH ₃ (CH ₂) ₅	(<i>Z</i>)-2-Hexyl-2-butenedioic acid

7



7c	R= <i>i</i> -Pr	(<i>Z</i>)-2-(1-Methylpropyl)-2-butenedioic acid
7d	R=PhCH ₂ CH ₂	(<i>E</i>)-2-(2-Phenylethyl)-2-butenedioic acid
7e	R=Ph(CH ₂) ₃	(<i>E</i>)-2-(3-Phenylpropyl)-2-butenedioic acid
7f	R=Cl(CH ₂) ₃	(<i>E</i>)-2-(3-Chloropropyl)-2-butenedioic acid
7g	R=CN(CH ₂) ₃	(<i>E</i>)-2-(3-Cyanopropyl)-2-butenedioic acid
7h	R= <i>n</i> -Bu	(<i>E</i>)-2-Butyl-2-butenedioic acid
7i	R=CH ₃ (CH ₂) ₅	(<i>E</i>)-2-Hexyl-2-butenedioic acid

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"... Einstein's space is no closer to reality than Van Gogh's sky. The glory of science is not in a truth more absolute than the truth of Bach or Tolstoy, but in the act of creation itself. The scientist's discoveries impose his own order on chaos, as the composer or painter imposes his; an order that always refers to limited aspects of reality, and is based on the observer's frame of reference, which differs from period to period as a Rembrandt nude differs from a nude by Manet."

- ARTHUR KOESTLER

Chapter I

Introduction

The term "carbonylation" was coined by W. Reppe during the 1930's and 1940's when his research team at BASF laboratories discovered a number of carbonylation reactions catalyzed or promoted by metal carbonyl compounds.¹ A carbonylation reaction is one which leads to the incorporation of one or more molecules of CO into a substrate; this reaction can occur as an insertion of CO into single bonds, or an addition of CO to multiple bonds and may be accompanied by the incorporation of other reagents.

Carbonylation reactions have had far-reaching effects on the development of the fields of homogeneous and heterogeneous catalyses in general, and organometallic chemistry in particular. Furthermore, some of the initial scientific discoveries made in the field of carbonylation have gradually evolved into large-scale commercial processes, which have had a great impact on the chemical industry worldwide. Noteworthy among commercial carbonylation processes are the "oxo" process (olefin hydroformylation), the Reppe process (hydrocarboxylation of acetylene to acrylic acid), and the Monsanto process (carbonylation of methanol to acetic acid). These processes are employed worldwide to prepare millions of tonnes of commodity chemicals each year. In addition, it has been predicted that the importance of carbonylation reactions in the total chemical output will continue to grow as several new carbonylation processes are expected to reach commercialization in mid-1990's.²

As mentioned above, acetylene carbonylation is an important commercial process for producing acrylic acid, which is, in turn, used to manufacture a wide variety of acrylic resins. Although this was one of the first carbonylation reactions discovered, its commercial utility has not achieved the same importance as those of olefin and alcohol carbonylation processes.

The main reasons for this are the relatively higher cost of alkynes as feedstocks and the complex nature of their carbonylation reactions, which often yield an array of different products. Consequently, only the carbonylation of acetylene, the simplest of alkynes, is carried out on a commercial scale. The commercial viability of this reaction stems mainly from the symmetrical structure of acetylene, which avoids the problems associated with controlling the regio- and stereoselectivity in alkyne carbonylation reactions.

The excitement generated by the discovery of alkyne carbonylation reactions, and the reports of the pioneering studies by Reppe and Roelen,³ stimulated considerable research activity in this area between 1950 and 1965, producing a large number of patents. As is often the case, however, the limited commercial utility of alkyne carbonylation resulted in a gradual decline in these activities, and by late 1960's alkyne carbonylation attracted much less attention from researchers as did olefin carbonylation. Throughout the 1970's and 1980's, most studies of alkyne carbonylation dealt with the carbonylation of alkynols to lactones, leaving the general problem of higher alkyne carbonylation unsolved. Nevertheless, as our knowledge of the fundamental principles of transition metal catalysis continually expands, suitable solutions will probably be found in the near future for many of the challenging problems remaining in catalysis, including alkyne carbonylation.

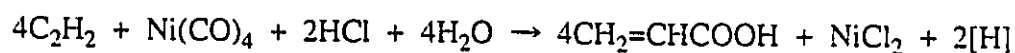
This thesis describes a study of the influence of various reaction conditions on the carbonylation of alkynes. The specific objective of the present study has been to find reaction conditions and procedures which will allow the efficient conversion of simple, aliphatic and aromatic alkynes to the corresponding unsaturated mono- and diacids. To this end, some of the more versatile procedures reported previously have served as starting points for this work, and by systematically studying the variables affecting these reactions (e.g., CO gas pressure, temperature, etc.), improved procedures and reaction conditions have been found.

Chapters II and III of this thesis describe the present study of alkyne hydrocarboxylation (monocarbonylation) and dicarbonylation, respectively; the last chapter will summarize the major results and will outline some conclusions. The remainder of the present chapter will present a brief overview of the literature of alkyne carbonylation as background to the ensuing discussions; more examples from previously reported studies will also be cited in chapters II and III for the purpose of evaluating the present results.

1.1. Alkyne Carbonylation: Literature Overview

Pino and Braca⁴ have reviewed the early stages in the development of this field and have concluded that alkyne carbonylation is an inherently complex reaction. Evidently, the outcome of this reaction is very strongly influenced by such factors as the type of metal catalyst, the solvent, the reaction temperature and pressure, the presence of hydrogen sources such as H₂ and H₂O, the type of acid or other promoters used, and the pH of the reaction medium. Possible products include ketones, aldehydes, esters, acids, lactones, hydroquinones, and oligomers of these products and of the starting alkyne.

The most widely used catalysts for alkyne carbonylation are the carbonyl complexes of Groups 8-10 metals, of which Ni(CO)₄ and Co₂(CO)₈, or their precursors, have been the most important catalysts and the only ones used in commercial processes. In general, these systems require high temperatures (100-200 °C) and pressures (30-200 atm); milder conditions (25-100 °C, 1-10 atm) usually lead to stoichiometric reactions. The stoichiometry of acetylene hydrocarboxylation was assumed by Reppe to be as follows:



Later studies⁵ showed, however, that the true stoichiometry of this reaction is much more complicated than that shown above. Hydrogen gas does not evolve from these reactions; instead, the hydrogen atoms seem to end up in by-products such as cinnamic acid, propionic acid, and other high-boiling derivatives (dimers, oligomers, etc.). Moreover, the type of acid used and the presence of alcohols have a large effect on the nature and amount of by-products formed; the amount of water also influences the outcome of acetylene hydrocarboxylation. The role of pH is not completely understood. It is known^{5,6}, for example, that an acidic medium is not always essential, and that hydrocarboxylation of alkynes can also be carried out in basic media. In neutral media, however, hydrocarboxylation is suppressed significantly.

Stoichiometric hydrocarboxylation of alkynes with Ni(CO)_4 has been studied in detail by Whiting and coworkers⁵. The scope of this reaction is fairly broad and accommodates the presence of various substituents on alkynes. The yields, however, are typically between 10 and 40%, and seldom higher than 60%; in addition, by-products form in most reactions. With terminal alkynes, the reaction rate decreases with increasing size of the substituent. The regioselectivity of the reaction of terminal alkynes is normally in favour of the regioisomer in which the carboxyl group is *gem* to the substituent; with internal alkynes, on the other hand, the two regioisomers form in almost equal amounts.

The requirement of stoichiometric amounts of Ni(CO)_4 in alkyne hydrocarboxylation detracts from the suitability of this reaction for industrial applications. Attempts by researchers to decrease the Ni(CO)_4 consumption has led to "semicatalytic" processes in which CO gas is used in addition to Ni(CO)_4 .⁴ These processes are conducted at 40-50 °C and pressures slightly above the vapour pressure of the reaction mixture. By feeding the gases (CO and acetylene) into a solution in which the stoichiometric hydrocarboxylation has already begun, modest catalytic turnovers can be obtained. (Approximately 20 moles of CO react per mole

of Ni(CO)_4 used.) Hydrochloric acid is the most suitable acid, and activators such as HgCl_2 seem to stabilize the catalytic agent. The above reaction conditions are suitable only for acetylene, however; with higher alkynes much more stringent conditions are necessary.

The main problem in the catalytic synthesis of acrylic acid from acetylene is the low reaction rate.⁴ High temperatures (180-200 °C) and high concentrations of CO and acetylene gases are required for optimum catalytic rates. The presence of cocatalysts such as Cu(II) complexes or salts is also helpful and increases the yields to as high as 90% based on acetylene and 85% based on CO. Most of the oligomeric by-products normally forming in this reaction can be converted to acrylic acid by pyrolysis, thereby avoiding significant material loss. Dicarboxylation of acetylene in the presence of nickel catalysts is also possible; the main product is succinic acid but several other products also form, rendering this reaction unsuitable for practical applications.

An important disadvantage of using nickel catalysts in alkyne carbonylation reactions is the formation of the volatile Ni(CO)_4 during the reaction. Ligands such as PPh_3 have been used to counteract this problem,⁷ but the presence of these ligands reduced the catalytic activity. The use of supported catalysts has also been investigated,⁸ but the reaction yields were generally lower and large amounts of by-products form.

Cobalt compounds can also be used in the stoichiometric and catalytic carbonylation of alkynes under mild conditions. In general, however, the stoichiometric carbonylation of alkynes with $\text{Co}_2(\text{CO})_8$ and HCo(CO)_4 is rather unsuccessful, because these compounds form very stable and unreactive complexes with alkynes.⁴ In contrast, under more severe conditions (100-200 °C, 200-300 atm of CO), cobalt compounds show high catalytic activity for alkyne carbonylation. A careful control of the ratio of CO to acetylene and the total pressure of these gases is essential for minimizing the formation of by-products such as cyclic ketones and oligomers. As was the case with nickel catalyzed systems, cobalt catalysts

are quite ineffective for the carbonylation of alkynes other than acetylene.

Some of the other metals used for alkyne carbonylation include iron, ruthenium, and rhodium. The reactivities of these metals have not been investigated systematically, but the existing reports indicate that they promote reactions quite different from those of nickel and cobalt. For instance, products such as quinones, hydroquinones, and lactones are often observed in the reactions of these metals with alkynes. In general, the catalytic reactions are very sluggish and the product distribution is poor. One exception is the Rh-catalyzed conversion of terminal and internal alkynes to lactones (furan-2(5H)-ones) reported by Takahashi⁹ (*vide infra*).

Among transition metals other than cobalt and nickel, palladium has shown the highest and most interesting reactivity. The main difference in the reactivities of Pd, Ni, and Co is that Pd-catalyzed carbonylation of alkynes usually leads to dicarbonylation, whereas Ni- and Co-catalyzed processes give mainly monocarbonylated products. In addition, Pd-catalyzed alkyne carbonylation usually requires milder conditions. A common feature of most Pd-catalyzed systems is that metallic palladium separates during the reaction and only by using such oxidants as CuCl_2/O_2 or thiourea/air can these reactions proceed catalytically.⁴ Considerable difficulties exist in explaining the mechanism of Pd-catalyzed alkyne carbonylation reactions; this is partly due to the scarcity of stable palladium complexes containing CO and alkyne ligands, which does not allow the formulation of sound reaction mechanisms. Another reason is that in most cases it is not even clear whether these reactions are homogeneous or heterogeneous.

The use of Pd-catalysts in alkyne carbonylation was first reported in a German patent issued in 1962,¹⁰ which was soon followed by many other publications. One of the earliest investigators who studied alkyne carbonylation with palladium compounds was J. Tsuji, whose research group used PdCl_2 in the presence of $\text{CuCl}_2/\text{HCl}/\text{O}_2$ to carbonylate a variety of

terminal and internal alkynes.¹¹ The predominant products of these reactions are the dicarbonylation products: maleic, fumaric, and succinic derivatives. Some of the by-products include the chloroesters and dimeric products. Halogenated alkynes often result in the formation of allenic derivatives; alkynols usually lead to lactones. Chiusoli and coworkers¹² have also studied Pd-catalyzed alkyne carbonylation extensively; instead of Cu(II) as reoxidant, however, they have used a combination of thiourea/air to oxidize the Pd(0). Heck¹³ has reported the use of Hg-compounds as promoters of the action of palladium in these reactions; this approach facilitates the use of mild reaction conditions, but the reactions are usually stoichiometric. Other promoters, such as SnCl₂, are more effective.¹⁴

Alper and coworkers have reported the use of PdCl₂/CuCl₂/HCl/O₂/CO in catalytic hydrocarboxylation and hydrocarboalkoxylation (hydroesterification) of olefins with water¹⁵ and alcohols¹⁶, respectively. In an extension of this work, Alper, Despeyroux, and Woell¹⁷ showed that this procedure can be used to carbonylate alkynes in alcoholic solvents. The reaction conditions are very mild (ambient temperature, atmospheric pressure) and the yields are generally high. Terminal alkynes give the dicarbonylated products (maleic and fumaric derivatives), whereas internal alkynes are monocarbonylated (hydrocarboalkoxylated) to the corresponding unsaturated esters. By analogy to the reaction of olefins, the possibility of the preparation of carboxylic acids from alkynes was briefly investigated by Alper and Hartstock.¹⁸ Replacing alcohols with a mixture of THF and water as solvent under analogous reaction conditions resulted in the carbonylation of alkynes to the corresponding maleic and fumaric acids; the yields of these reactions, however, were much lower and very few alkynes were reactive.

In 1987, Alper *et al.*¹⁹ reported the use of formate esters, instead of alcohols, in alkene hydroesterification. It was shown that the carbonyl moiety in the product esters arises from the CO gas and not the formate ester, suggesting that the formate is decarbonylated during

the reaction. This has not been demonstrated, however, and the mechanism of this novel reaction remains unknown. An attempt to extend the reaction of formate esters to alkynes was only partially successful, leading to a mixture of monosubstituted maleic and fumaric esters and acids.^{20a} The latter presumably arise from the reaction of the residual moisture in the reaction medium. This observation initiated the present study on the dicarbonylation of alkynes with formic acid. It was hoped that the use of formic acid would eliminate the problems encountered earlier in using $\text{H}_2\text{O}/\text{HCl}$ for converting alkynes to carboxylic acids. This study has led to a number of interesting results regarding the reaction mechanism,^{20b} as described in Chapter III.

In 1988, Alper, Saldana-Maldonado, and Lin²¹ were successful in affecting alkyne carbonylation with formate esters by changing the previously employed conditions ($\text{PdCl}_2/\text{CuCl}_2/\text{HCl}/\text{O}_2/\text{CO}$, ambient temperature and atmospheric pressure) to a completely different set of conditions: $\text{Pd}(\text{OAc})_2$ or $\text{Pd}(\text{dba})_2$, phosphine ligands, 100 °C, and 80 atm of CO gas. The main products under these conditions were unsaturated monoesters (hydrocarbalkoxylation or hydroesterification). The same products were also observed when dialkyl oxalates were used instead of alkyl formates.²² The novelty of these reactions lay in the use of formates and oxalates for the first time in alkyne carbonylations. The oxalate reaction was also interesting because it raised the possibility of a C-C bond cleavage during the catalysis.

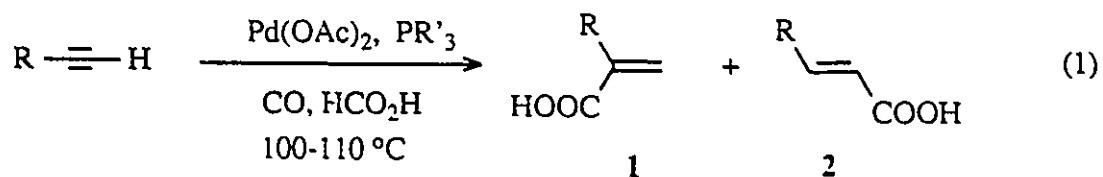
The observation that under non-oxidative conditions alkynes react by monocarbonylation rather than dicarbonylation, prompted a study of alkyne carbonylation in the presence of formic acid. This study has resulted in a general procedure for alkyne hydrocarboxylation, as described in the next chapter.

Chapter II

Hydrocarboxylation of Alkynes

2.1 Results and Discussion

Terminal alkynes can be hydrocarboxylated with formic acid in the presence of catalytic amounts of $\text{Pd}(\text{OAc})_2$ and phosphine ligands; this reaction requires a temperature of 100-110 °C and 120 psi of CO gas pressure, and gives 63-96% combined yields of the two regioisomers **1** and **2** (eq. 1).



The results of the catalytic hydrocarboxylation of terminal alkynes are summarized in Table 2.1. A close examination of these results reveals that the nature of the alkyne substituent R has a noticeable effect on the reaction yield, which decreases in the following order: $\text{Ph} > (\text{CH}_2)_5\text{CH}_3 \approx (\text{CH}_2)_n\text{X} > s\text{-Bu} = t\text{-Bu} > \text{SiMe}_3$ ($\text{X} = \text{Ph}, \text{CN}, \text{and Cl}$). Based on reported A-values,²³ the relative effective bulk of these substituents increases in the following approximate order: $\text{Me} \approx \text{Et} \approx \text{straight chain alkyl} < i\text{-Pr} \approx s\text{-Bu} < \text{SiMe}_3 < \text{Ph} < t\text{-Bu}$. A comparison of these two orders reveals that the effect of the R group on the yield of

Table 2.1 The Pd(OAc)₂ Catalyzed Hydrocarboxylation of Terminal Alkynes ^{a,b}

$ \text{R} \text{---} \text{C} \equiv \text{C} \text{---} \text{H} \xrightarrow[100-110\text{ }^{\circ}\text{C}]{\text{Pd(OAc)}_2, \text{PR}'_3, \text{CO, HCO}_2\text{H}} \text{HOOC} \text{---} \text{C}(\text{R})=\text{CH}_2 + \text{R} \text{---} \text{CH}=\text{CH} \text{---} \text{COOH} $ 1 2				
Entry	R	Yield (%)	Turnover No.	1 : 2
a	Ph	96	90	93 : 7
b	(CH ₂) ₂ Ph	86	83	94 : 6
c	(CH ₂) ₅ CH ₃	83	93	87 : 13
d	(CH ₂) ₃ CN	86	93	94 : 6
e	(CH ₂) ₃ Cl	77	79	89 : 11
f	CH(Me)Et	70	67	87 : 13
g	C(Me) ₃	70	76	21 : 79
h	SiMe ₃	63	67	0 : 100

a. The detailed experimental procedures are described in the Experimental section (pages 66-72).

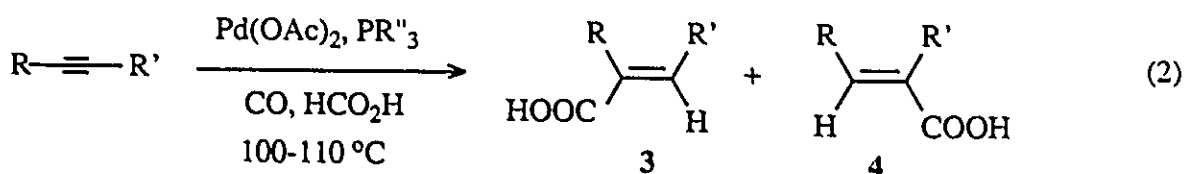
b. No hydrocarboxylation takes place when R = OEt, COMe, C(Me)=CH₂, and CO₂Me.

the hydrocarboxylation reaction is not strictly proportional to its relative steric bulk. Similarly, steric factors alone can not explain the regioselectivity observed in these catalytic reactions. For instance, the regioselectivity is 87-94% in favour of the 1,1-disubstituted isomer, **1**, with both the straight chain alkyl substituents and the much bulkier Ph and *sec*-Bu groups (entries a-f). The 1,2-disubstituted isomer, **2**, becomes the preferred product with the *t*-Bu group, and the exclusive product with SiMe₃ (entries g and h). It appears, therefore, that a combination of electronic and steric effects, as well as other factors, might be responsible for the observed trends in the reaction yield and regioselectivity.

Hydrocarboxylation does not proceed when R = COOMe, COMe, OEt, and C(Me)=CH₂. The ¹H NMR spectra of the reaction mixtures for these substrates contained only the resonances characteristic of the substituents R; the acetylenic or vinylic resonances, which would be expected if the starting alkyne or the hydrocarboxylation products were present, do not appear in these spectra. In addition, the non-solvent resonances in these spectra are often quite broad. Since these alkynes and their acid derivatives, which would form upon hydrocarboxylation, are very prone to dimerization, cyclotrimerization, and/or polymerization, it seems possible that they undergo these types of reactions much more readily than hydrocarboxylation. These types of side reactions are usually encountered in alkyne carbonylation reactions.^{13,24} In particular, terminal alkynes with R = COMe, COOR, and COOH have been reported⁵ to resist hydrocarboxylation, whereas dimerization takes place when R = COONa to give (*E,E*)-muconic acid. Tsuji^{11b} has reported that ethyl propynoate reacts with PdCl₂ (100 atm of CO gas, room temperature) to give a mixture of mono- and dicarbonylated products and dimers of both the starting alkyne and the carbonylated products.

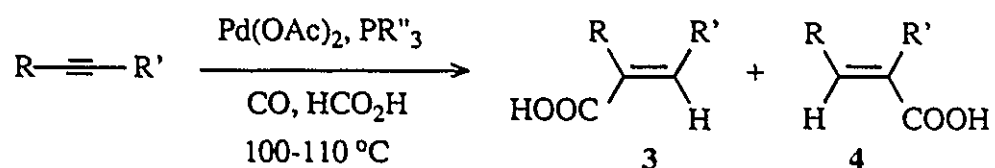
Internal alkynes also undergo catalytic hydrocarboxylation in the presence of Pd(OAc)₂, PPh₃, dppb (1,4-bis(diphenylphosphino)butane), and HCOOH at 100-110°C and

120 psi of CO gas; the products are the two regioisomers 3 and 4 (eq. 2, Table 2.2).



In principle, the hydrocarboxylation of internal alkynes can lead to a mixture of four isomeric products, two stereoisomers for each of the two possible regioisomers. Both the regio- and stereoselectivity of the reactions were determined from the ^1H NMR spectra of the reaction mixtures, on the basis of the following considerations. The regioisomers were readily distinguishable from the multiplicities and the coupling constants of their vinylic and allylic resonances. For instance, of the two products obtained from the hydrocarboxylation of 2-heptyne, one showed a quartet resonance at 6.98 ppm ($^3J_{\text{H-H}} = 7.2$, 1 H) and a corresponding triplet resonance at 2.28 ppm ($^3J_{\text{H-H}} = 7.2$, 2 H); these resonances clearly belong to 3a, the regioisomer with the vinylic H positioned *gem* to the methyl substituent. The other product showed a triplet of quartets at 6.89 ppm ($^3J_{\text{H-H}} = 7.5$, $^4J_{\text{H-H}} = 1.4$, 1 H) and a corresponding quartet at 2.18 ppm ($^3J_{\text{H-H}} = 6.8$, 2 H); these resonances were attributed to 4a, the regioisomer with the vinylic H positioned *gem* to the butyl substituent (Appendix C). The stereoisomers were distinguishable on the basis of the chemical shift of the vinylic resonance, which is more downfield when the vinylic H is *cis* to the carbonyl moiety.²⁵ Thus, all of the internal alkynes tested in the present system lead to a single stereoisomer arising from an overall *cis* addition of the "H" and "COOH" moieties to give *E* alkenoic acids. In other words, the reaction of internal alkynes is stereospecific and regioselective. Therefore, symmetrical alkynes yield only one product, whereas unsymmetrically substituted internal alkynes give rise to two regioisomers.

As in the hydrocarboxylation of terminal alkynes, both the yield and the regioselectivity

Table 2.2 The Pd(OAc)₂ Catalyzed Hydrocarboxylation of Internal Alkynes ^a

Entry	Alkyne		Yield (%)	Turnover No.	3 : 4
	R	R'			
a	Bu	Me	82	82	38 : 62
b	<i>i</i> -Pr	Me	58	59	20 : 80
c	Ph	Me	96	93	42 : 58
d	Ph	Et	91	91	64 : 36
e	Ph	Ph	89	90	---

a. The detailed experimental procedures are described in the Experimental section (pages 72-76).

tivity of this reaction vary with the alkyne substituents; in general, however, internal alkynes react less regioselectively than terminal alkynes. 2-Heptyne, for instance, gives an 82% combined yield and a 38:62 regioselectivity (entry a); the major product is the one in which the carboxyl group has been added to the acetylenic carbon bearing the less bulky substituent, 4. The poor regioselectivity in this case may be rationalized in terms of the similar sizes of the two substituents Bu and Me; consistent with this rationale, a large difference in the steric bulks of the two substituents would be expected to improve the regioselectivity. Indeed, replacing the Bu substituent in 2-heptyne with the more bulky *i*-Pr group improves the regioselectivity to 20:80, but it also causes a noticeable decline in the combined reaction yield (entry b). With 1-phenyl-1-propyne, on the other hand, the reaction yield is significantly higher and the regioselectivity is lower than would be expected on the basis of the relatively large size of the phenyl substituent (entry c). In comparison to the reaction of 2-heptyne, the effect of the Ph group on the regioselectivity seems to be much more similar to *n*-Bu than *i*-Pr. This anomalous behaviour is also apparent in the reaction of 1-phenyl-1-butyne in which the major regioisomer is the one in which the carboxyl group has been added to the carbon bearing the Ph group (entry d). In summary, the effect of the Ph group on the reactivity of the alkyne is more like that of a small, straight chain alkyl group than a larger group such as *i*-Pr. In other words, the electronic properties of the Ph group seem to prevail over its steric aspects.

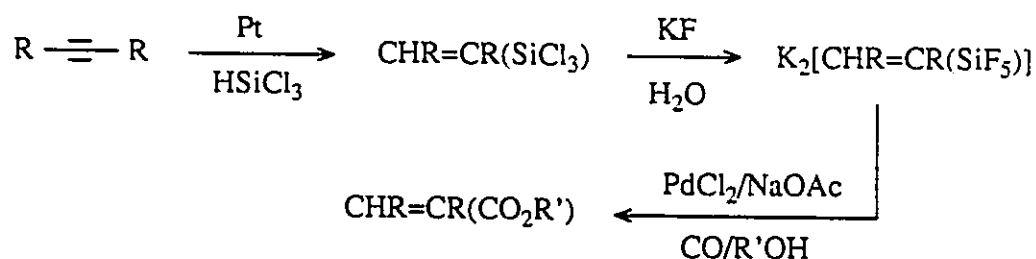
2.1.1 Comparison of the present results to literature reports

In general, hydrocarboxylation of alkynes in the present system requires relatively mild conditions and provides high yields and catalytic turnovers with simple alkynes; the product distribution is good with almost all terminal alkynes and with symmetrical internal alkynes. These results compare favourably with those reported by others on alkyne hydro-

carboxylation or hydrocarboalkoxylation (hydroesterification). One of the earliest examples of terminal alkyne hydrocarboxylation was reported by Jones, Shen, and Whiting⁵ who used Reppe's $\text{Ni}(\text{CO})_4/\text{H}_2\text{O}/\text{acid}$ system for stoichiometric carbonylation. This system was shown to tolerate a wide range of functional groups on the alkynes, but its use has not been continued by others mainly because of the toxicity of $\text{Ni}(\text{CO})_4$ and the low reaction yields.

In 1977, Knifton¹⁴ reported the hydrocarboalkoxylation of terminal alkynes in a system containing $[(\text{PR}_3)_2\text{PdCl}_2]\text{-SnCl}_2$. In contrast to the present results, the major product of carbonylation in this system is the linear α,β -unsaturated esters in 50% yields. A Pt-analogue of Knifton's system was reported by Watanabe *et al.*²⁴ Terminal alkynes such as 1-octyne are reported to react with CH_3OH and $[\text{HPt}(\text{SnCl}_3)(\text{PPh}_3)_2]$ (100°C , *ca.* 900 psi CO, 8h) to give $\text{CH}_2=\text{C}(\text{COOMe})(n\text{-C}_6\text{H}_{13})$ in 40-60% yields (20-30 turnovers). Under similar conditions, diphenylacetylene gives 65-85% yields of $\text{CHPh}=\text{C}(\text{COOMe})\text{Ph}$ (30-45 turnovers).

Alkyne carbonylation can be achieved indirectly by converting the alkyne to a metal alkenyl compound and carbonylating the latter via transmetalation. An example of such an approach has been reported by Kumada and coworkers.²⁶ Thus, alkynes are hydrosilylated with Pt/HSiCl_3 to give alkenylsilanes, which can be converted to alkenylpentafluorosilicates; the latter can then be carbonylated with palladium, as shown below:



A conceptually similar approach involves alkyne hydroboration, followed by trans-

metallation of the resultant alkenylboranes to give alkenylmercurials, and Pd-catalyzed carbonylation of the latter. The first two steps are readily accomplished by the method of Brown and Larock.²⁷ The usually difficult carbonylation step can also be accomplished relatively easily by using catalytic amounts of PdCl₂ and stoichiometric amounts of CuCl₂ at ambient or lower temperatures, as reported by Larock.²⁸ Conducting the reaction in alcohols gives esters and in moist THF gives acids. This approach has the advantage of tolerating a wide variety of functional groups; its disadvantage lies in the requirement of the two extra steps prior to the carbonylation reaction. This disadvantage is eliminated by including O₂ gas and small amounts of HCl in the PdCl₂/CuCl₂/CO system,¹⁷ thereby allowing the direct carbonylation of alkynes. This procedure results in dicarbonylation of terminal alkynes and monocarbonylation of internal alkynes; the yields are quite good, but turnover numbers are low. An alternative to CuCl₂/O₂/HCl as oxidant is thiourea/O₂, which has been used in Pd-catalyzed carbonylation of alkynes by Chiusoli.¹² This system gives interesting products with diynes such as dipropargylamines, but the yields are usually low and a number of by-products appear in most cases, especially with simple alkynes. Palladium black has been reported to convert phenylacetylene to methyl atropate and cinnamate in the presence of HI in methanol (100°C, 20 atm of CO gas, 2 h; 25-65% yields).²⁹ Interestingly, addition of triphenylphosphine or arsine to this system decreases the reaction yields; the opposite observation was made during this study for various metal catalyst precursors (*vide infra*).

Alper and coworkers have reported catalytic alkyne carbonylation with formate esters,²¹ oxalate esters,²² and aqueous NaOH.⁶ The first two processes are catalyzed by Pd(dba)₂/dppb (30 atm of CO gas pressure, 2-3 days) and give modest yields (30-60%). The novelty of these reactions lies in their unprecedented use of formate and oxalate esters, and it is believed that the sluggishness of these reactions is due to the difficult steps of sp² C-H bond activation in formates and C-C bond cleavage in oxalates. The third report describes the

NiCN₂-catalyzed hydrocarboxylation of terminal alkynes under phase transfer conditions. This system offers some advantages such as the use of an inexpensive nickel catalyst, low CO pressure requirement (1 atm), and high reaction yields (70-95%). The drawbacks include the low catalytic turnovers and the formation of byproducts arising from double bond isomerization in the strongly basic reaction medium. In addition, internal alkynes are unreactive in this system.

Alkyne hydrocarboxylation can also be achieved by carboxylation rather than carbonylation. Dunach and coworkers³⁰ have reported a Ni-catalyzed reductive electrocarboxylation process that hydrocarboxylates terminal and internal alkynes with CO₂. The yields and selectivities are good.

2.1.2 The process of optimizing reaction conditions

Most of the results presented in Tables 2.1 and 2.2 were obtained from reactions in which optimized experimental conditions were employed. The process by which these optimal conditions were determined is discussed in the following sections.

A. The role of phosphine ligands. Table 2.3 contains the results of a series of experiments carried out to examine the influence of the nature of phosphine ligands on the hydrocarboxylation of 1-octyne. The three monodentate phosphines PPh₃, PBu₃, and P(OPh)₃ were tested in order to establish the effect of phosphine basicity (*i.e.*, electron donating ability) and cone angle on the reaction. In terms of the relative orders of ligand basicity (PBu₃ > PPh₃ > P(OPh)₃) and cone angle (PPh₃ > PBu₃ > P(OPh)₃), as estimated by Tolman,³¹ only PPh₃ which has intermediate basicity and the largest cone angle promotes the hydrocarboxylation reaction (entries 1-3). This same ligand was also found to be the best in Watanabe's

Table 2.3 The Effects of Various Phosphines on the Catalytic Hydrocarboxylation of 1-Octyne*

$ \begin{array}{c} \text{R} \text{---} \text{C} \equiv \text{C} \text{---} \text{H} \xrightarrow[\text{CO, HCO}_2\text{H}]{\text{Pd(OAc)}_2, \text{PR}'_3} \begin{array}{c} \text{R} \\ \diagup \\ \text{C} = \text{C} \\ \diagdown \\ \text{HOOC} \end{array} + \begin{array}{c} \text{R} \\ \diagup \\ \text{C} = \text{C} \text{---} \text{CH}_2\text{COOH} \end{array} \\ \text{R = n-hexyl} \qquad \qquad \qquad 100\text{-}110\text{ }^\circ\text{C} \qquad \qquad \qquad \text{1c} \qquad \qquad \qquad \text{2c} \end{array} $				
Entry	Phosphine	Yield (%)	Turnover No.	1c : 2c
1	PPh ₃	83	93	87 : 13
2	P(OPh) ₃	0	—	—
3	PBu ₃	0	—	—
4	dppe	47	48	98 : 2
5	dppp	91	91	95 : 5
6	dppb	87	86	87 : 13
7	Ph ₂ P-CH=CH-PPh ₂	9	9	—

* The experimental details are described on pages 72-78.

[Pt/ Sn] system mentioned earlier;²⁴ in that system, however, P(OPh)_3 resulted in the exclusive formation of the 1,2-disubstituted regioisomer in low yields.

The bidentate ligands dppb, dppp (1,3-bis(diphenylphosphino)propane), dppe (1,3-bis(diphenylphosphino)ethane), and (*Z*)-Bis(diphenylphosphino)ethylene were also tested in order to determine the effect of chelation. The first two, dppb and dppp, showed very high yields, whereas their shorter chain congener, dppe, was less effective a ligand in terms of reaction yield, though it produced the highest regioselectivity (entries 4-6). The last ligand, which has the smallest "bite", resulted in a very low yield (entry 7).

Having determined that the nature of the phosphine ligand is a very important factor in the Pd(OAc)_2 -catalyzed hydrocarboxylation of alkynes, and that PPh_3 and dppb are suitable choices, further experiments were performed to establish the optimal ratio of the metal catalyst to these ligands. (Note: In the actual chronology of the experiments, dppp was tested long after the other ligands; therefore, although in hindsight dppp appears to be a better ligand than both PPh_3 and dppb, its effectiveness was not examined further.) The results of these experiments are summarized in Table 2.4; these results established the following two points:

I. In general, the presence of suitable phosphine ligands in this system is crucial for effective hydrocarboxylation of alkynes; otherwise, the starting materials are consumed in competing side reactions. One possible explanation for this observation is that suitable phosphine ligands help maximize the concentration of the active catalyst by preventing the loss of palladium metal. It is well known that in catalytic processes using a palladium compound as catalyst precursor, loss of palladium catalysts due to deposition of palladium metal is a distinct possibility.^{32,33}

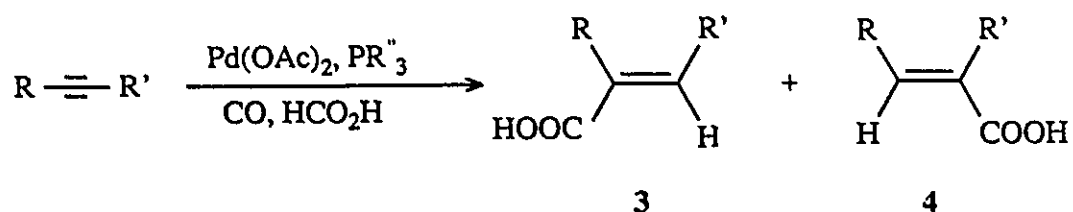
II. The optimal Pd(OAc)_2 : PPh_3 ratios for phenylacetylene and 1-octyne are 1:4 and 1:8, respectively (entries 2 and 5-7); the bidentate ligand dppb, in corresponding ratios, was

slightly better than PPh_3 for 1-octyne, but somewhat less effective for phenylacetylene (entries 3,8, and 9; note that since dppb is a bidentate ligand, $n/2$ equivalents of it are required to give the same ratio of metal to phosphorus atoms as would result with n equivalents of PPh_3 .)

Some preliminary results from our laboratories³⁴ had indicated that using a mixture of PPh_3 and dppb in the hydrocarboxylation of alkenes is sometimes superior to using either one alone; this prompted us to carry out a number of experiments using a mixture of these two phosphines. Although this approach was not advantageous with 1-octyne (entry 10) and was only slightly better for phenylacetylene (entry 4), it gave much better results with other terminal alkynes such as 3-methyl-1-pentyne and 3,3-dimethyl-1-butyne (entries 11-14). In addition, the effectiveness of using a mixture of PPh_3 and dppb was much more evident in the hydrocarboxylation of internal alkynes. As seen in Table 2.5, 2-heptyne did not undergo hydrocarboxylation with a 1:4 ratio of $\text{Pd}(\text{OAc})_2 : \text{PPh}_3$, and even with a 1:8 ratio only 9% yield was obtained (entries 1,2). In contrast, the same substrate gave 54% and 82% yields with dppb and a mixture of dppb plus PPh_3 , respectively (entries 3,4). With 1-phenyl-1-propyne and 1-phenyl-1-butyne, a 1:8 ratio of $\text{Pd}(\text{OAc})_2 : \text{PPh}_3$ gave only 32% yield, whereas using dppb either alone or in a mixture with PPh_3 greatly increased the reaction yields to 91-96% (entries 6, 7, 9, 10). Finally, the strong influence of dppb on the reaction yield is even more dramatically apparent in entry 8 of Table 2.5, which demonstrates that the presence of small amounts of dppb in the reactions using PPh_3 as the main ligand results in a 50% yield increase. An additional observation which is not reflected in the data tabulated in Table 2.5, but which is very important nonetheless, is that hydrocarboxylation of internal alkynes is much more consistently reproducible with dppb or a mixture of PPh_3 and dppb than with PPh_3 alone.

In summary, the best choice of ligands, and the one which is generally effective in the

Table 2.5 Influence of the Ratio of Pd : PPh₃ : dppb on the Catalytic Hydrocarboxylation of Internal Alkynes*



hydrocarboxylation of terminal and internal alkynes, is a mixture of PPh_3 and dppb. A $\text{Pd}(\text{OAc})_2 : \text{PPh}_3 : \text{dppb}$ ratio of 1:4:2 was commonly used in most reactions; as indicated above, however, the use of slightly less dppb or PPh_3 does not seem to affect the reaction yield appreciably. The observation that a mixture of two phosphine ligands is more effective in promoting the catalytic hydrocarboxylation of alkynes than either of the two ligands alone is novel and might hold promising prospects for other catalytic systems as well. Moreover, such "ligand synergism" might have important mechanistic implications. For instance, it suggests the possible involvement of two or more metal centres (which may contain one or more of the monodentate ligands) bridged to each other by the bidentate ligands.

B. The activities of various metal catalysts. The activities of a number of catalyst precursors in the hydrocarboxylation of terminal alkynes are shown in Table 2.6. The activity observed with $\text{Pd}(\text{OCOF}_3)_2$ is comparable to that of $\text{Pd}(\text{OAc})_2$, whereas PdCl_2 , which is very commonly used in Pd-catalyzed organic transformations, was much less active. Many reports have indicated³⁵ that chloride ions can strongly influence the catalytic activity of Pd catalysts, and it seemed reasonable that these might be responsible for the low reactivity of PdCl_2 in the present system. We set out to verify this possibility by examining the effect of removing the chloride ions from the reaction medium on the reaction yield. It was reasoned that adding some NaOAc to the reaction mixture would bring about a ligand exchange equilibrium, trapping the chloride ions as insoluble NaCl and removing them from the catalytic cycle. Thus, an experiment was conducted in which a mixture of PdCl_2 and NaOAc was used in an otherwise standard catalytic reaction. Entry 4 in Table 2.6 shows that the presence of NaOAc dramatically improved the activity of PdCl_2 to approximately the same level as $\text{Pd}(\text{OAc})_2$. Similarly, Milstein has shown^{35e} that the PdCl_2 -catalyzed allylic carbonylation (carbomethoxylation) of (+)-carvone occurs much more readily in the presence of

Table 2.6 The Activities of Various Catalysts in the Catalytic Hydrocarboxylation of Terminal Alkynes^a

Entry	Catalyst	Yield (%)	1 : 2
1	Pd(OAc) ₂ /PPh ₃	84	95 : 5
2	Pd(OCOF ₃) ₂ /PPh ₃	87	92 : 8
3	PdCl ₂ /PPh ₃	15 ^b	—
4	PdCl ₂ /NaOAc/PPh ₃ /dppb	77	96 : 4
5	Pd(PPh ₃) ₄	77	92 : 8
6	10% Pd/C	0	—
7	10% Pd/C /PPh ₃ /dppb	85	86 : 14
8	Ni(OAc) ₂ /PPh ₃ /dppb	74	92 : 8

a. The experimental details are described on pages 81-83.

b. Small amounts of the dicarbonylation products, anhydride and (Z)-diacid, as well as some unidentified species were also present.

carboxylic acid anions. Therefore, any one of $\text{Pd}(\text{OAc})_2$, $\text{Pd}(\text{OCOCF}_3)_2$, or a mixture of PdCl_2 and NaOAc can efficiently catalyze the hydrocarboxylation of alkynes.

In all three of the catalyst precursors discussed above the Pd centre is in a +2 oxidation state; to examine the activity of a Pd(0) catalyst precursor, $\text{Pd}(\text{PPh}_3)_4$ was used in an otherwise standard catalytic reaction (entry 5). Although this compound is somewhat less effective than $\text{Pd}(\text{OAc})_2$, it is nevertheless a good precatalyst; therefore, starting with a Pd(0) species does not hinder the catalysis significantly. This outcome is, in fact, not at all surprising in view of the fact that Pd(II) compounds often undergo *in-situ* reduction to Pd(0) when heated in a CO atmosphere.³⁶

A heterogeneous catalyst precursor such as palladium on carbon (Pd/C) does not, on its own, catalyze alkyne hydrocarboxylation (entry 6). Interestingly, in the presence of suitable phosphine ligands, Pd/C becomes quite an effective catalyst (entry 7). This observation raises the following questions: What is the role of the phosphine ligand in the reaction of Pd/C with alkynes? Is the catalysis occurring on the surface of the supported metal (*i.e.*, a heterogeneous process)? Or is the phosphine ligand "leaching" Pd metal out of the solid phase and into the liquid phase by forming homogeneous palladium phosphine species? While these questions were not pursued in the course of our study, analogy with other heterogeneously catalyzed processes points to the "leaching" idea as a reasonable possibility. In the heterogeneously catalyzed oxo process, for instance, the eventual "washing out" of the Co or Rh catalysts from the surface of the support is well documented.³⁷ Whatever the true reason may be, the observation that the combination of Pd/C and PR_3 leads to effective palladium phosphine catalysts is intriguing and might hold some promise for other reactions as well.

Another interesting result from Table 2.6 is that $\text{Ni}(\text{OAc})_2$ is very active in catalyzing the hydrocarboxylation of phenylacetylene. From an economic viewpoint, nickel analogues

palladium compounds would obviously be very desirable substitutes for use in large scale processes. For this reason, shortly after Reppe and coworkers reported their pioneering studies on the hydrocarboxylation of acetylene, a large number of patents appeared⁴ on the possibility of using Ni compounds as catalysts for the hydrocarboxylation and hydrocarboalkoxylation of acetylene and propargyl alcohol. For instance, NiI_2 or Ni(OAc)_2 supported on SiO_2 were used³⁸ for the catalytic synthesis of acrylic acid from acetylene at 170- 270 °C and 30-60 atm pressures of CO gas; the yields, however, were quite low and a large number of by-products formed. In addition, very little is known about Ni-catalyzed hydrocarboxylation of alkynes other than acetylene. The complexes $[\text{Ni}(\text{PR}_3)_2\text{Br}_2]$ ($\text{R} = \text{Ph}, \text{CH}_3\text{C}_6\text{H}_4, \text{CH}_3\text{OC}_6\text{H}_4$, etc.) have been used with 1-hexyne at 180-200 °C and CO pressures of 2-15 atm,³⁹ but again the yields and the rates are low. On the other hand, a variety of alkynes can be hydrocarboxylated by using Ni(CO)_4 as a stoichiometric reagent.⁵

The absence of reports on the successful use of nickel compounds as catalyst precursors for the hydrocarboxylation of alkynes prompted us to further explore the reactivity of the $\text{Ni(OAc)}_2/\text{PPh}_3/\text{dppb}/\text{HCOOH}$ system. Unfortunately, our preliminary results were not encouraging: of the 5 alkynes tested, only phenylacetylene undergoes hydrocarboxylation in the nickel system. Therefore, the present combination of catalyst and reagents is effective only for the most reactive alkyne. It is hoped that a closer examination of the various factors affecting this reaction (*e.g.*, nickel species, phosphine ligands, heat, solvent) may lead to a more generally applicable catalytic system. This task, however, was not pursued during the course of this study.

C. The effects of CO gas pressure, P_{CO} . The data tabulated in Table 2.7 and plotted in Figure 2.1 show that the presence of CO gas is essential for alkyne hydrocarboxylation: virtually no reaction occurs in its absence. The reaction yield is 57% with a pressure of 32 psi

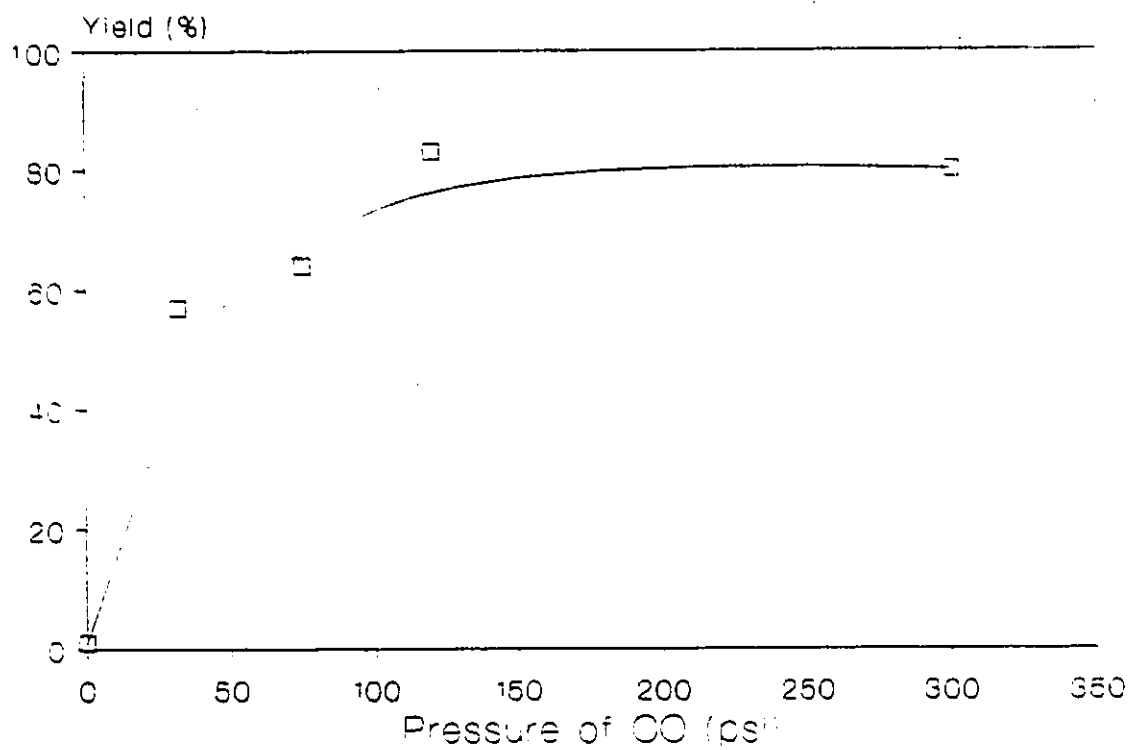
Table 2.7 The Effect of CO Pressure on the Catalytic Hydrocarboxylation of Alkynes^a

Entry	P _{CO} (psi)	Yield (%) ^b
1	0	1 ^c
2	32	57
3	75	64
4	120	83
5	300	80

a. The experimental details are described on page 84.

b. Yield refers to the combined yield of the regioisomeric unsaturated acids **1** and **2**.

c. Traces of other, unidentified products were also present.

Figure 2.1**The Effect of CO Pressure on the Catalytic Hydrocarboxylation of Alkynes**

(about 2.2 atm), and increases gradually with increasing P_{CO} up to a pressure of 120 psi (about 8.3 atm) at which point the yield seems to reach a plateau at 83%. Since the solubility of CO gas in solvents is proportional to (among other factors) P_{CO} , these results imply that sufficient concentrations of CO gas dissolved in the reaction medium is vital for the catalysis. Another possible inference is that the carbonyl moiety of the product acid probably originates from the CO gas rather than formic acid. Additional support for the latter assertion comes from a similar study carried out in our laboratories on alkene hydrocarboxylation with HCOOH .³⁴ Complementary experiments using ^{13}C -labelled starting materials (^{13}CO gas and H^{13}COOH) found that only in traces of the acid product did the carbonyl moiety originate from formic acid. It seems reasonable to conclude, therefore, that in the hydrocarboxylation of alkynes with formic acid, the carbonyl moiety of the product acid originates from the CO gas, and that each molecule of formic acid serves as a net source of one molecule of water (i.e., "H" and "OH" moieties). Indeed, water on its own has been shown to induce the catalytic hydrocarboxylation of alkynes, albeit in a much more sluggish manner than formic acid (*vide infra*). Some of the possible ways in which formic acid might provide a net molecule of water will be discussed later along with other mechanistic considerations.

D. The effects of temperature and reaction time. The data presented in Table 2.8 and plotted in Figure 2.2 indicate that a temperature of about 105°C is optimal for alkyne hydrocarboxylation: lower temperatures decrease the yield drastically and higher temperatures do not offer any advantages. As a result, for most experiments the temperature was maintained between 100 and 110°C.

Table 2.9 and Figure 2.3 show that catalytic hydrocarboxylation of alkynes in the present system proceeds fairly rapidly, such that the reaction is almost over in about 1.5 h (about one turnover per minute). Nevertheless, for the purpose of ensuring optimal results, in

Table 2.8 The Effect of Temperature on the Catalytic Hydrocarboxylation of Terminal Alkynes*

		$\begin{array}{c} \text{R} \\ \diagup \\ \text{HOOC}=\end{array}$		$\begin{array}{c} \text{R} \\ \diagup \\ \text{CH}=\text{CH}-\text{COOH} \end{array}$	
		1		2	
Entry	Temperature (°C)	Yield (%)	Turnover No.	1 : 2	
1	22	—	—	—	
2	60	7	7	92 : 8	
3	90	64	14	92 : 8	
4	105	88	90	94 : 6	
5	127	84	85	88 : 12	

* The experimental details are described on pages 84 and 85.

Figure 2.2

The Effect of Temperature on the Catalytic Hydrocarboxylation of Alkynes

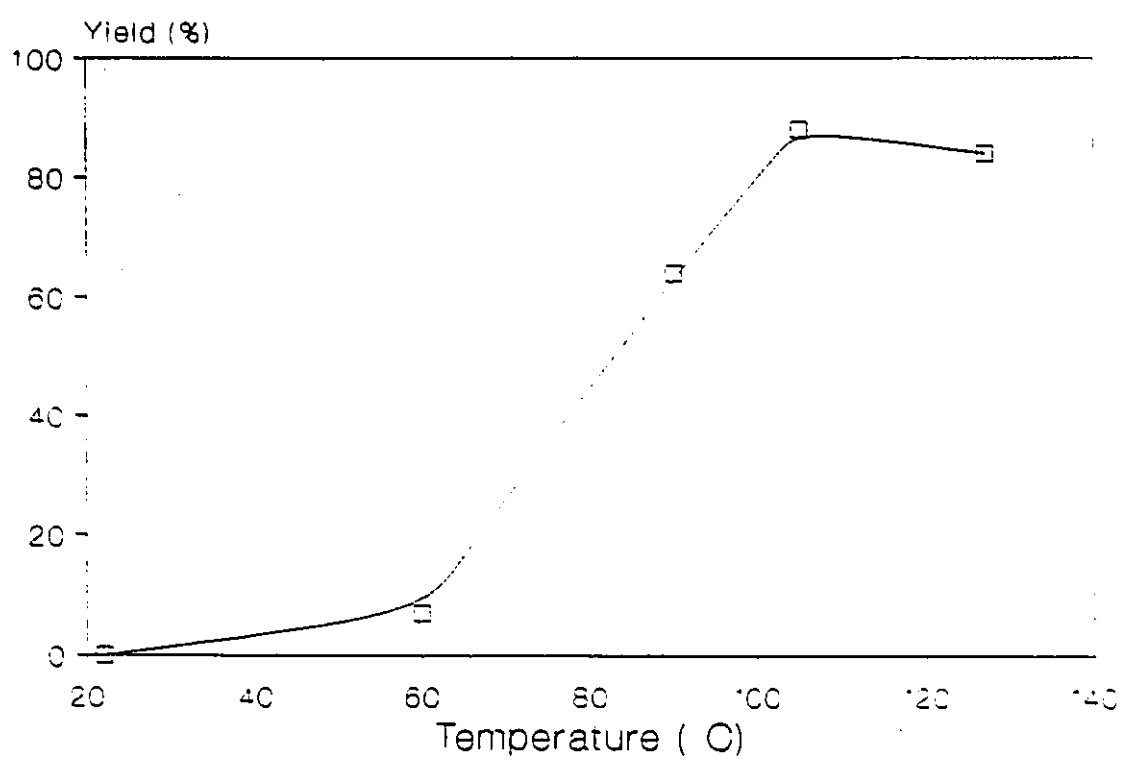


Table 2.9 The Effect of Reaction Time on the Catalytic Hydrocarboxylation of Phenylacetylene^a

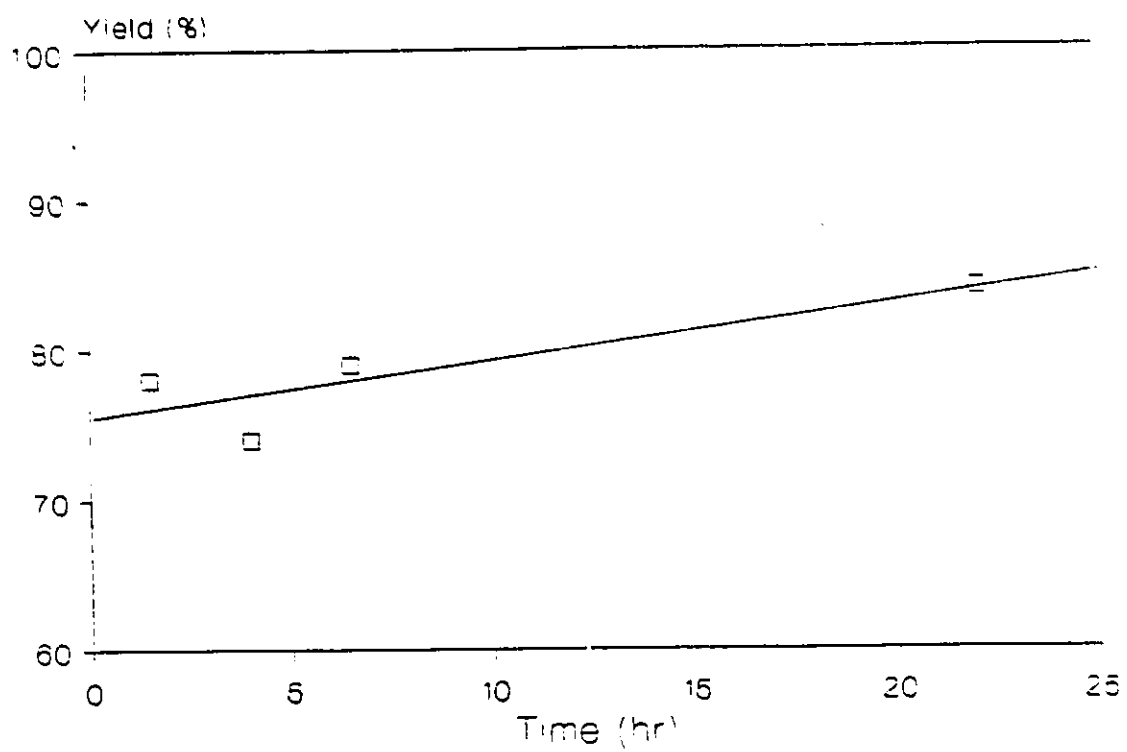
Entry	Time (hr)	Yield (%)	Turnover No.	1a : 2a ^b
1	1.5	78	82	96 : 4
2	4.0	74	72	90 : 10
3	6.5	79	80	92 : 8
4	22.0	84	85	95 : 5

a. The experimental details are described on pages 85 and 86.

b. 1a = atropic acid; 2a = cinnamic acid

Figure 2.3

The Effect of Reaction Time on the Catalytic Hydrocarboxylation of Phenylacetylene



most experiments the reaction was allowed to proceed for 15-24 h. It is noteworthy, however, that at least over the time range of 1.5-22 h, and the temperature range of 60-127 °C, the regioselectivity of the catalytic reaction remains unchanged within a rather narrow margin of experimental error. These observations indicate that the regioselectivity of the reaction is most probably determined during the main catalytic cycle and depends on steric and other factors influencing the reaction mechanism. In other words, the possibility of an independent isomerization process occurring parallel to the main catalytic process is slim. This point will be further elaborated later (*vide infra*).

E. Solvent effects. As seen from Table 2.10, among the solvents tested DME, acetone, and THF are the suitable choices in that order. Acetonitrile seems to be a particularly poor solvent perhaps because of its tendency to bond quite strongly to Pd, thereby competing with other ligands and substrates for coordination to the metal centre.

F. The effect of various acids. As implied by its name, hydrocarboxylation requires a source of "H" and "COOH" moieties in addition to the substrate, the alkyne in this case. A number of experimental observations (*vide supra*) have led us to the conclusion that the "CO" of the "COOH" moiety is supplied by the CO gas. Therefore, the only additional reagent necessary for this reaction is one which can serve as a net source of "H" and "OH". The most obvious reagent for this purpose, and the one most widely used in hydrocarboxylation of alkenes and alkynes, is water. As seen from Table 2.11, however, water is not a satisfactory reagent in the present system, since it gives either no reaction (entry 2) or only a low yield (entry 3). Note that no reaction takes place without an added source of "H" and "OH" (first entry); this is in contrast to the dicarbonylation of alkynes with $\text{PdCl}_2/\text{CuCl}_2/\text{CO}/\text{O}_2$ (described in Chapter III of this thesis) where the residual moisture is sufficient for the

Table 2.10 The Effects of Various Solvents on the Catalytic Hydrocarboxylation of Phenylacetylene*

Entry	Solvent	Yield (%)	1a : 2a
1	DME	84	95 : 5
2	Acetone	76	94 : 6
3	THF	75	92 : 8
4	CHCl ₃	10	80 : 20
5	CH ₃ CN	5	89 : 11

* The experimental details are described on page 86.

Table 2.11 The Effects of Various Acids on the Catalytic Hydrocarboxylation of Alkynes^a

Entry	Alkyne	Acid	Al:W:Ac ^b	Yield (%)	1 : 2
1	1-octyne	—	—	0	—
2	Ph— $\equiv$ —Ph	H ₂ O	100:218:0	0	—
3	Ph— $\equiv$ —H	H ₂ O	106:100:0	35	88:12
4	i-octyne	HCl _{aq}	104:102:30	30 ^c	—
5		CF ₃ CO ₂ H _{aq}	104:183:23	16	96:4
6		HCO ₂ H _{aq}	98:137:10	10	90:10
7		(-CO ₂ H) ₂ aq	100:164:11	12	99:1
8		99% CF ₃ CO ₂ H	103:0:222	28	91:9
9		98% HCO ₂ H	112:8:160	83	87:13
10		99% (-CO ₂ H) ₂	111:0:125	66	99:1

a. The experimental details are described on pages 86-88.

b. Molar ratio of alkyne : water : acid.

c. Other, unidentified products were also present in the product mixture.

reaction.

The poor reactivity of water prompted an examination of the effects of adding acids to the water reactions. Hydrochloric acid was tested first, since it is the most commonly used acid in the hydrocarboxylation of alkenes and alkynes. The use of this acid in the present system resulted in a low yield and the formation of by-products (entry 4). Low yields were also obtained with aqueous solutions of the organic acids CF_3COOH , HCOOH , and $(-\text{COOH})_2$ (entries 5-7). A closer examination of these results reveals that the reaction yield is more or less proportional to the amount of acid used; in other words, the reaction seems to require stoichiometric, rather than catalytic, amounts of H^+ . Accordingly, reactions in which formic and oxalic acids were present in stoichiometric or excess amounts gave good yields (entries 9, 10), but the yield was still quite poor with stoichiometric amounts of CF_3COOH (entry 8).

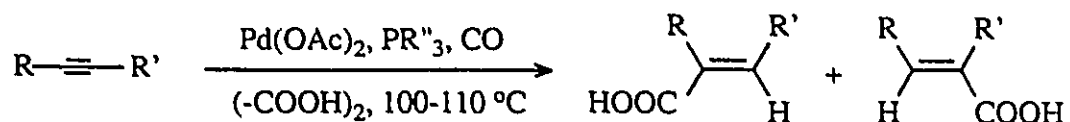
In contrast to the results discussed above, Whiting *et al.*⁵ have reported that in the stoichiometric hydrocarboxylation of phenylacetylene and 1-hexyne with $\text{Ni}(\text{CO})_4$, HCl gave the best results whereas oxalic and trichloroacetic acids were unreactive. The same authors also showed that phenylacetylene can be hydrocarboxylated in alkaline media. Similar observations have been made by others. In a 1951 patent,⁴⁰ Reppe showed that the compound $\text{K}_2\text{Ni}(\text{CN})_4$ catalyzes the synthesis of sodium or potassium acrylate from acetylene in aqueous alkaline medium at 100-180 °C and 30-60 atm pressure of CO gas. Recently, Alper and Amer⁶ have reported a much milder process for the catalytic hydrocarboxylation of terminal alkynes under phase transfer conditions.

How does hydrocarboxylation proceed in both basic and acidic media? In basic media, the nucleophilic attack by the hydroxyl anion on coordinated CO is thought to form metal hydroxycarbonyl species, which insert into the metal alkyne bond. The metal alkenyl intermediates thus formed and a hydride ligand, formed by the decarboxylation of a second

hydroxycarbonyl ligand, reductively eliminate to give the products. In acidic media, the metal is probably protonated first, and the hydride ligand thus formed inserts into the metal alkyne bond to give a metal alkenyl intermediate. Insertion of CO into the metal alkenyl bond and hydrolysis furnish the products. These mechanisms are, of course, only tentative postulates and, as we shall see later, considerable controversy exists among different research groups over the mechanistic details of carbonylation reactions in general, and alkyne carbonylation in particular.

G. Alkyne hydrocarboxylation with oxalic acid. Although formic acid was selected as the best choice of acid for alkyne hydrocarboxylation in the present system, the use of oxalic acid was also explored briefly (Table 2.12). Like formic acid, oxalic acid does not promote hydrocarboxylation in the absence of CO gas, which is to say that the CO moiety in the product originates from CO gas and not from oxalic acid. In comparison to formic acid reactions, the oxalic acid reactions are much more sensitive to the choice of phosphine ligands. For example, dppb is much better than PPh_3 in promoting the reaction of phenylacetylene with oxalic acid (entries 1, 2). This reaction is also quite sensitive to the ratio of oxalic acid to alkyne: a ratio of 1-2:1 seems to be optimal (entries 2, 3). The yields of the oxalic acid reactions are somewhat variable for different alkynes; in comparison to the corresponding reactions with formic acid, oxalic acid gives matching or higher yields for some alkynes (entries 8-10), and lower ones with others (entries 5-7). The mechanism for alkyne hydrocarboxylation with oxalic acid is probably similar to that for the formic acid reaction (*vide infra*).

H. The effects of metal catalyst to alkyne ratio. Table 2.13 contains the results of four reactions with varying ratios of phenylacetylene to $\text{Pd}(\text{OAc})_2$. Based on these results, 1%

Table 2.12 Catalytic Hydrocarboxylation of Alkynes Using Oxalic Acid^a

Entry	Alkyne		Pd : PPh ₃ : dppb	O:A ^b	Yield (%)	Turnover No.	Ratio ^c
	R	R'					
1	Ph	H	1 : 4 : 0	0.57	6	6	92 : 8
2			1 : 0 : 2.1	0.49	58	58	97 : 3
3			1 : 4 : 2.1	0.50	56	59	93 : 7
4			1 : 0 : 2.1	1.09	77	79	97 : 3
5	<i>n</i> -C ₆ H ₁₃	H	1 : 0 : 2.1	1.13	66	73	99 : 1
6			1 : 4 : 2	1.20	78	78	96 : 4
7			1 : 4 : 2.3	2.06	76	73	91 : 9
8	(CH ₂) ₃ CN	H	1 : 4.2 : 2.2	2.15	65	63	97 : 3
9	Ph(CH ₂) ₂	H	1 : 4 : 2.1	2.16	90	86	91 : 9
10	Ph	Me	1 : 4.2 : 2.1	2.10	96	95	48 : 52
11	Ph	Ph	1 : 4.2 : 2.1	2.03	88	90	—

a. The experimental details are described on pages 88-90.

b. Molar ratio of oxalic acid to alkyne used in the reaction.

c. This column represents the ratios of 1 : 2 when R' = H, and 3 : 4 when R' = Me or Ph.

Table 2.13 The Effect of Catalyst to Alkyne Ratio on the Catalytic Hydrocarboxylation of Phenylacetylene^a

Entry	Ph-CC-H / Pd	Yield (%)	Turnover No.	1a : 2a
1	24	75	18	92 : 8
2	94	96	90	93 : 7
3	509	36	183	89 : 11
4	502 ^b	33	165	95 : 5

a. The experimental details are described on page 91.

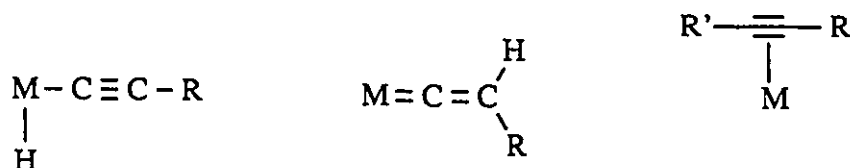
b. Twice as much dppb was used in this experiment compared to the previous entry.

$\text{Pd}(\text{OAc})_2$ was used in most of the reactions reported in the present study. Higher than 100 turnover numbers can be obtained by using less catalyst, but in these cases the reaction yield decreases significantly even with additional amounts of phosphine ligands (entries 3, 4).

Having discussed the experimental findings which led to the optimization of the reaction conditions for catalytic hydrocarboxylation of alkynes, it is necessary to deal with the implications of these findings for the mechanism of this reaction. Before embarking on this task, however, we will review the bonding modes of the major reagents present in the catalytic reaction media, and briefly discuss the various mechanisms reported in the literature. This will set the stage for proposing a plausible mechanism and discussing its merits in light of the experimental results obtained during the course of this study.

2.1.3 Bonding Modes

Phosphines and CO are two of the most ubiquitous ligands in transition metal chemistry, and much is known about their modes of bonding to metal centres.⁴¹ The interaction of transition metals with alkynes has also been studied extensively and several bonding modes have been reported.⁴² In principle, alkynes can interact with the metal centre in mononuclear complexes in three ways:

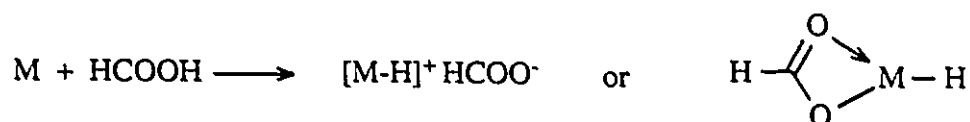


Oxidative addition of the sp C-H bond in terminal alkynes to give hydrido(alkynyl) or

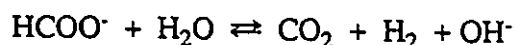
vinylidene complexes is possible with some metal complexes;⁴³ these modes of bonding, however, are unlikely to occur in the present system for the following reasons. As will be discussed later, hydrocarboxylation of 1-deuterio-4-phenyl-1-butyne, $\text{Ph}(\text{CH}_2)_2\text{-CC-D}$ under standard catalytic conditions, produces the corresponding unsaturated carboxylic acids with complete retention of the deuterium label. Any palladium deuteride species forming as a result of the oxidative addition of the deuterioalkyne to the metal catalyst would be expected to undergo rapid D/H exchange with the large excess of H^+ ions present in the reaction medium. Such an exchange process would reduce the concentration of the Pd-D species and diminish the likelihood of D-incorporation into the final product. Hence, the presence of the deuterium label in the final product rules out the oxidative addition of terminal alkynes. Moreover, assuming that the hydrocarboxylation of both terminal and internal alkynes proceeds via two very similar mechanisms, oxidative addition of the sp^2 C-H bond may not be considered because it is not available to internal alkynes. The involvement of metal vinylidines, which was initially suggested by Reppe in 1953,⁴ is also unlikely because it could not account for the 1,1-disubstituted product, $\text{CR}(\text{COOH})=\text{CH}_2$, which is the major product for all but two of the terminal alkynes studied. (Reppe also discarded this idea as soon as the hydrocarboxylation of internal alkynes was discovered.) Therefore, the most probable mode of bonding for alkynes in the present system is that in which the alkyne is coordinated to the metal in a π -fashion.

The interaction of formic acid with transition metals is less studied than those of phosphines, CO, and alkynes; nevertheless, enough is known about this interaction to allow a simple analysis here. In principle, one reactive moiety in formic acid is the sp^2 C-H bond, the activation of which would provide a metal hydrido(hydroxycarbonyl) complex, $[\text{MH}-(\text{COOH})]$. To be sure, sp^2 C-H bond activation has been observed with such carbonyl compounds as aldehydes⁴⁴ and alkyl formates,^{44,45} but not with formic acid. The more

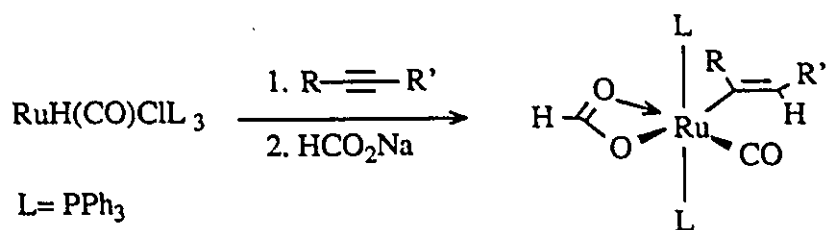
obvious reaction between a metal centre and HCOOH is the protonation of the metal to form, initially, a cationic hydrido species; the resultant formate anion can either act as a counter anion or coordinate to the metal centre:



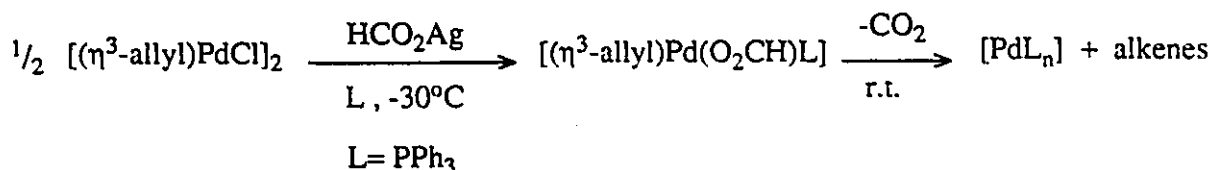
Transition metal formate complexes are usually unstable and readily decarboxylate to give metal hydrides and CO_2 .⁴⁶ In some cases, a metal formate complex and its hydride analogue interconvert in an equilibrium involving the insertion and elimination of CO_2 ,⁴⁷ occasionally, however, the decomposition proceeds by decarbonylation and the formation of water.⁴⁸ The formation of metal hydrides *via* metal promoted formate decarboxylation has been exploited in catalytic hydrogenolysis reactions,⁴⁹ reduction of alkenes, alkynes,⁵⁰ and nitro compounds,^{49,51} butadiene dimerization,⁵² and hydrogenation of carbonyl compounds.⁵³ Decarboxylation of formate ligands also allows the use of HCOO^- instead of CO in the studies of the water-gas shift reaction.⁵⁴



The stability of the formate ligand is variable and depends on many factors; in general, bases and higher temperatures accelerate its decomposition. Formate decarboxylation is not always facile, however, and a few well characterized complexes containing stable formate ligands are known. One such example is the thermally stable Ru(II) formate complex⁵⁵ shown below:



This compound is very interesting and relevant to the present discussion not only because it is a stable formate complex, but also because it has all the required ligands in the postulated catalytic intermediate in alkyne hydrocarboxylation (*vide infra*). Other examples of stable complexes containing formate ligands include $[\text{Rh}(\text{HCO}_2)_2\text{L}_2]_2$ ($\text{L}_2 = 2 \text{ CO}$, or cod), $[\text{Rh}(\text{HCO}_2)_2(\text{PR}_3)_2(\text{CO})]$ ($\text{R} = \text{Ph}$, or Cy), $[\text{Ir}(\text{PMe}_3)_2(\text{H})_2]^+[\text{HCOO}^-]$, and $[\text{Os}(\text{HCO}_2)_2(\text{PR}_3)_2(\text{CO})_2]$.^{45b,56} Yamamoto⁵⁷ has recently reported the synthesis and characterization (^1H , ^{13}C , and ^{31}P NMR) of a Pd(II) formate complex that is stable only at low temperatures; at room temperature, decomposition takes place *via* decarboxylation and reductive elimination:



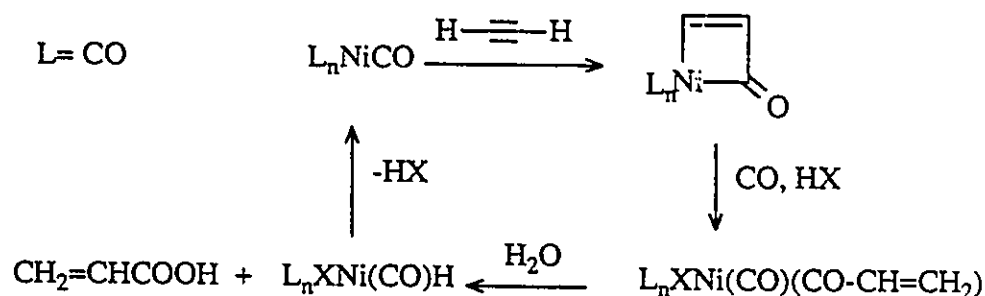
In summary, on the basis of the precedents cited above, it is reasonable to conclude that in the present system formic acid can react with the catalytically active Pd species to give a metal hydrido(formate) complex. The formate ligand in this complex might be either coordinated to the metal centre or act as a counter anion. In either case, the mechanism proposed for alkyne hydrocarboxylation contends that this putative intermediate is stable to decarboxylation in spite of the high temperature of the catalytic reaction (*vide infra*).

2.1.4 Possible reaction mechanisms

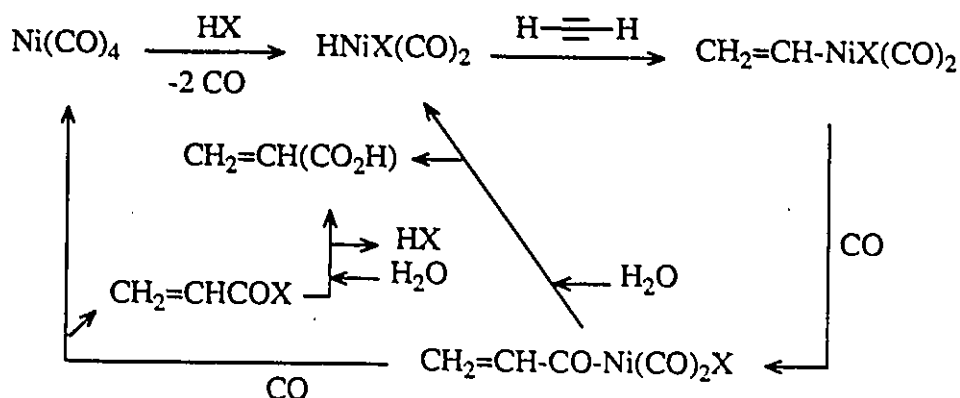
Some of the first mechanisms proposed for the $\text{Ni}(\text{CO})_4$ catalyzed hydrocarboxylation of acetylene by Reppe and other pioneers in this field had little basis in established mechanistic knowledge but are historically significant. These mechanisms have been presented in Pino's review⁴ and shall not be discussed here.

An interesting proposal put forth by Bird *et al.* in 1970⁵⁸ involves the insertion of a coordinated acetylene into a Ni-CO bond to form a metallacyclobutenone intermediate, which is then hydrolyzed by $\text{H}_2\text{O}/\text{HCl}$ to furnish the products (Scheme 2.1). (A few examples of such four-membered metallacycles have been synthesized by reacting cyclopropenones with iron and cobalt,⁵⁹ and platinum⁶⁰ compounds.)

Scheme 2.1

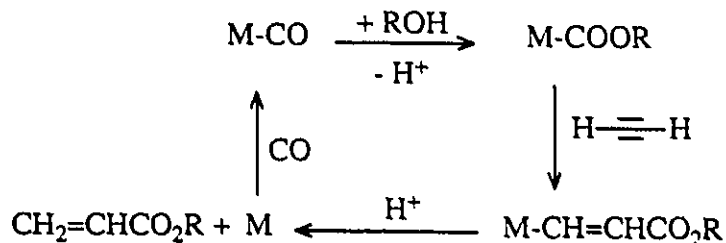


A second mechanism⁶¹ involves the formation of a Ni-H species: alkyne insertion into the Ni-H forms a nickel alkenyl intermediate, CO "insertion" forms a nickel acyl species, which then decomposes *via* different possible routes to provide the products (Scheme 2.2).

Scheme 2.2

Owing partly to the complex nature of alkyne hydrocarboxylation, and to a lack of detailed mechanistic studies in this field, the two mechanisms cited above are still considered to be plausible to date, 20-30 years after they were first proposed. The analogous hydrocarboalkoxylation of alkynes (ROH instead of H₂O) and both the hydrocarboxylation and hydrocarboalkoxylation of alkenes have been studied more carefully and are better understood, although even the mechanisms of these reactions remain elusive. The main theme arising from the latter studies is that transition metal-catalyzed hydrocarboalkoxylation of alkynes and alkenes can, in principle, proceed by either a hydride mechanism similar to that shown in Scheme 2.2 above, or by a mechanism involving a M-COOR intermediate (Scheme 2.3):

Scheme 2.3



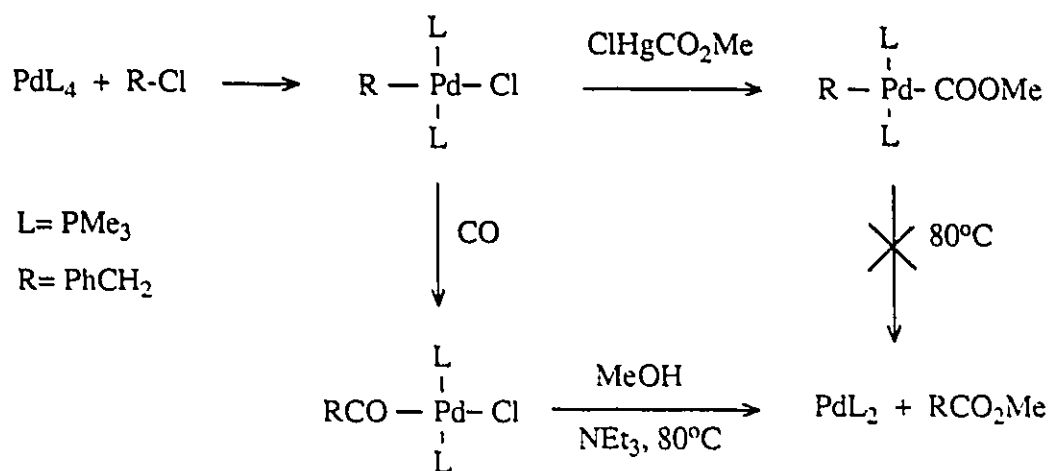
The mechanism involving M-COOH or M-COOR addition to alkynes or alkenes has been endorsed by Fenton,⁶² Norton,²⁵ and Milstein;⁶³ the mechanism involving hydride addition to alkynes or alkenes has been endorsed by Knifton,¹⁴ Tsuji,⁶⁴ and Toniolo.⁶⁵ Of these, the reports by Norton and Toniolo are most relevant to the present discussion and will be discussed here briefly.

Norton and coworkers have reported a detailed study of the Pd-catalyzed intramolecular cyclocarbonylation of alkynols to methylene lactones.²⁵ On the basis of their results and well precedented chemistry, the authors outline a mechanism similar to that shown in Scheme 2.3 above, involving (a) the nucleophilic attack on Pd-CO by the alcohol end of the alkynol substrate to form Pd-CO₂(CH₂)₂-CC-H, (b) intramolecular cycloaddition of the triple bond to the Pd-COOR bond to give an alkenyl intermediate, and (c) protic cleavage of the alkenyl ligand to form the methylene lactone.

An alternative mechanism involving the oxidative addition of the O-H bond and the formation of a metal hydride is less likely in this system for two reasons. First, the oxidative addition of the weakly acidic O-H bond of the alkynol would be difficult. Second, the formation of metal hydrides would be expected to facilitate isomerization of the *exo* double bond in the product lactone, and to give the endocyclic lactone which was never observed in the reaction. In contrast, the situation is quite different in our system, with formic acid

possessing a very acidic O-H bond and a weakly nucleophilic conjugate base, HCOO^- , both of which would favour a mechanism involving a hydride intermediate (*vide infra*).

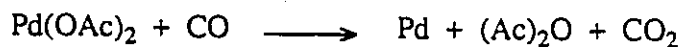
Toniolo and coworkers have studied the hydrocarboalkoxylation of alkenes catalyzed by *trans*- $[\text{PdCl}_2(\text{PPh}_3)_2]$ in the presence of additional PPh_3 at 95 °C and under 100-120 atm of CO gas pressure; the source of active hydrogens is the solvent alcohol.⁶⁵ These authors report isolating the acyl complexes *trans*- $[\text{PdCl}(\text{COR})(\text{PPh}_3)_2]$ (R= Et, Bu) and the carbomethoxy complex *trans*- $[\text{PdCl}(\text{COOMe})(\text{PPh}_3)_2]$ at the end of some catalytic reactions. When the acyl complex is used instead of *trans*- $[\text{PdCl}_2(\text{PPh}_3)_2]$, both catalytic and stoichiometric (in the absence of CO) reactions proceed very well. When, on the other hand, the carbomethoxy complex is used, neither catalytic nor stoichiometric reactions proceed. Moreover, the addition of bases such as trialkylamine or carboxylic acid anions, which are reagents known to promote the formation of Pd-COOR species, also failed to initiate any reaction with the carbomethoxy complex. Therefore, the authors conclude that the more probable mechanism for the hydrocarboalkoxylation of alkenes is the one which involves the insertion of the alkene double bond into an M-H bond, followed by CO migration to form a metal acyl complex, and alcoholysis of the acyl ligand to give the ester products (see Scheme 2.2 above). Mechanisms involving metal acyl complexes as the main catalytic intermediates have also been put forth for the carbonylation of organic halides. For instance, Milstein has shown⁶³ that carbonylation of benzylchloride catalyzed by $[\text{Pd}(\text{PMe}_3)_4]$ occurs *via* metal acyl, rather than carboalkoxy, intermediates (Scheme 2.4).

Scheme 2.4

2.1.5 The mechanism proposed for the present system

On the basis of the literature precedents discussed in the two preceding sections, and the experimental observations made during this study, the following tentative mechanism has been proposed for the $\text{Pd}(\text{OAc})_2$ -catalyzed hydrocarboxylation of alkynes with formic acid (Scheme 2.5).

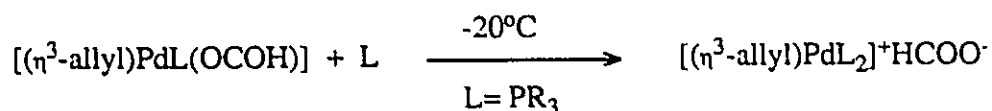
Beginning with step A, it is reasonable to assume that the trimeric, solid state structure of $\text{Pd}(\text{OAc})_2$ breaks down and the starting $\text{Pd}(\text{II})$ centre gets reduced to $\text{Pd}(0)$ in the CO atmosphere. These assertions find support in the findings of Moiseev³⁶ who proposed the following reaction:



According to Moiseev's report, if the above reaction is carried out in the absence of

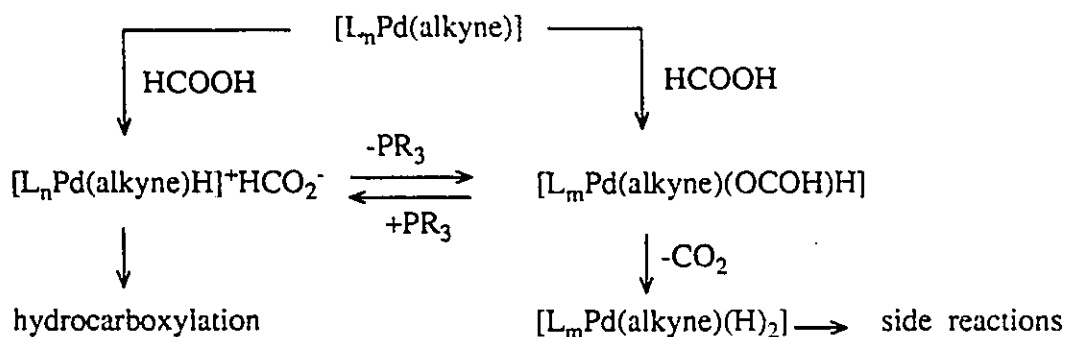
strongly coordinating ligands and in acetic acid as solvent, the tetranuclear clusters $[\text{Pd}(\text{CO})\text{OAc}]_4$ can be isolated in which the four Pd nuclei are held together by means of bridging carbonyl and acetate ligands, as well as Pd-Pd bonds. The presence of strongly coordinating ligands such as phenanthroline and bipyridine changes the tetrameric structure, depending on the Pd : ligand ratio. By drawing an analogy to these observations, we have supposed that in the present system the species $[\text{Pd}(\text{CO})_m(\text{PR}_3)_n]_x$ is formed in the presence of phosphine ligands and CO. The structure of this species will be assumed to be monomeric in order to simplify the arguments and illustrations; in principle, however, other structures containing two, three, or more nuclei can also be considered.

The complex $[\text{Pd}(\text{CO})_m(\text{PR}_3)_n]$ can then undergo ligand substitution (step B) and coordinate a molecule of alkyne. The central question is how this alkyne complex reacts with formic acid. We propose that formic acid reacts by forming a metal hydride species, in essence protonating the electron-rich metal centre (step C). Pd(0) species are electron-rich and are known⁶⁶ to form Pd-H bonds in the presence of strong acids. As discussed earlier, the formate anion can either coordinate to the metal to give a neutral compound, or act as a counter anion to the cationic species. The latter is more plausible in the present system for two reasons. First, the coordination of the formate anion would render it prone to decarboxylation, leading to a dihydride complex that would be incapable of inducing hydrocarboxylation and likely to cause alkyne hydrogenation to alkenes or alkanes. Second, unambiguous precedents exist^{57,67} for the displacement of weakly coordinating, labile anions (*e.g.*, chloride, acetate, triflate, formate) from the coordination sphere of metals by less labile ligands. In a relevant case, Yamamoto⁵⁷ has shown that a formate ligand can be displaced from the coordination sphere of Pd by phosphine ligands, as follows:



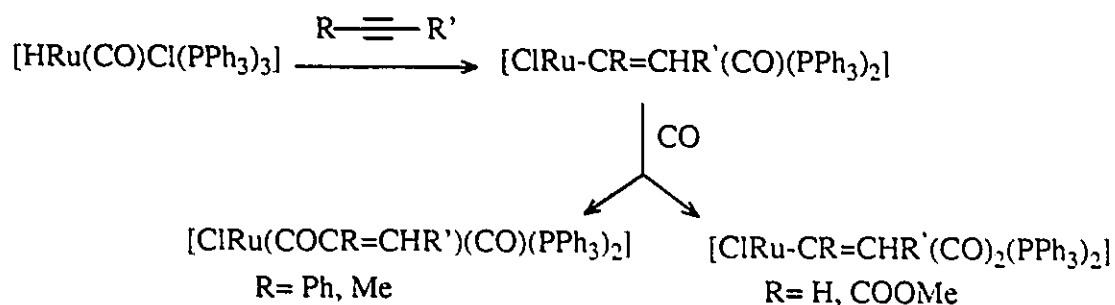
Therefore, it is conceivable that during the course of the catalysis in the present system, an equilibrium exists between two species in which the formate is either a non-coordinating counter anion or a ligand attached to the metal centre (Scheme 2.6). In the presence of suitable phosphine ligands, the formate will be displaced from the coordination sphere of the metal nucleus and the catalysis will proceed. The absence of suitable phosphine ligands, on the other hand, would drive the equilibrium partially or completely in the direction of the species with the coordinated formate. This, in turn, will facilitate formate decarboxylation and will lead to side reactions such as alkyne hydrogenation or polymerization.

Scheme 2.6



The hydrido(alkyne) intermediate, generated in step C (Scheme 2.5) from the protonation of the alkyne complex, would then undergo a 1,2-addition (insertion) of the alkyne triple bond to the Pd-H bond (step D). This kind of hydride additions, and the analogous alkyl additions, have been extensively studied for the past 20 years.⁶⁸ Evidently, the addition can take place either in a concerted manner or *via* a radical pathway, depending

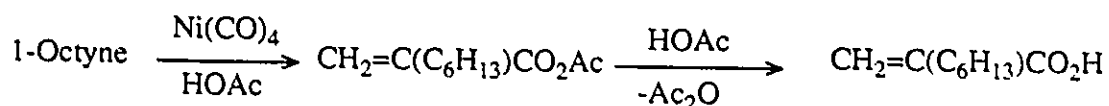
on the specific compound and the reaction conditions; the stereochemistry of the addition is also governed by a number of variables (*vide infra*). Regardless of the mode of hydride addition, an alkenyl ligand forms, which can then undergo a migratory insertion into a metal carbonyl bond to give a metal acyl compound (step E). Ros and coworkers have recently reported⁶⁹ exactly this sequence of reactions:



Interestingly, with these ruthenium alkenyl complexes the CO insertion step does not occur when the alkenyl carbon atom directly bonded to the metal centre bears a hydrogen or an electron withdrawing group like COOMe; instead, a dicarbonyl compound is formed. This observation is counter-intuitive, because the presence of electron withdrawing substituents in the indicated position should reduce the electron density at the metal centre, thereby weakening the M-CO backbonding and facilitating CO insertion. Whatever the reasons may be for this behaviour, it points to a possible reason why terminal alkynes bearing electron withdrawing substituents do not undergo hydrocarboxylation (*vide supra*).

The final step in the catalytic cycle is the cleavage of the palladium acyl intermediate which leads to the formation of the products and the regeneration of the catalyst (Scheme 2.5, step F). The most probable candidate for inducing such a cleavage is the formate counter anion which would give a mixed anhydride. Although our experimental results provide no direct evidence for the formation of a mixed anhydride, this idea seems feasible in light of a

few relevant observations made by others. For instance, in palladium-catalyzed carboxylation of vinyl triflates,⁷⁰ aryl halides,⁷¹ and optically active 1-arylethyl formates,⁷² the products have been presumed to form by a formate anion mediated cleavage of metal acyls to give mixed formic anhydrides as unstable intermediates. Moreover, Matsuda and coworkers⁷³ have shown that the $\text{Pd}(\text{OAc})_2/\text{NaOAc}$ catalyzed carboxylation of arenediazonium salts gives mixed aromatic acetic anhydrides, ArCOOAc , which are converted to aromatic acids upon work-up. Finally, Chiusoli and Cameroni^{12a} have reported that 1-octyne reacts with $\text{Ni}(\text{CO})_4$ in acetic acid to produce a mixed anhydride which can be detected by infrared spectroscopy; reaction with acetic acid converts the mixed anhydride to 2-methyleneoctanoic acid and acetic anhydride:



A remarkable point in the above reaction is that the same mixed anhydride and acid form even in the presence of methanol, indicating that cleavage by acetate anion is favoured over the nucleophilic attack by methanol to give the corresponding methyl ester. Of course, no competing nucleophiles are present in our system, making the formate anion-induced cleavage very plausible. Such a cleavage would result in a mixed formic acid anhydride, but these compounds are very unstable at higher than ambient temperatures⁷² and decompose readily to give the corresponding acid (Scheme 2.5, step G). In addition, this decomposition is autocatalytic in the presence of acids, bases, or water.⁷⁴

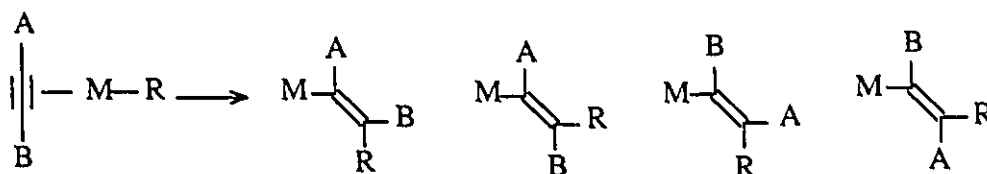
Alkyne hydrocarboxylation with oxalic acid probably follows a mechanism similar to that of the formic acid reaction. Thus, an analogous acyl intermediate would form in which oxalate is the counter anion; the cleavage of the metal acyl bond by the oxalate anion can then give a mixed oxalic anhydride, which would decompose to give the product acids.

The mechanism illustrated in Scheme 2.5 belongs to the class of "hydride" mechanisms discussed earlier. It is, of course, one possibility among a few other sequences of reactions which can be envisaged for the hydrocarboxylation of alkynes. An obvious alternative would be the "carboalkoxy" mechanism which has been favoured by Norton²⁵ and others (*vide supra*). Recall that it involves a nucleophilic attack on a M-CO species to form M-COOR (or M-COOH in the present case), which then undergoes insertion by the coordinated alkyne to give alkenyl intermediates. This mechanism was judged unlikely for the present system, because this type of nucleophilic attack generally occurs in basic, rather than acidic, reaction media.⁶³ Although in principle both water and the formate anion can act as nucleophiles in our reactions, the likelihood of this is not great because both of these are weak nucleophiles. In fact, the catalysis proceeds less efficiently with the more nucleophilic of these two reagents, *i.e.*, water.

Even though Scheme 2.5 presents a reasonable picture of "how" alkynes are hydrocarboxylated in the present system, it does not deal with some other mechanistic details, and falls short of explaining some of our experimental results. Some of these points are addressed in the following section.

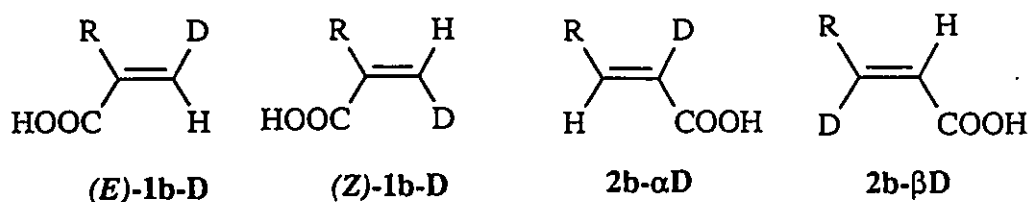
2.1.6 The alkyne insertion reaction

The insertion of π -coordinated alkynes into M-R (R= H, alkyl, alkenyl, or aryl) bonds has been known for over 30 years, and numerous examples of this reaction can be found in the literature of organometallic chemistry. Two main features of such insertions are the stereochemistry ("*cis*" vs. "*trans*") and the regiochemistry (α vs. β) of the addition step. Thus, the possible products of these reactions are shown below:



The stereo- and regiochemistry of the alkyne insertion step in the present catalytic reactions are discussed below in terms of the products of these reactions.

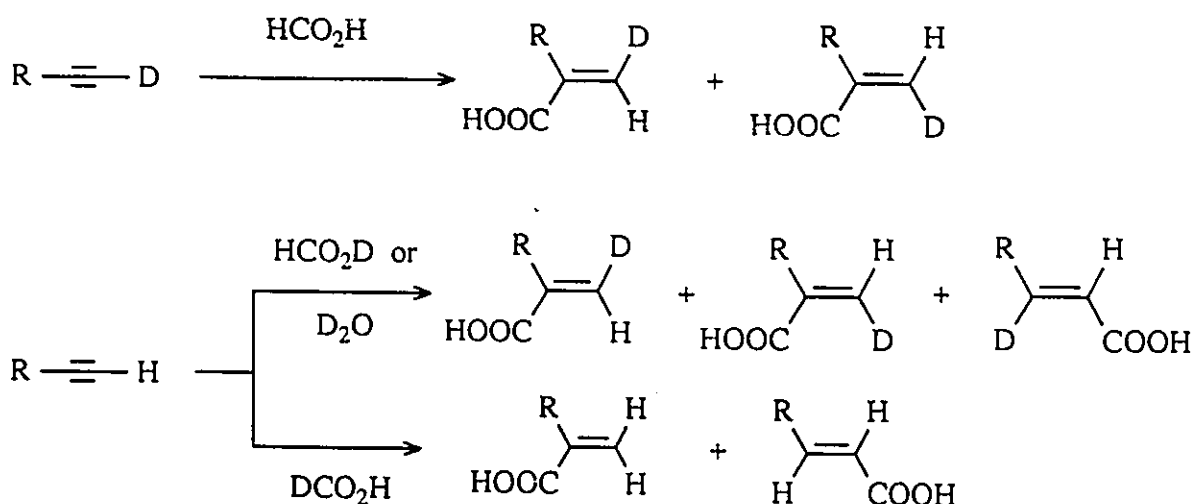
A. The stereochemistry of addition. With internal alkynes, the stereochemistry of addition was determined to be "cis" in both regioisomers by comparing the ^1H NMR chemical shifts of the vinyl protons to the corresponding values reported in the literature (*vide supra*). With the products of terminal alkyne reactions, however, the situation is somewhat more complicated. The 1,1-disubstituted product, for instance, is symmetrical at one end and yields no information about the stereochemistry of addition. If a terminal alkyne labelled at the C-1 position is used, the stereochemistry of this product would be distinguishable by ^1H NMR spectroscopy. Thus, the labelled alkyne 1-deuterio-4-phenyl-1-butyne was prepared and used in an otherwise standard catalytic experiment. The possible products of this reaction are shown below ($\text{R} = \text{PhCH}_2\text{CH}_2$):



The GC/MS spectra of the reaction products confirmed the incorporation of one

deuterium: $M^+ = 249$. The ^1H NMR spectrum of the product mixture consisted of two broad singlet resonances in the vinylic region. By comparison to the results of previous experiments with unlabelled 4-phenyl-1-butyne, these were assigned to (*E*)- and (*Z*)-**1b-D**; neither **2b- α D** nor **2b- β D** was detected in the reaction mixture. In accord with literature reports,²⁵ the more downfield vinylic resonance (6.32 ppm) was assigned to the (*E*) stereoisomer in which the H is cis to the carbonyl moiety. The integration of this resonance was 1.28 times more intense, indicating a 56:44 ratio for the (*E*) and (*Z*) products, respectively.

Three other experiments, complementary to the labelling experiment described above, were conducted by using *undeuterated* 4-phenyl-1-butyne with HCOOD , DCOOH , and D_2O . The experiment with HCOOD resulted in a 43:40:17 mixture of (*E*)- and (*Z*)-**1b-D**, and **2b- β D**, respectively. The experiment using DCOOH resulted in a 91:9 mixture of **1b** and **2b**, respectively, with no deuterium incorporation. When D_2O was used as the source of D^+ , the reaction yield was much less than that of the HCOOD reaction (7% vs. 63%), but the product distribution was not significantly different, consisting of (*E*)- and (*Z*)-**1b-D**, and **2b- β D** in a 33:45:22 ratio. These results can be summarized in the following reactions:



The following conclusions can be drawn from the above experiments:

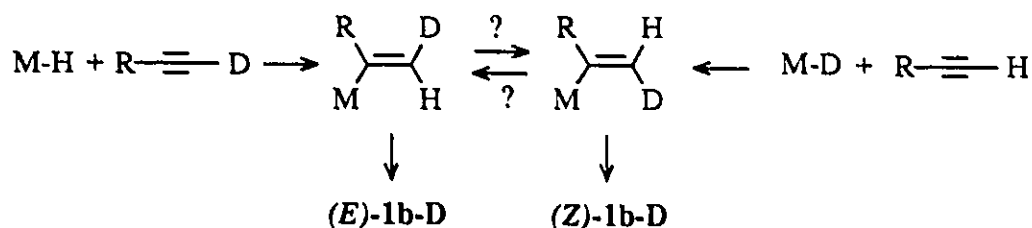
I. The retention of deuterium in the reaction of the labelled alkyne supports the assertion that during the course of the hydrocarboxylation reaction terminal alkynes do not undergo oxidative addition of the sp C-H bond.

II. That none of the above experiments lead to a product in which the incoming "H" (or "D") and "COOH" moieties end up being *gem* to each other, supports the exclusion of a metal vinylidene intermediate from the reaction mechanism proposed above.

III. That deuterium incorporation into a vinylic position in the product occurs with HCOOD but not with DCOOH demonstrates that formic acid reacts by protonating the metal centre, *i.e.*, by O-H(D) rather than sp^2 C-H(D) bond activation.

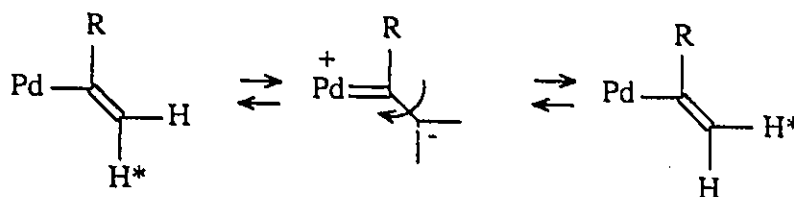
IV. The 1,1-disubstituted product, **1**, results from a combination of "*cis*" and "*trans*" additions of the "H" and "COOH" moieties, whereas the 1,2-disubstituted product, **2**, originates from a "*cis*" addition to give the (*E*) stereoisomer.

The first three of the above points had been mentioned earlier and do not warrant more discussion here, but the last one deserves some comment. The overall "*cis*" addition observed in both regioisomeric products of the internal alkyne reactions, and in the 1,2-disubstituted product of terminal alkynes can be attributed to a concerted insertion of the coordinated alkyne into the Pd-H bond. Such a process can not, however, explain the formation of a mixture of stereoisomers (*i.e.*, (*E*)- and (*Z*)-**1-D**) observed in the reaction of the labelled terminal alkyne above. The two stereoisomers in this case originate *via* either a concerted addition process followed by isomerization at the C=C bond of the coordinated alkenyl ligand,



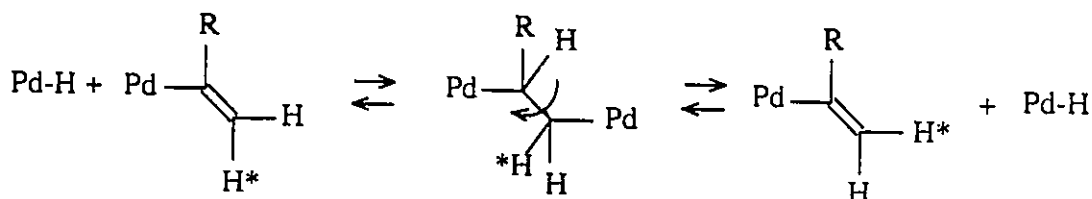
or a "*trans*" addition of the coordinated alkyne into the Pd-H bond. The literature of organo-metallic chemistry contains several reports of such net "*trans*" additions of alkynes into M-H or M-R bonds.⁷⁵⁻⁸⁷ For instance, Goldman⁷⁵ has also used deuterium labelling experiments to show that the 1,1-disubstituted alkenes formed by the insertion of terminal alkynes into a Rh-Ph bond have two stereoisomers arising from "*cis*" and "*trans*" additions. Jones⁷⁶ has isolated and characterized (X-ray) *cis* and *trans* rhodium alkenyl complexes arising from the insertion of electron poor alkynes into a Rh-H bond. Very recently, Tanke and Crabtree⁷⁷ showed that hydrosilylation of terminal alkynes can occur by either "*cis*" or "*trans*" additions of the alkyne into the M-H or M-SiR₃ bond. A theoretical study⁸⁸ has shown that a "*cis*" addition can occur by a more or less concerted process whereby the M-R bond approaches the alkyne in a coplanar, end-on manner to give the resultant *cis*-metal alkenyl species. The occurrence of "*trans*" additions, however, is not very well understood.

Through their sustained studies of alkyne insertions into Pt-H bonds, Clark and coworkers⁶⁸ have provided strong evidence for either radical or electron transfer mechanisms for the "*trans*" mode of addition. Some researchers have espoused these hypotheses,⁷⁶ but others have preferred other alternatives, such as bipolar *cis-trans* isomerization mechanisms.^{77,81-84} A typical example of such bipolar mechanisms can be envisaged here (Scheme 2.7) as an explanation for the observation of the "*trans*" addition products observed in the present study.

Scheme 2.7

The bipolar species shown above can be thought of as a metastable intermediate or simply as an extreme case of resonance delocalization. The main thrust of this mechanism is the notion that the C=C bond weakens enough to allow a rotation which results in the "trans" insertion product.

Another possibility involves a bimetallic intermediate, formed by an *intermolecular* hydride insertion into the metal alkenyl bond to give a μ^2 -alkyl ligand, shown below (Scheme 2.8); free rotation around the C-C single bond of this ligand followed by β -hydride elimination would allow *cis-trans* isomerization:

Scheme 2.8

In contrast, Otsuka *et al.*⁸⁷ have argued that most transition metal reaction mechanisms can not be adequately described in purely ionic, radical, or concerted terms, and most likely involve some combination of all of these concepts. They have put forth a concerted, kinetically and stereoelectronically controlled insertion mechanism with a four-

centred, bimolecular transition state which may be partially ionic or radical in character, depending on subtle stereoelectronic effects.

Evidently, the phenomenon of "*trans*" insertion can be explained by invoking a number of different mechanisms, none of which can be completely ruled out for all cases. The major difficulty in developing one generally acceptable and unifying mechanism is that the nature of these reactions and their stereochemical outcome are strongly influenced by such variables as solvent polarity, the presence of minute impurities like oxygen in the reaction media, the alkyne substituents, and, of course, the metal complex itself.⁶⁸ Consequently, no set of rules or guidelines exist to date for predicting *a priori* whether a given insertion will proceed in a "*cis*" or a "*trans*" manner.

B. Regiochemistry of addition. As discussed earlier, alkyne hydrocarboxylation in the present system produces two regioisomers in varying degrees of regioselectivity. With terminal alkynes, the regioselectivity is better than 80:20 in favour of the 1,1-disubstituted product with most substrates; the 1,2-disubstituted isomer is the main product with 3,3-dimethyl-1-butyne and the only one with (trimethylsilyl)acetylene (Table 2.1). With unsymmetrically substituted internal alkynes, on the other hand, the regioselectivity (ratio of 3:4) is generally lower, in the range of 35(±5):65(±5); with 4-methyl-2-pentyne, the regioselectivity is about 80:20.

Assuming that the alkyne inserts into a Pd-H rather than a Pd-COOH bond (Scheme 2.5), the question arises: What factors govern the regiochemistry of this reaction? More specifically, how do the electronic properties of the alkyne (*i.e.*, the degree of charge distribution between the triply bonded carbon atoms) and the steric bulk of the alkyne substituents control the regioselectivity? A survey of the reported cases of alkyne insertions into metal hydride bonds indicates that, like the stereochemistry of this reaction, the regiochemistry is

also variable, and factors like the solvent and the reaction temperature exert a strong influence over the regioselectivity. Schwartz has reported⁸⁹ that hydrozirconation of alkynes favours the addition of the hydride to the alkyne carbon bearing the more bulky substituent; the regioselectivity ranges from 55:45 for R= Et and R'= Me to 98:2 for R= *t*-Bu and R'= Me. In contrast, Pt-H bonds add to the alkyne carbon bearing the less bulky substituent.⁶⁸

Further examples can be found in the studies of Heck and Bergman on the analogous insertion of alkenes and alkynes into M-R (R= alkyl or aryl) bonds. Heck's results point to the predominance of steric factors in determining the regioselectivity of alkene insertions into Pd-R bonds.⁹⁰ Generally, these reactions lead to the addition of R to the least substituted carbon of the double bond. Similarly, Bergman and coworkers^{81a} have shown that alkyne insertion into Ni-Me and Ni-Ph bonds occurs at the less crowded carbon atom, thereby resulting in the formation of metal alkenyl ligands wherein the more bulky substituent is *gem* to the metal. These authors also demonstrated that electronic effects of the alkyne substituents are not crucial; instead, the regioselectivity is sensitive to only steric crowding. Curiously, however, "... it is the metal end of the Ni-CH₃ bond rather than the CH₃ group which behaves as the sterically *less* active substituent in the insertion transition state."^{81a}

The regioselectivity of the present system can also be attributed mainly to steric effects. Thus, with most of the terminal alkynes tested, the Pd-H bond tends to add preferentially to the less crowded carbon, *i.e.*, to the terminus. This is evident for terminal alkynes with small or medium sized substituents like (CH₂)₅CH₃, (CH₂)₃Cl, and *sec*-Bu. For alkynes with large substituents like *t*-Bu and SiMe₃, however, the opposite is true. These two cases can be rationalized by arguing that addition of Pd-H to the terminal carbon of these alkynes would place the sterically very demanding substituent closer to the metal and its other ligands. In other words, the energetics of the addition reaction are quite sensitive to the size of the substituent. Perhaps one exception to the above trend is phenylacetylene for which

addition to the terminal carbon is highly preferred (about 90-95%). This result is contrary to our expectations if the phenyl group is regarded to be at least as bulky as SiMe_3 .²³ Since phenylacetylene reacts like a terminal alkyne bearing a small substituent, we are forced to conclude that the electronic effects of the phenyl group effectively counteract its steric effects, thereby leading to the predominance of the 1,1-disubstituted products.

Steric effects also seem to be the main factor in determining the regioselectivity of internal alkyne reactions. The difference is that here the hydride adds to the more crowded carbon atom. One exception is in the hydrocarboxylation of 1-phenyl-1-butyne, where the hydride adds preferentially to the carbon bearing the less bulky Et group (68:32). It is as if in this case the effective steric bulk of the Et group is more than that of the Ph group! To complicate the matter further, the regioselectivities observed for the other three unsymmetrical alkynes ($\text{R} = \text{Bu}$, Ph, *i*-Pr and $\text{R}' = \text{Me}$) increases in the order *i*-Pr > Ph $\approx$ *n*-Bu, implying once again that the effective bulk of the Ph group is comparable to that of a small, straight chain alkyl group. It is noteworthy that regioselectivities of these reactions have been shown to be highly reproducible within a very narrow range of experimental error ($< \pm 5$) by repeating each experiment at least three times.

In summary, the regioselectivity of alkyne hydrocarboxylation in the present system seems to be affected mainly by steric bulk of the alkyne substituents. Based on the assumption that the alkyne inserts into the Pd-H bond of an intermediate in the catalytic cycle (Scheme 2.5), it was pointed out that with terminal alkynes the hydride tends to add to the less crowded, terminal carbon atom except for alkynes bearing very bulky substituents. With internal alkynes, the opposite was observed; however, the small number of the substrates tested do not allow any firm conclusions at this stage.

2.2 Experimental Section

General Comments. The solvents were distilled from appropriate drying agents (N_2 atmosphere). The gases (high purity grade) were purchased from commercial sources, and were passed through scrubbers (KOH, $CaCl_2$) prior to use. The alkynes (Farchan) were dried and distilled before use. The following materials were purchased from commercial sources and were used without further purification: acetone- d_6 , $CDCl_3$, D_2O , $HCOOH$, $DCOOH$, $HCOOD$, $PdCl_2$, $Fd(OAc)_2$, $Ni(OAc)_2$, 10% Pd/C , $Pd(OCOCF_3)_2$, $Pd(PPh_3)_4$, $CuCl_2$, PPh_3 , PBu_3 , $P(OPh)_3$, $dppb$, $dppp$, $dppe$, $t-BuLi$, oxalic acid.

^1H and ^{13}C NMR spectra were recorded on Varian Gemini 200-MHz and XL 300-MHz spectrometers at ambient temperature. ^1H NMR data are reported in the following format: chemical shift (multiplicity, coupling constant(s), assignment). The chemical shifts (δ) are measured in parts per million (ppm) and referenced to the residual solvent proton resonances which are internally calibrated against tetramethylsilane; coupling constants are in hertz. ^{13}C NMR data are reported in the following format: chemical shift (assignment). The chemical shifts are measured in ppm and referenced to the triplet resonance of $CDCl_3$ or the singlet resonance of the carbonyl carbon of acetone- d_6 , both of which are internally calibrated against tetramethylsilane. GC/MS analyses were performed on a VG 7070E mass analyzer, and high resolution mass spectra were recorded on a Kratos Concept 2H mass spectrometer.

2.2.1 General Procedure for The Catalytic Reactions

The catalytic reactions were carried out using a Parr stainless steel autoclave

equipped with a glass liner. The solvent and a stirring bar were placed inside the glass liner, and the starting materials were added in the following order: the metal catalyst, phosphine(s), alkyne, and formic acid (or other reagents). The liner was then placed inside the autoclave chamber which contained another 4 mL of the solvent. The autoclave was assembled, purged with CO gas by three fill-vent cycles, and then charged with CO gas up to the appropriate pressure. The autoclave assembly was then placed inside an oil bath sitting atop a heater/stirrer. The temperature of the oil bath was brought to the desired level and monitored during the reaction period.

After the reaction time had lapsed, the autoclave was taken out of the oil bath and allowed to cool. The gas(es) was vented, the autoclave disassembled, and the product mixture worked up as follows. The solvent was removed on the rotary evaporator, Et₂O was added to the residue, and the resulting mixture was transferred to a separatory funnel; filtration was often required at the latter step in order to remove insoluble materials (metal precipitates, phosphines, etc.). The Et₂O solution was extracted with 3 x 10 mL portions of a *ca.* 1 N aqueous NaOH solution, washed with 5 mL of distilled water, and dried over MgSO₄. Filtration of the Et₂O suspension, followed by removal of solvent, yielded an oily residue or a solid which was weighed and often, though not always, analyzed by ¹H NMR spectroscopy. Unless otherwise described, this residue consisted mainly of the starting phosphine(s) and other unidentified species.

The aqueous NaOH solution was made slightly acidic by adding 5 N HCl; this usually led to the formation of a cloudy, off-white suspension. Extraction of the aqueous suspension with Et₂O rendered the aqueous layer clear and colorless; this was discarded. The organic layer was dried over MgSO₄, filtered, concentrated, and kept under vacuum for 15-30 minutes. The resulting oil or solid was weighed and analyzed by NMR, IR, and GC/MS spectroscopy. When necessary, the product was further purified either by repeating the above

extraction procedure, or by esterification and column chromatography, as described for individual cases.

2.2.2 The Specific Experiments

This section contains detailed accounts of the individual experiments carried out during the course of this study. The majority of these accounts describe the experiments which were carried out to optimize the reaction conditions and to probe the reaction mechanism. The first thirteen, however, describe the experiments in which optimal reaction conditions were used and which, in general, gave the best results. The following items are included in each of the latter accounts:

- a. The name of the compound synthesized and its Chemical Abstracts registry number (Chemical Abstracts names in boldface type, other names inside the parentheses and in normal type, registry numbers in italic type and inside square brackets);
- b. The Arabic number which will be used throughout this thesis to refer to the corresponding compound (the Glossary of Compounds, included at the beginning of the thesis, also contains the compound names and the corresponding numerical designations);
- c. The experimental details and complete spectral data obtained for the characterization of the compounds.

α -Methylenebenzeneacetic acid [492-38-6] (Atropic acid), **1a**, and (*E*)-3-phenyl-2-propenoic acid [621-82-9] (cinnamic acid), **2a**. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (27 mg, 0.103 mmol), dppb (20 mg, 0.0469 mmol), phenylacetylene (98%, 255 mg, 2.45 mmol), formic acid (98%, 232 mg, 4.94 mmol), and DME (5 mL) for 18 h at 108 °C under 120 psi of CO gas pressure. The final reaction mixture

was worked up as described above (See "General Procedure for The Catalytic Reactions", section 2.2.1) to give 23 mg of a yellow oil from the organic layer and 356 mg of an off-white, crystalline solid from the aqueous layer. The ^1H NMR spectra of these materials revealed that the oil was a mixture of the phosphines and other unidentified species, and the solid was a 93:7 mixture of **1a** and **2a**, respectively. (Combined yield= 96%).

^1H NMR (δ , CDCl_3). **1a**: 8-10 (broad, COOH), 7.4 (m, phenyl protons), 6.53 (d, $^2J_{\text{H-H}} = 1.2$, vinylic proton *cis* to COOH), 6.01 (d, $^2J_{\text{H-H}} = 1.2$, vinylic proton *trans* to COOH); **2a**: 8-10 (broad, COOH), 7.79 (d, $^3J_{\text{H-H}} = 15.9$, vinylic proton *cis* to COOH), 7.4 (m, phenyl protons), 6.45 (d, $^3J_{\text{H-H}} = 16.0$, vinylic proton *gem* to COOH). The present data match those reported in the literature.^{6,91,92a}

^{13}C NMR (δ , CDCl_3). **1a**: 172.4 (C=O), 140.6 ($=\text{C}(\text{COOH})\text{Ph}$), 136.1 (*ipso* C of the phenyl ring), 129.6 ($=\text{CH}_2$), 128.4, 128.1 (*o*- & *m*-C of the phenyl ring), 128.3 (*p*-C of the phenyl ring).

GC/MS. Trimethylsilyl esters of **1a** & **2a**: $M^+ = 220$.

HRMS. High resolution MS, calculated for $\text{C}_9\text{H}_8\text{O}_2$: 148.161; found: 148.05254.

α -Methylene-benzenebutanoic acid [128038-39-1], **1b**, and **(E)-5-phenyl-2-pentenoic acid** [55320-96-2], **2b**. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), 4-phenyl-1-butyne (98%, 333 mg, 2.56 mmol), formic acid (98%, 160 mg, 3.47 mmol), and DME (6 mL) for 22 h at 105 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 389 mg of a pale yellow oil from the aqueous layer. Spectral analysis of this oil showed that it was a 94:6 mixture of **1b** and **2b**, respectively. (Combined yield= 86%)

^1H NMR (δ , CDCl_3). **1b**: 10.7 (br, COOH), 7.30 (m, phenyl protons), 6.32 (d, $^2J_{\text{H-H}} = 1.5$, vinylic proton *cis* to COOH), 5.62 (d, $^2J_{\text{H-H}} = 1.1$, vinylic proton *trans* to COOH), 2.84

(m, $\text{CH}_2\text{C}(\text{COOH})=$), 2.65 (m, $\text{Ph}-\text{CH}_2$); **2b**: 10.8 (br, COOH), 7.21 (m, phenyl protons), 5.85 (d, $^3J_{\text{H-H}} = 15.7$, $=\text{CH}(\text{COOH})$), 2.78 (m, $\text{CH}_2\text{CH}=\text{}$), 2.65 (m, PhCH_2). The resonance due to the second vinylic proton (dt, $=\text{CHCH}_2$) is presumed to be buried under the phenyl resonances. The present data match those reported in the literature.^{6,93}

¹³C NMR (δ , CDCl_3). **1b**: 172.8 (COOH), 141.2 ($\text{CH}_2-\text{C}(\text{COOH})=$), 139.2 (*ipso* carbon of the phenyl ring), 128.5 & 128.4 (*o*- and *m*-carbon atoms of the phenyl ring), 128.0 (*p*-carbon atom of the phenyl ring), 126.0 ($=\text{CH}_2$), 34.8 & 33.5 (PhCH_2CH_2); **2b**: 172.2 (COOH), 151.2 ($=\text{CH}(\text{COOH})$), 140.2 (*ipso* carbon of the phenyl ring), 128.4 & 127.9 (*o*- and *m*-carbon atoms of the phenyl ring), 126.2 (*p*-carbon atom of the phenyl ring), 121.1 ($\text{CH}_2-\text{CH}=\text{}$), 34.1 & 34.0 (PhCH_2CH_2).

GC/MS. Trimethylsilyl ester of **1b**: $M^+ = 248$; trimethylsilyl ester of **2b**: $M^+ - \text{CH}_3 = 233$.

2-Methyleneoctanoic acid [3760-10-9], 1c, and (E)-2-nonenic acid [14812-03-4], 2c. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (56 mg, 0.214 mmol), 1-octyne (98%, 328 mg, 2.98 mmol), formic acid (98%, 196 mg, 4.26 mmol), and DME (6 mL) for 29 h at 105 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 386 mg of a pale yellow oil from the aqueous layer. Spectral analysis of the latter showed that it was an 87:13 mixture of **1c** and **2c**, respectively. (Combined yield = 83%)

¹H NMR (δ , CDCl_3). **1c**: 6.26 (d, $^2J_{\text{H-H}} = 1.4$, vinylic proton *cis* to COOH), 5.62 (d, $^2J_{\text{H-H}} = 1.4$, vinylic proton *trans* to COOH), 2.27 (t, $^3J_{\text{H-H}} = 7.3$, $\text{CH}_2\text{C}(\text{COOH})=$), 1.45-1.26 (m, $\text{CH}_3(\text{CH}_2)_4$), 0.86 (t, $^3J_{\text{H-H}} = 6.4$, CH_3); **2c**: 7.07 (dt, $^3J_{\text{H-H}} = 15.6$ & 7.0, $=\text{CHCH}_2-$), 5.80 (dt, $^3J_{\text{H-H}} = 15.6$ & 1.6, $=\text{C}(\text{COOH})\text{H}$), 2.29 (m, $=\text{CHCH}_2-$), 1.45-1.26 (m, $\text{CH}_3(\text{CH}_2)_4$), 0.86 (t, $^3J_{\text{H-H}} = 6.4$, CH_3). The present data match those reported in the literature.⁶

¹³C NMR (δ , CDCl_3). **1c**: 173.2 (COOH), 140.3 ($\text{CH}_2-\text{C}(\text{COOH})=$), 126.9 ($=\text{CH}_2$),

31.6 ($\underline{\text{CH}_2\text{C}(\text{COOH})=}$), 31.4 ($-\underline{\text{CH}_2\text{CH}_2\text{C}(\text{COOH})=}$), 28.9 & 28.3 ($\text{CH}_3\text{CH}_2\underline{\text{CH}_2\text{CH}_2}$), 22.6 ($\text{CH}_3\underline{\text{CH}_2}$), 14.1 ($\underline{\text{CH}_3}$).

GC/MS. Trimethylsilyl ester of **1c**: $\text{M}^+ = 228$; trimethylsilyl ester of **2c**: $\text{M}^+ - \text{CH}_3 = 213$.

5-Cyano-2-methylenepentanoic acid, 1d, and (E)-6-cyano-2-hexenoic acid [56453-87-3], 2d. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (56 mg, 0.214 mmol), 5-cyano-1-pentyne (98%, 268 mg, 2.88 mmol), formic acid (98%, 218 mg, 4.73 mmol), and DME (5 mL) for 16 h at 100 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 345 mg of a pale yellow oil from the aqueous layer. Spectral analysis of the latter showed that it was a 94:6 mixture of **1d** and **2d**, respectively. (Combined yield= 86%)

^1H NMR (δ , CDCl_3). **1d**: 10.9 (br, COOH), 6.34 (s, vinylic proton *cis* to COOH), 5.72 (d, $^2J_{\text{H-H}} = 1.1$, vinylic proton *trans* to COOH), 2.43 (t, $^3J_{\text{H-H}} = 7.4$, $-\underline{\text{CH}_2\text{C}(\text{COOH})=}$), 2.33 (t, $^3J_{\text{H-H}} = 7.0$, $\text{NC}-\underline{\text{CH}_2}$), 1.84 (quintet, $^3J_{\text{H-H}} = 7.4$, $\text{NC}-\text{CH}_2\underline{\text{CH}_2}$); **2d** (ref. 126): 10.9 (br, COOH), 6.99 (dt, $^3J_{\text{H-H}} = 15.7$ & 6.8, $=\underline{\text{CHCH}_2-}$), 5.87 (dt, $^3J_{\text{H-H}} = 15.7$ & 0.8, $=\text{C}(\text{COOH})\underline{\text{H}}$), 2.39 (m, $=\text{CHCH}_2-$), 2.33 (t, $^3J_{\text{H-H}} = 7.0$, $\text{NC}-\underline{\text{CH}_2}$), 1.84 (quintet, $^3J_{\text{H-H}} = 7.4$, $\text{NC}-\text{CH}_2\underline{\text{CH}_2}$). The present data match those reported in the literature.²⁸

^{13}C NMR (δ , CDCl_3). **1d**: 172.1 ($\underline{\text{COOH}}$), 137.8 ($-\text{CH}_2\underline{\text{C}(\text{COOH})=}$), 129.1 ($=\underline{\text{CH}_2}$), 119.3 ($\underline{\text{CN}}$), 30.5 ($\underline{\text{CH}_2\text{C}(\text{COOH})=}$), 24.1 ($\text{NC}-\underline{\text{CH}_2}$), 16.5 ($\text{NCCH}_2\underline{\text{CH}_2}$).

GC/MS. Trimethylsilyl esters of **1d** & **2d**: $\text{M}^+ - \text{CH}_3 = 196$.

5-Chloro-2-methylenepentanoic acid [117929-81-4], 50e, and (E)-6-chloro-2-hexenoic acid [72448-94-3], 51e. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (55 mg, 0.210 mmol), 5-chloro-1-pentyne (98%, 283 mg, 2.76

nmol), formic acid (98%, 198 mg, 4.30 mmol), and DME (5 mL) for 16 h at 95 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 315 mg of a pale yellow oil from the aqueous layer. Spectral analysis of the latter showed that it was an 89:11 mixture of **1e** and **2e**, respectively. (Combined yield= 77%)

¹H NMR (δ , CDCl₃). **1e**: 6.33 (s, vinylic proton *cis* to COOH), 5.71 (d, ²J_{H-H} = 1.1, vinylic proton *trans* to COOH), 3.52 (t, ³J_{H-H} = 6.5, Cl-CH₂), 2.44 (t, ³J_{H-H} = 6.9, -CH₂-C(COOH)=), 1.94 (quintet, ³J_{H-H} = 7.3, Cl-CH₂CH₂CH₂); **2e**: 7.03 (dt, ³J_{H-H} = 15.6 & 7.0, =CH-CH₂), 5.86 (dt, ³J_{H-H} = 15.6, ⁴J_{H-H} = 1.5, =CH(COOH)), 3.52 (t, ³J_{H-H} = 6.5, Cl-CH₂), 2.44 (t, ³J_{H-H} = 6.9, -CH₂C(COOH)=), 1.94 (quintet, ³J_{H-H} = 7.3, Cl-CH₂CH₂CH₂). The present data match those reported in the literature.⁹⁴

¹³C NMR (δ , CDCl₃). **1e**: 172.7 (C=O), 138.3 (-CH₂C(COOH)=), 128.5 (=CH₂), 44.1 (ClCH₂), 30.9 (CH₂C(COOH)=), 28.7 (ClCH₂CH₂); **2e**: 171.2 (C=O), 151.0 (-CH₂C(COOH)=), 121.6 (=CH₂), 43.6 (ClCH₂), 30.5 (CH₂C(COOH)=), 29.3 (ClCH₂CH₂).

GC/MS. Trimethylsilyl esters of **1e** & **2e**: M⁺ - CH₃ = 205.

3-Methyl-2-methylenevaleric acid [25044-06-8] (3-methyl-2-methylenepentanoic acid), **1f**, and (*E*)-**4-methyl-2-hexenoic acid** [51724-49-3], **2f**. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), dppb (25 mg, 0.0586 mmol), 3-methyl-1-pentyne (98%, 210 mg, 2.56 mmol), formic acid (98%, 211 mg, 4.58 mmol), and DME (5 mL) for 17 h at 106 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 232 mg of a colourless oil from the aqueous layer. Spectral analysis of the latter showed that it was an 87:13 mixture of **1f** and **2f**, respectively. (Combined yield= 70%)

¹H NMR (δ , CDCl₃). **1f** (ref. 150): 6.31 (d, ²J_{H-H} = 1.0, vinylic proton *cis* to COOH), 5.59 (d, ²J_{H-H} = 0.8, vinylic proton *trans* to COOH), 2.58 (m, -CH(Me)CH₂), 1.39 (m,

CH₃CH₂CH(Me)), CH₃CH₂), 1.06 (d, ³J_{H-H} = 6.5, CH(Et)CH₃), 0.84 (t, ³J_{H-H} = 7.5, CH₃CH₂); **2f**: 6.97 (dd, ³J_{H-H} = 15.7 & 7.9, =CH(CH(Me)Et)), 5.77 (dd, ³J_{H-H} = 15.7, ⁴J_{H-H} = 1.2, =CH(COOH)), 2.20 (m, -CH(Me)CH₂), 1.55 (m, CH₃CH₂CH(Me)), 1.04 (d, ³J_{H-H} = 9.7, CH(Et)CH₃), 0.86 (t, ³J_{H-H} = 7.5, CH₃CH₂). The present data match those found in the literature.^{91,95}

¹³C NMR (δ, CDCl₃). **1f**: 173.4 (COOH), 145.2 (-CH(Me)C(COOH)=), 125.3 (=CH₂), 35.7 (CH(Me)Et), 28.6 (CH₃CH₂), 19.3 (CH₃CH(Et)), 11.6 (CH₃CH₂); **2f**: 172.7 (COOH), 157.5 (CH(COOH)=), 119.1 (=CH(CHMe)), 38.2 (CH(Me)Et), 28.7 (CH₃CH₂), 18.7 (CH₃CH(Et)), 11.8 (CH₃CH₂).

GC/MS. Trimethylsilyl esters of **1f** & **2f**: M⁺ = 200.

1160. 3,3-Dimethyl-2-methylenebutanoic acid [4423-82-9], **1g**, and (*E*)-4,4-dimethylpentenoic acid [16666-45-8], **2g**. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (27 mg, 0.103 mmol), dppb (23 mg, 0.0539 mmol), 3,3-dimethylbutyne (240 mg, 2.93 mmol), formic acid (98%, 253 mg, 5.50 mmol), and DME (5 mL) for 17.5 h at 102 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 266 mg of a pale yellow oil from the aqueous layer. Spectral analysis of the latter showed that it was a 21:79 mixture of **1g** and **2g**, respectively. (Combined yield = 70%)

¹H NMR (δ, CDCl₃). **1g** (ref. 175): 6.16 (s, vinylic proton *cis* to COOH), 5.62 (d, ²J_{H-H} = 0.9, vinylic proton *trans* to COOH), 1.20, (s, C(CH₃)₃); **2g**: 7.07 (d, ³J_{H-H} = 15.9, vinylic proton *cis* to COOH), 5.72 (d, ³J_{H-H} = 15.9, =CH(COOH)), 1.07 (s, C(CH₃)₃). The present data match those reported in the literature.^{96,97}

¹³C NMR (δ, CDCl₃). **1g**: 173.6 (COOH), 148.9 (=C(CMe₃)(COOH)), 124.2 (=CH₂), 34.6 (CMe₃), 29.3 (C(CH₃)₃); **2g**: 173.1 (COOH), 161.9 (=CH(COOH)), 116.1 (=CHC(Me)₃), 33.9 (CMe₃), 28.5 (C(CH₃)₃).

GC/MS. Trimethylsilyl esters of **1g** & **2g**: $M^+ = 200$.

(E)-3-Trimethylsilyl-2-propenoic acid [58207-98-0], **2h**. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), dppb (23 mg, 0.0539 mmol), (trimethylsilyl)acetylene (98%, 281 mg, 2.87 mmol), formic acid (98%, 266 mg, 5.77 mmol), and DME (5 mL) for 24 h at 101 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 262 mg of a pale yellow oil from the aqueous layer. Spectral analysis of the latter showed that it was **2h**. (Yield= 63%)

^1H NMR (δ , CDCl_3). **2h** (ref. 164): 7.37 (d, $^3J_{\text{H-H}} = 18.9$, $\text{SiMe}_3\text{CH=}$), 6.22 (d, $^3J_{\text{H-H}} = 18.9$, $=\text{CH}(\text{COOH})$), 0.12 (s, $\text{Si}(\text{CH}_3)_3$). The present data match those reported in the literature.⁹⁸

^{13}C NMR (δ , CDCl_3). **2h**: 171.3 (COOH), 153.0 ($=\text{CH}(\text{COOH})$), 133.2 ($=\text{CH}(\text{SiMe}_3)$), -2.0 ($\text{Si}(\text{CH}_3)_3$).

GC/MS. Trimethylsilyl ester of **2h**: $M^+ - \text{Me} = 201$.

(E)-2-ethylidene-hexanoic acid [105027-56-3], **3a**, and **(E)-2-methyl-2-heptenoic acid** [79140-80-0], **4a**. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), dppb (23 mg, 0.0539 mmol), 2-heptyne (257 mg, 2.68 mmol), formic acid (98%, 250 mg, 5.43 mmol), and DME (6 mL) for 23 h at 107 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 312 mg of a colourless oil from the aqueous layer. Spectral analysis of the latter showed that it was a 38:62 mixture of **3a** and **4a**, respectively. (Combined yield= 82%)

^1H NMR (δ , CDCl_3). **3a**: 6.98 (q, $^3J_{\text{H-H}} = 7.2$, $=\text{CHMe}$), 2.28 (t, $^3J_{\text{H-H}} = 7.1$, $=\text{C}(\text{COOH})-\text{CH}_2$), 1.81 (m, $\text{CH}_3-\text{C=}$), 1.34 (m, $\text{CH}_3(\text{CH}_2)_2$), 0.89 (t, $^3J_{\text{H-H}} = 7.0$, CH_2CH_3); **4a**: 6.89 (tq, $^3J_{\text{H-H}} = 7.5$, $^4J_{\text{H-H}} = 1.4$, $=\text{CHCH}_2$), 2.18 (q, $^3J_{\text{H-H}} = 6.8$, $=\text{CH}-\text{CH}_2$), 1.81 (m,

$=C(COOH)CH_3$), 1.34 (m, $CH_3(CH_2)_2$), 0.89 (t, $^3J_{H-H} = 7.1$, CH_2CH_3). The present data match those reported in the literature.^{6,18,99}

^{13}C NMR (δ , $CDCl_3$). **3a**: 173.8 ($\underline{C}OOH$), 140.0 ($=\underline{C}HMe$), 132.9 ($=\underline{C}(Me)COOH$), 31.1 ($\underline{C}H_2CH=$), 25.8 ($CH_3CH_2\underline{C}H_2$), 22.6 ($CH_3\underline{C}H_2$), 14.4 ($\underline{C}H_3-CH=$), 13.9 ($\underline{C}H_3CH_2$); **4a** (ref. 14): 174.0 ($\underline{C}OOH$), 145.5 ($=\underline{C}HCH_2-$), 126.9 ($=\underline{C}(Me)COOH$), 30.5 ($\underline{C}H_2CH=$), 28.6 ($CH_3CH_2\underline{C}H_2$), 22.4 ($CH_3\underline{C}H_2$), 13.8 ($\underline{C}H_3CH_2$), 11.9 ($\underline{C}H_3-C=$).

GC/MS. Trimethylsilyl esters of **3a** and **4a**: $M^+ = 214$.

(E)-2-(1-methylethyl)-2-butenic acid [94773-28-1], **3b**, and **(E)-2,4-dimethyl-2-pentenoic acid** [3876-52-6], **4b**. The general procedure was followed using $Pd(OAc)_2$ (6 mg, 0.027 mmol), PPh_3 (31 mg, 0.118 mmol), $dppb$ (23 mg, 0.0539 mmol), 4-methyl-2-pentyne (224 mg, 2.73 mmol), formic acid (98%, 262 mg, 5.69 mmol), and DME (5 mL) for 20 h at 101 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 203 mg of a colorless oil from the aqueous layer. Spectral analysis of the latter showed that it was a 20:80 mixture of **3b** and **4b**, respectively. (Combined yield= 58%)

^1H NMR (δ , $CDCl_3$). **3b**: 6.84 (q, $^3J_{H-H}=7.1$, vinylic proton), 2.91 (septet, $^3J_{H-H}=7.1$, $Me_2CH-C(COOH)=$), 1.79 (d, 7.1, $\underline{C}H_3CH=$), 1.16 (d, $^3J_{H-H}=7.0$, $(\underline{C}H_3)_2CH-C(COOH)=$); **4b**: 7.00 (dq, $^3J_{H-H}=9.8$, $^4J_{H-H}=1.4$, vinylic proton), 2.63 (m, $Me_2CH-CH=$), 1.82 (d, $^4J_{H-H}=1.4$, $\underline{C}H_3C(COOH)=$), 1.07 (d, $^3J_{H-H}=6.6$, $(\underline{C}H_3)_2CH-CH=$). The present data match those reported in the literature.^{100,101}

^{13}C NMR (δ , $CDCl_3$). **3b**: 173.4 ($\underline{C}OOH$), 137.8 ($=\underline{C}(COOH)(i-Pr)$), 124.8 ($=\underline{C}HMe$), 26.7 ($\underline{C}HMe_2$), 20.5 ($(\underline{C}H_3)_2CH$), 14.0 ($=CH\underline{C}H_3$); **4b**: 174.2 ($\underline{C}OOH$), 151.6 ($=\underline{C}H(i-Pr)$), 138.6 ($=\underline{C}Me(COOH)$), 28.0 ($\underline{C}H(Me)_2$), 21.7 ($(\underline{C}H_3)_2CH$), 11.8 ($\underline{C}H_3-C(COOH)=$).

GC/MS. Trimethylsilyl esters of **3b** & **4b**: $M^+ = 200$.

(E)- α -ethylidene-benzeneacetic acid [4412-10-6] (*(E)*-2-Phenylcrotonic acid), **3c**, and *(E)*-2-methyl-3-phenyl-2-propenoic acid [1895-97-2] (*(E)*- α -methylcinnamic acid), **4c**. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (23 mg, 0.0539 mmol), PPh₃ (30 mg, 0.115 mmol), 1-phenyl-1-propyne (99%, 300 mg, 2.59 mmol), formic acid (98%, 214 mg, 4.64 mmol), and DME (5 mL) for 16 h at 106 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 403 mg of a pale yellow oil (solidified slowly to an off-white solid) from the aqueous layer. Spectral analysis of the latter showed that it was a 42:58 mixture of **3c** and **4c**, respectively. (Combined yield= 96%)

¹H NMR (δ , CDCl₃). **3c**: 7.39 (m, phenyl protons), 7.31 (partly obscured by the multiplet resonance due to the aromatic protons) (m, =C(Me)H), 1.75 (d, ³J_{H-H} = 7.2, =CH(CH₃)); **4c**: 7.80 (d, ⁴J_{H-H} = 1.4, =CH(Ph)), 7.39 (m, phenyl protons), 2.12 (d, ⁴J_{H-H} = 1.4, =C(COOH)CH₃). The present data match those reported in the literature^{92b,102-104} and confirm the (*E*) conformation assigned to these compounds.

¹³C NMR (δ , CDCl₃). **3c**: 172.9 (COOH), 142.9 (=CHMe), 134.4 (=C(COOH)Ph), 129.0, 128.4, 128.7, 128.1 (Carbons of the phenyl ring), 15.8 (=CHCH₃); **4c**: 174.6 (COOH), 141.2 (=CHPh), 135.5 (=C(COOH)Me), 129.8, 128.4, 127.6, 127.5 (Carbons of the phenyl ring), 13.7 (=C(COOH)CH₃). Assignments of the non-aromatic carbons were confirmed by HETCOR and DEPT spectra.

GC/MS. Trimethylsilyl esters of **3c** & **4c**: M⁺= 234.

(E)- α -Propylidene-benzeneacetic acid [3127-88-6], **3d**, and *(E)*-2-(Phenyl-methylene)-butanoic acid [26197-64-8] (*(E)*- α -ethylcinnamic acid), **4d**. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), dppb (23 mg, 0.0539 mmol), 1-Phenyl-1-butyne (98%, 347 mg, 2.67 mmol), formic acid (98%, 256 mg, 5.58 mmol), and DME (5 mL) for 24 h at 101 °C under 120 psi of CO gas

pressure. Work-up in the usual manner gave 428 mg of a pale yellow oil from the aqueous layer. Spectral analysis of the latter showed that it was a 64:36 mixture of **3d** and **4d**, respectively. (Combined yield= 91%)

^1H NMR (δ , CDCl_3). **3d**: 10.3 (br, COOH), 7.33 (m, phenyl protons), 7.20 (t, $^3J_{\text{H-H}} = 7.5$, $=\text{CH}(\text{Et})$), 2.12 (quintet, $^3J_{\text{H-H}} = 7.6$, $=\text{CH}(\text{CH}_2\text{CH}_3)$), 1.02 (t, $^3J_{\text{H-H}} = 7.5$, CH_2CH_3); **4d**: 10.3 (br, COOH), 7.77 (s, $=\text{CH}(\text{Ph})$), 7.33 (m, phenyl protons), 2.55 (q, $^3J_{\text{H-H}} = 7.5$, CH_2CH_3), 1.19 (t, $^3J_{\text{H-H}} = 7.5$, CH_2CH_3). The present data match those reported in the literature.^{93,105}

^{13}C NMR (δ , CDCl_3). **3d**: 172.8 (COOH), 149.3 ($=\text{CH}(\text{Et})$), 134.7 ($=\text{C}(\text{COOH})\text{Ph}$), 132.7, 129.7, 128.7, 128.5, 128.0 (phenyl carbons), 23.2 (CH_3CH_2), 13.2 (CH_3CH_2); **4d**: 174.1 (COOH), 140.8 (CHPh), 135.4 ($=\text{C}(\text{COOH})\text{Et}$), 133.9, 129.5, 129.4, 128.2, 127.6 (phenyl carbons), 20.6 (CH_3CH_2), 13.8 (CH_3CH_2).

GC/MS. Trimethylsilyl esters of **3d** and **4d**: $M^+ = 248$.

(E)- α -(Phenylmethylene)-benzeneacetic acid [91-48-5] ((E)-2,3-diphenyl-2-propenoic acid), **3e**. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (23 mg, 0.0539 mmol), diphenylacetylene (99%, 482 mg, 2.71 mmol), formic acid (98%, 227 mg, 4.94 mmol), and DME (5 mL) for 16.5 h at 100 °C under 120 psi of CO gas pressure. Work-up in the usual manner gave 542 mg of a white solid from the aqueous layer. Spectral analysis of the latter showed that it was **3e**. (Yield= 89%)

^1H NMR (δ , CDCl_3). 7.92 (s, $=\text{CH}(\text{Ph})$), 7.37-7.06 (m, Ph). The present data match those reported in the literature.^{92c}

^{13}C NMR (δ , CDCl_3). 173.3 (COOH), 142.5 ($=\text{CPh}(\text{H})$), 135.2, 134.2, 131.6 (*ipso* carbons of the two rings and $\text{CPh}(\text{COOH})$), 130.8, 129.7, 128.7, 128.2 (*o*- and *m*-carbons of

the two rings), 129.5, 128.4 (*p*-carbons of the two rings).

MS. Direct probe, electron impact (*m/e*, relative intensity): 224.0 (100%), 179.0 (94%), 178.0 (73%).

The attempted hydrocarboxylation of some terminal alkynes

Methyl propynoate. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (29 mg, 0.111 mmol), methyl propynoate (H-CC-COOMe, 98%, 229 mg, 2.72 mmol), formic acid (98%, 139 mg, 3.03 mmol), and DME (6 mL) for 22 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave 36 mg of an orange oil from the aqueous layer. The ¹H NMR spectrum of this oil contained many resonances in the regions 9-6 ppm and 4-3 ppm. No further attempts were made to identify this mixture of products.

3-Butyn-2-one. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (29 mg, 0.111 mmol), 3-butyn-2-one (98%, 199 mg, 2.93 mmol), formic acid (98%, 204 mg, 4.43 mmol), and DME (5 mL) for 22.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave 70 mg of a red oil from the aqueous layer. The ¹H NMR spectrum of this oil showed very broad resonances; no further attempt was made to identify this material.

An analogous reaction in the presence of dppb also failed to hydrocarboxylate this alkyne.

2-Ethynylpropene. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), 2-ethynylpropene (98%, 188 mg, 2.85 mmol), formic acid (98%, 155 mg, 3.37 mmol), and DME (5 mL) for 22.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave 109 mg of a yellow oil from the aqueous layer, which showed very complicated and broad resonances in its ¹H NMR spectrum. No further attempt

was made to identify this material.

Ethyl ethynyl ether. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (58 mg, 0.221 mmol), ethyl ethynyl ether (50%, 185 mg, 2.65 mmol), formic acid (98%, 229 mg, 4.99 mmol), and DME (6 mL) for 21.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave 7 mg of a brown oil from the aqueous layer. The ^1H NMR of this oil was very complex; no further attempts were made to identify the mixture.

The effects of various phosphines

$\text{P}(\text{OPh})_3$. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), $\text{P}(\text{OPh})_3$ (64 mg, 0.206 mmol), 1-octyne (98%, 310 mg, 2.82 mmol), formic acid (98%, 263 mg, 5.72 mmol), and DME (10 mL) for 21 h at 95 °C under 120 psi of CO gas pressure. Standard work-up gave 5 mg of a pale yellow oil from the aqueous layer. No attempt was made to identify this oil.

PBu_3 . The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PBu_3 (95%, 35 mg, 0.174 mmol), 1-octyne (98%, 294 mg, 2.67 mmol), formic acid (98%, 158 mg, 3.43 mmol), and DME (5 mL) for 22 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave 47 mg of a dark brown oil from the organic layer and 9 mg of a pale yellow oil from the aqueous layer. These materials were not subjected to the usual analyses.

dppe. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), dppe (44 mg, 0.111 mmol), 1-octyne (98%, 300 mg, 2.73 mmol), formic acid (98%, 221 mg, 4.81 mmol), and DME (5 mL) for 18 h at 110 °C under 120 psi of CO gas pressure. Standard work-up gave a 98:2 mixture of **1c** and **2c**, respectively, in 47% combined yield.

dppp. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), dppp (97%, 21 mg, 0.0517 mmol), 1-octyne (98%, 294 mg, 2.67 mmol), formic acid (98%, 233 mg, 5.07 mmol), and DME (5 mL) for 21.5 h at 102 °C under 120 psi of CO gas pressure.

Standard work-up gave a 95:5 mixture of **1c** and **2c**, respectively, in 91% combined yield.

dppb. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (46 mg, 0.108 mmol), 1-octyne (98%, 292 mg, 2.65 mmol), formic acid (98%, 207 mg, 4.50 mmol), and DME (5 mL) for 17 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave an 87:13 mixture of **1c** and **2c**, respectively, in 87% combined yield.

(Z)-Ph₂P-CH=CH-PPh₂. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), (Z)-Ph₂P-CH=CH-PPh₂ (43 mg, 0.109 mmol), 1-octyne (98%, 305 mg, 2.77 mmol), formic acid (98%, 239 mg, 5.20 mmol), and DME (5 mL) for 22 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave a 95:5 mixture of **1c** and **2c**, respectively, in 9% combined yield.

The effects of Pd:PPh₃:dppb ratio on hydrocarboxylation of terminal alkynes

No phosphine. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), phenylacetylene (98%, 245 mg, 2.40 mmol), formic acid (98%, 119 mg, 2.58 mmol), and DME (5 mL) for 22 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave 4 mg of a pale yellow oil which was not subjected to any analysis.

1:4:0. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (29 mg, 0.111 mmol), phenylacetylene (98%, 276 mg, 2.71 mmol), formic acid (98%, 248 mg, 5.39 mmol), and DME (5 mL) for 21.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 94:6 mixture of **1a** and **2a**, respectively, in 88% combined yield.

1:0:2.3. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (26 mg, 0.061 mmol), phenylacetylene (98%, 238 mg, 2.33 mmol), formic acid (98%, 229 mg, 4.98 mmol), and DME (5 mL) for 16.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave an 89:11 mixture of **1a** and **2a**, respectively, in 77%

combined yield.

1:4:0. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (29 mg, 0.111 mmol), 1-octyne (98%, 295 mg, 2.68 mmol), formic acid (98%, 270 mg, 5.88 mmol), and DME (5 mL) for 8 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 93:7 mixture of **1c** and **2c**, respectively, in 49% combined yield.

1:8:0. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (87 mg, 0.332 mmol), 1-octyne (98%, 290 mg, 2.64 mmol), formic acid (98%, 210 mg, 4.56 mmol), and DME (5 mL) for 17 h at 95 °C under 120 psi of CO gas pressure. Standard work-up gave an 89:11 mixture of **1c** and **2c**, respectively, in 72% combined yield.

1:0:4. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (70 mg, 0.164 mmol), 1-octyne (98%, 293 mg, 2.66 mmol), formic acid (98%, 200 mg, 4.35 mmol), and DME (5 mL) for 26 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave a 90:10 mixture of **1c** and **2c**, respectively, in 78% combined yield.

1:4:1.9. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), dppb (22 mg, 0.0516 mmol), 1-octyne (98%, 312 mg, 2.84 mmol), formic acid (98%, 193 mg, 4.20 mmol), and DME (5 mL) for 25 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave an 87:13 mixture of **1c** and **2c**, respectively, in 79% combined yield.

1:8:0. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (56 mg, 0.214 mmol), 3-methyl-1-pentyne (98%, 217 mg, 2.64 mmol), formic acid (98%, 178 mg, 3.88 mmol), and DME (5 mL) for 19 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave an 86:14 mixture of **1f** and **2f**, respectively, in 54% combined yield.

1:4:0. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), 3,3-dimethylbutyne (232 mg, 2.83 mmol), formic acid (98%, 203 mg, 4.43 mmol), and DME (5 mL) for 16.5 h at 110 °C under 120 psi of CO gas pressure.

Standard work-up gave a 57:43 mixture of 1g and 2g, respectively, in 39% combined yield.

**The effects of Pd:PPh₃:dppb ratio on
hydrocarboxylation of internal alkynes**

2-Heptyne. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), 2-heptyne (98%, 47 mg, 0.490 mmol), formic acid (98%, 39 mg, 0.852 mmol), and DME (5 mL) for 16 h at 97 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the usual manner gave 30 mg of a white solid from the organic layer and nothing from the aqueous layer.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (56 mg, 0.214 mmol), 2-heptyne (276 mg, 2.88 mmol), formic acid (98%, 171 mg, 3.71 mmol), and DME (5 mL) for 16 h at 98 °C under 120 psi of CO gas pressure. Standard work-up gave a mixture of 3a and 4a in 9% combined yield.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (25 mg, 0.0586 mmol), 2-heptyne (264 mg, 2.75 mmol), formic acid (98%, 247 mg, 5.37 mmol), and DME (5 mL) for 16 h at 108 °C under 120 psi of CO gas pressure. Standard work-up gave a 35:65 mixture of 3a and 4a, respectively, in 56% combined yield.

1-Phenyl-1-propyne. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (56 mg, 0.214 mmol), 1-phenyl-1-propyne (313 mg, 2.70 mmol), formic acid (98%, 188 mg, 4.09 mmol), and DME (5 mL) for 16 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 43:57 mixture of 3c and 4c, respectively, in 32% combined yield.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (23 mg, 0.0539 mmol), 1-phenyl-1-propyne (99%, 308 mg, 2.66 mmol), formic acid (98%, 217 mg, 4.71 mmol), and DME (5 mL) for 16 h at 104 °C under 120 psi of CO gas pressure.

Standard work-up gave a 36:64 mixture of 3c and 4c, respectively, in 94% combined yield.

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), dppb (5 mg, 0.0117 mmol), PPh_3 (30 mg, 0.115 mmol), 1-phenyl-1-propyne (99%, 298 mg, 2.57 mmol), formic acid (98%, 270 mg, 5.88 mmol), and DME (5 mL) for 8 h at 108 °C under 120 psi of CO gas pressure. Standard work-up gave a 40:60 mixture of 3c and 4c, respectively, in 82% combined yield.

1-Phenyl-1-butyne. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (56 mg, 0.214 mmol), 1-phenyl-1-butyne (98%, 363 mg, 2.79 mmol), formic acid (98%, 247 mg, 5.37 mmol), and DME (5 mL) for 16 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave a 68:32 mixture of 3d and 4d, respectively, in 32% combined yield.

The activities of various catalysts

$\text{Pd}(\text{OAc})_2$. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), phenylacetylene (98%, 274 mg, 2.69 mmol), formic acid (98%, 137 mg, 2.98 mmol), and DME (5 mL) for 22 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 95:5 mixture of 1a and 2a, respectively, in 84% combined yield.

$\text{Pd}(\text{OCOCF}_3)_2$. The general procedure was followed using $\text{Pd}(\text{OCOCF}_3)_2$ (9.5 mg, 0.0286 mmol), PPh_3 (57 mg, 0.218 mmol), 1-octyne (98%, 285 mg, 2.59 mmol), formic acid (98%, 255 mg, 5.54 mmol), and DME (6 mL) for 21 h at 103 °C under 120 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of 1c and 2c, respectively, in 87% combined yield.

PdCl_2 . The general procedure was followed using PdCl_2 (6 mg, 0.0339 mmol), PPh_3 (28 mg, 0.107 mmol), 1-octyne (98%, 299 mg, 2.72 mmol), formic acid (98%, 188 mg, 4.09 mmol) and DME (5 mL) for 16.5 h at 105 °C under 120 psi of CO gas pressure. Standard

work-up gave a 43:34:22 mixture of **1c**, **5i** (hexylmaleic anhydride), and **7i** ((*E*)-2-hexyl-2-butenedioic acid), respectively, and other unidentified species. (Estimated yield of **1c** was 15%; for spectroscopic data on **5i** and **7i** see the Experimental section of Chapter III.)

PdCl₂/NaOAc. PdCl₂ (5 mg, 0.0282 mmol) and NaOAc (4 mg, 0.0488 mmol) were shaken for 15 min. in DME (2 mL). The general procedure was then followed using PPh₃ (27 mg, 0.103 mmol), dppb (24 mg, 0.0563 mmol), 1-octyne (98%, 288 mg, 2.62 mmol), formic acid (98%, 238 mg, 5.18 mmol), and DME (5 mL) for 20.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 96:4 mixture of **1c** and **2c**, respectively, in 77% combined yield.

Pd(PPh₃)₄. The general procedure was followed using Pd(PPh₃)₄ (27 mg, 0.0234 mmol), phenylacetylene (98%, 260 mg, 2.55 mmol), formic acid (98%, 119 mg, 2.58 mmol), and DME (5 mL) for 22 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of **1a** and **2a**, respectively, in 77% combined yield.

10% Pd/C. The general procedure was followed using 10% Pd/C (28 mg, 0.0263 mmol of Pd), 1-octyne (98%, 290 mg, 2.64 mmol), formic acid (98%, 253 mg, 5.50 mmol), and DME (5 mL) for 17 h at 100 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the usual manner gave 10 mg of an orange oil from the organic layer and 1 mg of an orange oil from the aqueous layer. These materials were not subjected to analysis.

10% Pd/C/PPh₃. The general procedure was followed using 10% Pd/C (28 mg, 0.0263 mmol of Pd), PPh₃ (28 mg, 0.107 mmol), dppb (23 mg, 0.0539 mmol), 1-octyne (98%, 294 mg, 2.67 mmol), formic acid (98%, 214 mg, 4.64 mmol), and DME (5 mL) for 20.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave an 84:16 mixture of **1c** and **2c**, respectively, in 85% combined yield.

Ni(OAc)₂. The general procedure was followed using Ni(OAc)₂ · 4 H₂O (9 mg, 0.0362

mmol), dppb (23 mg, 0.0539 mmol), PPh_3 (27 mg, 0.103 mmol), phenylacetylene (98%, 275 mg, 2.70 mmol), formic acid (98%, 270 mg, 5.88 mmol), and DME (5 mL) for 26 h at 107 °C under 120 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of **1a** and **2a**, respectively, in 74% combined yield.

$\text{Ni}(\text{OAc})_2$ reactions

The general procedure was followed using $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (7 mg, 0.028 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (24 mg, 0.0563 mmol), (trimethylsilyl)acetylene (98%, 266 mg, 2.71 mmol), formic acid (98%, 255 mg, 5.54 mmol), and DME (5 mL) for 17 h at 104 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the usual manner gave 28 mg of a white oily solid from the organic layer and 1 mg of a colorless oil from the aqueous layer.

The general procedure was followed using $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (7 mg, 0.028 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (23 mg, 0.0539 mmol), diphenylacetylene (99%, 495 mg, 2.78 mmol), formic acid (98%, 235 mg, 5.11 mmol), and DME (5 mL) for 22 h at 100 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the usual manner gave 490 mg of an off-white solid from the organic layer but nothing from the aqueous layer. The off-white solid from the organic layer was shown (^1H NMR, TLC) to be the starting material (*ca.* 98% recovery).

The general procedure was followed using $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ (7 mg, 0.028 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (23 mg, 0.0539 mmol), 4-methyl-2-pentyne (220 mg, 2.68 mmol), formic acid (98%, 250 mg, 5.43 mmol), and DME (5 mL) for 22 h at 104 °C under 120 psi of CO gas pressure. Standard work-up gave **3b** (*ca.* 1%) and other unidentified species.

The effect of CO pressure

No CO. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (58 mg, 0.221 mmol), 1-octyne (98%, 297 mg, 2.70 mmol), formic acid (98%, 240 mg, 5.22 mmol), and DME (5 mL) for 22 h at 105 °C under 30 psi of N₂ gas pressure. Standard work-up gave a mixture of **1c** (ca. 1%) and other unidentified species.

32 psi. The general procedure was followed using Pd(OAc)₂ (22 mg, 0.098 mmol), PPh₃ (107 mg, 0.408 mmol), dppb (90 mg, 0.211 mmol), phenylacetylene (98%, 238 mg, 2.33 mmol), formic acid (98%, 230 mg, 5.00 mmol), and DME (5 mL) for 23.5 h at 100 °C under 32 psi of CO gas pressure. Standard work-up gave a 90:5:5 mixture of **1a**, **2a**, and 2-phenylpropanoic acid, respectively in 57% combined yield.

75 psi. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), 1-octyne (98%, 65 mg, 0.588 mmol), formic acid (98%, 31 mg, 0.682 mmol), and acetone (1 mL) for 6.5 h at 90 °C under 75 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of **1c** and **2c**, respectively, in 64% combined yield.

300 psi. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (58 mg, 0.221 mmol), 1-octyne (98%, 306 mg, 2.78 mmol), formic acid (98%, 270 mg, 5.88 mmol), and DME (6 mL) for 21 h at 110 °C under 300 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of **1c** and **2c**, respectively, in 80% combined yield.

The effect of temperature

22 °C. The general procedure was followed using Pd(OAc)₂ (22mg, 0.098 mmol), PPh₃ (106 mg, 0.405 mmol), dppb (86 mg, 0.202 mmol), phenylacetylene (98%, 252 mg, 2.47 mmol), formic acid (98%, 218 mg, 4.74 mmol), and DME (5 mL) for 24.5 h at 22 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the usual manner gave 1 mg of a yellow oil from the aqueous layer.

60 °C. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (60 mg, 0.229 mmol), 1-octyne (98%, 299 mg, 2.72 mmol), formic acid (98%, 202 mg, 4.39 mmol), and DME (5 mL) for 15 h at 60 °C under 120 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of 1c and 2c, respectively, in 7% combined yield.

110 °C. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (29 mg, 0.111 mmol), dppb (23 mg, 0.0539 mmol), phenylacetylene (98%, 288 mg, 2.82 mmol), formic acid (98%, 252 mg, 5.48 mmol), and DME (5 mL) for 1.5 h at 110 °C under 120 psi of CO gas pressure. Standard work-up gave a 96:4 mixture of 1a and 2a, respectively, in 78% combined yield.

127 °C. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (29 mg, 0.111 mmol), phenylacetylene (98%, 278 mg, 2.73 mmol), formic acid (98%, 247 mg, 5.37 mmol), and DME (5 mL) for 21 h at 127 °C under 120 psi of CO gas pressure. Standard work-up gave an 88:12 mixture of 1a and 2a, respectively, in 84% combined yield.

The effect of reaction time

4 h. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (27 mg, 0.103 mmol), dppb (21 mg, 0.0492 mmol), phenylacetylene (98%, 258 mg, 2.53 mmol), formic acid (98%, 228 mg, 4.96 mmol), and DME (5 mL) for 4 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 90:10 mixture of 1a and 2a, respectively, in 74% combined yield.

6.5 h. The general procedure was followed using Pd(OAc)₂ (7 mg, 0.0312 mmol), PPh₃ (33 mg, 0.126 mmol), dppb (27 mg, 0.0633 mmol), phenylacetylene (98%, 323 mg, 3.17 mmol), formic acid (98%, 158 mg, 3.43 mmol), and DME (5 mL) for 6.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of 1a and 2a, respectively, in 80% combined yield.

The effects of various solvents

Acetone. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (29 mg, 0.111 mmol), phenylacetylene (98%, 290 mg, 2.84 mmol), formic acid (98%, 146 mg, 3.17 mmol), and acetone (5 mL) for 17 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave a 94:6 mixture of **1a** and **2a**, respectively, in 76% combined yield.

THF. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), phenylacetylene (98%, 305 mg, 2.99 mmol), formic acid (98%, 156 mg, 3.39 mmol), and THF (5 mL) for 16.5 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of **1a** and **2a**, respectively, in 75% combined yield.

CHCl_3 . The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (30 mg, 0.115 mmol), phenylacetylene (98%, 296 mg, 2.90 mmol), formic acid (98%, 161 mg, 3.49 mmol), and CHCl_3 (5 mL) for 17 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave an 80:20 mixture of **1a** and **2a**, respectively, in 10% combined yield.

CH_3CN . The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), phenylacetylene (98%, 284 mg, 2.79 mmol), formic acid (98%, 158 mg, 3.43 mmol), and CH_3CN (5 mL) for 17 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave an 89:11 mixture of **1a** and **2a**, respectively, in 5% combined yield.

The effects of various acids

None. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (29 mg, 0.111 mmol), 1-octyne (98%, 276 mg, 2.51 mmol), and DME (5 mL) for 16.5 h at 109 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the

usual manner gave 80 mg of a reddish-brown oily solid from the organic layer but nothing from the aqueous layer. Spectral analysis of the oily solid showed that it was a mixture of PPh_3 , 1-octyne, and other unidentified species.

Water. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (27 mg, 0.103 mmol), dppb (23 mg, 0.0539 mmol), diphenylacetylene (99%, 476 mg, 2.68 mmol), distilled water (105 mg, 5.83 mmol), and DME (5 mL) for 17 h at 101 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the usual manner gave 483 mg of a beige-brown solid from the organic layer and 1 mg of a white solid from the aqueous layer. The ^1H NMR spectrum and the TLC of the solid from the organic layer showed that it was the starting alkyne.

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (30 mg, 0.115 mmol), dppb (23 mg, 0.0539 mmol), phenylacetylene (98%, 290 mg, 2.84 mmol), distilled water (98%, 48 mg, 2.67 mmol), and DME (5 mL) for 22 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave an 88:12 mixture of **1a** and **2a**, respectively, in 35% combined yield.

HCl. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (31 mg, 0.118 mmol), 1-octyne (98%, 306 mg, 2.78 mmol), 37% HCl (78 mg, 0.795 mmol HCl, 2.72 mmol H_2O) and DME (5 mL) for 16.5 h at 96 °C under 120 psi of CO gas pressure. Standard work-up gave a mixture of **1c** and **2c** and other unidentified species.

$\text{CF}_3\text{CO}_2\text{H}/\text{H}_2\text{O}$. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (24 mg, 0.0563 mmol), 1-octyne (98%, 307 mg, 2.79 mmol), trifluoroacetic acid (99%, 70 mg, 0.614 mmol), H_2O (88 mg, 4.89 mmol), and DME (5 mL) for 17 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 96:4 mixture of **1c** and **2c**, respectively, in 16% combined yield.

$\text{HCO}_2\text{H}/\text{H}_2\text{O}$. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027

mmol), PPh_3 (29 mg, 0.111 mmol), dppb (23 mg, 0.0563 mmol), 1-octyne (98%, 289 mg, 2.63 mmol), distilled H_2O (66 mg, 3.67 mmol), formic acid (98%, 13 mg, 0.28 mmol), and DME (5 mL) for 12 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave a 90:10 mixture of **1c** and **2c**, respectively, in 10% combined yield.

Oxalic acid/ H_2O . The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (23 mg, 0.0563 mmol), 1-octyne (98%, 299 mg, 2.66 mmol), distilled H_2O (79 mg, 4.39 mmol), oxalic acid (99%, 27 mg, 0.30 mmol), and DME (5 mL) for 12 h at 104 °C under 120 psi of CO gas pressure. Standard work-up gave a 99:1 mixture of **1c** and **2c**, respectively, in 12% combined yield.

$\text{CF}_3\text{CO}_2\text{H}$. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (23 mg, 0.0539 mmol), 1-octyne (98%, 303 mg, 2.75 mmol), trifluoroacetic acid (99%, 678 mg, 5.95 mmol), and DME (5 mL) for 17 h at 106 °C under 120 psi of CO gas pressure. Standard work-up gave a 91:9 mixture of **1c** and **2c**, respectively, in 28% combined yield.

Oxalic acid. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), dppb (24 mg, 0.0563 mmol), 1-octyne (98%, 325 mg, 2.96 mmol), oxalic acid (99%, 301 mg, 3.34 mmol), and DME (5 mL) for 17 h at 98 °C under 120 psi of CO gas pressure. Work-up of the final reaction mixture in the usual manner gave 9 mg of a brown oil from the organic layer and 380 mg of a yellow oily solid from the aqueous layer. The latter was partitioned in H_2O and CHCl_3 to remove any oxalic acid present; the organic layer was dried (MgSO_4) and evaporated to yield a pale yellow oil (307 mg). Spectral analysis of this oil showed that it was a 99:1 mixture of **1c** and **2c**, respectively, in 66% combined yield.

Oxalic acid reactions

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28

mg, 0.107 mmol), phenylacetylene (98%, 287 mg, 2.82 mmol), oxalic acid (99%, 144 mg, 1.61 mmol), and DME (5 mL) for 22 h at 97 °C under 120 psi of CO gas pressure. Standard work-up gave a 90:10 mixture of **1a** and **2a**, respectively, in 6% combined yield.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (24 mg, 0.0563 mmol), phenylacetylene (98%, 272 mg, 2.67 mmol), oxalic acid (99%, 119 mg, 1.32 mmol), and DME (5 mL) for 17 h at 108 °C under 120 psi of CO gas pressure. Standard work-up gave a 97:3 mixture of **1a** and **2a**, respectively, in 58% combined yield.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), dppb (24 mg, 0.0563 mmol), phenylacetylene (98%, 287 mg, 2.82 mmol), oxalic acid (99%, 126 mg, 1.40 mmol), and DME (5 mL) for 21.5 h at 102 °C under 120 psi of CO gas pressure. Standard work-up gave a 93:7 mixture of **1a** and **2a**, respectively, in 56% combined yield.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (23 mg, 0.0539 mmol), phenylacetylene (98%, 281 mg, 2.76 mmol), oxalic acid (99%, 271 mg, 3.01 mmol), and DME (5 mL) for 18 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave a 97:3 mixture of **1a** and **2a**, respectively, in 77% combined yield.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), dppb (23 mg, 0.0539 mmol), 1-octyne (98%, 297 mg, 2.70 mmol), oxalic acid (99%, 292 mg, 3.25 mmol), and DME (5 mL) for 18 h at 107 °C under 120 psi of CO gas pressure. Standard work-up gave a 96:4 mixture of **1c** and **2c**, respectively, in 78% combined yield.

The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), dppb (26 mg, 0.0610 mmol), 1-octyne (98%, 284 mg, 2.58 mmol), oxalic acid (99%, 479 mg, 5.32 mmol), and DME (5 mL) for 16 h at 102 °C under 120 psi of CO gas pressure. Standard work-up gave a 91:9 mixture of **1c** and **2c**, respectively, in 76% combined

yield.

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (25 mg, 0.0586 mmol), 5-cyano-1-pentyne (98%, 242 mg, 2.60 mmol), oxalic acid (99%, 504 mg, 5.60 mmol), and DME (5 mL) for 21.5 h at 101 °C under 120 psi of CO gas pressure. Standard work-up gave a 97:3 mixture of **1c** and **2c**, respectively, in 65% combined yield.

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), dppb (24 mg, 0.0563 mmol), 4-phenyl-1-butyne (98%, 331 mg, 2.55 mmol), oxalic acid (99%, 497 mg, 5.52 mmol), and DME (5 mL) for 20 h at 108 °C under 120 psi of CO gas pressure. Standard work-up gave a 91:9 mixture of **1b** and **2b**, respectively, in 90% combined yield.

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), dppb (24 mg, 0.0563 mmol), PPh_3 (29 mg, 0.111 mmol), 1-phenyl-1-propyne (99%, 306 mg, 2.64 mmol), oxalic acid (99%, 499 mg, 5.54 mmol), and DME (5 mL) for 20 h at 114 °C under 120 psi of CO gas pressure. Standard work-up gave a 42:58 mixture of **3c** and **4c**, respectively, in 96% combined yield.

The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (29 mg, 0.111 mmol), dppb (24 mg, 0.0563 mmol), diphenylacetylene (99%, 487 mg, 2.74 mmol), oxalic acid (99%, 501 mg, 5.57 mmol), and DME (5 mL) for 26 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave **1e** in 88% yield.

No CO. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (28 mg, 0.107 mmol), dppb (25 mg, 0.0586 mmol), 1-octyne (98%, 289 mg, 2.63 mmol), oxalic acid (99%, 472 mg, 5.25 mmol), and DME (5 mL) for 16 h at 104 °C under 40 psi of N_2 gas pressure. Standard work-up gave **1c** in 1% yield.

The effect of catalyst to alkyne ratio

1:24. The general procedure was followed using Pd(OAc)₂ (23 mg, 0.102 mmol), PPh₃ (105 mg, 0.401 mmol), dppb (86 mg, 0.202 mmol), phenylacetylene (98%, 251 mg, 2.46 mmol), formic acid (98%, 228 mg, 4.96 mmol), and DME (5 mL) for 24 h at 100 °C under 120 psi of CO gas pressure. Standard work-up gave a 92:8 mixture of **1a** and **2a**, respectively, in 96% combined yield.

1:509. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), dppb (21 mg, 0.0492 mmol), phenylacetylene (98%, 1389 mg, 13.6 mmol), formic acid (98%, 1291 mg, 28.1 mmol), and DME (5 mL) for 23 h at 105 °C under 120 psi of CO gas pressure. Standard work-up gave an 89:11 mixture of **1a** and **2a**, respectively, in 36% combined yield.

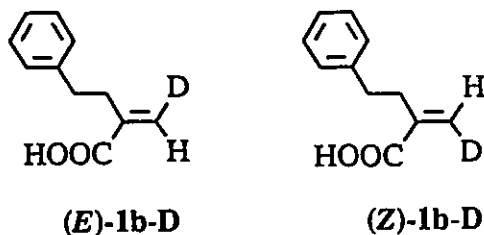
1:502. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), dppb (45 mg, 0.106 mmol), PPh₃ (27 mg, 0.103 mmol), phenylacetylene (98%, 1.365 g, 13.4 mmol), formic acid (98%, 1.327 g, 28.8 mmol), and DME (5 mL) for 24 h at 103 °C under 120 psi of CO gas pressure. Standard work-up gave a 95:5 mixture of **1a** and **2a**, respectively, in 33% combined yield.

2.2.3 Deuterium Labelling Experiments

Preparation of PhCH₂CH₂-CC-D. A septum-capped, 50 mL round bottomed flask containing a stirring bar was purged with N₂ and flame dried for 20 min. The flask was removed from the flame, allowed to cool to room temperature under N₂, and placed in a cold bath (acetone/dry ice, ca. -60 °C). A few minutes later, freshly distilled THF (10 mL) and PhCH₂CH₂-CC-H (98%, 899 mg, 6.91 mmol) were transferred into the flask via a syringe, and stirred for 5 min. Then, n-BuLi (1.88 M, 3.7 mL; standardized immediately prior to the experiment by titration against Ph₂CHCOOH) was added dropwise to the reaction mixture

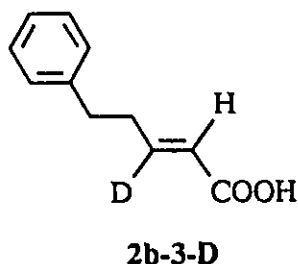
and stirred at $-60\text{ }^{\circ}\text{C}$ for ca. 10 min. The temperature of the bath was then allowed to rise to ca. $+2\text{ }^{\circ}\text{C}$ whereupon D_2O (99.9% D, ca. 1 mL) was added to the mixture and stirred for 15 min. (Addition of D_2O turned the colour of the mixture from brown-green to a pale yellow, and precipitated a gray solid.) The final mixture was filtered and extracted with Et_2O and water; the ether layer was dried over MgSO_4 , filtered, and the solvent removed to give a pale yellow liquid (736 mg, 81%). The ^1H NMR spectrum of this liquid indicated that greater than 95% deuterium incorporation had taken place at the acetylenic site; GC/MS of the liquid product confirmed this conclusion ($M^+ = 131$).

The Catalytic reaction of $\text{PhCH}_2\text{CH}_2\text{-CC-D}$ with HCOOH . The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (56 mg, 0.214 mmol), $\text{PhCH}_2\text{CH}_2\text{-CC-D}$ (331 mg, 2.53 mmol), HCOOH (98%, 174 mg, 3.79 mmol), DME (5 mL) for 15.5 h at $105\text{ }^{\circ}\text{C}$. Standard work-up gave 368 mg of a pale yellow oil (solidified slowly). The ^1H NMR spectrum of this material was similar to that of **1b** except for the unequal intensities of the vinylic resonances: the resonance at 6.32 ppm was 1.28 times more intense than the one at 5.62 ppm. Integration of these resonances showed that the product was a 56:44 mixture of (*E*)- and (*Z*)-**1b-D**, respectively, in 82% combined yield. The GC/MS spectrum of these products confirmed deuterium incorporation: the trimethylsilyl esters of (*E*)- and (*Z*)-**1b-D**: $M^+ = 249$.



The reaction of 4-phenyl-1-butyne with D_2O . The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (6 mg, 0.027 mmol), PPh_3 (33 mg, 0.126 mmol), 4-phenyl-1-butyne (355

mg, 2.73 mmol), D₂O (99.9%, 151 mg, 7.55 mmol), and DME (6 mL) for 16 h at 97 °C. Standard work-up gave 32 mg of a golden yellow oil (solidified slowly). The ¹H NMR spectrum of this material contained all the resonances for (*E*)- and (*Z*)-**1b-D** in addition to a broad resonance at 5.85 ppm which was assigned to **2b-3-D**. Integration of these resonances showed that the product was a 33:45:22 mixture of (*E*)- and (*Z*)-**1b-D**, and **2b-3-D**, respectively. (Combined yield = 7%)



The reaction of 4-phenyl-1-butyne with HCOOD. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (28 mg, 0.107 mmol), 4-phenyl-1-butyne (355 mg, 2.73 mmol), HCOOD (5% D₂O, 2% HCOOH, 93% HCOOD; 209 mg, 4.45 mmol of HCOOD and 0.55 mmol of D₂O), and DME (5 mL) for 17 h at 100 °C. Standard work-up gave 303 mg of a golden yellow oil (solidified slowly). The ¹H NMR spectrum of the latter confirmed the presence of (*E*)- and (*Z*)-**1b-D**, and **2b-3-D** in a 43:40:17 ratio, respectively. (Combined yield= 63%)

The reaction of 4-phenyl-1-butyne with DCOOH. The general procedure was followed using Pd(OAc)₂ (6 mg, 0.027 mmol), PPh₃ (32 mg, 0.122 mmol), 4-phenyl-1-butyne (350 mg, 2.69 mmol), DCOOH (95% in H₂O; 198 mg, 4.20 mmol of DCOOH and 0.56 mmol of H₂O), and DME (6 mL) for 16 h at 102 °C. Standard work-up gave a 91:9 mixture of **50b** and **51b**, respectively, in 79% yield; no deuterium incorporation had taken place.

Chapter III

Dicarbonylation of Terminal Alkynes

3.1 Results and Discussion

Phenylacetylene reacts with formic acid in the presence of PdCl_2 , CuCl_2 , and a mixture of CO/O_2 gases (1 atm, room temperature) to produce phenylmaleic anhydride, **5a**, in 75% yield.^{20b} Under the same conditions, 3,3-dimethyl butyne affords a 49% combined yield of *t*-butylmaleic anhydride, **5b**, and *t*-butylmaleic acid, **6b**, in a 95:5 ratio, respectively; 1-octyne, on the other hand, gives a mixture of hexylmaleic anhydride, **5i**, and the corresponding maleic and fumaric acids, **6i** and **7i**, respectively (eq. 3).

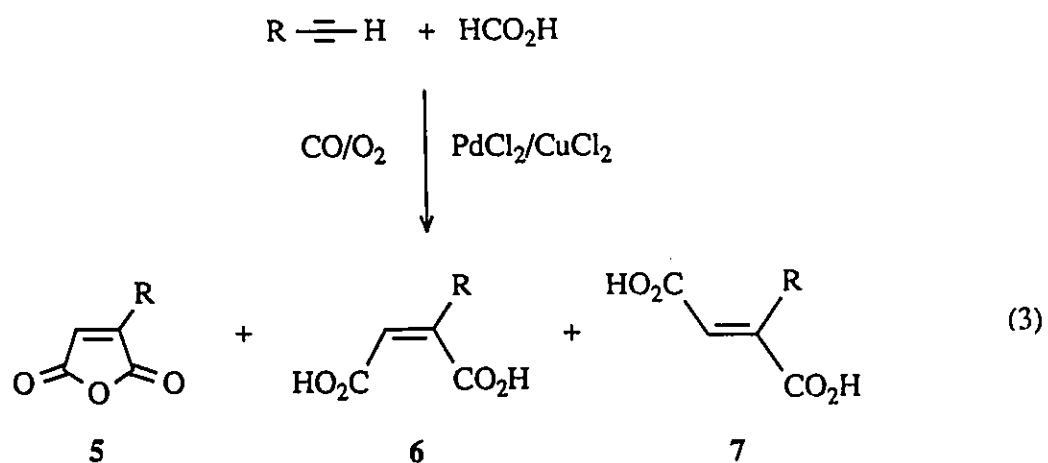
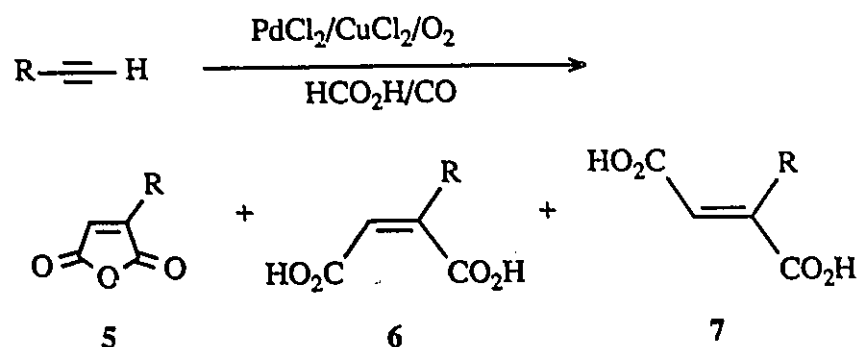


Table 3.1 summarizes the results of the reactions of terminal alkynes with formic acid. The following trends are apparent from these results. The maleic anhydride derivative 5 is the major product with all of the alkynes studied, but the product distribution depends on the steric bulk of the alkyne substituent. For instance, little or no 7 forms with alkynes bearing bulky substituents such as Ph, *t*-Bu, and CH(Me)Et (Table 3.1, entries a-c), whereas it constitutes about 25-35% of the product mixture with less bulky, straight chain alkyl substituents (entries d-i). The proportion of the maleic acid derivative 6 in the product mixture is also variable but independently of the size of the alkyne substituent. As will be discussed later, the most important factor influencing the formation of 6 is the amount of water present in the reaction medium.

In the starting alkyne, the presence of a chloro group remote from the triple bond seems to have no effect on the reaction (entry f), whereas a cyano group in the same position results in a lower yield (entry g). This effect might be due to the blocking of a coordination site on the metal centre of the catalyst by the pendant CN group. When the functional group is in the α -position, as in propynoic acid and its esters (H-CC-COOR; R = H, Me, Bu), intractable materials are obtained in which no carbonylation products could be identified. This result is in agreement with Heck's finding¹³ that polar substituents on both alkenes and alkynes cause substantial deactivating effects in Pd-catalyzed carbonylation of these substrates. Tsuji¹¹ has reported that propynoates undergo facile dimerization under the conditions of alkyne carbonylation reactions.

Finally, in the present system, the carbonylation reaction does not proceed with the internal alkynes 2-heptyne and 4-methyl-2-pentyne. These results are somewhat surprising in light of the earlier finding¹⁷ that internal alkynes are hydrocarboalkoxylated to disubstituted acrylates, CHR'=CR''(COOR), in a similar system using PdCl₂/CuCl₂/HCl/ROH. This and other observations, which will be discussed later, underline the sensitivity of alkyne carbo-

Table 3.1 PdCl₂-Catalyzed Dicarboxylation of Terminal Alkynes

Entry	R	Yield(%)*	product distribution		
			5	6	7
a	Ph	75(68)	100	0	0
b	<i>t</i> -Bu	49	95	5	0
c	CH(Me)Et	66	66	26	8
d	(CH ₂) ₂ Ph	53	75	0	25
e	(CH ₂) ₃ Ph	65	69	0	31
f	(CH ₂) ₃ Cl	59	70	5	25
g	(CH ₂) ₃ CN	30	62	11	27
h	(CH ₂) ₃ CH ₃	54	65	5	30
i	(CH ₂) ₅ CH ₃	68(59)	60	5	35

* The numbers in the parentheses represent isolated yields; the remaining are NMR yields. See the Experimental Section (pages 124-134) for reaction conditions and the details of yield assessments.

nylation reactions to factors such as the nature of acid and nucleophile employed.

3.1.1 Comparison of the present results to literature reports

Tsuiji has authored many of the earlier (1960-1970) reports on palladium-catalyzed alkyne dicarbonylation reactions. Generally speaking, most of the reactions that he and his coworkers studied resulted in many different products. For example, ethyl propynoate has been reported to undergo carbonylation in the presence of $\text{PdCl}_2/\text{HCl}/\text{EtOH}$ to produce the following products: diethyl fumarate, triethyl esters of ethylenetricarboxylate and 1,1,2-ethanetricarboxylate, and tetraethyl 1,3-butadiene-1,1,4,4-tetracarboxylate.^{11b} Similarly, other terminal and internal alkynes give rise to many products. Two exceptions are diphenylacetylene and propargyl alcohol, which give the corresponding lactones as the predominant product.^{11c,11e}

In 1968, Chiusoli¹² reported the use of PdCl_2 /thiourea/air for alkyne carbonylation. This system also results in a number of mono- and dicarbonylated products and, consequently, has not found synthetic utility. In 1971, Heck¹³ reported the $\text{PdCl}_2/\text{HgCl}_2/\text{ROH}$ promoted dicarbonylation of terminal and internal alkynes. Depending on the alkyne reacted, the products consisted of different proportions of the corresponding maleic and fumaric esters and, only with phenylacetylene, maleic anhydride; in some cases, chloroesters also formed. Not only was the product distribution of this system generally poor, but the reactions were mostly stoichiometric. In 1983, Alper¹⁷ reported the PdCl_2 -catalyzed dicarbonylation of terminal alkynes with alcohols. This system, which requires $\text{CuCl}_2/\text{O}_2/\text{HCl}$ to sustain catalysis, provides monosubstituted maleic and fumaric esters in 90-100% yields and good selectivities. As mentioned earlier, internal alkynes are also carbonylated in this system to form unsaturated esters in good yields.

Apart from the nickel-promoted hydrocarboxylation of alkynes studied by Reppe³ and Whiting,⁵ most alkyne carbonylation studies have used alcohols, as opposed to water, as the nucleophile. This is primarily because water usually leads to side reactions. One exception is the rhodium-catalyzed carbonylation of internal alkynes reported by Takahashi.⁹ This reaction uses $\text{Rh}_4(\text{CO})_{12}$, water, and trialkyl amines (100 °C, 100 atm of CO gas) to form furan-2(5H)-ones (lactones). With unsymmetrically substituted internal alkynes, various ratios of the two regioisomers form in combined yields of 50-90%.

Most of the above reports on alkyne dicarbonylation, including the present one, are of little synthetic value. In contrast, Tamaru and coworkers¹⁰⁶ have recently reported an attractive PdCl_2 -catalyzed process for dicarbonylation of alkynols to α -methylene- γ -butyrolactones under mild reaction conditions (1 atm of CO, room temperature, 1 day). The oxidant system consists of excess CuCl_2 /propylene oxide/ethyl orthoacetate; the yields and turnover numbers are very good.

In conclusion, the present system suffers from poor yields and selectivities, and low catalytic turnovers. One merit of this system is the formation of anhydrides as the major reaction product; as will be discussed later, this is thought to arise from substituting formic acid for HCl in the well known $\text{Pd/Cu/CO/O}_2/\text{HCl}$ system.

3.1.2 The process of optimizing the reaction conditions

Most of the results presented in Table 3.1 were obtained from reactions in which optimized experimental conditions were employed. The process by which these optimal conditions were determined is discussed next.

A. The effects of various Pd-compounds and other oxidants. A number of Pd-

compounds were tested in order to compare their catalytic activities to that of PdCl_2 . Before discussing the results of these reactions, however, it is necessary to address the question of what happens when no metal catalyst is used. Recently, Shvo and coworkers¹⁰⁷ reported that terminal alkynes can be oxidized to ketones at elevated temperatures in the presence of excess formic acid. As seen from the first entry in Table 3.2, 1-octyne does not react with formic acid at room temperature and in the absence of metal catalysts. This experiment established that a suitable metal catalyst is necessary for the carbonylation reaction, and ruled out the possibility that the carbonylation reaction products originate from a direct and uncatalyzed reaction between HCOOH and the alkyne.

Under the standard conditions employed for PdCl_2 -catalyzed reactions (i.e., $\text{CuCl}_2/\text{O}_2/\text{CO}/\text{HCOOH}$), the Pd(II) -compounds $\text{Na}_2[\text{PdCl}_4]$, Pd(OAc)_2 , and Pd(acac)_2 are less active than PdCl_2 (entries 2-4). Interestingly, the Pd(0) compound $\text{Pd}_2(\text{dba})_3$ is capable of catalyzing the dicarbonylation reaction in the presence of CuCl_2/O_2 (entries 5 and 6). The heterogeneous sources of Pd(0) such as Pd/C are also fairly active catalysts provided that CuCl_2/O_2 is present (entries 7-9), but Pd-black is inactive. In summary, of the Pd -compounds tested, 10% Pd/C shows catalytic activity comparable to that of PdCl_2 . Evidently, the oxidation state of the catalyst precursor is not as important a factor as the oxidative conditions. It is important to emphasize, however, that whereas PdCl_2 , and to a lesser extent other Pd(II) compounds, can bring about a stoichiometric alkyne dicarbonylation reaction in the absence of any oxidant, Pd(0) compounds fail to do so. This and other related observations (*vide infra*) suggest that the carbonylation reaction occurs in the presence of a species containing palladium in oxidation state of +2.

The most commonly used oxidant system for regenerating deactivated Pd -catalysts is $\text{CuCl}_2/\text{O}_2/\text{HCl}$. Although HCl is in most cases quite crucial, its presence in the present system leads to side reactions and poor carbonylation yields (*vide infra*); therefore, the

Table 3.2 The Effects of Various Pd-Compounds
On Dicarboxylation of 1-Octyne^a

Entry	Pd-compound	Yield(%) ^b
1	— ^c	—
2	Na ₂ [PdCl ₄]	44
3	Pd(OAc) ₂	25
4	Pd(acac) ₂	12
5	Pd ₂ (dba) ₃	47
6	Pd ₂ (dba) ₃ ^c	—
7	10% Pd/C	57
8	5% Pd/C	17
9	10% Pd/C ^c	—
10	Pd-black	traces
11	Pd-black ^c	—

a. The experimental details are described on pages 134-136.

b. Yield refers to the combined yield of the dicarboxylation products **5i**, **6i**, and **7i**.

c. No CuCl₂/O₂ was used.

standard oxidant used in the present system was CuCl_2/O_2 . Many other oxidant systems have also been used for oxidizing $\text{Pd}(0)$ to $\text{Pd}(\text{II})$, including thiourea/air,¹² benzoquinone,¹⁰⁸ KI/O_2 ,¹⁰⁹ alkyl nitrite,¹¹⁰ CuCl_2 /propylene oxide/ethyl orthoacetate ($\text{MeC}(\text{OEt})_3$),¹⁰⁶ TBHP (*t*-butyl hydroperoxide),³² and DTBP/ CuCl_2 /HCl (DTBP= di-*t*-butyl peroxide).¹¹¹ The latter system has been used as a replacement for oxygen in the CuCl -catalyzed oxidative carbonylation of alcohols to dialkyl oxalates, succinates, and carbonates,^{111a} and in the PdCl_2 -catalyzed single and double carbonylation of primary amines to carbamates and oxamates.¹¹² The advantages of using DTBP are twofold: it eliminates the risks associated with using mixtures of CO/O_2 , and avoids the catalyst deactivation often caused by the formation of water in O_2 systems. In addition, one by-product of the DTBP reaction, namely *t*-BuOH, is a useful gasoline supplement. The mechanism of catalyst regeneration in DTBP reactions is thought to involve the formation of either Cu-alkoxy complexes or alkoxy radicals arising from O-O bond homolysis.^{111b} Recently, CuCl was shown to react with dibenzoyl peroxide in pyridine to give $[\text{Cu}(\text{III})\text{Cl}(\text{PhCO}_2)_2(\text{py})_2]$,¹¹³ although it is not known whether this product arises from the oxidative addition of the peroxide or by the capture of the peroxy radicals by CuCl .

The use of DTBP in the dicarbonylation of terminal alkynes was briefly explored in the present study. As seen in Table 3.3, replacing O_2 by DTBP/HCl does not lead to a more effective oxidant (entry 2). Moreover, excluding either HCl or CuCl_2 does not improve the effectiveness of DTBP (entries 3 and 4). Finally, combining the two oxidant systems (i.e., using DTBP/HCl/ CuCl_2 / O_2 , entry 1) also does not prove advantageous. Therefore, in the present system O_2 is a better oxidant than DTBP.

B. The effect of catalyst to substrate ratio. Table 3.4 summarizes the reaction yields and turnover numbers for various Pd : alkyne ratios. It is interesting to note that the yields of

Table 3.3 The Effectiveness of DTBP^a As Oxidant
In Dicarboxylation of 1-Octyne^b

Entry	Oxidant System	Yield(%) ^c
1	DTBP/HCl/CuCl ₂ /O ₂	51
2	DTBP/HCl/CuCl ₂	38
3	DTBP/CuCl ₂	19
4	DTBP/HCl	8

a. DTBP= Di-*t*-butyl peroxide, (*t*-BuO)₂.

b. The experimental details are described on
pages 136 and 137.

c. Yield refers to the combined yield of the
dicarboxylation products **5i**, **6i**, and **7i**.

Table 3.4 The Effect of Catalyst to Substrate Ratio on Dicarboxylation of R-CC-H^a

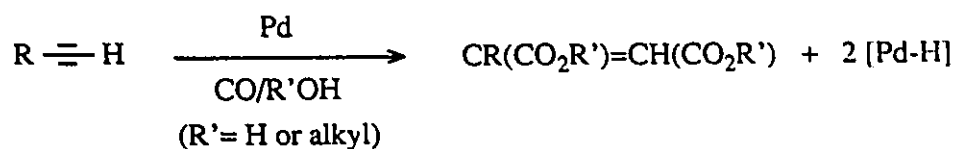
Entry	R	Pd:Alkyne	Yield(%)	5 : 6 : 7	Turnover No.
1	(CH ₂) ₅ CH ₃	1: 1	75	58:11:31	—
2		1: 9 ^b	77	60:3:37	7
3		1:40	17	40:20:40	7
4	Ph	1:20	50	100:0:0	10
5		1:22 ^c	40	100:0:0	9
6	(CH ₂) ₃ Cl	1:48	15	43:25:32	7

a. The experimental details are described on pages 137 and 138.

b. 1-Octyne and HCOOH were added dropwise over a 3-hour period.

c. Excess CuCl₂ was used (Pd:Cu= 1:10).

stoichiometric and catalytic reactions are similar (entries 1 and 2); in addition, higher than 1:10 Pd : alkyne ratios lead to lower yields but more or less the same turnover numbers (entries 2-6). The catalytic turnover numbers observed in the present system are quite low, probably as a result of competing side reactions. A likely side reaction is alkyne polymerization or oligomerization, which can become significant with higher Pd : alkyne ratios. Also, the continuous bubbling of CO and O₂ through the reaction mixture causes some loss of alkyne by evaporation, especially when more volatile alkynes are used. A partial solution to both these problems is to keep the alkyne concentration low by adding it dropwise (entry 2). Another possible side reaction is alkyne hydrogenation. The hydrogen (or the Pd-H species) required for this reaction might originate from the water gas-shift reaction (*vide infra*) or as a by-product of the dicarbonylation reaction, as follows:



C. The effects of CO/O₂ and the metals. The gases CO and O₂ are very crucial to the catalysis. As seen in the first entry of Table 3.5, without CO no carbonylation takes place even when sufficient amounts of HCOOH are present; instead, the alkyne undergoes cyclotrimerization and polymerization. In addition, it is better to bubble the CO gas *through* the reaction mixture, because lower yields are obtained when the gases are contained in a balloon attached to the reaction flask (entry 2). A 3:1 ratio of CO:O₂ was used in most reactions, but experiments showed that this ratio is not very important (entries 3 and 4). This is perhaps not surprising since these gases are usually in large excess with respect to the other components of the system (e.g., with a 3:1 ratio of CO:O₂, the ratio of Pd:CO:O₂ is roughly 1:500-1000:-200-300).

Table 3.5 The Effects of Gases and Metal Ratios on Dicarboxylation of Alkynes^a

Entry	PdCl ₂ :CuCl ₂	CO:O ₂	Yield (%)	5 : 6 : 7
1	1:2.0	O ₂ only	— ^b	
2	1:2.1	3:1 ^c	45	62 : 9 : 29
3	1:1.7	10:1	51	39 : 14 : 47
4	1:2.0	1:6	53	20 : 43 : 37
5	PdCl ₂ only	CO only	(66) ^d	35 : 30 : 35
6	CuCl ₂ only	3:1	—	
7	1:0.6	3:1	68	57 : 5 : 38
8	1:2.5	3:1	68	57 : 5 : 38
9	1:5.5	3:1	66	54 : 5 : 41
10	PdCl ₂ only	3:1	43	26 : 21 : 53
11	1:16	CO only	2 ^e	100 : 0 : 0

a. The experimental details are described on pages 138-141.

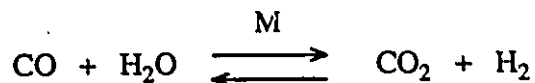
b. Polymers formed.

c. The gases were contained in a balloon attached to the reaction flask.

d. The yield is based on the PdCl₂, not the alkyne.

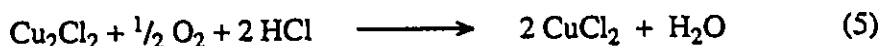
e. Phenylacetylene was used; Pd:Ph-CC-H= 1:14.

In transition metal catalyzed systems containing CO gas and water, it is conceivable that CO₂ and H₂ gases can evolve from the water gas-shift reaction, as follows:



This process usually occurs in basic media ¹¹⁴ and therefore would be unlikely to occur in the present system; nevertheless, the possibility that CO can be converted to CO₂ in the present system, and that it is in fact CO₂ which leads to the observed products, was examined by the following experiments. When CO₂ gas was used instead of CO in an otherwise standard reaction, no carbonylation took place. In addition, using a CO/CO₂ mixture (no O₂) resulted in a stoichiometric yield (10%). These results ruled out the possibility that CO₂ is in any way involved in the alkyne dicarbonylation reaction. In fact, it was shown that very little or no CO₂ is generated during the standard catalytic reaction conditions: when the outgoing gases were passed through an aqueous solution of Ba(OH)₂, only traces of a white precipitate (presumably BaCO₃) were detected in the solution.

In the absence of oxygen and CuCl₂, the carbonylation reaction proceeds stoichiometrically (66% yield with respect to PdCl₂; entry 5). In the absence of PdCl₂, however, no carbonylation takes place (entry 6). These results indicate that, of the two metal salts used, PdCl₂ is undoubtedly the catalyst precursor. In catalytic systems employing some combination of PdCl₂ and CuCl₂/O₂, the latter are generally assumed to act as Wacker-type regenerators (oxidants) of the "deactivated" palladium catalyst. In the Wacker process,¹¹⁵ CuCl₂ is considered to be the main oxidant for regenerating Pd^{II} (eq. 4); HCl and oxygen are needed in order to replenish CuCl₂ (eq. 5), and can be replaced by excess CuCl₂.



Some of our experimental results indicate, however, that at least in the present system the true functions of CuCl_2 and O_2 are far more complex than implied by equations 4 and 5. For instance, the relative amount of CuCl_2 used in the reaction does not seem to be a crucial factor (entries 7-9), such that even in the complete absence of CuCl_2 at least 4 catalytic turnovers are observed (entry 10). In contrast, excluding just oxygen from the system completely inhibits the catalysis *even when excess CuCl_2 is used* (entry 11); in this case, simply introducing oxygen into the system initiates the catalysis. Finally, HCl has detrimental effects on the carbonylation reaction: it lowers the yields of the dicarbonylated products and results in the formation of other, unidentified species.

These results have important implications for the mechanism of catalyst regeneration in this system and perhaps in many other Pd(II)/Cu(II)/O_2 (Wacker-type) systems. They imply that oxygen is much more necessary for the catalysis than is CuCl_2 , and seem to suggest that oxygen can oxidize Pd^0 to Pd^{II} independently of CuCl_2 . A search of the literature has revealed other reports^{116,117} supporting this possibility. The most widely accepted view is that the insertion of O_2 into the Pd-H bond of an intermediate species forms a palladium hydroperoxo complex¹¹⁸ which, in turn, gives Pd(II) and water (*vide infra*).

If, indeed, oxygen is the true oxidant in this system, then CuCl_2 , which is certainly beneficial for the overall catalytic process, must have a different function. One distinct possibility is that CuCl_2 may be involved in the formation of a heterometallic, Pd-Cu species which participates in the catalysis in some capacity. This possibility has been raised earlier by Fenton and Steinwand¹¹⁹ who proposed a Pd-Cu complex as the main catalytic species in the carbonylation of alcohols to oxalates. Hosokawa, Murahashi and coworkers^{32,116a} have

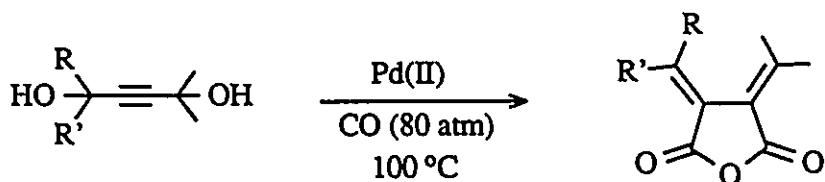
also argued that a Pd-Cu intermediate is involved in the oxidative cyclization of 2-allylphenols catalyzed by $\text{Pd}(\text{OAc})_2/\text{Cu}(\text{OAc})_2/\text{O}_2$. Furthermore, we have observed that the interaction of PdCl_2 , CuCl_2 , and CO in the absence of alkyne and HCOOH leads to a yellow solid which can serve as a catalyst precursor with catalytic activity comparable to that of $\text{PdCl}_2/\text{CuCl}_2$. That this compound contains CO ligand(s) is apparent from a single, strong absorption at 1985 cm^{-1} in the IR spectrum of this solid, and the fact that it does not form in the absence of CO. The full characterization of this material, however, has thus far eluded us because it is quite insoluble in most solvents, very unstable in the absence of CO, and does not form crystals. The results of elemental analyses performed on two samples of this material (see the Experimental Section) are provided below; the average values provided by these analyses have been compared to those calculated for the empirical formula $\text{PdCu}_2\text{Cl}_4(\text{CO})_4$:

	<u>Found</u>	<u>Calculated</u>
%Pd	24.1	21.8
%Cu	24.9	26.1
%Cl	28.2	29.1
%C	7.7	9.9
%H	0.9	0.0

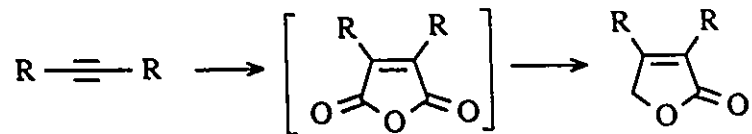
The discrepancies between the found and calculated values are in the range of 0.9-2.3%. Discrepancies of this magnitude would normally be considered too large to be acceptable; given the unstable nature of the species under discussion, however, the differences observed may be inevitable. For instance, the excess of Pd found in the analyzed samples (ca. +2.3%) might be due to the contamination of the samples by small amounts of

palladium metal which normally precipitates during the reaction. The deficiency of carbon (-2.2%), on the other hand, can be rationalized by invoking partial loss of CO either prior or during the analyses. A combination of Pd(0) precipitation and CO loss would also account for the observed discrepancies. Finally, the presence of small amounts of hydrogen in the analyzed samples implies the presence of contaminants such as residual solvent or moisture. Therefore, the results of elemental analyses and the IR spectrum provide partial support for the proposed formula; nevertheless, further evidence is needed for the unequivocal characterization of this species.

D. The role of formic acid. An unusual feature of the present catalytic system is its tendency to give substituted maleic anhydrides as the major reaction products. Most previous studies of alkyne carbonylation have reported the formation of the corresponding maleic and fumaric acids (with water as nucleophile) and esters (with alcohols as nucleophiles), in addition to other monocarbonylated products. To our knowledge, the only other reports of alkyne dicarbonylation to anhydrides are Heck's¹³ stoichiometric reaction using PdCl₂/HgCl₂/phenylacetylene/H₂O/acetone, and the catalytic synthesis of dimethylenesuccinic anhydrides by Tsuji^{11e} and Kiji¹²⁰:



In addition, there have been reports of Pd- and Rh-catalyzed carbonylation of alkynes to furan-2(5H)-ones,^{9,12} which are believed to arise from the *in-situ* reduction of the corresponding maleic anhydrides:



The use of HCOOH in the present system seemed at first to be the most probable cause for the preferential formation of anhydrides. We set out to examine this possibility by attempting to ascertain the specific roles of water and HCOOH in the catalytic system. When HCOOH was replaced by water in an otherwise standard reaction, a 53% total yield was obtained with a 5:6:7 ratio of 44:19:37 (Table 3.6, entry 1). Therefore, water is a sufficiently good nucleophile for bringing about anhydride formation, even though HCOOH gives somewhat higher total yields and anhydride proportions. Indeed, even when no water or HCOOH was added to the reaction mixture, a significant yield was obtained (entry 2). This result indicated that the reaction medium contained relatively large amounts of water, perhaps as the residual moisture in either the solvent, the gases, or the reagents used.

To our surprise, however, no matter how rigorously the solvent and the reagents were dried or distilled prior to their use, and in spite of scrubbing the gases, the reactions with no added water or HCOOH repeatedly resulted in about 40% yields. Only when 4Å molecular sieves were present in the reaction medium *during the entire course of the reaction* was it possible to almost completely suppress the carbonylation reaction (entry 3). MgSO₄ had a similar effect (entry 4), although it did not suppress the reaction to the same extent as did the molecular sieves; this is probably due to the lower effectiveness of MgSO₄ as a dessicant. Therefore, water seems to be generated during the reaction, and the presence of oxygen is probably responsible for this in some manner. As noted above, the formation of water from oxygen has been invoked by others^{116,117,121} and might result from hydroperoxo complexes

Table 3.6 The Effect of Water, Acids, and Bases on The Dicarbonylation of Terminal Alkynes^a

Entry	Reagents	Yield(%)	5 : 6 : 7
1	H ₂ O	53	44 : 19 : 37
2	—	41	54 : 12 : 34
3	4Å molecular sieves	6	80 : 0 : 20
4	MgSO ₄	12	71 : 0 : 29
5	90% HCOOH, 4Å mol. sieves	5	24 : 54 : 22
6	90% HCOOH, MgSO ₄	56	54 : 5 : 41
7	98-100% HCOOH (pK _a = 3.75)	57	62 : 10 : 28
8	Oxalic Acid (pK _a = 1.27)	68	36 : 25 : 39
9	Malonic Acid (pK _a = 2.85)	56	26 : 48 : 26
10	Acetic Acid (pK _a = 4.74)	48	37 : 37 : 26
11	Boric Acid (pK _a = 9.24)	61	31 : 39 : 30
12	Conc. HCl (pK _a = -2.2)	14 ^b	30 : 20 : 50
13	H ₂ O, EtN(Pr) ₂	—	

a. The experimental details are described on pages 141-144.

b. Other, unidentified products were also observed.

formed by the insertion of O_2 into a metal hydride bond¹²² (*vide infra*).

Having found that water can also result in anhydride formation, it was then necessary to understand why HCOOH results in higher total yields and anhydride proportions. Is HCOOH a more effective nucleophile than water? Or does it act merely as a promoter for the reaction of water? In order to determine whether HCOOH plays a direct role in the carbonylation reaction, it was necessary to carry out an experiment with only HCOOH, taking measures to ensure that any *in-situ* generated water would be removed. Thus, a standard HCOOH reaction was carried out in the presence of 4Å molecular sieves. This reaction gave almost no carbonylation (entry 5), implying that water, not HCOOH, is the true nucleophile in the carbonylation reaction. This possibility, however, was not supported by the outcome of an analogous HCOOH reaction with $MgSO_4$, which gave a 56% yield (entry 6).

The large difference in the yields of these two reactions is difficult to explain. On the one hand, the high yield of the $MgSO_4$ reaction might be due not to the reaction of HCOOH, but rather to the relatively lower effectiveness of $MgSO_4$ in removing water from the reaction medium. On the other hand, it is possible that 4Å molecular sieves inhibit the reaction more effectively because they trap both water and HCOOH, whereas $MgSO_4$ traps only water, allowing HCOOH to react and the reaction to proceed almost unhindered.

If HCOOH does not act as a nucleophile, its role might be to provide H^+ ions which could be conducive to the catalysis; in that case, there should be acids other than HCOOH with similar effects on the reaction. As seen from the results of Table 3.6 (entries 7-12), oxalic, boric, acetic, and malonic acids lead to reaction yields which are comparable to that of HCOOH, and higher than the yield of the reaction with no added water or HCOOH; HCl leads to much lower yields and other products. Therefore, acidic conditions are indeed favourable for the catalysis; there is, however, no correlation between the pK_a values of the acids used on the one hand and, on the other hand, their effects on either the yield or the

anhydride proportion. This is in accord with the results of Whiting *et al.*⁵ who found that the Ni(CO)_4 -promoted synthesis of acrylic acid from alkynes was independent of the pK_a of the acids used. Bases completely inhibit the reaction (entry 13). It is noteworthy that under similar conditions (i.e., $\text{PdCl}_2/\text{CuCl}_2/\text{CO}/\text{base}/\text{ROH}$) terminal alkynes have been reported to undergo either oxidative carboalkoxylation to produce acetylenecarboxylates ($\text{R}'\text{-CC-COOR}$), or oxidative coupling to form diynes.¹²³

In summary, the presence of HCOOH is beneficial for the catalysis in terms of both yields and anhydride proportion. Our results, however, do not clarify the precise reason(s) for these effects, and the role of HCOOH in the catalysis remains unknown.

E. Solvent and additive effects. The present catalytic system is quite sensitive to a number of factors, including the solvent. As seen from Table 3.7, the suitability of the solvent follows the order $\text{THF} > \text{Acetone} > \text{Dioxane} \approx \text{CH}_3\text{CN} > \text{EtOAc} > \text{C}_6\text{H}_6$. No obvious correlation seems to exist between the solvent polarity and its suitability for the reaction. For instance, while CH_3CN is the most polar of the solvents tested, it is not the most suitable one for the reaction; this might be due to the well known ability of this solvent to compete with substrates for coordination to palladium.

Alkali metal halides and I_2 have been used as promoters for Pd-catalyzed alkyne carbonylations.^{29,120,109} In the present system, however, LiCl was found to have no promoting effect, while NaI inhibited the catalysis both in the presence and absence of CuCl_2 . Small amounts of I_2 did not influence the reaction, but larger amounts suppressed the dicarbonylation and gave small amounts of an unidentified product.

Bystrom, Larsson, and Åkermark¹⁰⁸ have recently reported that addition of PPh_3 to a catalytic system consisting of Pd(OAc)_2 , Cu(OAc)_2 , hydroquinone, and O_2 inhibits the catalytic acetoxylation of olefins; this effect was attributed to the oxidation of the phosphine

Table 3.7 The Effects of Solvents on Dicarboxylation of 1-Octyne*

Entry	Solvent	Yield (%)	5 : 6 : 7
1	THF	68	60 : 5 : 35
2	Acetone	57	36 : 37 : 27
3	1,4-Dioxane	44	54 : 8 : 38
4	CH ₃ CN	42	17 : 56 : 27
5	EtOAc	25	50 : 9 : 41
6	C ₆ H ₆	11	59 : 24 : 17

* The reactions were carried out at room temperature for 6 hours.
See the Experimental Section for details (page 144).

by oxygen. We have examined the effects of using the phosphines PPh_3 , PCy_3 , and dppb and the phosphites P(OPh)_3 and P(OiPr)_3 in various ratios with respect to PdCl_2 , with or without CuCl_2/O_2 ; the catalysis was completely inhibited in all cases. Therefore, the carbonylation proceeds best in the absence of any ligand or solvent which can compete with CO and the alkyne for coordination sites on the catalyst.

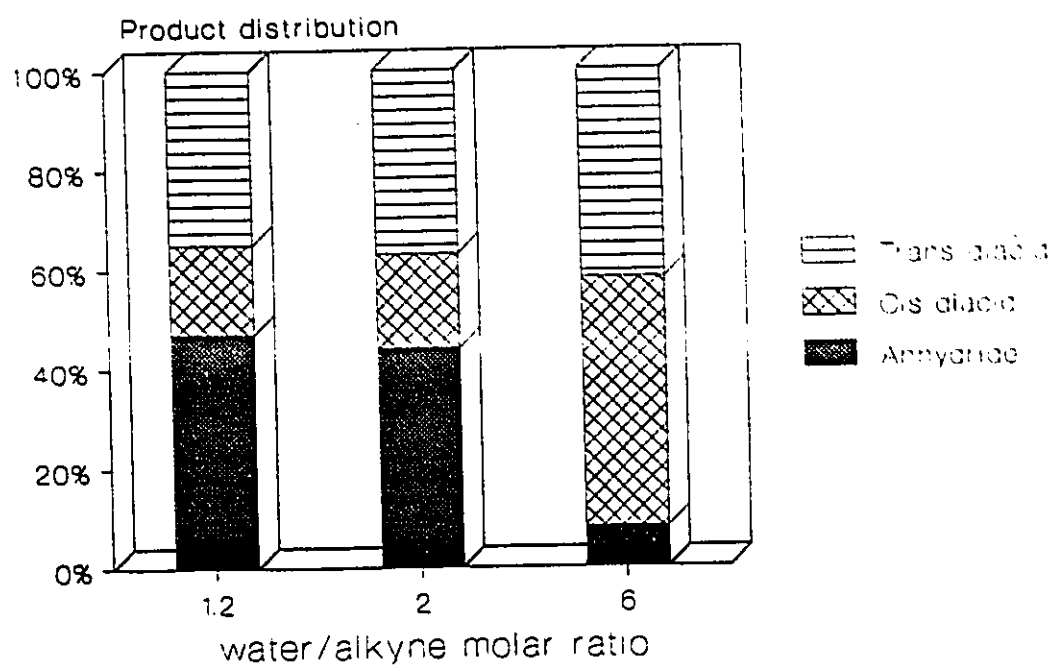
3.1.3 The Mechanism of the Carbonylation Reaction

Having discussed the experimental findings which led to the optimization of the reaction conditions for dicarbonylation of terminal alkynes, it is now possible to deal with the implications of these findings for the mechanism of this reaction. This section describes one possible sequence of reactions which lead to the observed products. In postulating a plausible mechanism, analogies have been drawn to the precedents found in the literature of organo-metallic chemistry in general, and the alkyne dicarbonylation reports in particular.

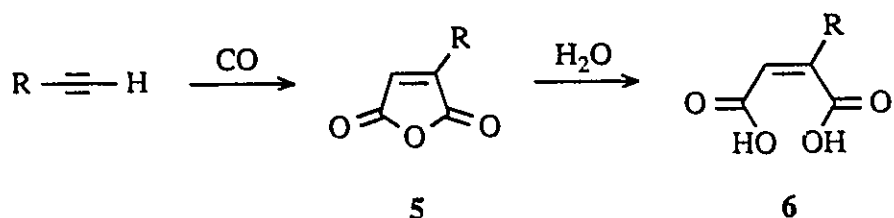
Although in the present system the maleic anhydride derivative **5** is the major product in all standard catalytic reactions with terminal alkynes, the proportions of the three products can vary significantly (Table 3.1). As mentioned earlier, the proportion of the fumaric acid derivative **7** is affected by the steric bulk of the alkyne substituent. The possible implications of this steric factor for the mechanism of alkyne insertion will be discussed later (*vide infra*). In addition, more of the maleic acid derivative **6** forms with a given alkyne when larger amounts of water are present in the reaction medium. This can be seen from the plot of the relative amounts of water present in the reaction mixture versus the product distribution (Figure 3.1). This plot also shows that the increase in the proportion of **6** comes almost completely at the expense of the corresponding anhydride derivative **5**. The simplest

Figure 3.1

The Relationship Between Water : Alkyne Molar Ratio and the Product Distribution.



explanation for this observation would be a *post facto* hydrolysis of the preformed anhydride, as shown below:



Our experimental results indicate, however, that the hydrolysis of the anhydride alone can not account for the formation of **6**: when pure anhydride **5** was stirred for 6 hours under the conditions of the catalytic reactions, a 97:3 mixture of the starting anhydride and the corresponding maleic acid **6**, respectively, was recovered (Table 3.8, entry 1). Even when this experiment was repeated in the presence of excess water, an 89:11 mixture of **5**:**6** was obtained (entry 2). Therefore, once the anhydride **5** is produced in the reaction, no more than 11% of it hydrolyzes to the corresponding diacid **6**. Conversely, once the diacid **6** is formed, it does not dehydrate appreciably to the corresponding anhydride **5** or isomerize to give the fumaric acid derivative **7** (entry 3).

Table 3.8 Hydrolysis and Dehydration Control Experiments

Entry	Starting Material	Products
		5 : 6 : 7
1	5 / HCOOH	97 : 3 : 0
2	5 / H ₂ O	89 : 11 : 0
3	6 / HCOOH	11 : 89 : 0

These results indicate that, under the conditions of the catalytic reactions, **5** and **6** do

not interconvert significantly, or isomerize to give **7**. Therefore, we can conclude that, to a large extent, these three products originate from three distinct, but interdependent, reaction pathways. Moreover, the relative contributions of these three pathways to the overall reaction are, to a good approximation, reflected in the product ratios. This conclusion is central to our proposed mechanism for the dicarbonylation of terminal alkynes (Scheme 3.1).

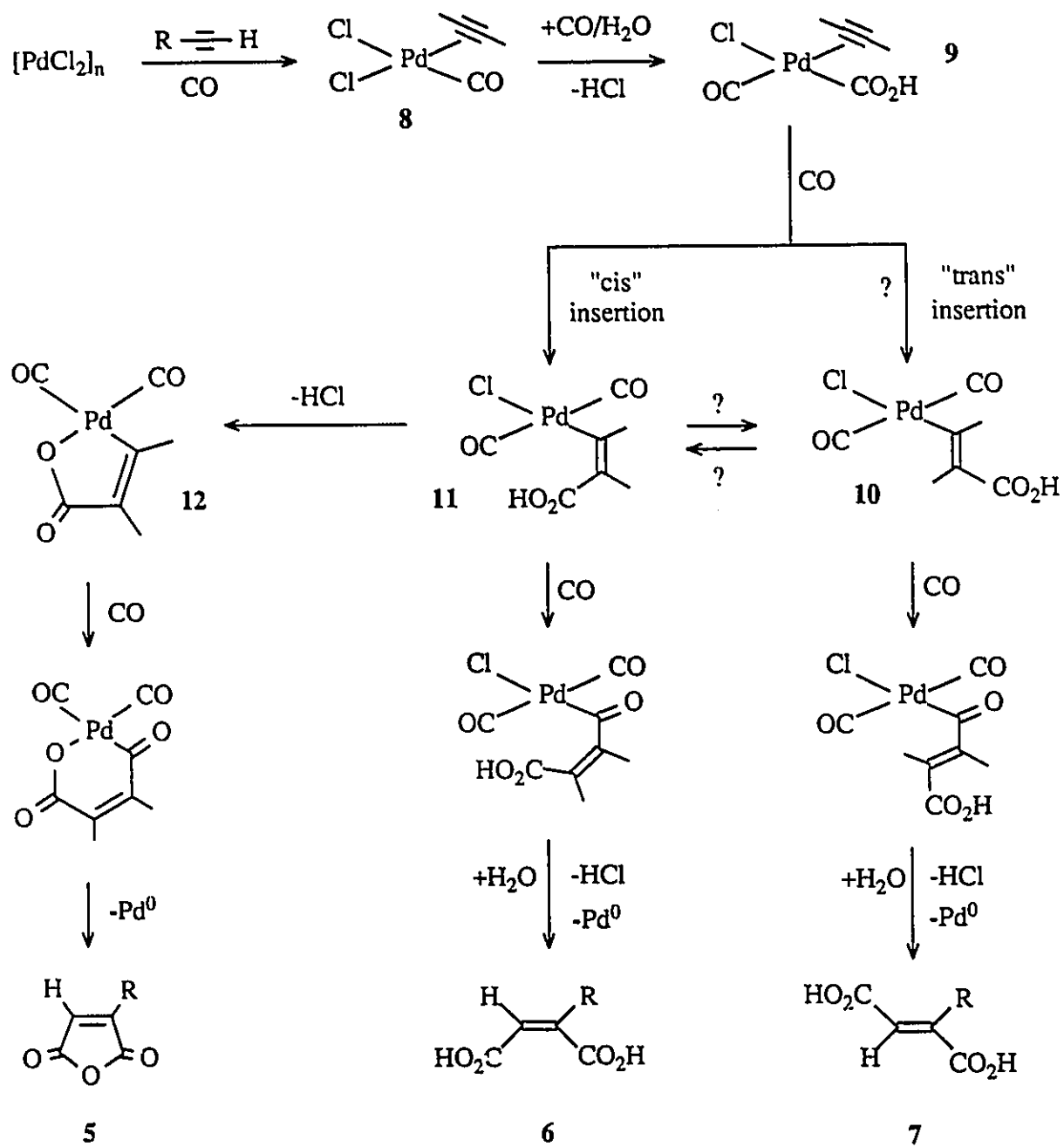
The mechanism shown in Scheme 3.1 is, in principle, very similar to that proposed by Heck¹³ for the dicarboalkoxylation of alkynes. Thus, coordination of CO and the alkyne to PdCl₂ can form complex **8**. Nucleophilic attack of water on the coordinated CO would give, after loss of HCl and the incorporation of another CO, the hydroxycarbonyl species **9**. The next step is the insertion of the coordinated alkyne into Pd-COOH, giving either **10** ("trans" insertion) or **11** ("cis" insertion); the stereochemistry of this insertion step will be discussed in the next section.

Complex **10** can undergo "migratory insertion" of CO into the metal alkenyl bond followed by the nucleophilic attack of water to give **7**. (Alternatively, the nucleophilic attack by water can take place first to form, after losing HCl, an alkenyl(carboxy) complex; this complex can then reductively eliminate the fumaric acid derivative **7** and Pd⁰.)

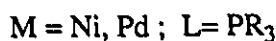
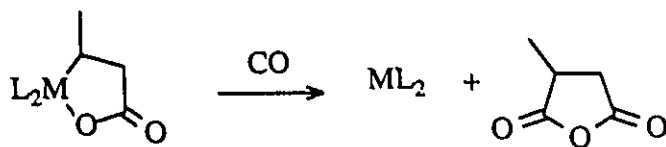
Complex **11** can undergo "migratory insertion" of CO, nucleophilic attack by water followed by loss of HCl, and reductive elimination to give the maleic acid derivative **6**. (As in the case of complex **10**, nucleophilic attack by water on complex **11** can take place first, followed by loss of HCl and reductive elimination to give to the same product.)

An alternative pathway for **11** is the oxidative addition of the carboxy O-H bond, followed by loss of HCl to give the metallalactone **12**. This complex is believed to be the main precursor to the maleic anhydride derivatives **5**. Yamamoto and coworkers¹²⁴ have synthesized and characterized complexes quite similar to **12**, and showed that these complexes undergo carbonylation to give the corresponding cyclic anhydrides, as shown

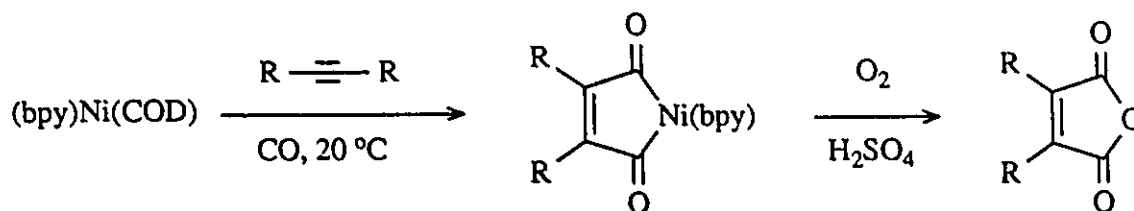
Scheme 3.1



below:



Therefore, it is reasonable to assume that **12** undergoes carbonylation and reductive elimination to give **5**. An interesting alternative involves the oxygen-induced cleavage of a metallacyclopentenedione, which might form by the insertion of two molecules of CO into the metal alkyne moiety. This sequence of steps was recently reported by Hoberg and Herrera¹²⁵ for a nickel complex, as shown below:



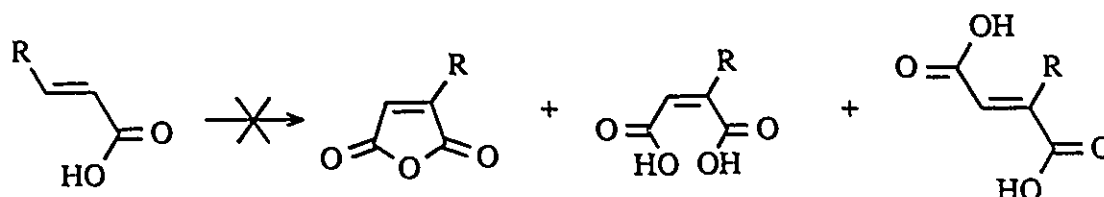
bpy= 2,2'-Bipyridine

COD= 1,5-Cyclooctadiene

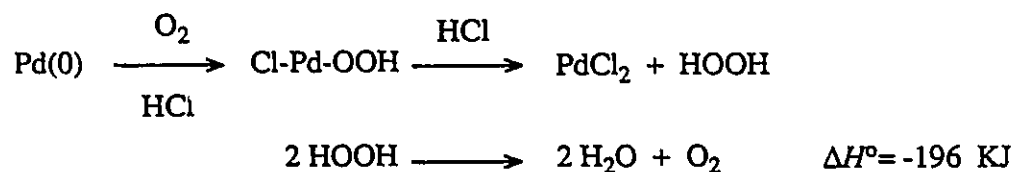
According to the overall reaction mechanism as depicted in Scheme 3.1, the products **5** and **6** both originate from the species **11**; one equivalent of water is required for the formation of **6** from **11**, whereas no water is required for the formation of **5**. This is consistent with the earlier described observation that the presence of excess water in the reaction medium changes the ratio of **5**:**6** in favour of **6**, without seriously affecting the proportion of **7** in the product distribution (Figure 3.1).

The present mechanism does not involve the formation of monocarbonylated products

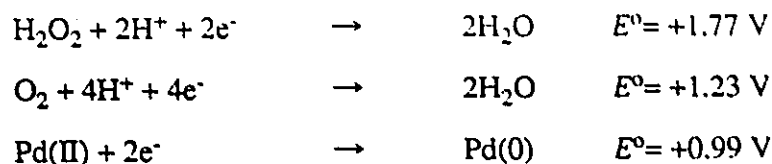
(enoic acids) as intermediates to the dicarbonylated products. This is based on the observation that *trans*-2-octenoic acid is not carbonylated under the catalytic reaction conditions:



Finally, the reduced palladium must be oxidized in order for the catalysis to proceed. As discussed earlier, our experimental results are consistent with a process in which oxygen is the main oxidant. One such process, involving a hydroperoxo complex, has been described by others.^{116,117} A slightly revised version of this process can be represented by the following sequence of steps.



These equations account for both the oxidation of Pd(0) to Pd(II) and the generation of water during the reaction. The HCl molecules required in the above steps are produced during the carbonylation reaction by the nucleophilic attack of water followed by loss of HCl (see Scheme 3.1). The role of CuCl₂ can be one of facilitating the oxidation of Pd⁰ in the above process by forming a Pd/Cu/CO complex, as proposed earlier. Both hydrogen peroxide and oxygen can, in theory, oxidize Pd(0) via redox processes according to the following reduction potentials:



These values refer to aqueous conditions, however, and are not directly applicable to the present argument.

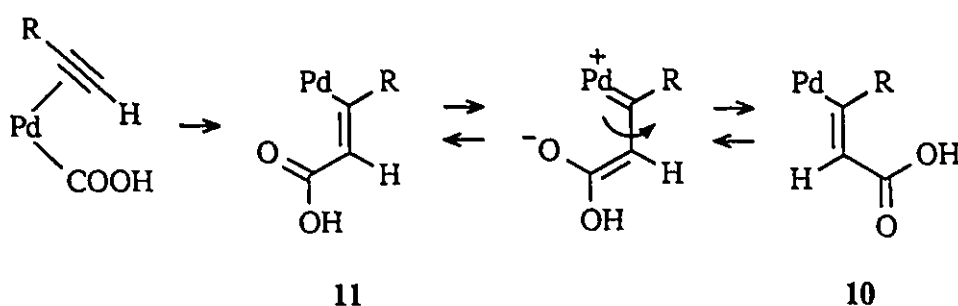
3.1.4 Alkyne Insertion Mechanism

The mechanism depicted in Scheme 3.1 accounts for the formation of the fumaric derivative **7** by invoking an overall "trans" insertion of the alkyne into the carboxy ligand to form the vinyl complex **10**. Strictly speaking, such a "trans" insertion is not the only possible route for the formation of **7**. In some cases, the product which appears to be the result of a "trans" insertion is, in fact, obtained from the (Z)-(E) isomerization of the "cis" insertion product. One relevant example is the HCo(CO)_4 -catalyzed hydrogenation of dimethyl acetylenedicarboxylate, where it was shown⁷⁹ that the major product, dimethyl fumarate, results not from a "trans" insertion but from a (Z)-(E) isomerization of the "cis" insertion product, dimethyl maleate. Palladium has also been shown¹²⁶ to affect such (Z)-(E) isomerizations with mixtures of styrenes. Therefore, it is possible that the "cis" insertion products are the *kinetic* products of the reaction, whereas the formal "trans" insertion products are the *thermodynamic* products.

In our system, however, it has been established that, once formed, the "cis" addition products **5** and **6** do not isomerize to **7** under the reaction conditions (Table 3.8); hence, these types of (Z)-(E) isomerizations can not explain the formation of **7**. This raises the possibility that a "trans" insertion is the source of **7**. An important question here is how such "trans"

insertions might take place.

A review of the literature on the insertion of alkynes into transition metal hydride and alkyl bonds reveals an abundance of precedents for the overall "trans" addition reaction, which occur either as the exclusive mode of addition or in conjunction with the "cis" addition.⁸⁰⁻⁸⁷ In spite of this abundance of examples, however, there are very few detailed mechanistic studies and little is known about the mechanism of "trans" insertions. Some workers have favoured a concerted "cis" insertion of the alkyne into the metal hydride or alkyl bond in the initial stage, followed by a cis-trans isomerization of the thus formed vinyl ligand. Others have proposed radical mechanisms for some insertion reactions. These and other ideas have been discussed in detail in the previous chapter (Alkyne Hydrocarboxylation), and shall not be repeated here. Suffice it to say that our results can be explained by the following cis-trans isomerization postulate:



The equilibrium distribution of **10** and **11** would presumably be determined by a number of factors, including the steric interactions between the R and the carboxyl groups. Thus, less of the "trans" insertion product **10**, and hence the fumaric derivative **7**, would be expected with bulky R groups; this is borne out by our results (Table 3.1).

3.2 Experimental Section

General Comments. The following materials were purchased from commercial sources and were used without further purification: acetone- d_6 , $CDCl_3$, $HCOOH$, D_2O , $PdCl_2$, $Pd(OAc)_2$, $Na_2[PdCl_4]$, $Pd(acac)_2$, 10% and 5% Pd/C , Pd -black, $CuCl_2$, $NiCl_2$, $NiBr_2$, $Ni(OAc)_2$, $Ni(CN)_2 \cdot 4H_2O$, di-*t*-butyl peroxide (DTBP), malonic acid, oxalic acid, acetic acid, boric acid, PPh_3 , PCy_3 , $P(OPh)_3$, $P(i-PrO)_3$, dppb, NaI , I_2 , $LiCl$, 4Å molecular sieves, $EtN(i-Pr)_2$. $Pd_2(dba)_3 \cdot CHCl_3$ was prepared according to a published procedure.¹²⁷

IR spectra were recorded on a Perkin-Elmer 783 spectrometer or a Bomem MB-100 FTIR. The elemental analyses were performed by Chemische Laboratoria, Groningen, Holland. Additional details on solvents, gases, alkynes, ^1H and ^{13}C NMR spectra, and GC/MS analyses can be found in the General Comments section of Chapter II.

3.2.1 General Procedure for The Catalytic Reactions

The catalytic reactions were carried out in a 2- or 3-neck flask containing a stirring bar and connected to an oil bubbler through a cold water condenser. The CO/O_2 gas mixture was bubbled through the reaction flask via a gas inlet adaptor extending down below the surface of the solvent. Unless otherwise indicated, the gas mixture consisted of approximately 9 mL/min of CO and 3 mL/min of O_2 . The starting materials were usually added in the following order: solvent, metal compounds ($PdCl_2$, $CuCl_2$, etc.), alkyne, and $HCOOH$ (or other reagents). The reaction mixture was then stirred at room temperature and, unless otherwise indicated, the CO/O_2 gas flow was maintained throughout the duration of the reaction.

The final reaction mixture was worked-up as follows. The solvent was evaporated and the residual material was extracted with diethyl ether/water. The ethereal layer was dried over MgSO_4 , filtered, evaporated to dryness, and held under vacuum for 20-30 min. The resultant oil or solid was weighed prior to analysis or chromatographic separation.

Quantitative analyses of the reaction products were carried out by ^1H NMR spectroscopy (acetone-d_6) using an accurately weighed quantity of maleic acid as internal standard. Integration of the vinylic proton resonances of the carbonylated products (*ca.* 6.95 ppm for the monosubstituted maleic anhydrides **5**, 6.75 ppm for the corresponding fumaric acids **7**, and 5.95 ppm for the corresponding maleic acids **6**) against that of the standard (*ca.* 6.40 ppm) gave both the total yields and the product ratios. In some experiments, the products were isolated by standard basification/neutralization extractions and/or column chromatography (silica gel, 1:2 methylene chloride:hexane followed by 1:1 ethyl acetate:hexane), and characterized on the basis of IR, ^1H and ^{13}C NMR, and GC/MS spectra.

3.2.2 The Specific Experiments

This section contains detailed accounts of the individual experiments carried out during the course of this study. The majority of these accounts describe the experiments which were carried out to optimize the reaction conditions and to probe the reaction mechanism. The first nine, however, describe the experiments in which optimal reaction conditions were used and which, in general, gave the best results. The following items are included in these:

- a. The name of the compound synthesized and its Chemical Abstracts registry number (Chemical Abstracts names in boldface type, other names inside the parentheses and in normal type, registry numbers in italic type and inside square brackets);

b. The Arabic number which will be used throughout this thesis to refer to the corresponding compound (the Glossary of Compounds, included at the beginning of the thesis, also contains the compound names and the corresponding numerical designations);

c. The experimental details and complete spectral data obtained for the characterization of the compounds.

3-Phenyl-2,5-furandione [36122-35-7] (Phenylmaleic anhydride), **5a**. The general procedure was followed using PdCl₂ (26 mg, 0.15 mmol), CuCl₂ (40 mg, 0.30 mmol), phenylacetylene (167 mg, 1.64 mmol), HCOOH (90%, 146 mg, 3.17 mmol), and THF (4 mL) for 7 h. The reaction mixture was worked-up as described above (see "General Procedure for Catalytic Reactions", section 3.2.1) to give 246 mg of a yellow powder from the organic layer. Spectral analysis of this material (as described above) revealed that it was **5a**. (¹H NMR yield= 74%)

Column chromatography with 1:1 CH₂Cl₂: hexane as eluent gave 192 mg of **5a**. (Isolated yield= 68%)

¹H NMR (δ, acetone-d₆). 7.91 (m, *ortho* protons of the phenyl ring), 7.56 (m, *meta* and *para* protons of the phenyl ring), 7.04 (s, =CH). The present data match those reported in the literature.¹²⁸

¹³C NMR (δ, CDCl₃). 164.5 and 163.6 (C=O), 146.8 (=CPh), 132.7 (=CH), 129.3 and 128.9 (*ortho*- and *meta*-carbon atoms of Ph), 126.8 (*ipso*-carbon atom of Ph), 124.4 (*para*-carbon atom of Ph).

GC/MS (m/e, relative intensity). M⁺= 174 (48%), 102 (100%), 76 (13%).

IR (CDCl₃, cm⁻¹). 1855 (m), 1815 (sh), 1770 (s), 1620 (w), 1500 (w), 1455 (w), 1060 (w).

tert-Butylmaleic anhydride [18261-07-9], **5b**, and *tert*-butylmaleic acid [18305-61-8], **6b**. The general procedure was followed using PdCl₂ (39 mg, 0.22 mmol), CuCl₂ (54 mg, 0.40 mmol), 3,3-dimethyl-1-butyne (300 mg, 3.66 mmol), HCOOH (90%, 310 mg, 6.74 mmol), and THF (15 mL) for 5 h. Work-up of the final reaction mixture in the usual manner gave 419 mg of an orange, crystalline solid from the organic layer. Spectral analysis of this material revealed that it contained a 95:5 mixture of **5b** and **6b**, respectively. (Combined yield= 49%)

¹H NMR (δ, CDCl₃). **5b**: 6.50 (s, =CH), 1.33 (s, C(CH₃)₃); **6b**: 6.14 (s, =CH), 1.33 (s, C(CH₃)₃). The present data match those reported in the literature.¹²⁹

¹³C NMR (δ, CDCl₃). **5b**: 164.0 and 163.4 (CO₂CO), 161.4 (=CCMe₃), 126.9 (=CH), 33.4 (CMe₃), 28.0 (C(CH₃)₃).

GC/MS (m/e, relative intensity). **5b** and **6b**: 154 (1%), 139 (22%), 126 (100%), 111 (100%), 110 (100%), 95 (100%), 83 (100%), 81 (100%).

IR (Nujol, cm⁻¹). **5b**: 3160 (m), 2950 (s), 1865 (sh), 1840 (sh), 1780 (s, br), 1630 (m).

1-(Methylpropyl)maleic anhydride [134566-86-2] (*sec*-butylmaleic anhydride), **5c**, (*Z*)-2-(1-methylpropyl)-2-butenedioic acid [134566-91-9] (*sec*-butylmaleic acid), **6c**, and (*E*)-2-(1-methylpropyl)-2-butenedioic acid [6621-99-4] (*sec*-butylfumaric acid), **7c**. The general procedure was followed using PdCl₂ (28 mg, 0.16 mmol), CuCl₂ (41 mg, 0.31 mmol), 3-methyl-1-pentyne (141 mg, 1.72 mmol), HCOOH (90%, 117 mg, 2.54 mmol), and THF (15 mL) for 6 h. Work-up of the reaction mixture in the usual manner gave 247 mg of a dark oil from the organic layer. Spectral analysis of this material revealed that it contained a 66:26:8 mixture of **5c**, **6c**, and **7c**, respectively. (Combined yield= 66%)

¹H NMR (δ, acetone-d₆). **5c**: 6.94 (d, ⁴J_{H-H}= 1.3, =CH), 2.70 (m, =CCH(Me)Et), 1.67 (m, CH(CH₂CH₃)CH₃), 1.24 (d, ³J_{H-H}= 6.9, CH(CH₃)Et), 0.93 (t, ³J_{H-H}= 7.5, CH₂CH₃); **6c**:

5.82 (d, $^4J_{\text{H-H}} = 1.0$, $=\text{C}(\text{COOH})\underline{\text{H}}$), 2.62 (m, $=\text{C}(\text{COOH})\underline{\text{CH}}(\text{Me})\text{Et}$), 1.73 (m, $\text{CH}(\underline{\text{CH}_2}\text{-CH}_3)\text{CH}_3$), 1.12 (d, $^3J_{\text{H-H}} = 6.7$, $\text{CH}(\underline{\text{CH}_3})\text{Et}$), 0.88 (t, $^3J_{\text{H-H}} = 7.1$, $\text{CH}_2\underline{\text{CH}_3}$); **7c**: 6.66 (s, $=\text{C}(\text{COOH})\underline{\text{H}}$), 2.91 (m, $=\text{C}(\text{COOH})\underline{\text{CH}}(\text{Me})\text{Et}$), 1.78 (m, $\text{CH}(\underline{\text{CH}_2}\text{CH}_3)\text{CH}_3$), 1.17 (d, $^3J_{\text{H-H}} = 6.4$, $\text{CH}(\underline{\text{CH}_3})\text{Et}$), 0.91 (t, $^3J_{\text{H-H}} = 7.2$, $\text{CH}_2\underline{\text{CH}_3}$). The present data match those reported in the literature.^{18,130}

^{13}C NMR (δ , acetone- d_6) **5c**: 167.1 and 165.7 ($\underline{\text{CO}_2\underline{\text{CO}}}$), 158.7 ($=\underline{\text{C}}\text{CH}(\text{Me})\text{Et}$), 129.4 ($=\underline{\text{CH}}$), 34.0 ($\underline{\text{CH}}(\text{Me})\text{Et}$), 28.6 ($\underline{\text{CH}_2}\text{CH}_3$), 18.4 ($\text{CH}(\underline{\text{CH}_3})\text{Et}$), 11.9 ($\text{CH}_2\underline{\text{CH}_3}$); **7c**: 168.1 and 162.3 ($\underline{\text{COOH}}$), 152.7 ($=\underline{\text{C}}(\text{COOH})\text{CH}(\text{Me})\text{Et}$), 127.6 ($=\underline{\text{C}}(\text{COOH})\text{H}$), 36.1 ($\underline{\text{CH}}(\text{Me})\text{Et}$), 28.9 ($\underline{\text{CH}_2}\text{CH}_3$), 19.5 ($\text{CH}(\underline{\text{CH}_3})\text{Et}$), 13.0 ($\text{CH}_2\underline{\text{CH}_3}$).

GC/MS (m/e , relative intensity). **5c**: $\text{M}^+ = 154$ (12%), 126 (100%), 112 (46%), 111 (57%), 98 (85%), 95 (45%), 81 (50%), 67 (80%); trimethylsilyl diesters of **6c** and **7c**: $\text{M}^+ = 316$ (5%), 301 (22%), 147 (100%).

IR (CHCl_3 , cm^{-1}). **5c**: 2973 (s), 1841 (sh), 1775 (s), 1467 (s), 1378 (m), 953 (s); **6c**: 3493-2878 (br), 1708 (s), 1638 (m), 1356 (s), 989 (w); **7c**: 3652-2936 (br), 1701 (s), 1645 (sh), 1411 (w), 954 (s).

3-(2-Phenylethyl)-2,5-furandione [134566-87-3] ((2-phenylethyl)maleic anhydride), **5d**, and (*E*)-2-(2-phenylethyl)-2-butenedioic acid [5469-48-7] ((2-phenylethyl)fumaric acid), **7d**. The general procedure was followed using PdCl_2 (40 mg, 0.23 mmol), CuCl_2 (56 mg, 0.42 mmol), 4-phenyl-1-butyne (289 mg, 2.22 mmol), HCOOH (90%, 186 mg, 4.04 mmol), and THF (20 mL) for 7 h. Work-up of the reaction mixture in the usual manner gave 462 mg of an orange solid from the organic layer. Spectral analysis of this material revealed that it contained a 75:25 mixture of **5d** and **7d**, respectively. (Combined yield = 53%)

^1H NMR (δ). **5d** (CDCl_3): 7.30-7.13 (m, Ph), 6.45 (t, $^4J_{\text{H-H}} = 1.5$, $=\underline{\text{CH}}$), 2.92 (m, $\text{Ph}\underline{\text{CH}_2}$), 2.87 (m, $\text{PhCH}_2\underline{\text{CH}_2}$); **7d** (acetone- d_6): 7.26 (m, Ph), 6.76 (s, $=\text{C}(\text{COOH})\underline{\text{H}}$), 4.03

(br, COOH), 3.01 (m, PhCH_2), 2.80 (m, PhCH_2CH_2). The present data match those reported in the literature.¹⁸

^{13}C NMR (δ , acetone- d_6). **5d**: 166.5 and 164.8 (CO_2CO), 152.8 ($=\text{C}-\text{CH}_2$), 140.3 ($=\text{CH}$), 129.4, 128.7, 128.5, 126.6 (Ph), 32.4 (PhCH_2), 27.1 (PhCH_2CH_2); **7d**: 168.1 and 167.0 (COOH), 148.0 ($=\text{C}(\text{COOH})\text{CH}_2$), 142.5 ($=\text{C}(\text{COOH})\text{H}$), 129.1 (*ortho*- and *meta*-carbon atoms of Ph), 128.0 (*ipso*-carbon atom of Ph), 126.7 (*para*-carbon atom of Ph), 36.0 (CMe_3), 30.7 (CH_3).

GC/MS (*m/e*, relative intensity). **5d**: M^+ = 202 (23%), 129 (63%), 91 (100%); high resolution MS: calculated for $\text{C}_{12}\text{H}_{10}\text{O}_3$: 202.1381; found: 202.0604; **7d**: M^+ = 220 (3%), 91 (100%); trimethylsilyl diester of **7d**: M^+ = 364.

IR (Nujol, cm^{-1}). **5d**: 2950 (s), 1840 (sh), 1765 (s), 1495 (s), 1165(m); **7d**: 3300-2500 (br), 1700 (s), 1640 (sh), 1490 (sh), 1185 (s).

3-(3-Phenylpropyl)-2,5-furandione [134566-88-4] ((3-phenylpropyl)maleic anhydride), **5e**, and (*E*)-2-(3-phenylpropyl)-2-butenedioic acid [134566-94-2] ((3-phenylpropyl)fumaric acid, **7e**). The general procedure was followed using PdCl_2 (30 mg, 0.17 mmol), CuCl_2 (52 mg, 0.39 mmol), 5-phenyl-1-pentyne (279 mg, 1.94 mmol), HCOOH (90%, 137 mg, 2.97 mmol), and THF (5 mL) for 5.5 h. Work-up in the usual manner gave 407 mg of a dark solid from the organic layer. Spectral analysis of this material revealed that it contained a 69:31 mixture of **5e** and **7e**, respectively. (Combined yield = 65%)

^1H NMR (δ , acetone- d_6) **5e**: 7.3-7.1 (m, Ph), 6.94 (t, $^4\text{J}_{\text{H-H}} = 1.8$, $=\text{CH}$), 2.73 (t, $^3\text{J}_{\text{H-H}} = 7.4$, PhCH_2), 2.57 (td, $^3\text{J}_{\text{H-H}} = 7.4$, $^4\text{J}_{\text{H-H}} = 1.6$, $=\text{CCH}_2$), 1.88 (m, PhCH_2CH_2); **7e**: 7.3- 7.1 (m, Ph), 6.79 (s, $=\text{C}(\text{COOH})\text{H}$), 2.85 (t, $^3\text{J}_{\text{H-H}} = 7.2$, $=\text{CCH}_2$), 2.72 (t, $^3\text{J}_{\text{H-H}} = 7.4$, PhCH_2), 1.91 (m, PhCH_2CH_2).

^{13}C NMR (δ , acetone- d_6). **5e**: 166.2 and 164.8 (CO_2CO), 142.9 ($=\text{CCH}_2$), 133.2

(=CH), 129.8, 128.9, 127.3 and 126.4 (Ph), 35.8 (=C(CH₂), 33.1 (PhCH₂), 23.8 (PhCH₂CH₂);
7e: 168.3 and 167.0 (COOH), 148.5 (=C(COOH)CH₂), 134.6 (=C(COOH)H), 129.1, 129.0,
 127.6 and 126.5 (Ph), 36.5 (=C(COOH)CH₂), 31.7 (PhCH₂), 28.3 (PhCH₂CH₂).

MS (m/e, relative intensity). **7e**: 216 (9%), 188 (12%), 143 (16%), 129 (41%), 112 (74%), 105 (76%), 91 (100%).

IR (CHCl₃, cm⁻¹). **5e**: 2923 (s), 1845 (w), 1746 (m), 1606 (m), 1257 (sh) 1167 (s); **7e**:
 3490-2566 (br), 1695 (s), 1646 (sh), 1287 (s), 1096 (w).

3-Chloropropyl-2,5-furandione [134566-89-5] ((3-chloropropyl)maleic anhydride),
5f, (*Z*)-2-(3-chloropropyl)-2-butenedioic acid [134566-92-0] ((3-chloropropyl)maleic acid),
6f, and (*E*)-2-(3-chloropropyl)-2-butenedioic acid [134566-95-3] ((3-chloropropyl)fumaric
 acid), **7f**. The general procedure was followed using PdCl₂ (36 mg, 0.20 mmol), CuCl₂ (54
 mg, 0.40 mmol), 5-chloro-1-pentyne (197 mg, 1.92 mmol), HCOOH (90%, 202 mg, 4.39
 mmol), and THF (15 mL) for 6 h. Work-up in the usual manner gave 334 mg of an orange
 solid from the organic layer. Spectral analysis of this material revealed that it contained a
 70:5:25 mixture of **5f**, **6f**, and **7f**, respectively. (Combined yield= 59%)

¹H NMR (δ, acetone-d₆). **5f**: 7.05 (t, ⁴J_{H-H}= 1.3, =CH), 3.63 (t, ³J_{H-H}= 6.9, Cl-CH₂),
 2.73 (t, ³J_{H-H}= 7.3, =CCH₂), 1.97 (quintet, ³J_{H-H}= 7.3, CH₂CH₂CH₂); **6f**: 6.42 (s, =CH), 3.63
 (t, ³J_{H-H}= 6.9, Cl-CH₂), 2.90 (t, ³J_{H-H}= 7.3, =CCH₂), 1.97 (quintet, ³J_{H-H}= 7.3, CH₂CH₂CH₂);
7f: 6.83 (s, =CH), 3.63 (t, ³J_{H-H}= 6.9, Cl-CH₂), 2.90 (t, ³J_{H-H}= 7.3, =CCH₂), 1.97 (quintet,
³J_{H-H}= 7.3, CH₂CH₂CH₂).

¹³C NMR (δ, acetone-d₆). **5f**: 168.2 and 167.1 (CO₂CO), 143.6 (=CCH₂), 133.1
 (=CH), 45.9 (CH₂Cl), 33.8 (=CCH₂), 26.2 (CH₂CH₂Cl); **6f**: 166.6 and 164.3 (COOH), 148.3
 (=C(COOH)CH₂), 130.1 (=C(COOH)H), 46.1 (CH₂Cl), 34.7 (=C(COOH)CH₂), 24.8 (CH₂-
 CH₂Cl); **7f**: 168.2 and 167.1 (COOH), 147.5 (=C(COOH)CH₂), 128.6 (=C(COOH)H), 45.6

($\underline{\text{CH}_2\text{Cl}}$), 33.2 ($=\text{C}(\text{COOH})\underline{\text{CH}_2}$), 26.5 ($\underline{\text{CH}_2\text{CH}_2\text{Cl}}$).

GC/MS (m/e, relative intensity). **5f**: M^+ = 176 & 174, 139 (91%), 112 (59%), 111 (42%), 110 (40%), 104 (21%), 102 (65%); **6f** and **7f**: 176 (0.4%), 174 (0.5%), 139 (75%), 112 (45%), 111 (35%), 102 (45%).

IR (CHCl_3 , cm^{-1}). **5f**: 2960 (s), 1843 (sh), 1776 (s), 1643 (sh), 1432 (m), 891 (s); **7f**: 3668-2632 (br), 1709 (s), 1640 (sh), 1435 (m), 921 (w).

3-Cyanopropyl-2,5-furandione [134566-90-8] ((3-cyanopropyl)maleic anhydride), **5g**, (**Z**)-2-(3-cyanopropyl)-2-butenedioic acid [134566-93-1] ((3-cyanopropyl)maleic acid), **6g**, and (**E**)-2-(3-cyanopropyl)-2-butenedioic acid [134566-96-4] ((3-cyanopropyl)fumaric acid), **7g**. The general procedure was followed using PdCl_2 (37 mg, 0.21 mmol), CuCl_2 (54 mg, 0.40 mmol), 5-cyano-1-pentyne (204 mg, 2.19 mmol), HCOOH (90%, 203 mg, 4.41 mmol), and THF (15 mL) for 6 h. Work-up in the usual manner gave 196 mg of a yellow oily solid from the organic layer. Spectral analysis of this material revealed that it contained a 62:11:27 mixture of **5g**, **6g**, and **7g**, respectively. (Combined yield = 30%)

^1H NMR (δ , acetone- d_6). **5g**: 7.08 (t, $^4\text{J}_{\text{H-H}} = 1.7$, $=\underline{\text{CH}}$), 2.72 (td, $^3\text{J}_{\text{H-H}} = 7.4$, $^4\text{J}_{\text{H-H}} = 1.7$, $=\underline{\text{CCH}_2}$), 2.64 (t, $^3\text{J}_{\text{H-H}} = 7.0$, $\underline{\text{CH}_2\text{CN}}$), 1.86 (m, $\underline{\text{CH}_2\text{CH}_2\text{CN}}$); **6g**: 5.91 (m, $=\text{C}(\text{COOH})\underline{\text{H}}$), 2.37 (td, $^3\text{J}_{\text{H-H}} = 6.7$, $^4\text{J}_{\text{H-H}} = 2.6$, $=\text{C}(\text{COOH})\underline{\text{CH}_2}$), 2.59 (t, $^3\text{J}_{\text{H-H}} = 7.3$, $\underline{\text{CH}_2\text{CN}}$), 1.86 (m, $\underline{\text{CH}_2\text{CH}_2\text{CN}}$); **7g**: 6.85 (s, $=\text{C}(\text{COOH})\underline{\text{H}}$), 2.87 (t, $^3\text{J}_{\text{H-H}} = 7.4$, $=\text{C}(\text{COOH})\underline{\text{CH}_2}$), 2.51 (t, $^3\text{J}_{\text{H-H}} = 7.1$, $\underline{\text{CH}_2\text{CN}}$), 1.89 (m, $\underline{\text{CH}_2\text{CH}_2\text{CN}}$).

^{13}C NMR (δ , acetone- d_6). **5g**: 167.1 and 165.6 ($\underline{\text{CO}_2\text{CO}}$), 152.8 ($=\underline{\text{CCH}_2}$), 130.8 ($=\underline{\text{CH}}$), 120.4 ($\underline{\text{CN}}$), 25.6 ($=\underline{\text{CCH}_2}$), 23.7 ($\underline{\text{CH}_2\text{CN}}$), 16.9 ($\underline{\text{CH}_2\text{CH}_2\text{CN}}$); **7g**: 168.1 and 167.3 ($\underline{\text{COOH}}$), 146.9 ($=\underline{\text{C}}(\text{COOH})\underline{\text{CH}_2}$), 129.1 ($=\underline{\text{C}}(\text{COOH})\underline{\text{H}}$), 120.6 ($\underline{\text{CN}}$), 27.8 ($=\text{C}(\text{COOH})\underline{\text{CH}_2}$), 26.1 ($\underline{\text{CH}_2\text{CN}}$), 16.5 ($\underline{\text{CH}_2\text{CH}_2\text{CN}}$).

GC/MS (m/e, relative intensity). Trimethylsilyl diester of **6g**: M^+ = 312 (23%), 237

(4%), 197 (3%), 149 (12%), 147 (100%), 113 (3%), 73 (80%); trimethylsilyl diester of **7g**: M^+ = 312 (45%), 237 (24%), 197 (43%), 147 (68%), 113 (29%), 73 (100%)

IR (CHCl₃, cm⁻¹). **5g**: 2953 (s), 2252 (w), 1851 (sh), 1781 (s), 1457 (sh) 1429 (m), 989 (w); **7g**: 3453-2857 (br), 2253 (w), 1725 (s), 1644 (w), 1415 (w), 892 (s).

Butylmaleic anhydride [100378-66-3], **5h**, (**Z**)-2-butyl-2-butenedioic acid [69665-12-9] (butylmaleic acid), **6h**, and (**E**)-2-butyl-2-butenedioic acid [5469-36-3] (butylfumaric acid), **7h**. The general procedure was followed using PdCl₂ (19 mg, 0.11 mmol), CuCl₂ (31 mg, 0.23 mmol), 1-hexyne (93 mg, 1.13 mmol), HCOOH (90%, 43 mg, 0.93 mmol), and THF (20 mL) for 6 h. Work-up in the usual manner gave 130 mg of a yellow solid from the organic layer. Spectral analysis of this material revealed that it contained a 65:5:30 mixture of **5h**, **6h**, and **7h**, respectively. (Combined yield= 54%)

¹H NMR (δ, acetone-d₆). **5h**: 6.95 (t, ⁴J_{H-H} = 1.7, =CH), 2.53 (td, ³J_{H-H} = 7.2, ⁴J_{H-H} = 1.5, =CCH₂), 1.43 (m, (CH₂)₂CH₃), 0.92 (t, ³J_{H-H} = 7.3, CH₃); **6h**: 5.90 (t, (t, ⁴J_{H-H} = 1.5, =C(COOH)H), 2.40 (td, ³J_{H-H} = 7.1, ⁴J_{H-H} = 1.5, =C(COOH)CH₂), 1.42 (m, (CH₂)₂CH₃), 0.91 (t, ³J_{H-H} = 7.0, CH₃); **7h**: 6.76 (br, =C(COOH)H), 2.79 (t, ³J_{H-H} = 7.1, =C(COOH)CH₂), 1.42 (m, (CH₂)₂CH₃), 0.90 (t, ³J_{H-H} = 7.2, CH₃). The present data match those reported in the literature.^{18,131,132}

¹³C NMR (δ, acetone-d₆). **5h**: 167.5 and 166.3 (CO₂CO), 153.5 (=CCH₂), 128.7 (=CH), 36.3 (=CCH₂), 28.5 (CH₂CH₂CH₃), 23.1 (CH₂CH₃), 14.4 (CH₃); **6h**: 164.5 and 163.9 (COOH), 148.1 (=C(COOH)CH₂), 126.2 (=C(COOH)H), 33.3 (=CCH₂), 28.3 (CH₂CH₂CH₃), 23.7 (CH₂CH₃), 14.1 (CH₃); **7h**: 168.74 and 167.4 (COOH), 148.3 (=C(COOH)CH₂), 127.5 (=C(COOH)H), 32.2 (=C(COOH)CH₂), 28.1 (CH₂CH₂CH₃), 23.4 (CH₂CH₃), 14.1 (CH₃).

GC/MS (m/e, relative intensity). **5h**, **6h**, and **7h**: 154 (17%), 126 (38%) 112 (100%), 111 (60%), 84 (68%).

IR (CHCl₃, cm⁻¹). 6h: 3677-2858 (br), 1708 (s), 1604 (sh), 1266 (w), 1016 (w); 7h: 3677-2858 (br), 1715 (s), 1649 (w), 1433 (w), 1104 (w).

Hexylmaleic anhydride [90926-71-9], 5i, (Z)-2-hexyl-2-butenedioic acid [104505-48-8] (hexylmaleic acid), 6i, and (E)-2-hexyl-2-butenedioic acid [71033-48-2] (hexylfumaric acid), 7i. The general procedure was followed using PdCl₂ (21 mg, 0.12 mmol), CuCl₂ (40 mg, 0.30 mmol), 1-octyne (134 mg, 1.22 mmol), HCOOH (90%, 130 mg, 2.54 mmol), and THF (15 mL) for 7.5 h. Work-up in the usual manner gave 240 mg of a yellow-brown solid from the organic layer. Spectral analysis of this material revealed that it contained a 70:5:25 mixture of 5i, 6i, and 7i, respectively. (Combined ¹H NMR yield= 68%)

Column chromatography with a 1:1 mixture of CH₂Cl₂:hexane as eluent gave 90 mg of 1i (41%) and 44 mg of 3i (18%). (Combined isolated yield= 59%)

¹H NMR (δ). 5i (acetone-d₆): 6.96 (t, ⁴J_{H-H}= 1.7, =CH), 2.54 (td, ³J_{H-H}= 7.3, ⁴J_{H-H}= 1.7, =CCH₂), 1.68 (quintet, ³J_{H-H}= 7.8, =CCH₂CH₂CH₂), 1.35 (m, (CH₂)₃CH₃), 0.89 (t, ³J_{H-H}= 6.8, CH₃); 6i: 5.87 (t, ⁴J_{H-H}= 1.6, =C(COOH)H), 2.37 (td, ³J_{H-H}= 7.2, ⁴J_{H-H}= 1.1, =C(COOH)CH₂), 1.53 (m, =C(COOH)CH₂CH₂), 1.45-1.20 (m, (CH₂)₃CH₃), 0.89 (t, ³J_{H-H}= 6.6, CH₃); 7i (CDCl₃): 6.85 (s, =C(COOH)H), 2.79 (t, ³J_{H-H}= 7.1, =C(COOH)CH₂), 1.51 (m, =C(COOH)CH₂CH₂), 1.46-1.24 (m, (CH₂)₃CH₃), 0.87 (t, ³J_{H-H}= 6.6, CH₃). The present data matches those reported in the literature.^{18,132}

¹³C NMR (δ, acetone-d₆). 5i: 168.3, 166.2 (CO₂CO), 146.3 (=CCH₂), 130.2 (=CH), 34.1 (=CCH₂), 27.9 (=CCH₂CH₂), 25.4 (CH₂(CH₂)₂CH₃), 24.1 (CH₂CH₂CH₃), 20.9 (CH₂-CH₃), 13.6 (CH₃); 6i: 165.4 and 163.9 (COOH), 149.2 (=C(COOH)CH₂), 128.3 (=C(COOH)H), 33.2 (=C(COOH)CH₂), 28.4 (=C(COOH)CH₂CH₂), 25.1 (CH₂(CH₂)₂CH₃), 22.1 (CH₂CH₂CH₃), 20.3 (CH₂CH₃), 13.7 (CH₃); 7i: 167.4 and 166.1 (COOH), 148.0 (=C(COOH)CH₂), 126.1 (=C(COOH)H), 30.9(=C(COOH)CH₂), 28.6 (=C(COOH)CH₂CH₂),

26.9 ($\text{CH}_2(\text{CH}_2)_2\text{CH}_3$), 23.2 ($\text{CH}_2\text{CH}_2\text{CH}_3$), 21.8 (CH_2CH_3), 12.9 (CH_3).

GC/MS (m/e, relative intensity). **5i**: $\text{M}^+ = 182$ (35%), 154 (55%), 110 (20%); **6i** and **7i**: $\text{M}^+ = 200$ (5%), 182 (98%), 164 (12%), 154 (24%), 148 (100%).

IR (Nujol, cm^{-1}). **5i**: 2947 (s), 1853 (sh), 1767 (s), 1465 (w), 1429 (s), 986 (m); **6i** and **7i**: 3400-2500 (br), 1705 (s), 1645 (sh), 1200 (m), 1150 (m), 940 (s), 910 (s).

The reactions of propynoic acid and its esters

The general procedure was followed using PdCl_2 (34 mg, 0.19 mmol), CuCl_2 (54 mg, 0.40 mmol), propynoic acid (121 mg, 1.73 mmol), HCOOH (90%, 155 mg, 3.37 mmol), and THF (15 mL) for 5 h. Work-up in the usual manner gave 137 mg of a brown solid from the organic layer. The ^1H NMR spectrum of this material was very complex, and GC/MS analysis indicated the presence of a few species arising, perhaps, from the decomposition of a high molecular weight oligomer. No further attempts were made to characterize this material. Analogous reactions with methyl and butyl propynoates instead of propynoic acid gave the same results.

Internal alkyne reaction

The general procedure was followed using PdCl_2 (31 mg, 0.18 mmol), CuCl_2 (45 mg, 0.34 mmol), 3-methyl-2-pentyne (170 mg, 2.07 mmol), HCOOH (90%, 185 mg, 4.03 mmol), and THF (5 mL) for 5.5 h. Work-up in the usual manner gave 74 mg of an orange oil from the organic layer. Spectral analysis of this material revealed that no carbonylation products had formed.

Testing various metal catalysts

Blank reaction: No metal catalyst. The general procedure was followed using

1-octyne (202 mg, 1.84 mmol), HCOOH (90%, 259 mg, 5.63 mmol) and THF (25 mL) for 5 h. Work-up in the usual manner gave 7 mg of a yellow oil. Spectral analysis of this material showed that it contained 1-octyne and HCOOH.

Na₂[PdCl₄]. The general procedure was followed using Na₂[PdCl₄] (49 mg, 0.17 mmol), CuCl₂ (51 mg, 0.38 mmol), 1-octyne (210 mg, 1.91 mmol), HCOOH (90%, 125 mg, 2.72 mmol), and THF (5 mL) for 6.5 h. Standard work-up resulted in a 61:6:33 mixture of 5i, 6i, and 7i, respectively, in 44% combined yield, plus small amounts of unidentified products.

Pd-black. The general procedure was followed using Pd-black (17 mg, 0.16 mmol), CuCl₂ (43 mg, 0.32 mmol), 1-octyne (180 mg, 1.64 mmol), HCOOH (90%, 149 mg, 3.23 mmol), and THF (5 mL) for 5 h. Standard work-up resulted in only traces of 5i, 6i, and 7i.

Another experiment using Pd-black in the absence of CuCl₂/O₂ gave no products.

Pd₂(dba)₃. The general procedure was followed using Pd₂(dba)₃ (141 mg, 0.14 mmol), CuCl₂ (55 mg, 0.41 mmol), 1-octyne (154 mg, 1.40 mmol), HCOOH (90%, 167 mg, 3.62 mmol), and THF (5 mL) for 6 h. Standard work-up resulted in a 50:20:30 mixture of 5i, 6i, and 7i, respectively in 47% combined yield.

Repeating the above experiment in the absence of CuCl₂/O₂ resulted in no carbonylation.

Pd/C. The general procedure was followed using 10% Pd/C (157 mg, 0.15 mmol), CuCl₂ (52 mg, 0.39 mmol), 1-octyne (181 mg, 1.65 mmol), HCOOH (90%, 131 mg, 2.86 mmol), and THF (5 mL) for 12 h. Standard work-up resulted in a 55:9:36 mixture of 5i, 6i, and 7i, respectively, in 57% combined yield.

A similar experiment was carried out using 5% Pd/C, as follows: 5% Pd/C (142 mg, 0.067 mmol), CuCl₂ (26 mg, 0.19 mmol), 1-octyne (183 mg, 1.66 mmol), HCOOH (90%, 106 mg, 2.31 mmol), and THF (5 mL) for 6.5 h. Standard work-up resulted in a 64:4:32 mixture of 5i, 6i, and 7i, respectively, in 17% combined yield.

Repeating the above experiments in the absence of CuCl_2/O_2 resulted in no carbonylation.

$\text{Pd}(\text{acac})_2$. The general procedure was followed using $\text{Pd}(\text{acac})_2$ (54 mg, 0.18 mmol), CuCl_2 (57 mg, 0.43 mmol), 1-octyne (218 mg, 1.98 mmol), HCOOH (90%, 144 mg, 3.13 mmol), and THF (5 mL) for 5.5 h. Standard work-up resulted in a 23:77 mixture of **5i** and **7i**, respectively, in 12% combined yield.

$\text{Pd}(\text{OAc})_2$. The general procedure was followed using $\text{Pd}(\text{OAc})_2$ (38 mg, 0.17 mmol), CuCl_2 (50 mg, 0.37 mmol), 1-octyne (188 mg, 0.37 mmol), HCOOH (90%, 178 mg, 3.87 mmol), and THF (5 mL) for 7.5 h. Standard work-up resulted in a 46:22:32 mixture of **5i**, **6i**, and **7i**, respectively, in 25% combined yield.

Nickel compounds. No carbonylation of 1-octyne took place when PdCl_2 was replaced by the nickel compounds NiCl_2 , NiBr_2 , $\text{Ni}(\text{acac})_2$, or $\text{Ni}(\text{CN})_4 \cdot 4\text{H}_2\text{O}$ in the general procedure.

Di-*t*-butyl peroxide (DTBP) as oxidant

$\text{DTBP}/\text{HCl}/\text{CuCl}_2/\text{O}_2$. The general procedure was followed using PdCl_2 (30 mg, 0.17 mmol), CuCl_2 (55 mg, 0.41 mmol), 1-octyne (212 mg, 1.93 mmol), HCOOH (90%, 118 mg, 2.56 mmol), DTBP (573 mg, 3.92 mmol), conc. HCl (2 drops), and THF (5 mL) for 5 h. Standard work-up resulted in a 45:10:45 mixture of **5i**, **6i**, and **7i**, respectively, in 51% combined yield.

$\text{DTBP}/\text{HCl}/\text{CuCl}_2$. An experiment similar to the above but excluding O_2 was carried out using: PdCl_2 (37 mg, 0.21 mmol), CuCl_2 (59 mg, 0.44 mmol), 1-octyne (267 mg, 2.43 mmol), HCOOH (90%, 161 mg, 3.50 mmol), DTBP (364 mg, 2.49 mmol), conc. HCl (2 drops), and THF (5 mL) for 4.5 h. Standard work-up resulted in a 61:10:29 mixture of **5i**, **6i**, and **7i**, respectively, in 38% combined yield.

DTBP/CuCl₂. Another experiment was carried out using DTBP and CuCl₂ and in the absence of HCl/O₂: PdCl₂ (29 mg, 0.16 mmol), CuCl₂ (52 mg, 0.39 mmol), 1-octyne (203 mg, 1.85 mmol), HCOOH (90%, 250 mg, 5.44 mmol), DTBP (278 mg, 5.44 mmol), and THF (5 mL) for 4.5 h; only CO gas was used. Standard work-up resulted in a 56:13:31 mixture of **5i**, **6i**, and **7i**, respectively, in 19% combined yield, in addition to some unidentified products.

DTBP/HCl. DTBP and HCl were used in an experiment in the absence of CuCl₂/O₂ using PdCl₂ (29 mg, 0.16 mmol), 1-octyne (197 mg, 1.79 mmol), HCOOH (90%, 148 mg, 3.21 mmol), di-*t*-butyl peroxide (826 mg, 5.66 mmol), conc. HCl (2 drops), and THF (5 mL) for 6 h; only CO gas was used. Standard work-up resulted in a 47:25:28 mixture of **5i**, **6i**, and **7i**, respectively, in 8% combined yield, in addition to some unidentified products.

Effects of Pd:alkyne ratio

1:1. The general procedure was followed using PdCl₂ (90 mg, 0.51 mmol), CuCl₂ (77 mg, 0.58 mmol), 1-octyne (56 mg, 0.51 mmol), HCOOH (90%, 51 mg, 1.00 mmol), and THF (25 mL) for 5 h. Standard work-up resulted in a 58:11:31 mixture of **5i**, **6i**, and **7i**, respectively, in 75% combined yield.

Slow addition of alkyne. The general procedure was followed using PdCl₂ (50 mg, 0.28 mmol), CuCl₂ (41 mg, 0.31 mmol), 1-octyne (292 mg, 2.66 mmol), HCOOH (90%, 242 mg, 5.26 mmol), and THF (50 mL) for 6 h. The mixture of 1-octyne/HCOOH was added slowly (over 3 h) to the reaction mixture via an addition funnel. Standard work-up resulted in a 60:3:37 mixture of **5i**, **6i**, and **7i**, respectively, in 77% combined yield.

1:40. The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (46 mg, 0.34 mmol), 1-octyne (745 mg, 6.77 mmol), HCOOH (90%, 563 mg, 12.2 mmol), and THF (5 mL) for 10.5 h. Standard work-up resulted in a 40:20:40 mixture of **5i**, **6i**, and **7i**, respectively, in 17% combined yield.

1:20. The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (46 mg, 0.34 mmol), phenylacetylene (352 mg, 3.45 mmol), HCOOH (90%, 309 mg, 6.71 mmol), and THF (5 mL) for 14.5 h. Standard work-up resulted in **5a**. (Yield= 50%)

1:20 (More CuCl₂). The general procedure was followed using PdCl₂ (29 mg, 0.16 mmol), CuCl₂ (218 mg, 1.63 mmol), phenylacetylene (367 mg, 3.60 mmol), HCOOH (90%, 336 mg, 7.29 mmol), and THF (5 mL) for 14.5 h. Standard work-up resulted in **5a**. (Yield= 40%)

1:48. The general procedure was followed using PdCl₂ (52 mg, 0.29 mmol), CuCl₂ (46 mg, 0.34 mmol), 5-chloro-1-pentyne (1464 mg, 14.0 mmol), HCOOH (90%, 1107 mg, 24.07 mmol), and THF (15 mL) for 11 h. Standard work-up resulted in a 43:25:32 mixture of **5f**, **6f**, and **7f**, respectively, in 15% combined yield.

Influence of gases and metal ratios

No CO. The general procedure was followed using PdCl₂ (33 mg, 0.19 mmol), CuCl₂ (49 mg, 0.37 mmol), 1-octyne (203 mg, 1.85 mmol), HCOOH (90%, 218 mg, 4.74 mmol), and THF (5 mL) for 9.5 h. Only O₂ was bubbled through the reaction mixture. Standard work-up resulted in 200 mg of a red oil which contained none of the expected carbonylation products, and seemed to consist of trimers or oligomers of 1-octyne.

Closed system experiment. The general procedure was followed using PdCl₂ (31 mg, 0.18 mmol), CuCl₂ (48 mg, 0.36 mmol), 1-octyne (186 mg, 1.69 mmol), HCOOH (90%, 165 mg, 3.58 mmol), and THF (5 mL) for 7 h. Standard work-up resulted in a 62:9:29 mixture of **5i**, **6i**, and **7i**, respectively, in 45% combined yield.

CO:O₂= 10:1. Bubbling CO through a stirred suspension of PdCl₂ (33 mg, 0.19 mmol) and CuCl₂ (42 mg, 0.31 mmol) in THF (15 mL) for 3 hours produced a slightly soluble, yellow solid. 1-Octyne (206 mg, 1.81 mmol) and water (65 mg, 3.61 mmol) were

added to the yellow mixture and a 10:1 CO/O₂ mixture was bubbled through for 10 hours. Standard work-up resulted in a 39:15:46 mixture of **5i**, **6i**, and **7i**, respectively, in 51% combined yield.

CO:O₂ = 1:6. The general procedure was followed using PdCl₂ (20 mg, 0.11 mmol), CuCl₂ (30 mg, 0.22 mmol), 1-octyne (101 mg, 0.92 mmol), H₂O (35 mg, 1.94 mmol), and THF (30 mL) for 5 h, using a 1:6 ratio of CO:O₂ gas mixture. Standard work-up resulted in a 20:43:37 mixture of **5i**, **6i**, and **7i**, respectively, in 53% combined yield.

CO₂/CO. The general procedure was followed using PdCl₂ (32 mg, 0.18 mmol), CuCl₂ (48 mg, 0.36 mmol), 1-octyne (196 mg, 1.78 mmol), HCOOH (111 mg, 2.41 mmol), and THF (5 mL) for 5.5 h, using a 1:2 ratio of CO₂:CO gas mixture. Standard work-up resulted in a 71:7:22 mixture of **5i**, **6i**, and **7i**, respectively, in 10% combined yield.

CO₂/O₂. The general procedure was followed using PdCl₂ (33 mg, 0.19 mmol), CuCl₂ (50 mg, 0.37 mmol), 1-octyne (203 mg, 1.85 mmol), HCOOH (125 mg, 2.72 mmol), and THF (5 mL) for 6.5 h, using a 1:3 ratio of CO₂:O₂ gas mixture. Standard work-up resulted in a black oil which contained none of the expected carbonylation products.

CO₂ trapping. The general procedure was followed using PdCl₂ (27 mg, 0.15 mmol), CuCl₂ (39 mg, 0.29 mmol), 1-octyne (181 mg, 1.65 mmol), HCOOH (200 mg, 4.35 mmol), and THF (5 mL) for 7.5 h, using a 3:1 ratio of CO:O₂ gas mixture. The outgoing gases were directed through a solution of Ba(OH)₂ (ca. 6 g, in 50 ml of water) into the oil bubbler. Standard work-up resulted in a 50:17:33 mixture of **5i**, **6i**, and **7i**, respectively, in 55% combined yield. The Ba(OH)₂ solution contained traces of a white solid, too little to be filtered and weighed.

No CuCl₂/O₂. The general procedure was followed using PdCl₂ (8 mg, 0.045 mmol), 1-octyne (55 mg, 0.50 mmol), H₂O (24 mg, 1.33 mmol), and THF (20 mL) for 5 h, using only CO gas. Standard work-up resulted in a 35:30:35 mixture of **5i**, **6i**, and **7i**, respectively, in 6%

combined yield.

No Pd. The general procedure was followed using CuCl_2 (45 mg, 0.34 mmol), 1-octyne (114 mg, 1.07 mmol), HCOOH (95 mg, 2.07 mmol), and THF (15 mL) for 5 h, using a 3:1 ratio of $\text{CO}:\text{O}_2$ gas mixture. Standard work-up resulted in traces of an unidentified species.

Pd:Cu= 1:0.56. The general procedure was followed using PdCl_2 (21 mg, 0.12 mmol), CuCl_2 (9 mg, 0.067 mmol), 1-octyne (144 mg, 1.31 mmol), HCOOH (125 mg, 2.71 mmol), and THF (15 mL) for 12 h, using a 3:1 ratio of $\text{CO}:\text{O}_2$ gas mixture. Standard work-up resulted in a 57:5:38 mixture of **5i**, **6i**, and **7i**, respectively, in 68% combined yield.

Pd:Cu= 1:2.5. The general procedure was followed using PdCl_2 (21 mg, 0.12 mmol), CuCl_2 (40 mg, 0.30 mmol), 1-octyne (134 mg, 1.22 mmol), HCOOH (130 mg, 2.54 mmol), and THF (15 mL) for 7.5 h, using a 3:1 ratio of $\text{CO}:\text{O}_2$ gas mixture. Standard work-up resulted in a 57:5:38 mixture of **5i**, **6i**, and **7i**, respectively, in 68% combined yield.

Pd:Cu= 1:5.5. The general procedure was followed using PdCl_2 (22 mg, 0.12 mmol), CuCl_2 (91 mg, 0.68 mmol), 1-octyne (144 mg, 1.31 mmol), HCOOH (126 mg, 2.74 mmol), and THF (15 mL) for 12 h, using a 3:1 ratio of $\text{CO}:\text{O}_2$ gas mixture. Standard work-up resulted in a 54:5:41 mixture of **5i**, **6i**, and **7i**, respectively, in 66% combined yield.

No CuCl_2 (CO/O_2). The general procedure was followed using PdCl_2 (22 mg, 0.12 mmol), 1-octyne (134 mg, 1.22 mmol), H_2O (48 mg, 2.67 mmol), and THF (20 mL) for 9.5 h, using a 3:1 ratio of $\text{CO}:\text{O}_2$ gas mixture. Standard work-up resulted in a 26:21:53 mixture of **5i**, **6i**, and **7i**, respectively, in 43% combined yield.

Pd:Cu= 1:16 (No O_2). The general procedure was followed using PdCl_2 (16 mg, 0.090 mmol), CuCl_2 (199 mg, 1.49 mmol), phenylacetylene (126 mg, 1.24 mmol), HCOOH (138 mg, 3.00 mmol), and THF (20 mL) for 3 h; only CO was bubbled through the reaction mixture. Standard work-up resulted in 232 mg of a reddish, oily solid which consisted mainly

of unidentified products and some **5a** (2%).

The yellow complex

Synthesis and IR Spectrum. Bubbling CO through a stirred suspension of PdCl₂ (29 mg, 0.16 mmol) and CuCl₂ (50 mg, 0.37 mmol) in THF (15 mL) for 4 hours produced a sparingly soluble, yellow solid. The reaction mixture was filtered under CO using standard Schlenk techniques, and the yellow solid thus isolated was stored under CO. IR (nujol) spectrum of the solid showed a strong absorption at 1985 cm⁻¹. The results of elemental analysis performed on this material are as follows: %C: 7.72; %H: 0.94; %Cl: 28.17; %Cu: 24.86; %Pd: 24.09.

Catalytic Activity. Bubbling CO through a stirred suspension of PdCl₂ (33 mg, 0.19 mmol) and CuCl₂ (42 mg, 0.31 mmol) in THF (15 mL) for 3 hours produced a slightly soluble, yellow solid. 1-Octyne (206 mg, 1.81 mmol) and water (65 mg, 3.61 mmol) were added to the yellow mixture and a 10:1 CO/O₂ mixture was bubbled through for 10 hours, during which the color of the mixture turned black. Standard work-up resulted in a 39:15:46 mixture of **5i**, **6i**, and **7i**, respectively, in 51% combined yield. Thus, the yellow complex can act as a catalyst precursor in the dicarbonylation of alkynes.

Effects of water, acids, and bases

Water. The general procedure was followed using PdCl₂ (25 mg, 0.14 mmol), CuCl₂ (47 mg, 0.35 mmol), 1-octyne (144 mg, 1.31 mmol), H₂O (47 mg, 2.61 mmol), and THF (5 mL) for 6 h. Standard work-up resulted in a 44:19:37 mixture of **5i**, **6i**, and **7i**, respectively, in 53% combined yield.

Blank reaction: No water or formic acid. The general procedure was followed using PdCl₂ (21 mg, 0.12 mmol), CuCl₂ (19 mg, 0.14 mmol), 1-octyne (130 mg, 1.18 mmol), and

THF (15 mL) for 4 h. Standard work-up resulted in a 54:12:34 mixture of **5i**, **6i**, and **7i**, respectively, in 41% combined yield.

Molecular sieves. The general procedure was followed using PdCl₂ (28 mg, 0.16 mmol), CuCl₂ (20 mg, 0.15 mmol), 1-octyne (188 mg, 1.71 mmol), 4A molecular sieves (1g), and THF (25 mL) for 10 h. Standard work-up resulted in an 80:20 mixture of **5i**, and **7i**, respectively, in 6% combined yield.

MgSO₄. The general procedure was followed using PdCl₂ (29 mg, 0.16 mmol), CuCl₂ (27 mg, 0.20 mmol), 1-octyne (173 mg, 1.57 mmol), MgSO₄ (1g), and THF (25 mL) for 5 h. Standard work-up resulted in a 71:29 mixture of **5i** and **7i**, respectively, in 12% combined yield.

Molecular sieves and HCOOH. The general procedure was followed using PdCl₂ (22 mg, 0.12 mmol), CuCl₂ (32 mg, 0.24 mmol), 1-octyne (298 mg, 2.71 mmol), HCOOH (90%, 279 mg, 6.07 mmol), 4A molecular sieves (1g), and THF (25 mL) for 5 h. Standard work-up resulted in a 24:54:22 mixture of **5i**, **6i**, and **7i**, respectively, in 5% combined yield.

MgSO₄ and HCOOH. The general procedure was followed using PdCl₂ (26 mg, 0.15 mmol), CuCl₂ (22 mg, 0.16 mmol), 1-octyne (154 mg, 1.40 mmol), HCOOH (90%, 167 mg, 3.63 mmol), MgSO₄ (500 mg), and THF (15 mL) for 3 h. Standard work-up resulted in a 54:5:41 mixture of **5i**, **6i**, and **7i**, respectively, in 56% combined yield.

50% HCCOH. The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (48 mg, 0.36 mmol), 1-octyne (193 mg, 1.76 mmol), HCOOH (98%, 80 mg, 1.75 mmol), H₂O (37 mg, 2.06 mmol), and THF (5 mL) for 6 h. Standard work-up resulted in a 47:18:35 mixture of **5i**, **6i**, and **7i**, respectively, in 44% combined yield.

98-100% HCOOH. The general procedure was followed using PdCl₂ (29 mg, 0.16 mmol), CuCl₂ (44 mg, 0.33 mmol), 1-octyne (182 mg, 1.66 mmol), HCOOH (98- 100%, 151 mg, 3.28 mmol), and THF (5 mL) for 7 h. Standard work-up resulted in a 62:10:28 mixture of

5i, 6i, and 7i, respectively, in 57% combined yield.

Oxalic acid. The general procedure was followed using PdCl₂ (32 mg, 0.18 mmol), CuCl₂ (51 mg, 0.38 mmol), 1-octyne (197 mg, 1.79 mmol), oxalic acid (329 mg, 3.66 mmol), and THF (5 mL) for 15 h. Standard work-up resulted in a 36:25:39 mixture of **5i**, **6i**, and **7i**, respectively, in 68% combined yield.

Malonic acid. The general procedure was followed using PdCl₂ (32 mg, 0.18 mmol), CuCl₂ (51 mg, 0.38 mmol), 1-octyne (208 mg, 1.89 mmol), malonic acid (371 mg, 3.57 mmol), and THF (5 mL) for 11 h. Standard work-up resulted in a 26:48:26 mixture of **5i**, **6i**, and **7i**, respectively, in 56% combined yield.

Acetic acid. The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (42 mg, 0.31 mmol), 1-octyne (183 mg, 1.66 mmol), glacial acetic acid (209 mg, 3.48 mmol), and THF (5 mL) for 11 h. Standard work-up resulted in a 37:37:26 mixture of **5i**, **6i**, and **7i**, respectively, in 48% combined yield.

Boric acid. The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (44 mg, 0.33 mmol), 1-octyne (181 mg, 1.65 mmol), boric acid (201 mg, 3.25 mmol), and THF (5 mL) for 12 h. Standard work-up resulted in a 31:39:30 mixture of **5i**, **6i**, and **7i**, respectively, in 61% combined yield.

HCl. The general procedure was followed using PdCl₂ (22 mg, 0.12 mmol), CuCl₂ (34 mg, 0.25 mmol), 1-octyne (128 mg, 1.16 mmol), conc. HCl (500 mg, 5 mmol; 17.6 mmol of H₂O), and THF (30 mL) for 10 h. Standard work-up resulted in a 30:20:50 mixture of **5i**, **6i**, and **7i**, respectively, in 14% combined yield, in addition to other unidentified products.

NaOH. The general procedure was followed using PdCl₂ (23 mg, 0.13 mmol), CuCl₂ (20 mg, 0.15 mmol), 1-octyne (148 mg, 1.45 mmol), NaOH pellets (198 mg, 4.95 mmol), and THF (30 mL) for 2.5 h. Standard work-up resulted in a 6:55:29 mixture of **5i**, **6i**, and **7i**, respectively, in 6% combined yield.

EtN(*i*-Pr)₂. The general procedure was followed using PdCl₂ (56 mg, 0.32 mmol), CuCl₂ (90 mg, 0.67 mmol), 1-octyne (380 mg, 3.46 mmol), H₂O (102 mg, 5.67 mmol), EtN(*i*-Pr)₂ (270 mg, 2.09 mmol), and THF (40 mL) for 5 h. Standard work-up resulted in 178 mg of a dark oil which contained none of the expected carbonylation products.

Solvent Effects

Acetone. The general procedure was followed using PdCl₂ (31 mg, 0.18 mmol), CuCl₂ (46 mg, 0.34 mmol), 1-octyne (186 mg, 1.69 mmol), HCOOH (90%, 158 mg, 3.42 mmol), and acetone (5 mL) for 11 h. Standard work-up resulted in a 36:37:27 mixture of **5i**, **6i**, and **7i**, respectively, in 57% combined yield.

1,4-Dioxane. The general procedure was followed using PdCl₂ (32 mg, 0.18 mmol), CuCl₂ (54 mg, 0.40 mmol), 1-octyne (202 mg, 1.84 mmol), HCOOH (176 mg, 3.84 mmol), and dioxane (5 mL) for 11 h. Standard work-up resulted in a 54:8:38 mixture of **5i**, **6i**, and **7i**, respectively, in 44% combined yield.

CH₃CN. The general procedure was followed using PdCl₂ (28 mg, 0.16 mmol), CuCl₂ (43 mg, 0.32 mmol), 1-octyne (163 mg, 1.48 mmol), HCOOH (90%, 140 mg, 3.04 mmol), and CH₃CN (25 mL) for 5.5 h. Standard work-up resulted in a 17:56:27 mixture of **1i**, **2i**, and **3i**, respectively, in 42% combined yield.

EtOAc. The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (45 mg, 0.34 mmol), 1-octyne (192 mg, 1.75 mmol), HCOOH (90%, 169 mg, 3.68 mmol), and EtOAc (5 mL) for 15 h. Standard work-up resulted in a 50:9:41 mixture of **5i**, **6i**, and **7i**, respectively, in 25% combined yield.

Benzene. The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (45 mg, 0.34 mmol), 1-octyne (184 mg, 1.67 mmol), HCOOH (189 mg, 4.11 mmol), and benzene (5 mL) for 12 h. Standard work-up resulted in a 59:24:17 mixture of **5i**, **6i**, and

7i, respectively, in 11% combined yield.

Additive effects

LiCl. The general procedure was followed using PdCl₂ (40 mg, 0.23 mmol), CuCl₂ (59 mg, 0.44 mmol), 4-phenyl-1-butyne (291 mg, 2.24 mmol), HCOOH (90%, 183 mg, 3.98 mmol), LiCl (39 mg, 0.92 mmol), and THF (25 mL) for 7 h. Standard work-up resulted in a 74:26 mixture of 5i and 7i, respectively, in 53% combined yield.

LiCl. The general procedure was followed using PdCl₂ (28 mg, 0.16 mmol), CuCl₂ (44 mg, 0.33 mmol), 5-cyano-1-pentyne (166 mg, 1.78 mmol), HCOOH (90%, 161 mg, 3.50 mmol), LiCl (102 mg, 2.37 mmol), and THF (20 mL) for 7 h. Standard work-up resulted in a 70:16:14 mixture of 5g, 6g, and 7g, respectively, in 27% combined yield.

LiCl. The general procedure was followed using PdCl₂ (21 mg, 0.12 mmol), CuCl₂ (31 mg, 0.23 mmol), 5-cyano-1-pentyne (114 mg, 1.23 mmol), HCOOH (90%, 136 mg, 2.96 mmol), LiCl (34 mg, 0.79 mmol), and THF (20 mL) for 5 h. Standard work-up resulted in a 60:13:27 mixture of 5g, 6g, and 7g, respectively, in 23% combined yield.

LiCl. The general procedure was followed using PdCl₂ (20 mg, 0.11 mmol), CuCl₂ (32 mg, 0.24 mmol), 5-cyano-1-pentyne (106 mg, 1.14 mmol), HCOOH (90%, 102 mg, 2.22 mmol), LiCl (10 mg, 0.23 mmol), and THF (20 mL) for 5 h. Standard work-up resulted in a 46:9:45 mixture of 5g, 6g, and 7g, respectively, in 17% combined yield.

LiCl. The general procedure was followed using PdCl₂ (29 mg, 0.16 mmol), CuCl₂ (43 mg, 0.32 mmol), 5-chloro-1-pentyne (164 mg, 1.60 mmol), HCOOH (90%, 151 mg, 3.28 mmol), LiCl (34 mg, 0.79 mmol), and THF (20 mL) for 6.5 h. Standard work-up resulted in a 78:6:16 mixture of 5f, 6f, and 7f, respectively, in 57% combined yield.

Iodine. The general procedure was followed using PdCl₂ (31 mg, 0.18 mmol), CuCl₂ (46 mg, 0.34 mmol), 5-chloro-1-pentyne (167 mg, 1.63 mmol), HCOOH (90%, 149 mg, 3.23

mmol), I_2 (235 mg, 0.93 mmol), and THF (20 mL) for 6.5 h. Standard work-up resulted in **5f**. (yield= 14%)

Iodine (Pd:I₂= 1:1). The general procedure was followed using $PdCl_2$ (33 mg, 0.19 mmol), $CuCl_2$ (51 mg, 0.38 mmol), iodine (48 mg, 0.19 mmol), 1-octyne (198 mg, 1.80 mmol), $HCOOH$ (90%, 194 mg, 4.23 mmol), and THF (5 mL) for 8.5 h. Standard work-up resulted in a 38:22:40 mixture of **5i**, **6i**, and **7i**, respectively, in 59% combined yield.

Iodine (Pd:I₂= 1:10). The general procedure was followed using $PdCl_2$ (32 mg, 0.18 mmol), $CuCl_2$ (51 mg, 0.38 mmol), iodine (461 mg, 1.82 mmol), 1-octyne (203 mg, 1.85 mmol), $HCOOH$ (90%, 174 mg, 3.78 mmol), and THF (5 mL) for 8.5 h. Standard work-up resulted in **5i**. (yield= 29%)

NaI. The general procedure was followed using $PdCl_2$ (31 mg, 0.18 mmol), $CuCl_2$ (47 mg, 0.35 mmol), NaI (522 mg, 3.48 mmol), 1-octyne (202 mg, 1.84 mmol), $HCOOH$ (90%, 188 mg, 4.09 mmol), and THF (5 mL) for 18 h. Standard work-up resulted in **7i**. (yield= 6%)

NaI (Without $CuCl_2$). The general procedure was followed using $PdCl_2$ (33 mg, 0.19 mmol), NaI (506 mg, 3.38 mmol), 1-octyne (213 mg, 1.94 mmol), $HCOOH$ (90%, 153 mg, 3.33 mmol), and THF (5 mL) for 18 h. Standard work-up resulted in 12 mg of an orange oil from the organic layer. This material was not subjected to any analysis.

PPh_3 . The general procedure was followed using $PdCl_2$ (29 mg, 0.16 mmol), $CuCl_2$ (45 mg, 0.34 mmol), PPh_3 (217 mg, 0.83 mmol), 1-octyne (184 mg, 1.67 mmol), $HCOOH$ (90%, 158 mg, 3.44 mmol), and THF (5 mL) for 6 h. Work-up of the final reaction mixture in the usual manner gave 90 mg of a reddish oily solid from the organic layer. Spectral analysis of this material revealed that it contained a mixture of the phosphine and other unidentified species; no carbonylation products were detected.

PCy_3 . The general procedure was followed using $PdCl_2$ (32 mg, 0.18 mmol), $CuCl_2$ (44 mg, 0.33 mmol), PCy_3 (250 mg, 0.89 mmol), 1-octyne (199 mg, 1.81 mmol), $HCOOH$

(90%, 193 mg, 4.19 mmol), and THF (5 mL) for 6 h. Work-up of the final reaction mixture in the usual manner gave 242 mg of a reddish oil from the organic layer. Spectral analysis of this material revealed that it contained a mixture of the phosphine and other unidentified species; no carbonylation product was detected.

dppb. The general procedure was followed using PdCl_2 (32 mg, 0.18 mmol), CuCl_2 (48 mg, 0.36 mmol), dppb (140 mg, 0.33 mmol), 1-octyne (184 mg, 1.67 mmol), HCOOH (90%, 134 mg, 2.91 mmol), and THF (20 mL) for 6 h. Standard work-up resulted in a mixture of the phosphine and **5i**. (Yield of **5i** = 4%)

dppb (No CuCl_2/O_2). The general procedure was followed using PdCl_2 (23 mg, 0.13 mmol), dppb (52 mg, 0.12 mmol), 1-octyne (150 mg, 1.36 mmol), HCOOH (90%, 134 mg, 2.91 mmol), and THF (25 mL) for 5 h. Work-up of the final reaction mixture in the usual manner gave 18 mg of a yellow oil from the organic layer. Spectral analysis of this material revealed that it contained a mixture of the phosphine and some unidentified species.

$\text{P}(\text{OPh})_3$. The general procedure was followed using PdCl_2 (29 mg, 0.16 mmol), CuCl_2 (45 mg, 0.34 mmol), $\text{P}(\text{OPh})_3$ (262 mg, 0.84 mmol), 1-octyne (819 mg, 1721 mmol), HCOOH (90%, 161 mg, 3.50 mmol), and THF (5 mL) for 6 h. Work-up of the final reaction mixture in the usual manner gave 180 mg of a dark oil from the organic layer. Spectral analysis of this material revealed that it contained a mixture of the phosphite and other unidentified species; no carbonylation products were detected.

$\text{P}(\text{O}(i\text{-Pr}))_3$. The general procedure was followed using PdCl_2 (29 mg, 0.16 mmol), CuCl_2 (44 mg, 0.33 mmol), $\text{P}(\text{O}(i\text{-Pr}))_3$ (162 mg, 0.78 mmol), 1-octyne (188 mg, 1.71 mmol), HCOOH (90%, 147 mg, 3.19 mmol), and THF (5 mL) for 6 h. Work-up of the final reaction mixture in the usual manner gave 123 mg of a dark oil from the organic layer. Spectral analysis of this material revealed that it contained a mixture of the phosphine and other unidentified species; no carbonylation product was detected.

PCy₃ (Without O₂). The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), CuCl₂ (47 mg, 0.35 mmol), PCy₃ (165 mg, 0.59 mmol), 1-octyne (183 mg, 1.66 mmol), HCOOH (90%, 145 mg, 3.15 mmol), and THF (5 mL) for 6 h. Only CO gas was bubbled through the reaction mixture. Work-up of the final reaction mixture in the usual manner gave 153 mg of a reddish oil from the organic layer. Spectral analysis of this material revealed that it contained a mixture of the phosphine and some unidentified species; no carbonylation product was detected.

PCy₃ (Without O₂/CuCl₂). The general procedure was followed using PdCl₂ (30 mg, 0.17 mmol), PCy₃ (153 mg, 0.55 mmol), 1-octyne (197 mg, 1.79 mmol), HCOOH (90%, 150 mg, 3.27 mmol), and THF (5 mL) for 6 h. Only CO gas was bubbled through the reaction mixture. Work-up of the final reaction mixture in the usual manner gave 220 mg of a reddish oil from the organic layer. Spectral analysis of this material revealed that it contained a mixture of the phosphine and some unidentified species; no carbonylation product was detected.

Hydrolysis and dehydration control experiments

Hydrolysis of the Maleic Anhydride Derivative with HCOOH. **5i** was used in place of the terminal alkyne under standard catalytic reaction conditions using PdCl₂ (22 mg, 0.12 mmol), CuCl₂ (32 mg, 0.24 mmol), 90% HCOOH (248 mg, 5.40 mmol), **5i** (130 mg, 0.71 mmol), and THF (5 mL). Standard work-up resulted in a 97:3 mixture of **5i** and **6i**, respectively; no traces of **7i** was detected.

Hydrolysis of the Maleic Anhydride Derivative with Water. The above experiment was repeated with water instead of 90% HCOOH: PdCl₂ (21 mg, 0.12 mmol), CuCl₂ (31 mg, 0.23 mmol), H₂O (54 mg, 3.0 mmol), **5i** (112 mg, 0.62 mmol), and THF (5 mL). Analogous work-up and analysis revealed an 89:11 mixture of **5i** and **6i**; no **7i** was detected.

Dehydration of the Maleic Acid Derivative. The above experiment was repeated with **6i** using PdCl₂ (0.19 mmol), CuCl₂ (0.19 mmol), 90% HCOOH (0.94 mmol), **6i** (0.50 mmol), and THF (5 mL). Standard work-up resulted in an 89:11 mixture of **6i** and **5i**, respectively; no **7i** was detected.

The Attempted Carbonylation of trans-2-Octenoic Acid

PdCl₂ (42 mg, 0.24 mmol) and CuCl₂ (62 mg, 0.46 mmol) were stirred in THF (20 mL), and a 3:1 mixture of CO/O₂ was bubbled through the mixture. After 10 min, *trans*-2-octenoic acid (302 mg, 2.13 mmol) and 90% HCOOH (174 mg, 3.77 mmol) were added, and the stirring continued for 6 hours. Work-up as usual gave a pale yellow liquid (298 mg) whose ¹H nmr spectrum was that of the starting acid.

Chapter IV

Concluding Remarks

Chapters II and III of this thesis have described the results of a research study on the Pd-catalyzed carbonylation of alkynes. This study consists of two main parts, the hydrocarboxylation and dicarbonylation reactions. The first part presents the conversion of terminal and internal alkynes to α,β -unsaturated carboxylic acids (substituted acrylic acids) in high yields and turnover numbers. The regioselectivity of this reaction is quite good with terminal alkynes, but poorer with internal alkynes. The presence of suitable phosphine ligands was shown to be crucial to the catalysis.

The catalytic cycle proposed for hydrocarboxylation starts with a Pd(0) species that undergoes a sequence of reactions leading to the conversion of the reactants to products and the regeneration of the active catalyst, the original Pd(0) species (Scheme 2.5). During this catalytic cycle, the oxidation state of the Pd centre changes from 0 to +2 and back to 0.

In contrast, in the catalytic cycle proposed for terminal alkyne dicarbonylation, the Pd centre is in the +2 oxidation state at the beginning and remains so until the end of the cycle when it is reduced to Pd(0). The catalyst is thus "deactivated" and oxidants are required for regenerating the active Pd(II) species. The presence of oxidants is therefore vital for sustaining the catalytic reaction.

The oxidant system used in this study consisted of CuCl_2 and O_2 . The latter was demonstrated to be the main oxidant: whereas the catalysis can proceed in the complete absence of CuCl_2 , excluding O_2 from the reaction medium effectively inhibits any catalysis.

Some speculative suggestions have been put forth for the respective roles of O_2 and $CuCl_2$, but further study is necessary for testing these ideas and improving our understanding of the oxidation step. Such an understanding will undoubtedly allow significant improvements in the reaction yield and the turnover numbers.

Although the alkyne hydrocarboxylation and dicarbonylation reactions described here are fundamentally different from each other, they both use the same basic elements, namely: Pd(II)-salts (e.g., $Pd(OAc)_2$), alkynes, formic acid, and CO gas. It is interesting to note, therefore, that through judicious selection of appropriate reaction conditions and additional reagents, one can promote either hydrocarboxylation (high temperature and pressure, phosphine ligands) or dicarbonylation (ambient temperature and pressure, $CuCl_2/O_2$). In this respect, the work presented in this thesis exemplifies the extent of control that can be exercised over the reactivity of Pd-compounds in catalytic organic transformations.

Claims to Original Research

1. The first examples of metal-catalyzed hydrocarboxylation of terminal and internal alkynes with formic and oxalic acids.
2. The first examples of metal-catalyzed dicarbonylation of terminal alkynes with formic acid.
3. An examination of the respective roles of CuCl_2 and oxygen as the oxidants in Pd-catalyzed, oxidative carbonylation of terminal alkynes.

References

1. Mullen, A., *New Syntheses With Carbon Monoxide*; Falbe, J., Ed.; Springer-Verlag: New York, 1980; pp. 243-308.
2. Waller, F. J. *J. Mol. Catal.* **1985**, *31*, 123.
3. (a) Reppe, W. Ger. Patent, 855 110, 1939; (b) Reppe, W. *Ann.* **1948**, *1*; (c) Roelen, O. Ger. Patent, 849 548, 1938; U.S. Patent, 2 327 066, 1943; Belg. Patent, 436 625, 1939; (d) Roelen, O. *Angew. Chemie* **1948**, *A.60(3)*, 213; (e) Reppe, W.; Stadler, R. U.S. Patent, 3 023 237, 1953; (f) Reppe, W.; Kutepow, N. v.; Raff, P.; Henkel, E.; Friedrich, H.; Himmele, W. Ger. Patent, 965 323, 1954; (g) Reppe, W.; Friedrich, H.; Henkel, E.; Kutepow, N. v.; Himmele, W. Ger. Patent, 1 003 721, 1954.
4. Pino, P.; Braca, G. "Organic Syntheses via Metal Carbonyls"; Pino, P.; Wender, I., eds.; John Wiley and Sons: New York, 1977; Vol. 2, pp. 419-516.
5. (a) Jones, E. R., Shen, T. Y., and Whiting, M. C. *J. Chem. Soc.* **1951**, 766122; (b) Jones, E. R. H.; Shen, T. Y.; Whiting, M. C. *J. Chem. Soc.* **1950**, 230; (c) *ibid.*, **1951**, 48; (d) Jones, E. R. H.; Whitham, G. H.; Whiting, M. C. *J. Chem. Soc.* **1954**, 1865.
6. Amer, I.; Alper, H. *J. Organomet. Chem.* **1990**, *383*, 573.
7. Yamamoto, K. *Bull. Chem. Soc. Japan* **1954**, *27*, 505.
8. (a) Bhattacharayya, S.; Bhattacharayya, D. *J. Appl. Chem.* **1966**, *18*; (b) *ibid.*, 202; (c) Bhattacharayya, S.; Sen, A. *ibid.* **1963**, 498; (d) *ibid.*, *Ind. eng. Chem., Proc. Des. Develop.* **1964**, *3(2)*, 169.
9. (a) Doyama, K.; Joh, T.; Onitsuka, K.; Shiomara, T.; Takahashi, S. *J. Chem. Soc., Chem. Commun.* **1987**, 649.177; (b) Mise, T.; Hong, P.; Yamazaki, H. *Chem. Lett.*

- 1981, 993; (c) Doyama, K.; Joh, T.; Takahashi, S.; Shiomara, T. *Tetrahedron Lett.* **1986**, *27*, 4497; (d) Joh, T.; Doyama, K.; Onitsuka, K.; Shiohara, T.; Takahashi, S. *Organometallics* **1991**, *10*, 2493.
10. (a) Jacobsen, G.; Spathe, H. Ger. Patent, 1 138 760, 1962; (b) *Chem. Abstr.* **1963**, *58*, 6699.
 11. (a) Tsuji, J.; Morikawa, M.; Iwamoto, N. *J. Am. Chem. Soc.* **1964**, *86*, 2095; (b) Tsuji, J.; Nogi, T. *J. Org. Chem.* **1966**, *31*, 2641; (c) Tsuji, J.; Nogi, T. *J. Am. Chem. Soc.* **1966**, *88*, 1289; (d) Tsuji, J.; Nogi, T. *Tetrahedron Lett.* **1966**, 1801; (e) Nogi, T.; Tsuji, J. *Tetrahedron* **1969**, *25*, 4099.
 12. (a) Chiusoli, G. P.; Camerini, A. *Chim. Ind. (Milan)* **1964**, *46*, 1063; (b) Chiusoli, G. P.; Venturello, C.; Merzoni, S. *Chem. Ind. (London)* **1968**, 977; (c) Cassar, L.; Chiusoli, G. P.; Guerrieri, F. *Synthesis* **1973**, 509; (d) Chiusoli, G.P.; Costa, M.; Pergreffi, P.; Reverberi, S.; Salerno, G. *Gazz. Chim. Ital.* **1986**, 691.
 13. Heck, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 2712.
 14. (a) Knifton, J. F. *J. Mol. Catal.* **1977**, *2*, 293; (b) Knifton, J. *J. Org. Chem.* **1977**, *41*, 293; (c) *ibid.*, *41*, 2885.
 15. Alper, H.; Woell, J. B.; Despeyroux, B.; Smith, D. J. H. *J. Chem. Soc., Chem. Commun.* **1983**, 1270.
 16. Despeyroux, B.; Alper, H. *Ann. N. Y. Acad. Sci.* **1983**, *415*, 148.
 17. Alper, H.; Despeyroux, B.; and Woell, J. B. *Tetrahedron Lett.* **1983**, *24*, 5691.
 18. Hartstock, F. W., Ph. D. Thesis, University of Ottawa, 1987, pp. 71-73.
 19. Mlekuz, M.; Joo, F.; Alper, H. *Organometallics*, **1987**, *6*, 1591.
 20. (a) Davit Zargarian and Howard Alper, unpublished results; (b) Zargarian, D.; Alper, H. *Organometallics* **1991**, *10*, 2914.
 21. Alper, H.; Saldana-Maldonado, M.; Lin, I. J. *J. Mol. Catal.* **1988**, *49*, L27.

22. Alper, H.; Saldana-Maldonado, M. *Organometallics* **1989**, *8*, 1124.
23. March, J. "Advanced Organic Chemistry"; John Wiley & Sons: New York, 1985; p. 126, Table 2, and references 159 and 173 therein.
24. Tsuji, Y.; Kondo, T.; Watanabe, Y. *J. Mol. Catal.* **1987**, *40*, 295.
25. Murray, T. F.; Norton, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 4107.
26. Tamao, K.; Kakui, T.; Kumada, M. *Tetrahedron Lett.* **1979**, 619.
27. (a) Larock, R. C.; Brown, H. C. *J. Organomet. Chem.* **1972**, *36*, 1; (b) Larock, R. C.; Gupta, S. K.; Brown, H. C. *J. Am. Chem. Soc.* **1972**, *94*, 4371.
28. Larock, R. C. *J. Org. Chem.* **1975**, *40*, 3237.
29. Mori, K.; Mizoroki, T.; Ozaki, A. *Chem. Lett.* **1975**, *1*, 39.
30. (a) Dunach, E.; Derien, S.; Perichon, J. *J. Organomet. Chem.* **1989**, *364*, C33; (b) Dunach, E.; Perichon, J. *J. Organomet. Chem.* **1988**, *352*, 239; (c) *ibid. Synlett* **1990**, 143.
31. (a) Tolman, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 2953; (b) *ibid.*, 2956.
32. Hosokawa, T.; Murahashi, S.-I. *Acc. Chem. Res.* **1990**, *23*, 49.
33. James, D. E.; Stille, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 1810.
34. Bassam El-Ali and H. Alper, unpublished results.
35. a) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630; b) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033; (c) Backvall, J. E.; Bystrom, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619; (d) Waegell, B. *Organometallics in Organic Synthesis*; de Meijere, A., tom Dieck, H., Eds.; Springer-Verlag: Berlin, Heidelberg, 1987; p. 203; (e) Milstein, D. *Organometallics*, **1982**, *1*, 888.
36. Moiseev, I. I. *Pure Appl. Chem.* **1989**, *61*, 1755.
37. Reference 4, pp. 54-55, and references therein.

38. For the patent literature see reference 4 and the references 139-144 therein. For some research reports see reference 8.
39. Sakakibara, Y.; Okamoto, T. *Bull. Inst. Chem. Res. Kyoto Univ.* **1967**, *45*, 175.
40. See reference 4 and reference 40 therein.
41. Most elementary textbooks on organometallic chemistry contain detailed description of bonding between transition metals and phosphine and CO ligands. For one example see: "Principles and Applications of Organotransition Metal Chemistry", Collman, J. P.; Hegedus, L. S., Eds.; University Science Books: 1980.
42. Carty, A. J. *Pure & Appl. Chem.* **1982**, *54*, 113.
43. (a) "Synthesis and Characterization of A Series of Rhodium Alkynyl Compounds", Zargarian, D.; M.Sc. Thesis, University of Waterloo, 1987; (b) Marder, T. B.; Zargarian, D.; Calabrese, J. C.; Herskovitz, T. H.; Milstein, D. *J. Chem. Soc., Chem. Commun.* **1987**, 1484.
44. (a) Milstein, D. *Organometallics* **1982**, *1*, 1549; (b) Thorn, D. L. *Organometallics* **1982**, *1*, 197.
45. (a) Milstein, D. *J. Am. Chem. Soc.* **1986**, *108*, 3525; (b) Keim, W.; Becker, J.; Trzeciak, A. M. *J. Organomet. Chem.* **1989**, *372*, 447, and references therein.
46. (a) Aguilo, A. *J. Catal.* **1969**, *13*, 283; (b) Strauss, S. H.; Whitmire, K. H.; Shriver, D. F. *J. Organomet. Chem.* **1979**, *174*, C59; (c) Chatt, J.; Shaw, B. L. *J. Chem. Soc.* **1962**, 5075; (d) Yoshida, T.; Ueda, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3941.
47. Immirzi, A.; Musco, A. *Inorg. Chim. Acta* **1977**, *22*, L35.
48. Halpern, J.; Kemp, A. L. W. *J. Am. Chem. Soc.* **1966**, *88*, 5147.
49. (a) Oshima, M.; Yamazaki, H.; Shimizu, I.; Nisar, M.; Tsuji, J. *J. Am. Chem. Soc.* **1989**, *111*, 6280; (b) Tsuji, J.; Yamakawa, T. *Tetrahedron Lett.* **1979**, 613; (c)

- Helquist, P. *Tetrahedron Lett.* **1978**, 1913; (d) Hutchins, R. O.; Learn, K. *J. Org. Chem.* **1982**, *47*, 4382; (e) Hey, H.; Arpe, H.-J. *Angew. Chem., Internat. Ed. Eng.* **1973**, *12*, 928; (f) Cortese, N. A.; Heck, R. F. *J. Org. Chem.* **1977**, *42*, 3491.
50. Vol'pin, M. E.; Kukolev, V. P.; Chernyshev, V. O.; Kolomnikov, I. S. *Tetrahedron Lett.* **1971**, 4435.
 51. Watanabe, Y.; Ohta, T.; Tsuji, Y.; Hiyoshi, T.; Tsuji, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2440.
 52. (a) Gardner, S.; Wright, D. *Tetrahedron Lett.* **1972**, 163; (b) Neilan, J. P.; Laine, R. M.; Cortese, N.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 3455; (c) Roffia, P.; Gregorio, G.; Conti, F.; Pregaglia, G. F.; Ugo, R. *J. Organomet. Chem.* **1973**, *55*, 405.
 53. Coffey, R. S. *J. Chem. Soc., Chem. Commun.* **1967**, 923.
 54. (a) Darensbourg, D. J.; Rokicki, A. *Organometallics* **1982**, *1*, 1685; (b) Weiller, B. H.; Liu, J.-P.; Grant, E. R. *J. Am. Chem. Soc.* **1985**, *107*, 1595.
 55. Loumhrari, H.; Matas, L.; Ros, J.; Torres, M. R.; Perales, A. *J. Organomet. Chem.* **1991**, *403*, 373.
 56. Pruchnik, F.; Wajda, K. *Inorg. Chim. Acta* **1980**, *40*, 203.
 57. Oshima, M.; Shimizu, I.; Yamamoto, A.; Ozawa, F. *Organometallics* **1991**, *10*, 1221.
 58. Ayrey, G.; Bird, C. W.; Briggs, E. M.; Harmer, A. F. *Organomet. Chem., Syn.* **1970/71**, *1*, 187.
 59. Bird, C. W.; Briggs, E. M.; Hudec, J. *J. Chem. Soc., C* **1967**, 1862.
 60. Wong, W.; Singer, S. J.; Pitts, W. D.; Watkins, S. F.; Baddley, W. H. *J. Chem. Soc., Chem. Commun.* **1972**, 672.
 61. (a) Heck, R. F. *J. Am. Chem. Soc.* **1963**, *85*, 2013; (b) Pauson, P. L. *Proc. Chem. Soc.* **1960**, 297; (c) Happel, J.; Umemura, S.; Sakakibara, Y.; Blanck, H.; Kunichika,

- S. Ind. Eng. Chem., Process Des. Develop.* **1975**, *14*, 44.
62. Fenton, D. M. *J. Org. Chem.* **1973**, *38*, 3192.
63. Milstein, D. *Acc. Chem. Res.* **1988**, *21*, 428.
64. Tsuji, J. *Acc. Chem. Res.* **1969**, *2*, 144.
65. Cavinato, G.; Toniolo, L. *J. Organomet. Chem.* **1990**, 398, 187.
66. Stille, J. K.; James, D. E. *J. Am. Chem. Soc.* **1975**, *97*, 674.
67. Vrieze, K.; Praat, A. P.; Cossee, P. J. *J. Organomet. Chem.* **1968**, *12*, 533.
68. Clark, H. C.; Ferguson, G.; Goel, A. B.; Janzen, E. G.; Ruegger, H.; Siew, P. Y.; Wong, C. S. *J. Am. Chem. Soc.* **1986**, *108*, 6961, and references therein.
69. Torres, M. R.; Perales, A.; Loumrhari, H.; Ros, J. *J. Organomet. Chem.* **1990**, 384, C61.
70. Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1985**, *26*, 1109.
71. Pri-Bar, I.; Buchman, O. *J. Org. Chem.* **1988**, *53*, 624.
72. Baird, J. M.; Kern, J. R.; Lee, G. R.; Morgans, Jr., D. J.; Sparacino, M. L. *J. Org. Chem.* **1991**, *56*, 1928.
73. Nagira, K.; Kikukawa, K.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1980**, *45*, 2365.
74. (a) Schijf, R.; Stevens, W. *Recl. Trav. Chim. Pays-Bas* **1966**, *85*, 627; (b) Fife, W. K.; Zhang, Z.-d. *J. Org. Chem.* **1986**, *51*, 3744.
75. Boese, W. T.; Goldman, A. S. *Organometallics* **1991**, *10*, 782.
76. Jones, W. D.; Chandler, V. L.; Feher, F. J. *Organometallics* **1990**, *9*, 164.
77. Tanke, R.; Crabtree, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 7984.
78. Blackburn, T. F.; Schwartz, J. J. *Chem. Soc., Chem. Commun.* **1977**, 157.
79. Taylor, P. and Orchin, M. *J. Organomet. Chem.* **1971**, *26*, 389.
80. Rice, C.; Oliver, J. D. *J. Organomet. Chem.* **1978**, *145*, 121.
81. (a) Huggins, J. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 3002; (b)

- Tremont, S. J.; Bergman, R. G. *J. Organomet. Chem.* **1977**, *140*, C12.
82. (a) Booth, B. L.; Hargreaves, R. G. *J. Chem. Soc. A* **1970**, 308; (b) Booth, B. L.; Hargreaves, R. G. *J. Organomet. Chem.* **1971**, *33*, 365; (c) Booth, B. L.; Lloyd, A. D. *J. Organomet. Chem.* **1972**, *35*, 195.
 83. (a) Harbourne, D.; Stone, F. G. A. *J. Chem. Soc. A* **1968**, 1765; (b) Bruce, M. I.; Harbourne, D.; Waugh, F.; Stone, F. G. A. *J. Chem. Soc. A* **1968**, 895; (c) Blackmore, T.; Bruce, M. I.; Stone, F. G. A. *J. Chem. Soc., Dalton* **1974**, 106.
 84. Hart, D. W.; Schwartz, J. J. *J. Organomet. Chem.* **1975**, *87*, C11.
 85. Eisch, J. J.; Manfre, R.; Konar, D. H. *J. Organomet. Chem.* **1978**, *159*, C13.
 86. Appleton, T. G.; Chisholm, M. H.; Clark, H. C. *J. Am. Chem. Soc.* **1972**, *94*, 8912.
 87. (a) Otsuka, S.; Nakamura, A. *Adv. Organomet. Chem.* **1976**, 245; (b) Nakamura, A.; Otsuka, S. *J. Mol. Catal.* **1976**, 285.
 88. Thorn, D. L.; Hoffmann, R. *J. Am. Chem. Soc.* **1978**, *100*, 2079.
 89. Hart, D. W.; Blackburn, T. F.; Schwartz, J. J. *Am. chem. Soc.* **1975**, *97*, 679.
 90. Heck, R. F. *J. Am. Chem. Soc.* **1971**, *93*, 6896.
 91. Outurquin, F.; Paulmier, C. *Synthesis* **1989**, 690.
 92. (a) Charles J. Pouchert, "The Aldrich Library of NMR Spectra", Ed. II, Vol. 2, 2(2)171A; (b) *ibid.*, 2(2)171B; (c) *ibid.*, 2(2)171D.
 93. Nunez, M. T.; Martin, V. S. *J. Org. Chem.* **1990**, *55*, 1928.
 94. Cooke, Jr., M. P.; Widener, R. K. *J. Org. Chem.* **1987**, *52*, 1381.
 95. Baker, R.; Head, J. C.; Swain, C. J. *J. Chem. Soc., Perkin Trans. I* **1988**, 85.
 96. Stubblefield, V. S.; Wilson, J. W. *J. Org. Chem.* **1979**, *44*, 193.
 97. Griesbaum, K.; Volpp, W. *Chem. Ber.* **1988**, *121*, 1795.
 98. Hermeling, D.; Schafer, H. *Chem. Ber.* **1988**, *121*, 1151.
 99. Myrbo, B.; Ila, H.; Junjappa, H. *J. Org. Chem.* **1983**, *48*, 5327.

100. Lee, V. J.; Branfman, A. R.; Herrin, T. R.; Rinehart, Jr., K. L. *J. Am. Chem. Soc.* **1978**, *100*, 4225.
101. Henin, F.; Mortezaei, R.; Muzart, J.; Pete, J.-P.; Piva, O. *Tetrahedron* **1989**, *45*, 6171.
102. a) Schauble, J. H.; Walter, G. J.; morin, J. G. *J. Org. Chem.* **1974**, *39*, 755; b) Tsuda, T.; Yoshida, T.; Saegusa, T. *J. Org. Chem.* **1988**, *53*, 607.
103. Bisson, R.; Yeats, R. B.; Warnhoff, E. W. *Can. J. Chem.* **1972**, *50*, 2851.
104. (a) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434; (b) Tanikaga, R.; Miyashita, K.; Ono, N.; Kaji, A. *Synthesis* **1982**, 131.
105. Slougui, N.; Rousseau, G. *Synthetic Commun.* **1982**, *12*, 401.
106. Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1991**, *56*, 1099.
107. Menashe, N.; Reshef, D.; Shvo, Y. *J. Org. Chem.* **1991**, *56*, 2912.
108. Bystrom, S. E.; Larsson, E. M.; Akermark, B. *J. Org. Chem.* **1990**, *55*, 5674.
109. Pri-Bar, I.; Alper, H. *Can. J. Chem.* **1990**, *68*, 1544.
110. Brechot, P.; Chauvin, Y.; Commereuc, D.; Saussine, L. *Organometallics* **1990**, *9*, 26.
111. (a) Morris, G. E.; Oakley, D.; Pippard, D. A.; Smith, D. J. H. *J. Chem. Soc., Chem. Commun.* **1987**, 410; (b) Morris, G. E.; Oakley, D.; Pippard, D. A.; Smith, D. J. H. *J. Chem. Soc., Chem. Commun.* **1987**, 411.
112. Alper, H.; Vasapollo, G.; Hartstock, F. W.; Mlekuz, M.; Smith, D. J. H.; Morris, G. E. *Organometallics* **1987**, *6*, 2391.
113. Speier, G.; Fulop, V. *J. Chem. Soc., Chem. Commun.* **1990**, 905.
114. "Advanced Inorganic Chemistry", Cotton, F. A.; Wilkinson, G., Eds; John Wiley & Sons: 1980, p.1290.
115. "Principles and Applications of Organotransition Metal Chemistry", Collman, J. P.;

- Hegedus, L. S., Eds.; University Science Books: 1980; pp. 605-611.
116. a) Hosokawa, T.; Uno, T.; Inui, S.; Murahashi, S-I. *J. Am. Chem. Soc.* **1981**, *103*, 2318; b) Hosokawa, T.; Miyagi, S.; Murahashi, S-I.; Sonoda, A. *J. Org. Chem.* **1978**, *43*, 2752.
117. Iataaki, H.; Yoshimoto, H. *J. Org. Chem.* **1973**, *38*, 76.
118. Kataoka, H.; Watanabe, K.; Goto, K. *Tetrahedron Lett.* **1990**, *31*, 4181.
119. Fenton, D. M.; Steinwand, P. J. *J. Org. Chem.* **1974**, *39*, 701.
120. Kiji, J.; Konishi, H.; Okano, T.; Kometani, S.; Iwasa, A. *Chem. Lett.* **1987**, 313.
121. (a) Rivetti, F.; Romano, U. *J. Organomet. Chem.* **1979**, *174*, 221; (b) Romano, U.; Tesei, R.; Mauri, M. M.; Rebora, P. *Ind. Eng. Chem. Prod. Res. Dev.* **1980**, *19*, 396.
122. a) Johnston, L. E.; Page, J. A. *Can. J. Chem.* **1969**, *47*, 4241; b) Robert, H. L.; Symes, W. R. *J. Chem. Soc. A* **1968**, 1450.
123. Tsuji, J.; Takahashi, M.; Takahashi, T. *Tetrahedron Lett.* **1980**, *21*, 849.
124. a) Osakada, K.; Doh, M-K.; Ozawa, F.; Yamamoto, A. *Organometallics* **1990**, *9*, 2197; b) Yamamoto, T.; Sano, K.; Yamamoto, A. *J. Am. Chem. Soc.* **1987**, *109*, 1092.
125. Hoberg, H.; Herrera, A. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 927.
126. Giles, R. G. F.; Lee Son, V. R.; Sargent, M. V. *Aust. J. Chem.* **1990**, *43*, 777.
127. Ishii, Y. *Ann. N. Y. Acad. Sci.* **1974**, *239*, 114.
128. Paquette, L. A.; Gardlik, J. M.; McCullough, K. J.; Samodral, R.; DeLucca, G.; Ouellette, R. J. *J. Am. Chem. Soc.* **1983**, *105*, 7649.
129. Funabiki, T.; Mizoguchi, A.; Sugimoto, T.; Yoshida, S.; Tada, S.; Tsuji, M.; Sakamoto, H. *J. Am. Chem. Soc.* **1986**, *108*, 2921.
130. (a) Ipaktchi, T.; Weinreb, S. M. *Tetrahedron Lett.* **1973**, 3895; (b) Bates, R. B.; Cutler, R. S.; Freeman, R. M. *J. Org. Chem.* **1977**, *42*, 4162.

131. Akhtar, M.; Botting, N. P.; Cohen, M. A.; Gani, D. *Tetrahedron* **1987**, *43*, 5899.
132. Anderson, N. H.; Ollis, W. D.; Thorpe, J. E.; Ward, A. D. *J. Chem. Soc., Perkin Trans. (I)* **1975**, 825.

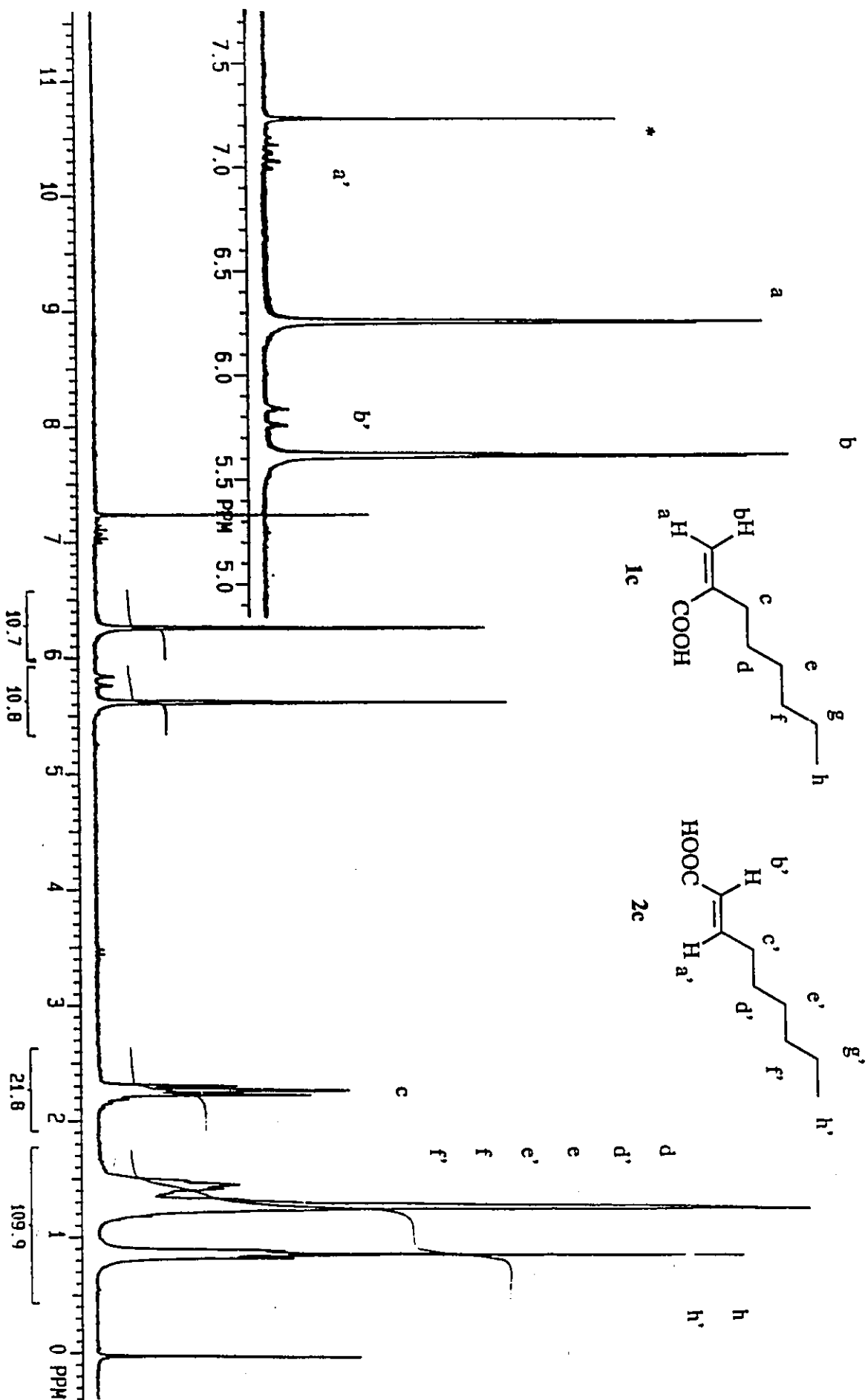
Appendix A

¹H NMR spectrum of compounds **1c** and **2c**

Instrument= Varian Gemini 200 MHz

Solvent= CDCl₃

(The singlet resonance due to residual CHCl₃ is indicated on the spectrum by " * "; the chemical shifts and the coupling constants are listed in the Experimental section, 2.2.)



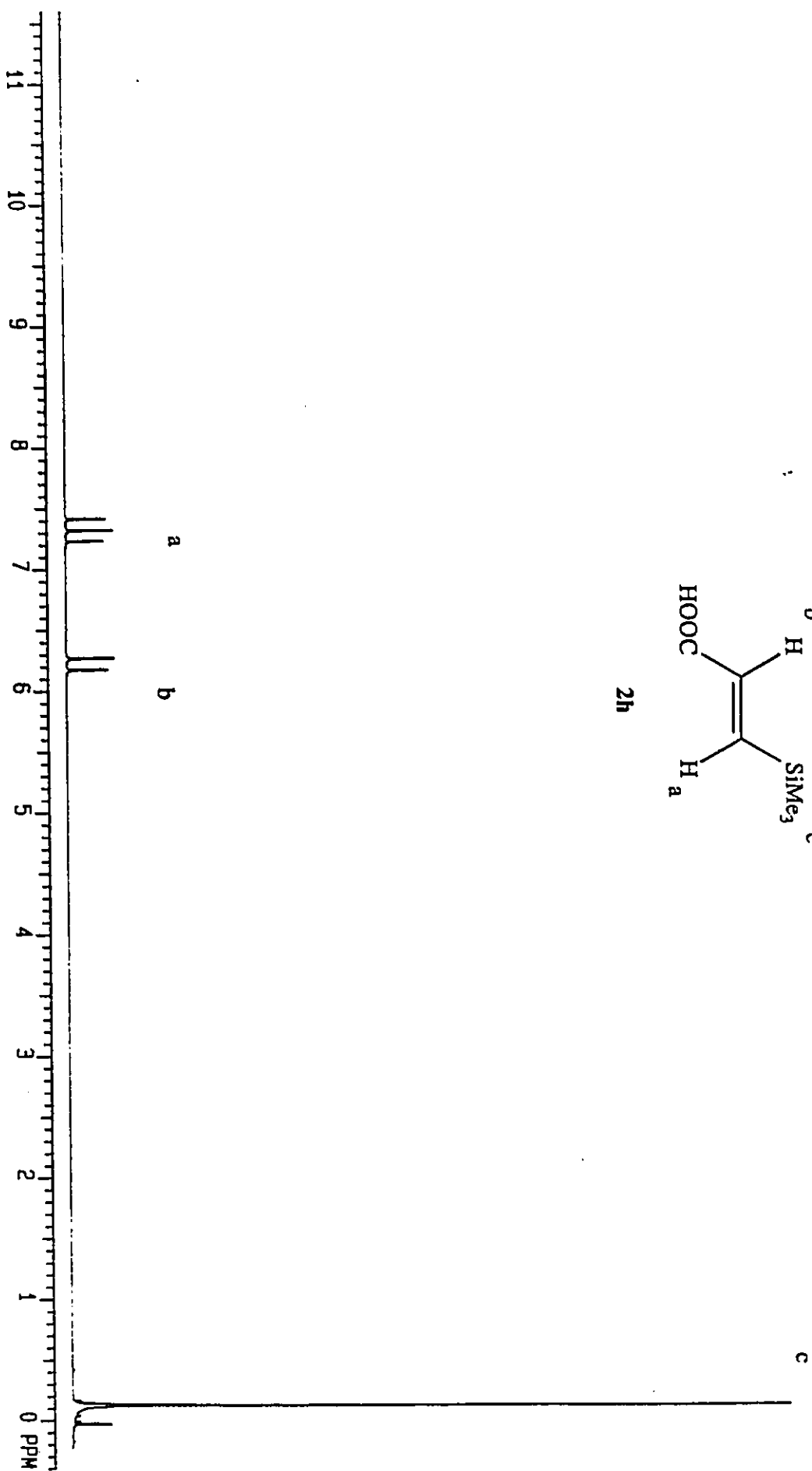
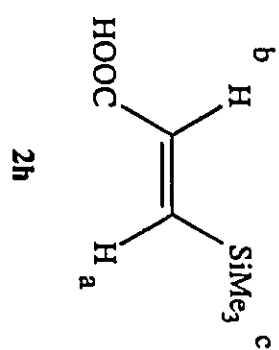
Appendix B

^1H NMR spectrum of compound **2h**

Instrument= Varian Gemini 200 MHz

Solvent= CDCl_3

(The singlet resonance due to residual CHCl_3 is indicated on the spectrum by " * "; the chemical shifts and the coupling constants are listed in the Experimental section, 2.2.)



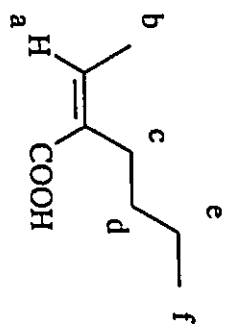
Appendix C

^1H NMR spectrum of compounds 3a and 4a

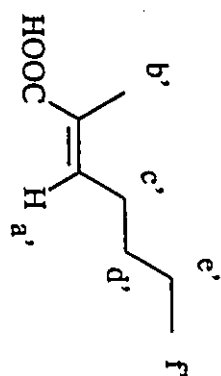
Instrument= Varian 300 MHz

Solvent= CDCl_3

(The singlet resonance due to residual CHCl_3 is indicated on the spectrum by " * "; the chemical shifts and the coupling constants are listed in the Experimental section, 2.2.)



3a



4a

