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To My Family

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CHAPTER EIGHT

EXPERIMENTAL SECTION

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I would like to express my gratitude to my supervisor, Professor Howard Alper, for teaching me a great deal of new and exciting chemistry and encouraging me to try my own ideas even though they did not always work. Without his support the work presented in this thesis would not have been possible. He is a great teacher and friend, and I will cherish forever the excellent times we had in Ottawa.

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Abstract

A systematic investigation has been carried out on the palladium-catalyzed thiocarbonylation and related reactions of unsaturated substrates such as propargylic and allylic alcohols, 1,2-and 1,3-dienes, and conjugated enynes with thiols and carbon monoxide. Results of these reactions are described in this thesis.

It has been first demonstrated that the reaction of allylic alcohols with thiols and CO in the presence of catalytic quantities of $Pd(OAc)_2$ (3 mol%), triphenylphosphine (12 mol%), and *p*-TsOH (5 mol%) leads to a novel reaction, namely thiocarbonylation, to afford β,γ-unsaturated thiol esters in good to excellent yields. Other catalyst systems such as $Pd_2(dba)_3 \cdot CHCl_3/PPh_3/p$-TsOH, $Pd(PPh_3)_4/p$-TsOH, and $Pd(OAc)_2$/dppb/*p*-TsOH are also effective for this transformation. The thiocarbonylation reaction is believed to proceed *via* a η^3-allylpalladium intermediate. The reaction occurs in a highly regioselective manner, at the least hindered allylic terminal carbon of the substrate, to give the products. The new carbonylation procedure was readily applied to a variety of allylic alcohols, and to both aromatic and aliphatic thiols.

Palladium (0) as well as palladium (II) complexes with added phosphine ligands catalyze the thiocarbonylation of propargylic compounds. Depending on the reaction conditions employed, the reaction can afford mono- and di-thioesters or β-thio-substituted γ-lactones as the principal products in good yields, respectively. Thus, in the presence of 3 mol% of $Pd(OAc)_2$, 5 mol% of *p*-TsOH, and 12 mol% of PPh_3, propargylic alcohols react with thiols in THF under 400 psi of carbon monoxide at 100°C to give

monothioesters in excellent yields. β-Thio-α,β-unsaturated-γ-lactones can be prepared in high yields by the thiolactonization of propargylic alcohols using $Pd(PPh_3)_4$ as the catalyst and DME as the solvent. Propargylic mesylates undergo dithiocarbonylation when they are treated with catalytic amounts of $Pd(PPh_3)_4$. This reaction exclusively gives dithioesters under milder conditions (90°C, 400 psi).

A series of mono- and di-substituted allenes undergo direct thiocarbonylation with thiols and carbon monoxide to form the corresponding unsaturated thioesters in 73-94% isolated yields. This reaction requires catalytic quantities of $Pd(OAc)_2$ (3 mol%) and triphenylphosphine (12 mol%) in THF under an atmosphere of CO (400 psi) at 100 °C for 48 h. The reaction is believed to proceed *via* a π-allylpalladium complex. The reaction exhibits high regioselectivity, in which the thiophenyl group adds to the less substituted double bond of allenes.

Palladium complexes can also catalyze the thiocarbonylation of 1,3-conjugated enynes. In the presence of catalytic quantities of $Pd(OAc)_2$ and 1,3-bis(dipenylphosphino)propane, the efficient reaction of 1,3-enynes bearing a terminal triple bond with thiols and carbon monoxide affords 2-(phenylthiocarbonyl)-1,3-dienes in good yields. This thiocarbonylation takes place with high chemo- and regio-selectivity, with the attack by the phenylthiocarbonyl group occurring exclsively at carbon-2 of the 1,3-conjugated enyne. Under the reaction conditions, an enyne bearing a hydroxyl group in the allylic position affords a sulfur-substituted seven-membered lactone in 74% yield.

Three-component coupling reaction of conjugated dienes, thiols and carbon monoxide affords an atom-economical thiocarbonylation of dienes to form β,γ-unsaturated thioesters as the sole products. A catalyst system based on $Pd(OAc)_2$ and

Ph_3P shows excellent catalytic activity. Using a chiral ligand, such as (R,R)-DIOP instead of PPh_3, results in the first examples of asymmetric thiocarbonylation. The reaction displays excellent enantioselectivity and a wide variety of optically active thioesters (up to 89% ee) are synthesized in good to excellent yields from easily accessible prochiral starting materials. The thiocarbonylation occurs in a highly regioselective manner and the selectivity is dependent an the steric characteristics and stability of the η^3-allylpalladium intermediate.

2,3-Dihydro-*4H*-benzothiopyran-4-one derivatives are synthesized by carbonylative heteroannulation of o-iodothiophenols with 1,2-dienes, catalyzed by $Pd(OAc)_2$ with 1,1'-bis(diphenylphosphino)ferrocene. Product yields are dependent on catalyst, ligand, solvent, base as well as the concentration of the allene.

The regioselectivity of the reaction of *o*-iodothiophenols with unsymmetrical allenes is generally quite high. The terminal disubstituted allene reacts with *o*-iodothiophenols to give only the exo-methylene products. The reaction is slower when the allene contains an electron-withdrawing group, but it can proceed to completion by prolonging the reaction time. A very bulky allene, tetramethylallene, can be also employed in this reaction to afford the corresponding product is good yield.

List of Schemes

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List of Abbreviations

Ac	Acetyl
Ar	Aryl
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
BDPP	2,4-Bis(diphenylphosphino)pentane
Boc	*N*-t-Butoxycarbonyl
Bu	Butyl
COD	1,5-Cyclooctadiene
COSY	Correlated Spectroscopy
Cy	Cyclohexyl
d	Doublet
dba	Dibenzylideneacetone
DME	Dimethoxyethane
DIOP	2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane
dppb	1,4-Bis(diphenylphosphino)butane
dppe	1,2-Bis(diphenylphosphino)ethane
dppf	1,1'-Bis(diphenylphosphino)ferrocene
dppp	1,3-Bis(diphenylphosphino)propane
EDA	Ethylenediamine
ee	Enantiomeric Excess
Et	Ethyl

GC	Gas Chromatography
HPLC	High Performance Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
Hz	Hertz
IR	Infrared Spectroscopy
L	Ligand
LDA	Lithium Diisopropyl Amide
Me	Methyl
Me-DuPHOS	1,2-Bis(2,5-dimethylphospholano)benzene
MS	Mass Spectrometry
NMR	Nuclear Magnetic Resonance
NuH	Nucleophile
PEG	Polyethylene Glycol
Ph	Phenyl
ppm	Parts per Million (δ scale)
Pr	Propyl
PROPHOS	1,2-Bis(diphenylphosphino)propane
psi	Pounds per Square Inch
PTC	Phase Transfer Catalysis or Phase Transfer Catalyst
p-TsOH	*para*-Toluenesulfonic Acid
PYRPHOS	3,4-Bis(diphenylphosphanyl)pyrrolidine
q	Quartet
R_L	Larger Substitutent

R_S	Smaller Substitutent
RT or r.t.	Room Temperature
s	Singlet
t	Triplet
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilyl
TON	Turn Over Number

CHAPTER 1

GENERAL INTRODUCTION

This thesis will describe our research on palladium-catalyzed thiocarbonylation and related reactions.

In the general introduction to follow, we will focus on the major catagories of carbonylation reactions. The basic chemistry of thiol esters will be also discussed in Chapter 1, because most of products presented in this thesis are thiol esters. Thiocarbonylation reactions of allylic and propargylic compounds will be described in Chapters 2 and 3. Specifically, we have investigated mono-, di-thiocarbonylation, and thiolactonization of allylic and propargylic alcohols as well as the corresponding mesylates and carbonates. In Chapters 4, 5, and 6 our efforts in the thiocarbonylation of unsaturated substrates such as allenes, enynes, and 1,3-dienes are described. Palladium-catalyzed carbonylative heteroannulation reactions of allenes with o-iodothiophenols and carbon monoxide are reported in Chapter 7.

PART ONE: INTRODUCTION TO CARBONYLATION CHEMISTRY

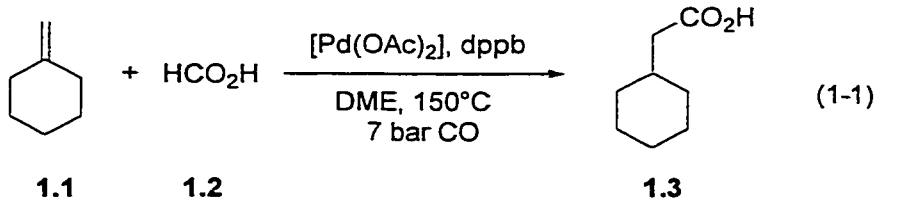
Carbonylation is the reaction in which carbon monoxide, along or together with other compounds, is introduced into a particular substrate. The first well-defined carbonylation was discovered by Otto Roelen[1] during his studies of the high pressure, cobalt-catalyzed Fisher-Tropsch synthesis of hydrocarbons from carbon monoxide and hydrogen in 1948. It was observed that addition of CO/H_2 to ethylene led to the formation of 1-propanal in high yield.[2] This type of reaction is called hydroformylation since it results in the addition of a hydrogen atom and a formyl group across a C=C bond. Initially the usefulness of hydroformylation reactions was limited as they usually required high temperatures and pressures as well as large amounts of toxic or unstable catalysts, such as $[Ni(CO)_4]$, $[Fe(CO)_5]$ or $[HCo(CO)_4]$. They did, however, become the basis of several industrial processes, including the synthesis of 1-butanal from propene and acrylic acid from acetylene.[3] Until the 1960's carbonylation chemistry was not considered to be a practical synthetic method for the preparation of fine organic chemicals. However, with the discovery of stable precursors for very active catalysts based on organophosphine complexes of either palladium or rhodium, for example, $[PdCl_2(PPh_3)_2]$ or $[RhCl(CO)(PPh_3)_2]$, this is no longer the case and many carbonylations can now be carried out below 100°C and at atmospheric pressure. Moreover, the scope and understanding of carbonylation has grown to such an extent that it is now considered an efficient technique for synthetic organic chemistry.[4] Transition metal catalyzed carbonylation reactions cover a wide range of applications, from large scale industrial

processes[5] (e.g. Monsanto process for the preparation of acetic acid from methanol and the hydroformylation of propene to afford butanal) to the preparation of fine chemicals[6] (e.g. ring expansion carbonylation,[4] asymmetric carbonylation[7]). Research efforts continue towards developing better catalytic systems for known processes, and new carbonylation reactions for the synthesis of potentially useful compounds.

1.1 Carbonylation of Alkenes

1.1.1. Hydrocarbonylation and related reactions

Catalytic hydrocarbonylation and hydroesterification of alkenes have attracted considerable attention during the last 20 years. Major synthetic studies have been focused on the development of highly regioselective methods. In general, Pd and Rh species were found to be the best catalysts for these reactions.[8] A recent example employed [$Pd(OAc)_2$] immobilized on montmorillonite in the presence of triphenylphosphine and an acid promoter for the hydroesterification of aryl and alkyl olefins. For aryl olefins the reaction is regiospecific for the branched isomer of aromatic esters, while aliphatic olefins afford branched chain esters with a regioselectivity of only 3/1 (B/L).[9] Selective hydrocarboxylation reactions to give linear acid derivatives, catalyzed by $Pd(OAc)_2$/1,4-bis(diphenylphosphino)butane (dppb) in the presence of formic acid (Eq. 1-1) [10], or by Pd on carbon in the presence of dppb and formic or oxalic acid,[11] have been described.



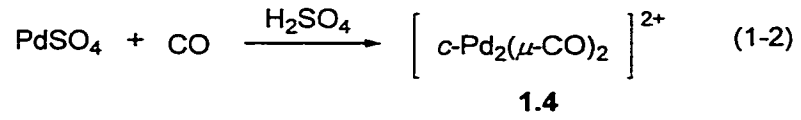
(1-1)

1.1 **1.2** **1.3**

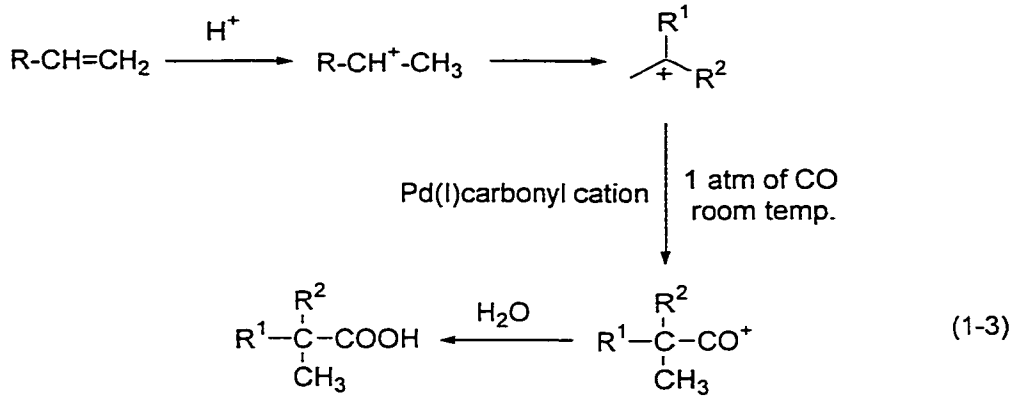
The regioselectivity of the hydroesterification of alkyl acrylates catalyzed by $[PdCl_2L_2]$ complexes (L= tertiary phosphine ligand) could be controlled by variation of the ligands. Use of a monodentate tertiary phosphine results in carbonylation to the branched isomer, while with bidentate tertiary phosphines the linear product is preferentially formed.[12] Similar regioselective control by changing the ligand was reported in the palladium-catalyzed carbonylation of formate esters.[13]

Depending on the reaction conditions, the carbonylation of dienes could lead to unsaturated and/or saturated mono and/or diacids or diesters. Examples include the formation of esters of 3,8-monodienoic acid by palladium acetate-catalyzed carbonylation of butadiene in alcohol[14] and the oxidative carbonylation of butadiene in methanol catalyzed by $[PdCl_2]$ to give dimethyl-2-butene-1,4-dicarboxylate.[15] The Pd-catalyzed hydrocarboxylation of substituted 1,3-dienes affords unsaturated mono acids in the presence of phosphine ligands and formic acid.[16]

A new palladium catalyst was found to exhibit high catalytic activity for the carbonylation of olefins.[17] Cyclo-*bis*(mu-carbonyl)dipalladium(I) cation (**1.4**) with bridging CO ligands was formed by reductive carbonylation of $[PdSO_4]$ in concentrated H_2SO_4 (Eq. 1-2). When an olefin was added, a tertiary carboxylic acid was obtained in



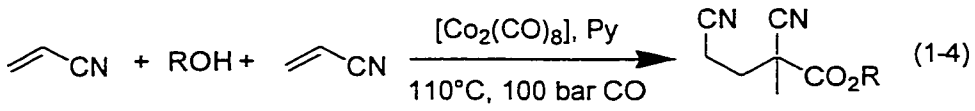
1.4 (1-2)



(1-3)

high yields at room temperature and atmospheric pressure of CO (Eq. 1-3). For environmental and economic reasons a water-soluble complex Rh/PPA(Na^+)/DPPEA was made and successfully applied in the carbonylation of olefins.[18]

In order to prepare polyfunctional intermediates as building blocks *via* tandem reaction Marko *et al.* developed an efficient one pot hydroesterification-Michael addition process (Eq. 1-4).[19]

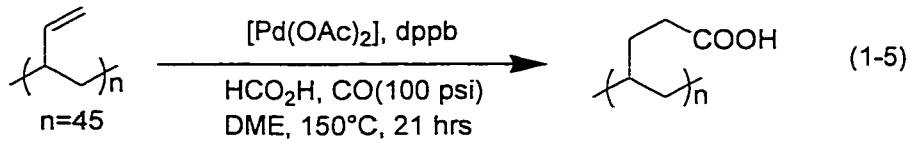


1.5 **1.6** **1.5** **1.7** (1-4)

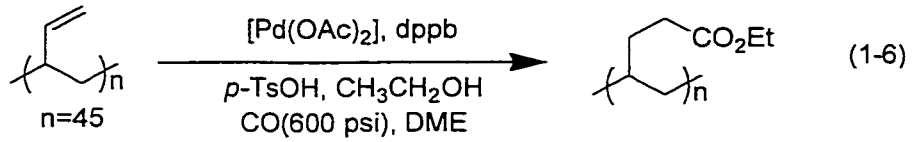
Thus, hydroalkoxycarbonylation of acrylonitrile (**1.5**) with alcohols proceeds in the presence of catalytic amounts of [$Co_2(CO)_8$] and pyridine bases to yield 2,4-dicyano-2-

methylbutanoic acid esters (**1.7**). The yield of the desired products (up to 90%) strongly depends on the pyridine/cobalt ratio.

Using different homogeneous catalytic systems, Alper *et al.* reported that the hydrocarboxylation of 1,2-polybutadiene (Mw 2400) was achieved with partial to full conversion of pendant double bonds in a highly regioselective manner.[20] The use of $[Pd(OAc)_2]$/1,4-bis(diphenylphosphino)butane (dppb)/HCOOH or $[Pd(OAc)_2]$/dppb/ROH leads to linear polyacids or polyesters, respectively (Eqs. 1-5 and 1-6).



1.8 **1.9** (1-5)



1.8 **1.10** (1-6)

1.1.2. Oligomerization and polymerization with CO

Several Pd(II) catalyst systems have been reported to catalyze the alternating copolymerization of olefins, particularly ethylene with CO to yield low-cost polyketones (Eq. 1-7).[21] Rhodium catalysts have also been used for copolymerization.[22]

$$n\,H_2C{=}CH_2 \;+\; n\,CO \;+\; CH_3OH \xrightarrow[115°C]{\text{Pd cat., HX}} H(CH_2CH_2CO)_nOCH_3 \qquad (1\text{-}7)$$

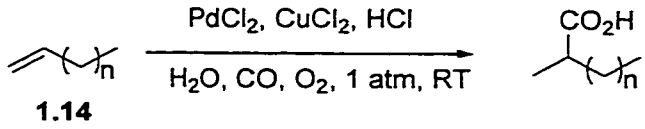
1.11 **1.12** **1.13**

The catalyst systems used in copolymerizations have employed palladium(II) salts in protic solvents together with an acid, mono- or bidentate phosphines, or bidentate nitrogen ligands and oxidants such as benzoquinone. Drent *et al.* developed an efficient homogeneous Pd catalyst system for the terpolymerization of ethylene, propylene and carbon monoxide. The catalyst system was an equimolar combination of 1,3-bis(diphenylphosphino)propane (dppp) as a ligand with a Pd(II) species in which the counter ions were weakly coordinating.[23] The reaction was suggested to proceed *via* alternating sequence of CO and alkene insertion in Pd-C bonds.[23] An alternative mechanism involving Pd carbene intermediates was recently proposed.[24] It has been reported that the alternative copolymerization of CO and 4-tert-butylstyrene represents an example of living alternating copolymerization, which is very rare.[25]

1.1.3. Oxidative carbonylation

A lot of attention has been paid by industry to the oxidative carbonylation of styrene as a method to produce cinnamic acid derivatives. The catalyst systems used contain Pd and Cu salts as well as other metals as co-catalysts. A study of the most active catalyst system consisting of $PdCl_2$, $CuCl_2$, $Cu(OAc)_2$ and $Mn(OAc)_2$ showed that putting $Mn(OAc)_2$ as additive substantially increased the activity.[26]

Alper *et al.* showed that a combination of $PdCl_2$, $CuCl_2$, HCl, H_2O, O_2 and CO promoted the regioselective hydrocarboxylation of polymeric olefins (**1.14**) at room temperature under 1 atmosphere of CO (Eq. 1-8).[27]

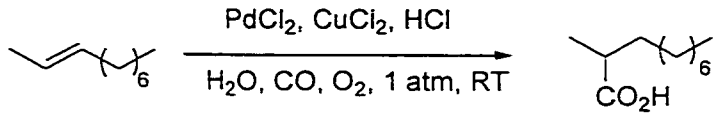


1.14

(1-8)

1.15, n=7, 100% yield
1.16, n=5, 82% yield

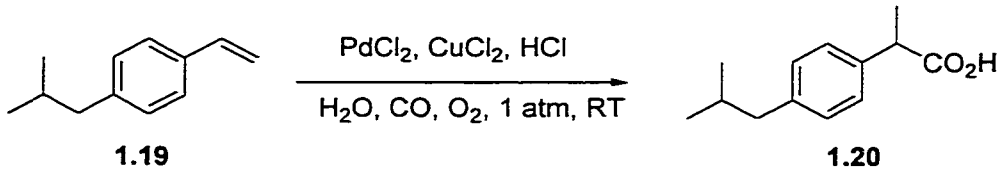
The branched isomer was obtained exclusively for all of the terminal olefins studied. Even more remarkably, the reaction of internal olefins with the C=C functional group at the 2-position also gave regioselectively only the 2-methylalkanoic acid (**1.18**) (Eq. 1-9).



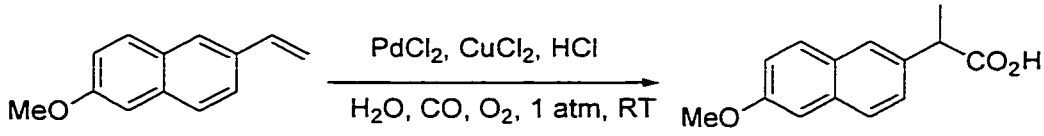
1.17 **1.18**

(1-9)

The application of this system to styrene and its derivatives was also highly successful. For example, using $PdCl_2$:$CuCl_2$ in a 1:2 ratio under 1 atmosphere of CO, the hydrocarbonylation of 4-isobutylstyrene (**1.19**) was catalyzed to give the product in 89% yield. 6-Methoxy-2-vinylnaphthalene (**1.21**) was also hydrocarboxylated in excellent selectivity. The addition of a chiral phosphate derived from BINAP to the reaction mixture gave carboxylic acids with up to 89% ee.[28] The products ibuprofen (**1.20**) and naproxen (**1.22**) from the hydrocarbonylation of **1.19** and **1.21** respectively, are potent analgesics (Eq. 1-10 and 1-11).

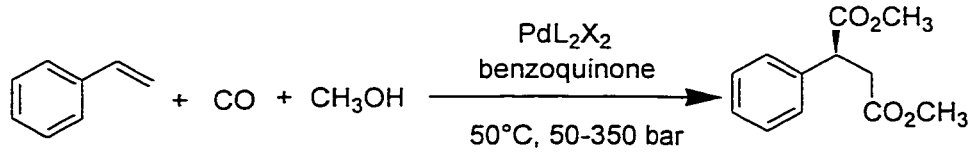


1.19 **1.20** (1-10)



1.21 **1.22** (1-11)

Bisalkoxycarbonylation of olefins to succinate derivatives has been developed with various catalyst systems. Among the catalysts employed, $PdCl_2$ with butyl nitrite[29], PdI_2 with O_2 and KI[30], and $Pd(acac)_2$ with di-tert-butylperoxide[31] are most often used. The first stereoselective version of this reaction was developed by Consiglio *et al.* (Eq. 1-12).[32]



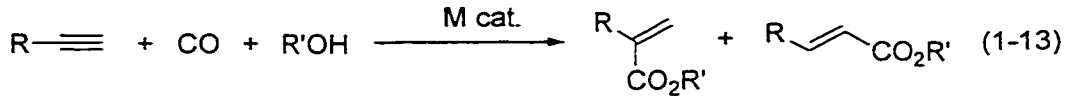
1.23 **1.24** (1-12)

The bisalkoxycarbonylation of styrene(**1.23**) using chiral PdL_2X_2 complexes and benzoquinone proceeds with enantiomeric excesses of up to 93% in the presence of a chiral phosphine ligand, although the chemoselectivity of the reaction is lower.

1.2 Carbonylation of Alkynes

1.2.1. Hydrocarboxylation and related reactions

In principle the same catalyst can be used for the carbonylation of alkynes as for the carbonylation of alkenes. Most of the synthetic work in the area of alkyne carbonylation has been devoted to developing new catalyst systems to control the regio- and stereoselectivities in the products. Using terminal alkynes instead of acetylene hydrocarboxylation reactions can give 2- or 3-substituted acrylic acid derivatives (Eq. 1-13).



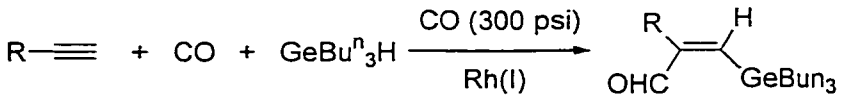
1.25 **1.26** **1.27**

The selective formation of 2-substituted acrylate esters has been described using nickel cyanide under phase transfer conditions[33] or with a Pd-phosphine catalytic system.[34] Moreover, hydroaminocarbonylation of terminal alkynes also proceeds regioselectively in the presence of palladium complexes with iodide promoters in diethylamine under considerably mild conditions.[35] This chemistry has been used for the synthesis of pharmacologically interesting amino acids.[36]

Treatment of alkynes with carbon monoxide in the presence of a bimetallic catalyst system consisting of $CoCl_2$, KCN, and $NiCN_2$ has been shown to give saturated carboxylic acids with good selectivity for the branched-chain isomer.[37] Biscarboxylations of alkynes to produce maleic and fumaric acid derivatives in the

presence of Pd catalysts and an oxidant have been reported.[38] Recently developed electrochemical reoxidation of palladium(0)[39] or using PdI_2 with iodide promoters as catalyst[40], avoided the use of stoichiometric quantities of a reoxidant, e.g. $CuCl_2$.

The germylformylation of terminal alkynes catalyzed by a rhodium(I) complex was described.[41] The zwitterionic rhodium complex, $[(cod)Rh^{+}(\eta^{6}\text{-}C_6H_6BPh_3)^{-}]$ (cod=cycloocta-1,5-diene), is an excellent catalyst for the reaction of terminal alkynes with tri-*n*-butylgermane and CO. The reaction occurs with high levels of regio- and stereoselectivity and affords (*Z*)-3-germylalk-2-enals (**1.29**) in good yields (Eq. 1-14).



1.25 **1.28** **1.29** (1-14)

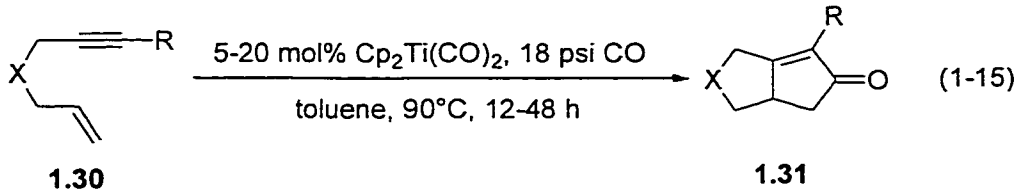
Similar reactions, such as inter-[42] and intra-molecular[43] silylformylation, as well as aminocarbonylations,[44] have been extensively studied in the past few years. These reactions are totally regio- and stereoselective.

In addition to monomeric alkynes, poly(2-methylvinylacetylene) (PVA) can be functionalized by palladium(II)-catalyzed hydrocarboxylation, hydroesterification, and iodoarene/CO coupling reactions to give new polymers containing pendant functional groups of α,β-unsaturated carboxylic acids, esters, and ketones, respectively.[45] The catalytic processes used provide unique methods to synthesize these polymers in a stereocontrolled manner.

1. 2. 2. Other Reactions

Currently there is much interest in tandem procedures, which can generate several bonds in only one step, as they provide a simple, efficient route to complex organic molecules. Such examples of transition metal-catalyzed syntheses include the preparation of cyclopentenones (Pauson-Khand reaction),[46] cyclopentadienones,[47], and furanones.[48]

A Pauson-Khand type conversion of enynes to bicyclic cyclopentenones, employing the commercially available precatalyst titanocene dicarbonyl, was recently reported by Buchwald *et al.* (Eq 1-15).[49]

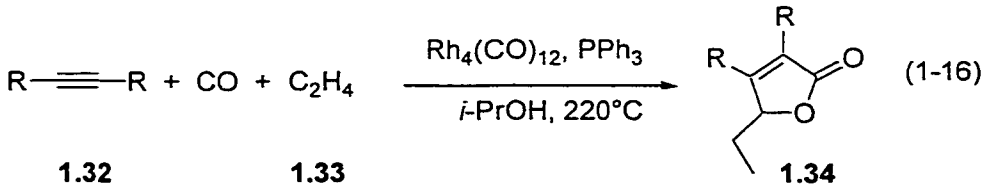


1.30 **1.31** (1-15)

X=O, NR', $C(R^1)(R^2)$; R, R', R^1 or R^2= H, alkyl, aryl, or $-CO_2Et$

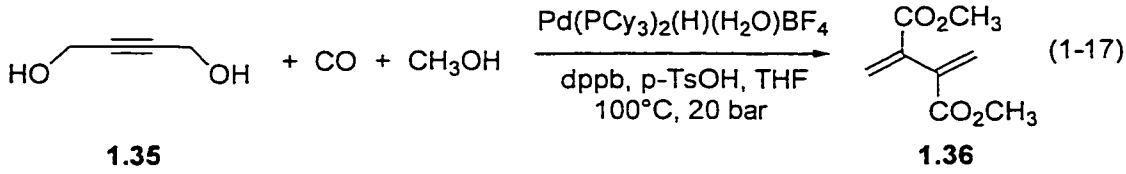
This methodology shows excellent functional group tolerance for a group 4 metallocene-catalyzed process. The titanocene catalyst has proven capable of cyclizing a variety of both 1,6- and 1,7-enynes and 1,1- and 1,2-disubstituted olefin-containing enynes. Moreover, a new active heterogeneous Pauson-Khand catalyst using cobalt metal supported on mesoporous silica, MCM-41, was developed.[50] The catalyst systems are air-stable and reusable, and quite effective for many intramolecular cycloaddition reactions. In addition, important features of the catalytic reaction are its experimental simplicity and the high conversion rate.

Rh-catalyzed synthesis of 2(*5H*)-furanones from alkynes under water-gas shift reaction[51] conditions was studied.[52] Both internal and terminal alkynes could be employed as substrates. The furanone framework is formed by the reaction of the alkyne with one molecule of hydrogen and two molecules of CO. 5-Ethyl-2(*5H*)-furanones were prepared by $Rh_4(CO)_{12}$-catalyzed carbonylation of an alkyne and ethylene in the presence of alcohols as the hydrogen source (Eq. 1-16).[53] Note that the chemoselectivity changed



(1-16)

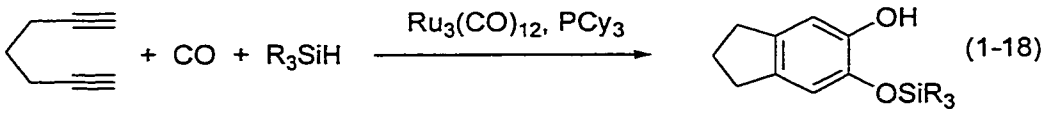
to 1-penten-3-one using only hydrogen.[54] Furanones were also formed when propargylic alcohols were carbonylated with bis(dibenzylidene acetone)-Pd and dppb.[55] The reaction of CO with propargylic derivatives has been widely studied.[56,57] Depending on the catalyst used (Ni, Pd, etc.) it is possible to synthesize dienoic acids (Eq. 1-17), allenic acids, or unsaturated diacids.[55]



(1-17)

Despite multiple functionalization possibilities none of these reactions have been used commercially. An interesting example of the carbonylation of 1,6-diynes was reported by Murai *et al.* seven years ago.[58] 1,6-Heptadiyne (**1.37**) reacts with CO and

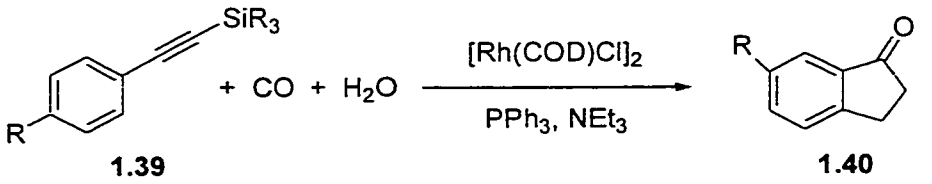
tert-butyldimethylsilane in the presence of $Ru_3(CO)_{12}$ and tricyclohexylphosphine to give a 5,6-dihydroxyindan derivative (**1.38**) (Eq. 1-18). A mechanistic study showed that the ruthenium carbonyl complex rearranged during the catalytic cycle to form a oxacarbyne complex.



(1-18)

1.37 **1.38**

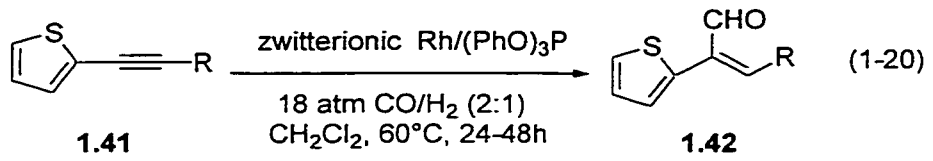
Another example of potentially useful cyclocarbonylation leads to indenones, which are valuable intermediates, for example, in the preparation of metallocene ligands. Under water-gas shift reaction conditions aryltrimethylsilylacetylenes (**1.39**) undergo rhodium-catalyzed desilylative carbonylation to give 2,3-dihydro-*1H*-inden-1-one (**1.40**) (Eq. 19).[59]



(1-19)

1.39 **1.40**

The regioselective hydroformylation of acetylenic thiophenes (**1.41**) was developed by Van den Hoven and Alper.[60] The reaction was catalyzed by a zwitterionic rhodium catalyst $(\eta^6\text{-}C_6H_5BPh_3)^-Rh^+$(1,5-COD) and triphenyl phosphite. This catalytic system afforded the α,β-unsaturated aldehyde (**1.42**) with the aldehyde and thiophene attached to the same olefin carbon atom (Eq. 1-20).



1.41 1.42 (1-20)

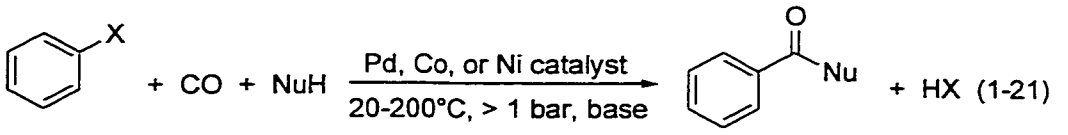
Assistance of sulfur from the heterocycle provided excellent regioselectivity and yields when the acetylenic unit was a propargyl ether or ester, phenylacetylene, or an enyne.[60b]

1.3 Carbonylation of Organic Halides

1.3.1. Reactions of Aryl- and Vinyl-X

Since the discovery of the Heck reaction, carbonylation reactions of aryl- and vinyl halides have been extensively studied.[61] Many efforts have been undertaken in the extension of this kind of chemistry by the use of new starting materials and by combining the carbonylation step with new modes of trapping reactions of the intermediate acyl-metal complex. The combination of metal-catalyzed C-C coupling reactions with carbonylation chemistry to develop regio- and stereoselective atom economic cascade reactions has been a major subject of interest.

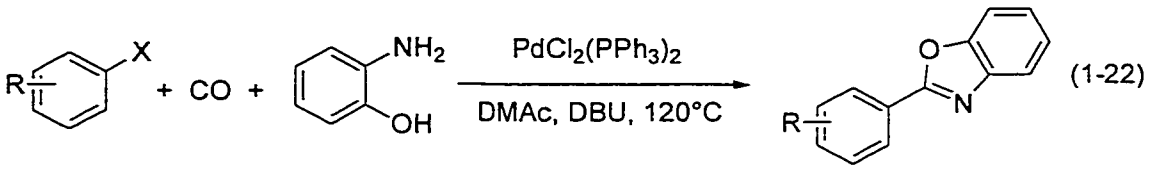
In most cases aryl halides, especially bromides and iodides, are used as starting materials and transition metals such as Pd or Co, which are capable of oxidative addition to a C-X bond, as the catalysts.[62] Depending on the reaction media it is possible to synthesize either acids,[63] esters,[64] amides,[65] and acid fluorides (Eq. 1-21).[66]



1.43 **1.44**

Nu = OH, OR, NR_2, F, or Cl
X = I, Br, Cl, N_2X, OSO_2R, or IO_2

Moreover, aryloxazoles,[67] anhydrides,[68] and imides[69] are also accessible *via* carbonylative Heck reactions (Eq. 1-22).



1.45 **1.46** **1.47**

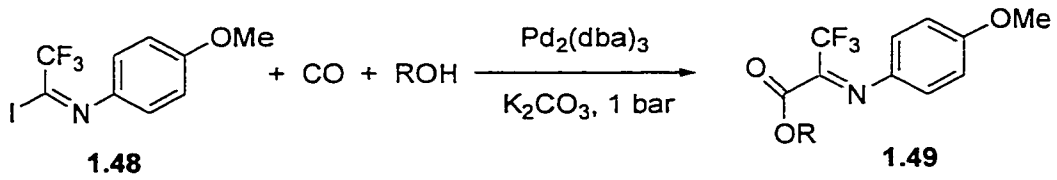
X = Br or I

Carbonylation of aromatic halides with Pd catalysts and phase transfer systems, for example polyethylene glycol (PEG),[70] or water-soluble catalysts[70] gave benzoic acids in good yields. A study on the application of heterogeneous catalysis for the carbonylation of aryl halides showed that a Pd species supported on active carbon gave excellent results.[71] The carbonylation activity increased with the addition of a small amount of water to the reaction solvent methanol, but a mixture of benzoic acid and methyl benzoate was formed.

For alkoxycarbonylation reactions, solid-liquid phase transfer conditions were found to lead to improved yields of butylbenzoic acid ester,[72] compared to the reaction conditions originally reported by Heck et al. Heat resistant aromatic polyesters and

polyamides[73] could be synthesized by Pd-catalyzed alkoxycarbonylations as well. For the preparation of model compounds for polyesters a study of the effect of added base for Pd-catalyzed aryloxycarbonylation was performed.[74] Sodium acetate and tertiary amines lead only in low yield to the desired product, while cyclic amidines drastically increased the rate of reaction and the yield.[74]

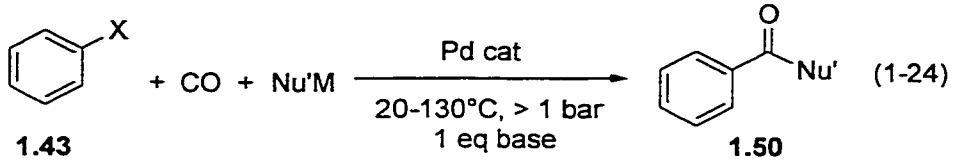
An excellent method to make fluorinated amino acids has been designed by Uneyama *et al.*[75] Palladium catalyzed carbonylation of an imidoyl iodide in the presence of benzyl alcohol afforded the corresponding imino ester, which could undergo further transformation to give quaternary amino acids (Eq. 1-23).



1.48 **1.49** (1-23)

Palladium-catalyzed carbonylation of an imidoyl iodide in the presence of benzyl alcohol afforded the corresponding imino ester, with further transformations giving quaternary amino acids.

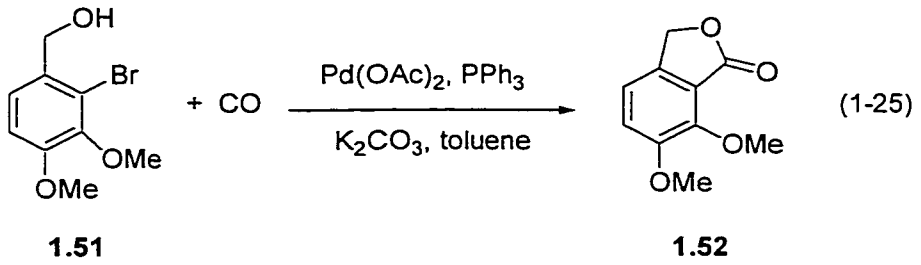
Besides typical benzoic and vinylic acid derivatives, aldehydes,[76] ketones,[77] aroyl cyanides,[78] aroyl acetylenes,[79] and their derivatives[80] are accessible *via* nucleophilic attack of the intermediate acyl metal complex by the corresponding hydrogen or carbon nucleophiles (Eq. 1-24).



(1-24)

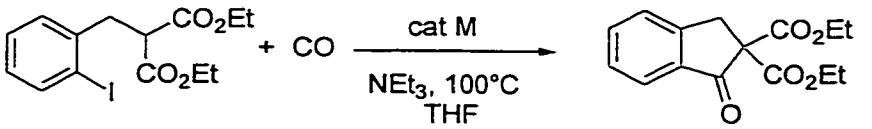
X = Br, I, OSO_2R
M = Na, K, BR_3, SnR_3, AlR_2, HgR
Nu' = H, CN, alkyl, aryl, vinyl, alkynyl

Instead of intermolecular reactions of the acyl palladium complex a number of intramolecular trapping reactions have been developed and used in organic synthesis in recent years. Some typical examples[81] include the carbonylation of 2-halophenols, anilines or *O*-alkynyl-benzyl alcohols to *O*- or *N*- heterocycles (Eq. 1-25), intramolecular enolate or enamine trapping to isocoumarins or quinolinones.



(1-25)

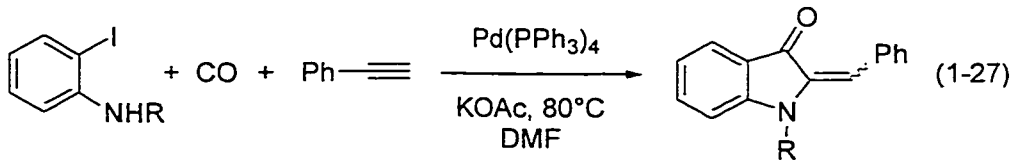
The feasibility of different late transition-metal complexes as catalysts for the formation of indanones and tetralones by the carbonylative cyclization has been investigated. The results showed that apart from palladium, copper and nickel complexes are also able to catalyze reactions (Eq. 1-26).[82]



1.53 **1.54** (1-26)

cat M = Pd, Ni, Cu

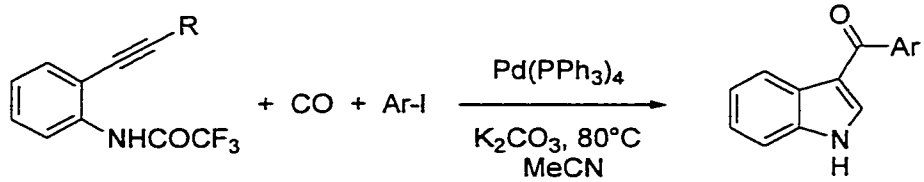
Related tandem reactions with three components (aromatics, alkynes and CO) were used for the synthesis of derivatives of flavone,[83] aurone,[84] indoxyl[85] and furanones,[86] benzopyranones,[87] benzoxazinones,[88] as well as pyrido[3,2-*e*]-1,3-oxazinones.[89] The synthetic potential of this methodology is illustrated by the variety of products which can be prepared by minor changes of the reactants. This is clearly demonstrated by the reaction of 2-haloanilines with CO and alkynes, a one-pot reaction to give indoxyl derivatives (Eq. 1-27).[85]



1.55 **1.56** (1-27)

76%

It is believed that the reaction is initiated by oxidative addition of a palladium(0) complex to the aryl halide. Interestingly, the resulting arylpalladium(II) complex reacts preferentially with CO and not the alkyne. As shown in Eq. 1-28, and contrary to the previous example, the consecutive reaction with an alkyne as the first step, and CO and another aryl halide as the second step, leads to 3-acylindoles.[90]



(1-28)

1.57 **1.58**

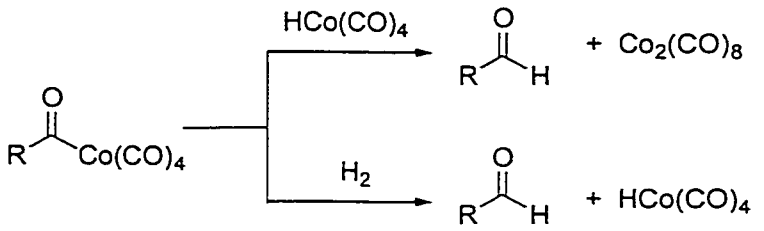
1. 3. 2. Reactions of Benzyl- and Allyl-X

The transition metal-catalyzed carbonylation of allylic and benzylic derivatives is a valuable method for the synthesis of 3, 4-unsaturated carboxylic acid derivatives and aryl acetic derivatives, respectively. Catalysts used for this type of transformation are complexes of Ni,[91] Co,[92] Rh,[93] Pt,[94] Fe,[95] but mainly Pd catalysts[96] have been employed for activity and selectivity reasons.

Unlike aryl halides, benzylic and allylic derivatives are susceptible to nucleophilic attack and elimination reactions. Thus, over the past 15 years for the carbonylation of allylic compounds, many efforts have been directed to the development of milder and more selective reaction conditions, e. g. atmospheric pressure carbonylations[97] and expanding synthetic methods (e. g. via tandem reactions). In the case of the catalytic carbonylation of allylic and benzylic halides, two-phase systems with phase transfer conditions have been introduced and extensively used.[72a] Usually the reactions were performed with an excess of base in a biphasic system with a metal catalyst in the organic phase. Surfactants are used as phase transfer catalysts. They appear to have an important transport function allowing the cobalt carbonyl salt to transfer from the aqueous to the organic phase.

Interestingly, Amer and Alper showed that certain lanthanide salts can effectively promote nickel cyanide catalyzed carbonylations.[91a] The Lewis acid character of the lanthanide compound presumably accelerates carbonyl insertion of the benzyl metal complex. This type of co-catalysis may well be applicable to other types of Lewis acids as well.[98]

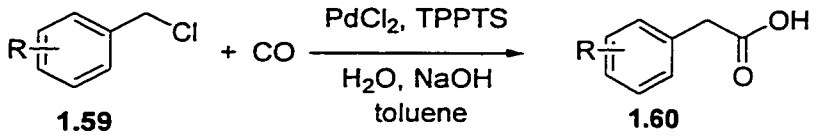
It has been reported that the carbonylation of benzyl chloride to phenylacetic acid is used in industry (Eq. 1-29).



(1-29)

The carbonylation is conducted in a two-phase medium of a non-polar solvent and 40% aqueous NaOH solution with a cobalt carbonyl complex and a benzyltrialkylammonium surfactant.[99]

A major drawback of most carbonylations of benzylic and allylic halides is that these reactions need a large amount of catalyst (usually 10-20 mol%) and phase transfer reagent (5-10 mol%) in order to get high conversions and yields. Recently, a new approach[100] was developed, in which water-soluble Pd catalysts, with TPPTS as the ligand, was employed and the TON was up to 1500 (Eq. 1-30).

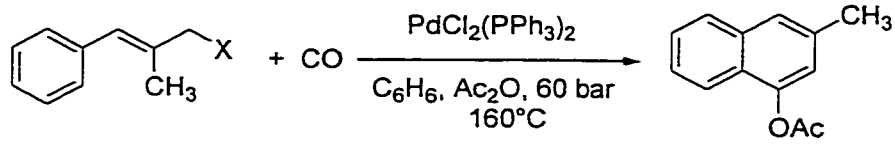


1.59 **1.60** (1-30)

TPPTS = sodium trissulfonatophenylphosphine

The carbonylation of allylic and benzylic alcohol derivatives such as acetates,[101] carbonates,[102] ethers,[103] phosphonates[104] as well as alcohols themselves[105] is an area of considerable interest. The reactivity of the leaving group of allylic substrates decreases in the order Br> $OP(O)(OEt)_2$> Cl> $OCOCF_3$> OCO_2Et> OCOPh> OCOMe. No reactivity was found for OPh, NEt_2 and OH. For allylic acetates, carbonylation has been a problem for some time. It has been shown that for the intermediate η^3-allylpalladium acetate complex the back reaction to form allyl acetates proceeds faster than the insertion of CO into the complex.[106] Introduction of bromide ion as the co-catalyst leads to a fast ligand exchange of the acetate with bromide. Therefore the resulting bromide complexes could be carbonylated in moderate to good yields (57-90%).[107]

Allylic halogenides containing an additional functional group in a suitable position, such as an alkene moiety or a hydroxy group, produce the corresponding cyclopentenone derivatives or lactones *via* Pd catalyzed carbonylation.[108] The related cyclocarbonylation of cinnamyl halides or acetates to form polycyclic aromatics, such as naphthol derivatives, have been reported (Eq. 1-31).



(1-31)

1.61a: X=OAc
1.61b: X=Br

1.62

Moreover, the synthetic utility of the method was demonstrated by the synthesis of acetoxybenzofurans, acetoxyindoles, and acetoxycarbazoles.[109]

1.4 Carbonylation of Aldehydes

The carbonylation of aldehydes has been widely used for the synthesis of glyoxylic acids and ethylene glycols.[110] For example, hydrocarbonylation of formaldehyde (**1.63**) to glycolaldehyde has been carried out homogeneously using Co, Ru or, most successfully, Rh catalysts (Eq. 1-32).[110]

$$\underset{\textbf{1.63}}{CH_2O} + CO + H_2 \xrightarrow{\text{Rh cat.}} \underset{\textbf{1.64}}{HOCH_2CHO} \qquad (1\text{-}32)$$

Best results are obtained in amidic solvents with Rh catalysts and acid promoters. The catalyst consists of $Rh(acac)(CO)_2$ with aromatic phosphines such as tri(4-chlorophenyl)phosphine as ligands.

Basic phosphine ligands tend to give rise to methanol. Thus, it has been concluded that a cationic Rh hydride is the key intermediate of the reaction. If it is

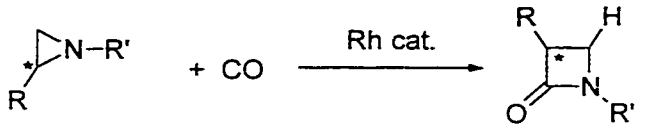
sufficiently acidic, it will activate formaldehyde by protonation to form an Rh-CH_2-OH species, whereas if it is too hydridic, it will give rise to Rh-OCH_3 and to methanol as observed for basic phosphines.[111] Besides hydrocarbonylation, direct carboxylation to glyoxylic acid is of commercial interest, but has not been investigated much. Acid catalyzed carbonylation, e. g. with H_2SO_4, zeolites or sulfonated resins were described[112] under severe reaction conditions. Other aldehydes besides formaldehyde are much more difficult to carbonylate. An exception is the recently published carbonylation of electron-rich aromatic aldehydes to phenylacetic acid derivatives by palladium-phosphine systems in the presence of HCl.[113]

Amidocarbonylation is another type of reactions for the carbonylation of aldehydes,[114] in which the addition reaction of an acid amide to an aldehyde and subsequent carbonylation of the adduct using cobalt carbonyl as the catalyst yield N-acyamino acid.[115-118] Later, it was found that in addition to aldehydes, acetals,[119-120] olefins,[121-122] and benzylic substituted compounds[123-124] can be used as starting materials in this particular reaction as well.

1.5 Other Carbonylation Reactions

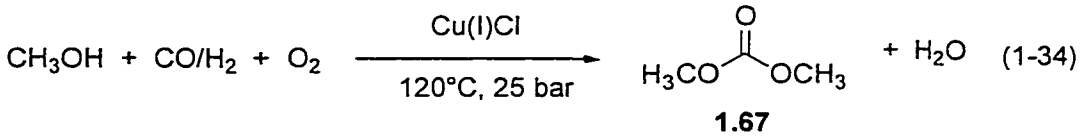
As a special type of carbonylation, the ring expansions of strained heterocyclic compounds like aziridines,[125] azetidines,[126] epoxides,[127] and thiiranes[128] have been nicely developed. Most of the work in this area is described by Alper *et al.*[129] In the case of

aziridines (**1.65**), the focus has been on enantioselective reactions to β-lactams (**1.66**) (Eq. 1-33).[130]



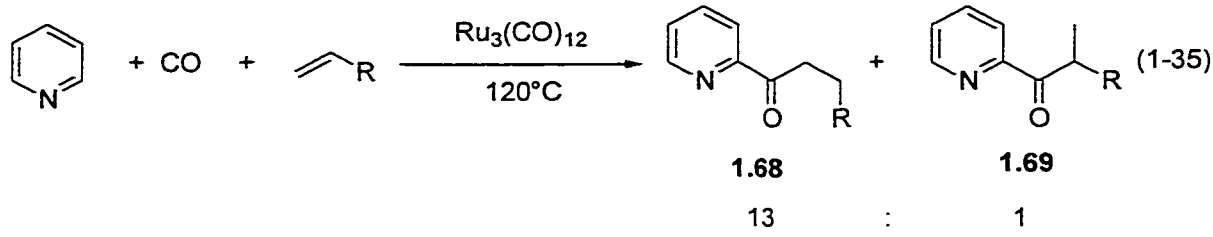
1.65 **1.66** (1-33)

Examples of other processes in the area of carbonylation include the syntheses of dimethyl carbonate and dialkyl oxalates. For the production of dimethyl carbonate, a slurry of CuCl in methanol is treated with a mixture of syngas and oxygen (Eq. 1-34).[131]



1.67 (1-34)

Carbonylation of unactivated hydrocarbons catalyzed by transition metal complexes is currently an area of great interest as it provides a route to functionalized molecules from cheap, readily available starting materials.[132] For example, phenylacetaldehyde can be synthesized from toluene and CO in the presence of Rh complexes.[133] An industrial application is the catalytic regioselective acylation of pyridine with CO and olefins[134] in the presence of ruthenium carbonyl cluster (Eq. 1-35).

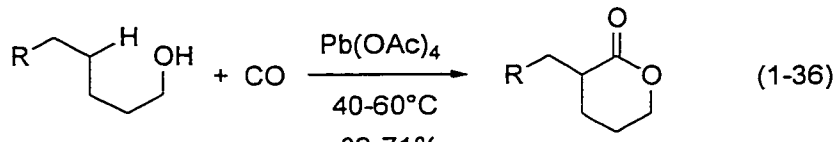


1.68 **1.69**

13 : 1

It is believed that the cluster framework remains intact during the course of the acylation reaction. TON of 160/h (and 65% yield) have been observed for the reaction with 1-hexene.

A new lactone synthesis starting from saturated alcohols *via* radical carbonylation has been reported (Eq. 1-36).[135]



1.70 **1.71**

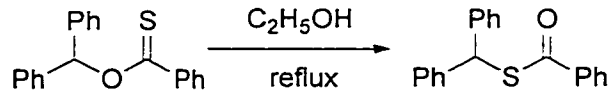
In the presence of a stoichiometric amount of lead tetraacetate an oxygen-centered radical was generated from a primary or secondary alcohol. After a 1,5-hydrogen shift the central carbon radical is trapped by CO. Finally, oxidation and cyclization yield the lactones.

Other radical carbonylations[136] to macrolides, cyclopentanones, and functionalized cyclopentanes were reported as well.

PART TWO: INTRODUCTION TO THIOL ESTER CHEMISTRY

1.6 General Background

A group of derivatives of thiols, which have a structure unit like R^1SCOR^2, are called thiol esters. Thiol esters are thermodynamically more stable than their thione ester isomers (C=O stronger than C=S); so, possible interconversions between them strongly favour the former (Eq. 1-37).



1.72 **1.73** (1-37)

Presumably because resonance interaction of the type summarized in Figure 1-1 is less important than the corresponding one for carboxylate esters shown in Figure 1-2, thiol esters tend to be more reactive towards carbonyl addition and more prone to enolization than carboxylate esters.[137]

Figure 1-1 Resonance of Thiol Esters

Figure 1-2 Resonance of Carboxylate Esters

1.7 Application of Thiol Esters

The chemistry of thiol esters has important biosynthetic implications in that coenzyme A, which is, in many respects, simply a complex thiol with a long tail possessing a nucleotide end group (abbreviated as CoASH), owes its special role in nature to the reactions of its acyl derivatives. Thus, acetyl coenzyme A (Figure 1-3) is

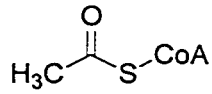


Figure 1-3 Acetyl Coenzyme A

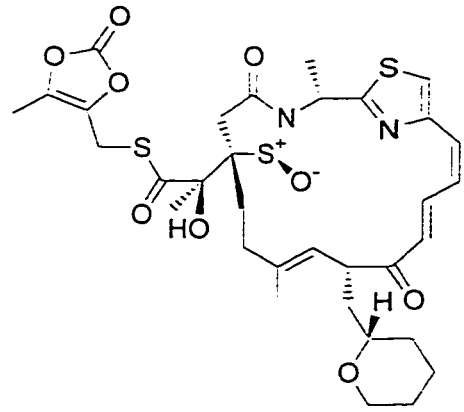
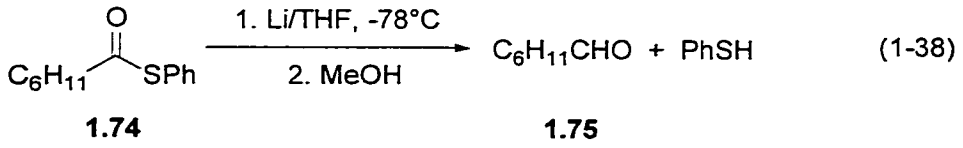


Figure 1-4 KF 22678

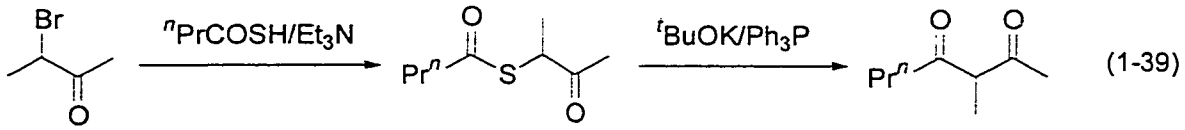
one of nature's important two carbon building blocks, the precursor both of fatty acids and of a large group of naturally occurring aromatic and heteroaromatic (polyketide derived) compounds.[138] Thiol esters also play an important role in the development of thiol drugs; they protect the unstable thiol moiety, increase the activity of the drugs, and mask the undesired odor and taste of the native thiol. A typical and representative example is KF22678 (Figure 6-4), a novel thioester derivative of leinamycin with the 1-oxo-1,2-dithiolane-3-one moiety.[139] KF22678 shows broad spectrum antitumor activity against human carcinoma xenografts (lung, colon, ovary and prostate).[139]

Organic compounds with a thiol ester group can be subjected to a wide range of synthetic transformations. For example, thiol esters are the only acyl derivatives that undergo reduction with alkai metals to give, after protonation of the intermediate, aldehydes (Eq. 1-38).[140]



1.74 **1.75**

Other reducing agents for this transformation involve diisobutylaluminum hydride (DIBAL)[141] and triethylsilane.[142] Similarly, thiol esters have been used for the synthesis of ketones, via organocuprates,[143] Grignard reagents[144] or silylacetylenes.[145] Another ingenious approach to ketones is by sulfur activated carbanionic cyclization followed by sulfur extrusion (Eq. 1-39).[137b]



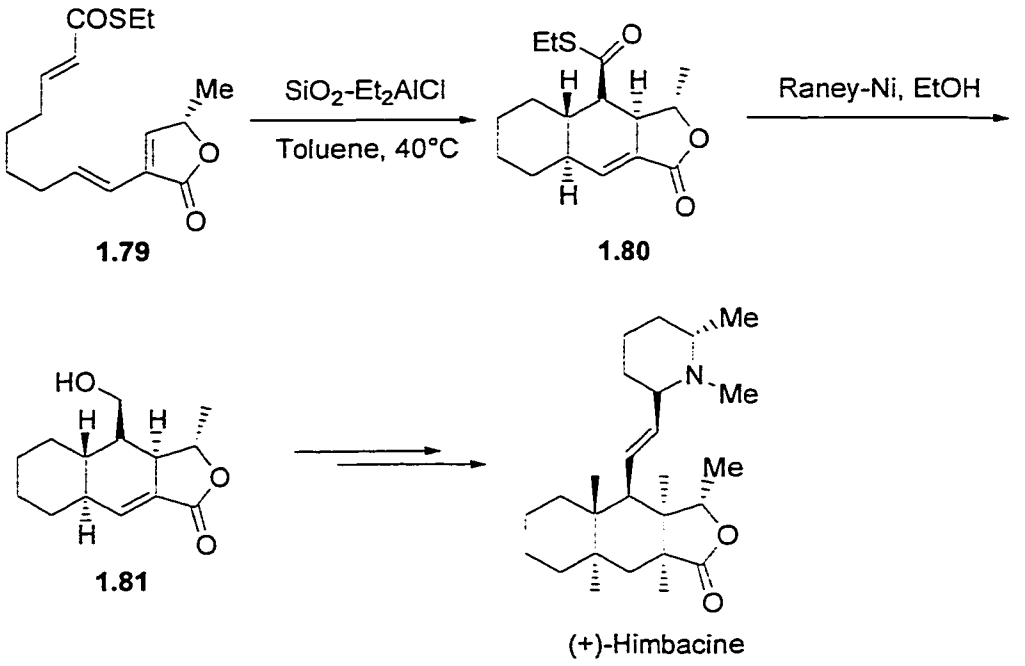
1.76 **1.77** **1.78**

Also, they can be transformed to the hydroxymethyl moiety with sodium borohydride[146] or other strong reducing agents.[147]

Thiol esters have been widely used in the synthesis of naturally occuring products and complex molecules. For example, the Diels-Alder reactions of α, β-unsaturated thioesters have been used as key steps in the course of two alkaloid total syntheses.[148]

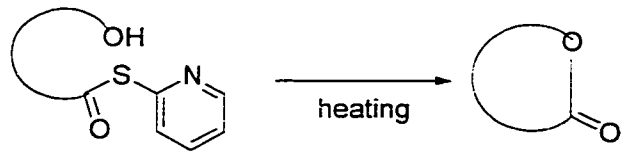
The features of thioesters as dienophiles are that they are more reactive than normal esters and the thioester group directs the regio- and stereochemistry of the cycloaddition reactions.[149] The chemistry of thioester groups differs from the chemistry of esters. In a synthesis of himbacine, a thioester cycloaddition was followed by its reduction to an alcohol using RaNi, without reduction of an appended lactone (Scheme 6-1).[150]

Scheme 1-1 Thiol Esters in the Synthesis of (+)-Himbacine



1.79 1.80 1.81

Macrolactonization through thiol esters was accomplished by simply heating the thiol esters at high dilution in an aromatic hydrocarbon (Eq. 1-40).[151]



1.82 1.83 (1-40)

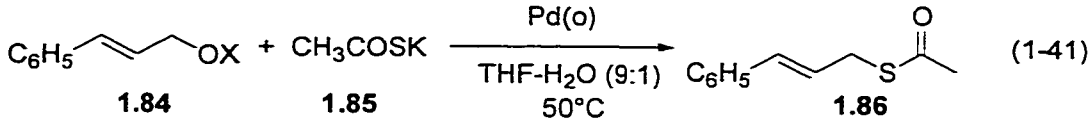
Yields are remarkably high, e.g., 88% for formation of a 16-membered lactone and the method has been used successfully in several syntheses.[151]

Recently, application of this functional group has expanded into the total synthesis of proteins by chemical ligation of benzyl thiol esters,[152] use as an acyl donor in the resolution of secondary alcohols catalyzed by lipase,[153] solid phase peptide synthesis,[154] and as cephalosporin derivatives which have been tested as elastase inhibitors.[155] Enolates of 2-pyridyl thiol esters have been used as substrates in the synthesis of β-lactams[156] and diastereoselective aldol condensations,[157] while the thiophenyl and pentafluorothiophenyl[158] derived thiol esters have been used as coupling reagents in the synthesis of amides.

1.8 Synthesis of Thiol Esters

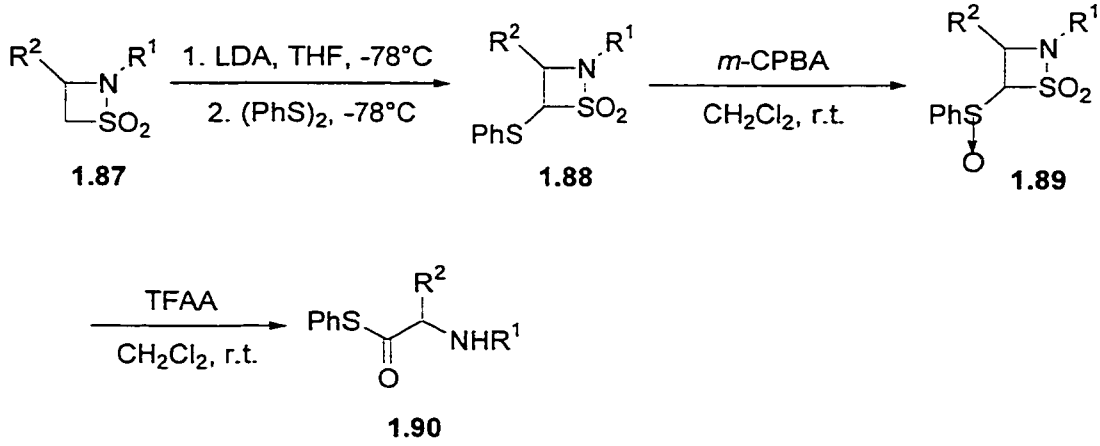
Preparations of thiol esters mainly involve either the direct coupling of a thiol with the parent carboxylic acid and an activating agent,[159] the coupling of a heavy metal thiolate with an acid chloride[160] or metal thiolate coupled with an acid anhydride.[161] Other syntheses of thiol esters include: use of triphenylphosphine with a carboxylic acid and thiophenol,[162] coupling of arenediazonium salts with thiocarboxylates[163] and

palladium-catalyzed alkylation of various allylic acetates by potassium thioacetate (Eq. 1-41).[164]



Biologically important thiol esters, such as α-amino acid thioesters, can be synthesized by the reaction of 2-aminoalk-2-enals with thiols[165] and Pummerer reactions (Scheme 1-2).[166]

Scheme 1-2 Synthesis of α-Amino Acid Thioesters



1.9 Aims of Research

Although a large number of catalytic systems have been developed for the carbonylation of a wide range of compounds, carbonylation chemistry has still not achieved its full potential. The search for the improvement of carbonylation technology continues, with the goal of increasing the diversity of possible substrates and reaction products. The analysis of literature data on the carbonylation of unsaturated organic compounds with various nucleophiles shows that these reactions provide convenient, efficient and one-step methods for the preparation of a variety of carbofunctionalized derivatives. However, there are very few reports in the literature on transition metal-catalyzed carbonylative reactions employing organosulfur compounds as direct substrates.

The project undertaken involves an examination of the thiocarbonylation and related reactions of allylic and propargylic compounds, allenes, enynes, and 1,3-conjugated dienes. The purpose of this investigation is to challenge the widespread acceptance that organosulfur compounds are poisons to transition metal catalysts,[167] to develop novel transformations with high chemo-, regio- and stereo-selectivities as well as atom-economy, and to synthesize valuable sulfur-containing compounds which are of interest as intermediates in organic synthesis.

CHAPTER 2

HIGHLY REGIOSELECTIVE THIOCARBONYLATION OF ALLYLIC ALCOHOLS WITH THIOLS AND CARBON MONOXIDE CATALYZED BY PALLADIUM COMPLEXES

2.1. Introduction: Carbonylation of Allylic Compounds

2.1.1. General Scope

The transition metal catalyzed carbonylation of allylic compounds has been the subject of many investigations. The first report on the carbonylation of allylic chlorides, which was catalyzed by $Ni(CO)_4$, appeared in 1959.[168] After a few years, the carbonylation of the same substrates catalyzed by Pd(0) under a high pressure of CO and at high temperature was discovered.[169] Later on, it was found that the carbonylation could be carried out most conveniently under mild conditions using allylic carbonates or chlorides among several allylic substrates.[56b] As shown in Scheme 2-1, allylic carbonates (**2.1**) can be converted to β, γ-unsaturated esters (**2.2**) under neutral conditions using $Pd(OAc)_2$ and PPh_3.[97b] Another practical method is the carbonylation of allylic chlorides which can be carried out at room temperature under 1 atm pressure of CO in an alcohol in the presence of K_2CO_3 using $Pd(OAc)_2$ as a catalyst without adding phosphine ligands.[170]

A number of studies on the carbonylation of several allylic substrates have been carried out under various conditions, which are summarized in Table 2-1.

Scheme 2-1. Carbonylation of Allylic Compounds

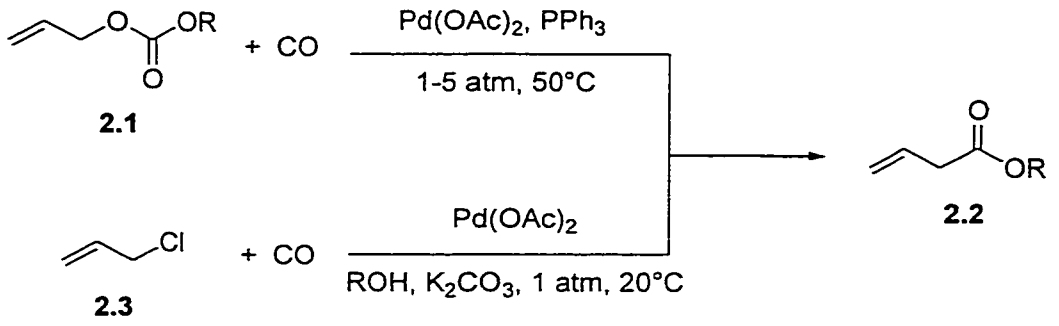
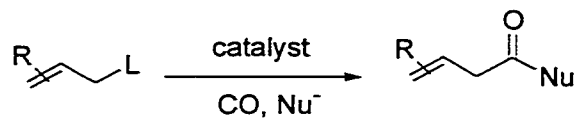
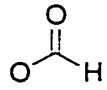
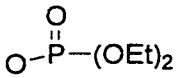


Table 2-1. Carbonylation of allylic substrates

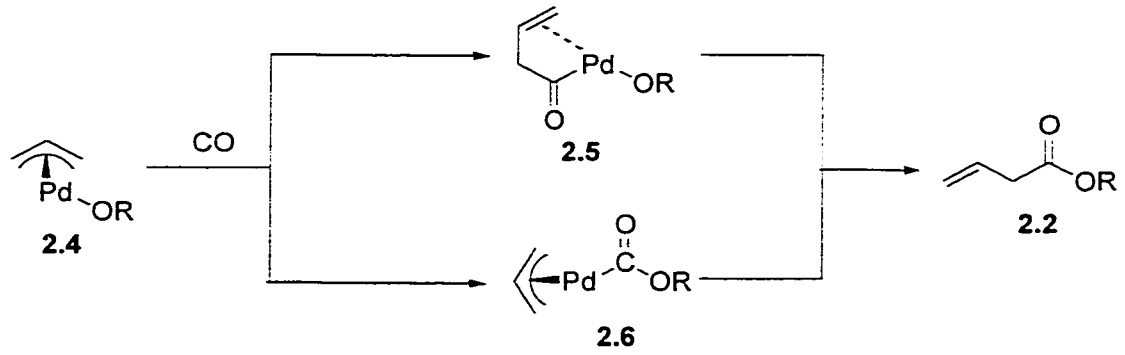


Allyl compd. L	Catalyst	Medium	Conditions CO, atm/temp., °C	Product Nu	Ref.
Cl, Br	Na_2PdCl_4	aq-NaOH	1/30-50	OH	96
	$Pd_2(dba)_3$-PPh_3	Toluene	20-60/rt-60	OH	171
	$Pd_2(dba)_3$-PPh_3	ROH/*i*-$PrNEt_2$	30/50	OR	101
OH	$Pd(PPh_3)_4$	THF/LiCl/$Ti(OR)_4$	25/100	OR	105a
OAc	$PdCl_2(PPh_3)_2$	ROH/NaBr	30/50	OR	101
OMe	[π-allylPdCl]$_2$	Toluene	30-40/100-120	OMe	103a
NR_2	$Pd(OAc)_2$-dppp	Toluene	30/110	NR_2	172
Cl	$PdCl_2(PPh_3)_2$	THF/$HNEt_2$	100/rt	$C(O)NEt_2$	171

2.1.2. Mechanistic Considerations

The catalytic carbonylation of allylic compounds are considered to proceed *via* a π-allyl intermediate **2.4**, which is formed by the oxidative addition of palladium(0) to various allylic compounds (esters, carbonates, etc.), followed by insertion of carbon monoxide into either the allyl-palladium bond (**2.4**→ **2.5**→ **2.2**) or the palladium-oxygen bond (**2.4**→ **2.6**→ **2.2**) of the intermediate **2.2** (Scheme 2-2).[56b]

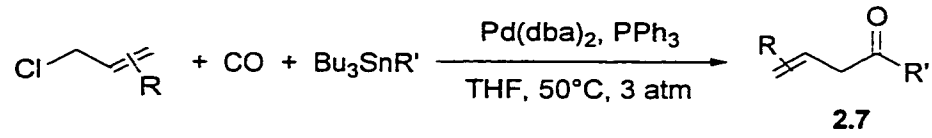
Scheme 2-2. Carbonylation of π-Allylpalladium Complex



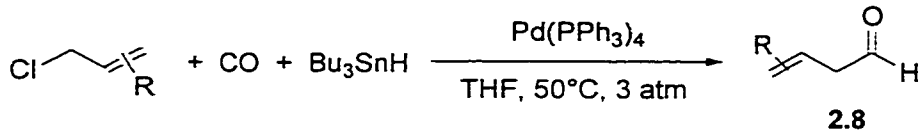
2.1.3. Synthetic Applications

The carbonylation of allylic compounds can afford β, γ-unsaturated carboxylic acids and esters as well as other carbonyl derivatives. For example, unsaturated ketones **2.7** can be prepared by adding organostannanes (Eq. 2-1),[173] or organozinc reagents[174] under mild conditions. Similarly, a 3-enyl aldehyde **2.8** can be obtained by the reaction of tributyltin hydride (Eq. 2-2).[76c]

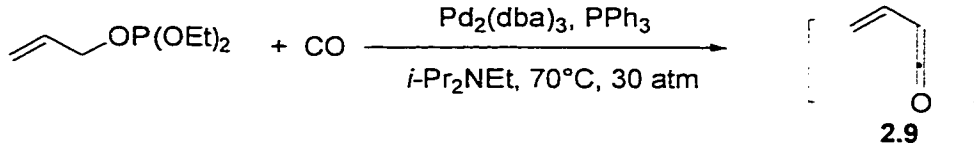
As shown in eq. 2-3, the β-lactam **2.11** was obtained by the carbonylation of allyl phosphate in the presence of the imine **2.10**. The reaction was explained by the [2+2] cycloaddition of the imine with the ketene **2.9** which is formed from allyl phosphate as an intermediate.[175]



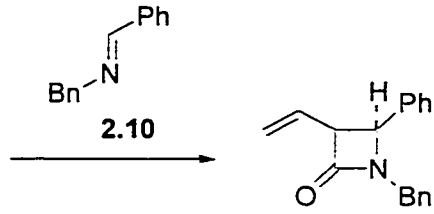
2.7 (2-1)



2.8 (2-2)

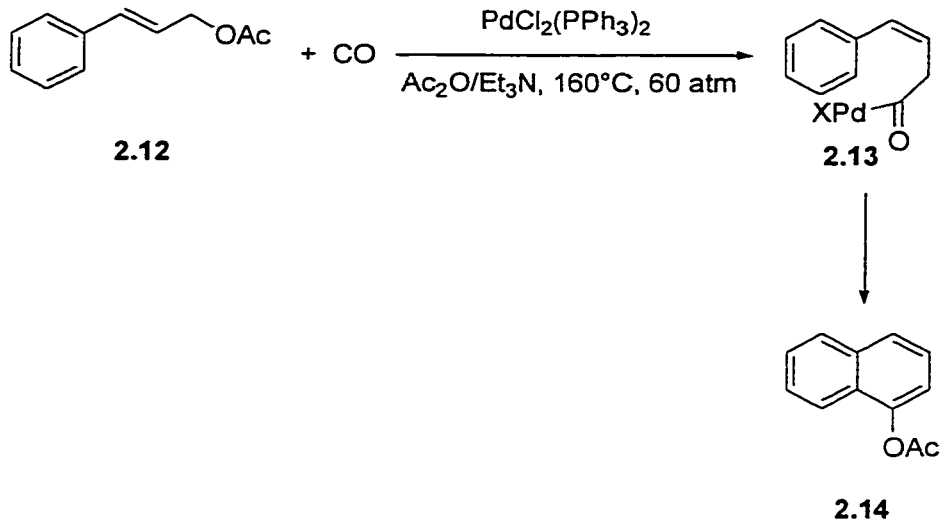


2.9



2.11 (2-3)

Interestingly, cyclocarbonylation of arylallylic acetate **2.12** took place in the presence of *tert*-amine and acetic anhydride (Eq. 2-4). The reaction offers a useful synthetic method for acetates of phenol and naphthol derivatives **2.14**.[176] The key step is the intramolecular Friedel-Crafts type acylation of the aromatic ring with the acylpalladium intermediates **2.13**.



2.12 2.13 2.14 (2-4)

2.2. Aim of the Research

Although reactions using alcohols,[177] amines,[178] carbon nucleophiles,[179] and organometallic reagents[180] to trap allylpalladium intermediates have been well established, much less attention has been paid to reactions with organic sulfur compounds,[181] in which thiopalladation would be involved. This might be partly because chalcogen compounds often bind strongly to the transition metals,[182] thus poisoning the catalysts and making catalytic reactions ineffective.[167, 183] However, if CO could insert into the S-Pd bond of the anticipated intermediate then carbonylation should occur. Furthermore, as mentioned already, the carbonylation of allylic compounds has some applications in organic synthesis. In order to extend the field of carbonylation chemistry as well as to explore the possibility of thiocarbonylation, we investigated the carbonylative addition reaction of allylic alcohols with thiols and carbon monoxide.

In addition, effective methods for the carbonylation reaction of allyl carbonates,[97b] esters,[107, 109b] amines,[184] and ethers[103a, 185] have been developed. However, the

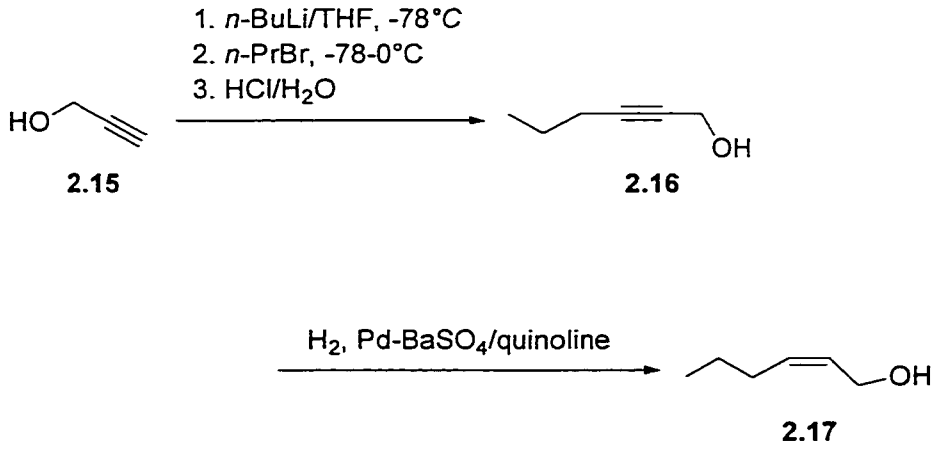
carbonylation of allyl alcohols has been little studied in spite of the ready availability of the starting materials, as the reaction requires high pressure of carbon monoxide.[105a, 186] The present methodology is concerned with allyl alcohols as direct starting materials under reasonably mild conditions.

2.3. Results and Discussion

2.3.1. Synthesis of Starting Materials

cis-2-Hexen-1-ol **2.17** was prepared (Scheme 2-3) by a modified literature procedure.[187]

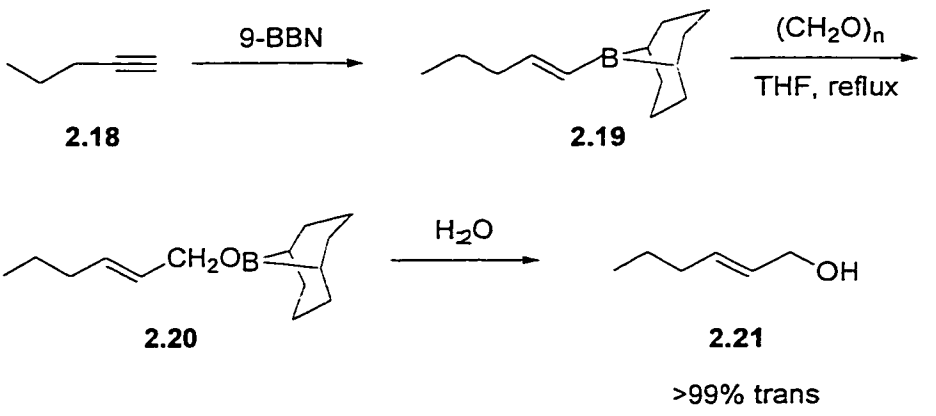
Scheme 2-3. Synthesis of *cis*-2-Hexen-1-ol



Alkylation of propargylic alcohol **2.15** with *n*-PrBr and *n*-BuLi in THF yielded **2.16** in 82% yield, which was then hydrogenated over Pd-$BaSO_4$ poisoned with quinoline to give **2.17** with >99% stereochemical purity as checked by GC.[188]

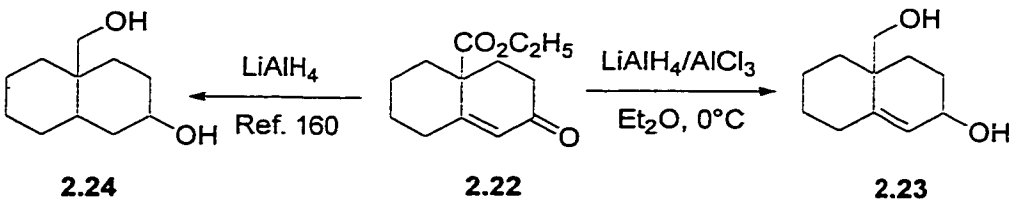
Attempts to prepare *trans*-2-hexen-1-ol (**2.21**) by the reduction of **2.16** with $LiAlH_4$ gave a mixture of stereoisomers in a 9:1 (*trans*: *cis*) ratio. In order to get defined stereochemistry, a Grignard-like addition of *B*-alkenyl-9-borabicyclo[3.3.1]nonanes to aldehydes was used successfully (Scheme 2-4).[189]

Scheme 2-4. Synthesis of *trans*-2-Hexen-1-ol



10-Hydroxymethyl-$\Delta^{1,9}$-2-octalol (**2.23**) was prepared by a modified literature procedure (Scheme 2-5).[190] Using $LiAlH_4$ as the reduction agent resulted in the formation of saturated diols (**2.24**).

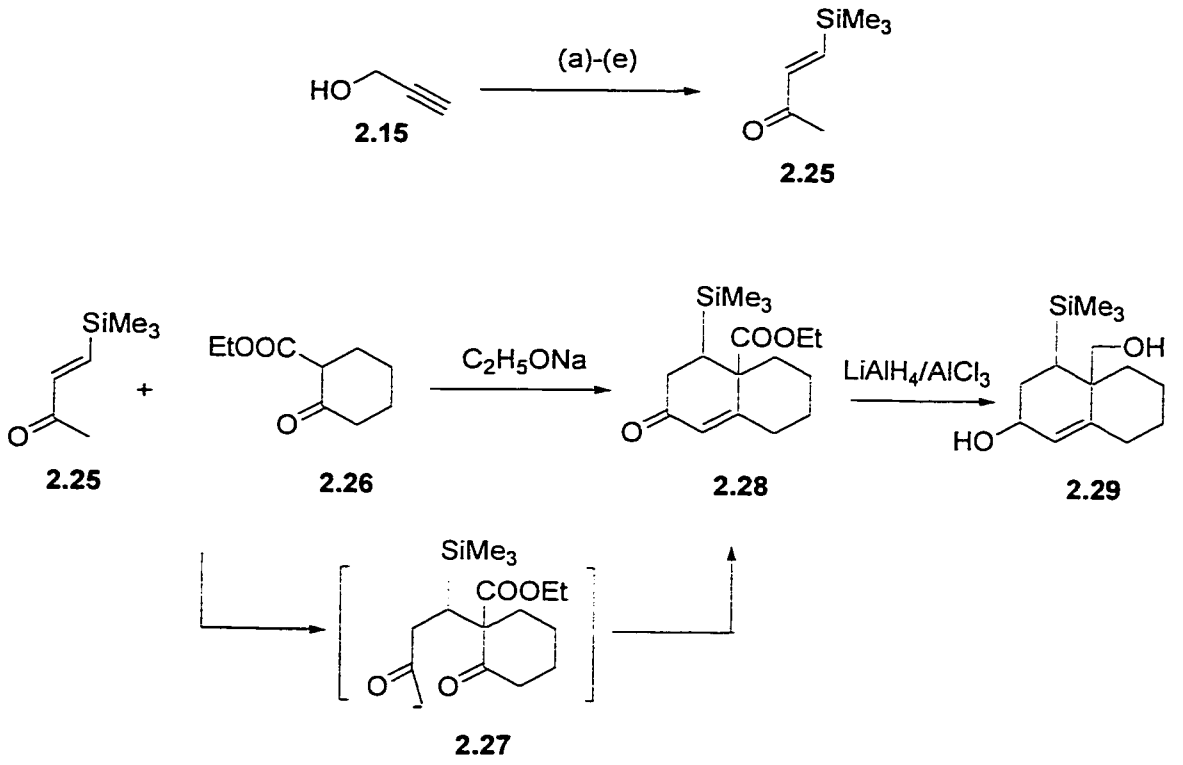
Scheme 2-5. Synthesis of 10-Hydroxymethyl-$\Delta^{1,9}$-2-Octalol



2.24 **2.22** **2.23**

6-(Hydroxymethyl)-5-(trimethylsilyl)bicyclo[4.4.0]dec-1-ol (**2.29**) was made according to a method by Hwu and Furth (Scheme 2-6).[191]

Scheme 2-6. Synthesis of 6-Hydroxymethyl)-5-(Trimethylsilyl)bicyclo[4.4.0]dec-1-en-3-ol



(a) (1) EtMgBr (2.9 equiv), ether; (2) Me_3SiCl (2.3 equiv), room temperature; (3) aqueous H_2SO_4; 99%; (b) Red-Al (1.4 equiv), ether; 84%; (c) PCC (1.1 equiv), CH_2Cl_2, room temperature; 78%; (d) MeMgI (2.5 equiv), ether, room temperature; 86%; (e) CrO_3 (1.1 equiv), H_2SO_4, water, acetone, 0°C; 92%.

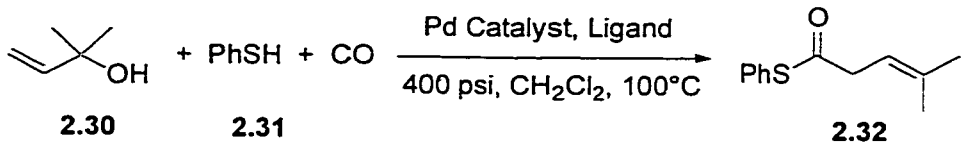
By modifying the literature procedure reported by Carter *et al.*,[191a] trimethylsilyl enone **2.25** was obtained from propargylic alcohol **2.15**. The trimethyl enone (**2.25**) was treated with β-keto ester (**2.26**) in the presence of sodium alkoxides to give **2.28** in 52% yield (Scheme 2-6). Reduction of **2.28** in anhydrous ether with $LiAlH_4/AlCl_3$ gave the corresponding alcohol **2.29** as the only product in 73% yield.

Allyl carbonates (**2.33a**[192] and **2.81**[193]) and phosphate (**2.33b**)[194] were prepared following the known procedure.

2.3.2. Reaction Conditions for Thiocarbonylation

We chose 2-methyl-3-buten-2-ol (**2.30**) as a model substrate and investigated its reaction with thiophenol (**2.31**), carbon monoxide and catalytic quantities of a variety of palladium complexes under different conditions. The effect of different catalytic systems on the thiocarbonylation of **2.30** is presented in Table 2-2.

Table 2-2. Effects of Different Catalytic Systems on the Thiocarbonylation of 2.30 with Thiophenol (2.31) and CO in CH_2Cl_2[a]

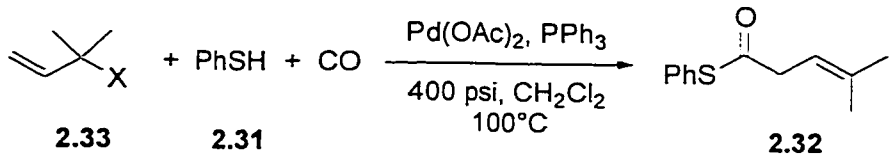


2.30 **2.31** **2.32**

entry	catalyst	additive	time(h)	temp.(°C)	yield(%)[b]
1	none	none	48	100	0
2	$Pd(PPh_3)_4$	none	48	100	8
3	$Pd(PPh_3)_4$	*p*-TsOH	72	100	63
4	$Pd(PPh_3)_4/PPh_3$	*p*-TsOH	48	100	82
5	$Pd(PPh_3)_4$/dppb	*p*-TsOH	48	100	77
6	$Pd(OAc)_2$	none	72	120	0
7	$Pd(OAc)_2$	*p*-TsOH	72	120	0
8	$Pd(OAc)_2/PPh_3$	none	72	120	4
9	$Pd(OAc)_2/PPh_3$	*p*-TsOH	48	100	93
10	$Pd(OAc)_2$/dppb	*p*-TsOH	48	100	88
11	$Pd(OAc)_2$/dppp	*p*-TsOH	48	100	64
12	$Pd(OAc)_2/PPh_3$	HCl	48	100	47
13	$Pd(OAc)_2$/dppe	*p*-TsOH	60	100	17
14	$Pd_2(dba)_3 \bullet CHCl_3/PPh_3$	*p*-TsOH	60	100	84

[a]Reaction conditions: **2.30** (2 mmol), **2.31** (2 mmol), catalyst (0.06 mmol), ligand PPh_3 (0.24 mmol), dppb (0.12 mmol), dppp (0.12 mmol) or dppe (0.12 mmol) (if used), *p*-TsOH (0.1 mmol) or HCl (0.1 mmol) (if used), 400 psi CO and CH_2Cl_2 (10 mL). [b]Isolated yield based on thiophenol.

Among the catalytic systems examined, $Pd(OAc)_2$ with PPh_3 and *p*-toluenesulfonic acid (*p*-TsOH) exhibited excellent catalytic activity to afford the thiocarbonylation product **2.32** in 93% isolated yield (Table 2-2, entry 9). In the absence of the catalyst or *p*-TsOH, **2.32** was not obtained at all or was obtained in a very low yield (Table 2-2, entries 1, 2, 6, and 8). The function of *p*-TsOH is to protonate the hydroxyl group of the substrate so as to eliminate H_2O to form a π-allyl palladium complex. Using HCl in place of *p*-TsOH (Table 2-2, entry 12), the reaction also afforded **2.32**, but the yield was much lower, probably because the poor solubility of HCl in CH_2Cl_2 decreases the degree of protonation of the hydroxyl group. Thiocarbonylation of allylic carbonate (**2.33a**), and phosphonate (**2.33b**) can be carried out without *p*-TsOH or HCl (Eq. 2-5).



(2-5)

2.33 **2.31** **2.32**

2.33a: X=OCO_2CH_3 91%

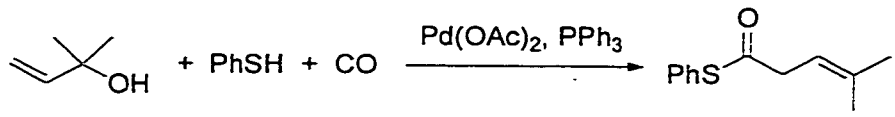
2.33b: X=$OP(O)(OMe)_2$ 93%

It further demonstrates that the function of the acid is to assist the elimination of hydroxyl group.

Palladium(0) complexes, such as $Pd(PPh_3)_4$ and $Pd_2(dba)_3 \bullet CHCl_3$ with added phosphine and *p*-TsOH are also excellent catalytic systems for this transformation (Table 2-2, entries 4, 5, and 14). However, palladium catalysts without added phosphine ligand (Table 2-2, entries 3 and 7) were less effective for this reaction. The bidentate phosphine, 1,3-bis(diphenylphosphino)propane (dppp) and 1,4-bis(diphenylphosphino)butane (dppb), were also useful as added ligands for the $Pd(OAc)_2$-catalyzed reaction, and afford **2.32** in 64 and 88% yield, respectively (Table 2-2, entries 10 and 11), but 1,2-bis(diphenylphosphino)ethane (dppe) is almost ineffective. This can be explained by the fact that CO insertion into a Pd-C bond occurs faster for those alkylpalladium diphosphine complexes containing a more flexible metal-ligand chelate ring.[195]

Table 2-3 indicates some results of the effect of varying the reaction conditions. Using the $Pd(OAc)_2$-PPh_3/*p*-TsOH catalyst system, we found that the reaction works well in CH_2Cl_2, 1,2-dimethoxyethane (DME), or THF but less so in toluene and diethyl ether (Table 2-3, entries 1-5). A decrease to 100 psi or increase to 800 psi of CO pressure resulted in the formation of by-products (Table 2-3, entries 6 and 7). Prolonged heating, 80 h versus 48 h, and increasing or decreasing reaction temperature reduced the yield of **2.32** (Table 2-3, entries 8-10). In addition, an excess of **2.30** did not change the reaction yield, but resulted in lactonization of the unreacted alcohol.[196]

Table 2-3. Effect of Reaction Conditions on the Palladium-Catalyzed Thiocarbonylation of 2.30 with Thiophenol and CO[a]



2.30 **2.31** **2.32**

entry	solvent	temp.(°C)	pressure(psi)	time(h)	yield(%)[b]
1	CH_2Cl_2	100	400	48	93
2	DME	100	400	48	90
3	THF	100	400	48	90
4	Toluene	100	400	48	54
5	Ether	100	400	48	47
6	CH_2Cl_2	100	100	60	53[c]
7	CH_2Cl_2	100	800	48	87[d]
8	CH_2Cl_2	50	400	48	61[e]
9	CH_2Cl_2	150	400	48	74
10	CH_2Cl_2	100	400	80	58

[a]Reaction of 2 mmol of **2.30** and 2 mmol of PhSH in the presence 0.06 mmol of $Pd(OAc)_2$, 0.24 mmol of PPh_3 and 0.1 mmol of *p*-TsOH. [b]Isolated yield based on thiophenol. [c]7% of the substitution reaction product, 4-phenylthioyl-2-methyl-2-butene, was found. [d]3% of dithiocarbonylation product was isolated. [e]23% of substrate was recovered.

2.3.3. Thiocarbonylation of Thiols with Various Acyclic Allylic Alcohols

The carbonylative coupling reaction of a series of acyclic allylic alcohols was effected using 1 equiv of a thiol or mercaptan, 3 mol% of $Pd(OAc)_2$, 12 mol% of PPh_3, and 5 mol% of *p*-TsOH, in CH_2Cl_2 at 400 psi CO for 48 h at 100°C. The β,γ-unsaturated thioesters were isolated in 56-93% yield (Table 2-4). Arenethiols and alkanethiols can be employed successfully in the reaction (Table 2-4, entries 1-7) together with primary, secondary, and tertiary acyclic allylic alcohols (Table 2-4, entries 8, 11, and 16). It is noteworthy that allylic alcohols containing terminal or internal C=C bonds with alkyl or phenyl substituents reacted with similar efficiency. The reaction exhibits high regioselectivity. Insertion of carbon monoxide occurs at the least substituted terminal allylic carbon to give linear thioesters rather than branched ones (Table 2-4, entries 8-10, 16, and 20). α,β-Unsaturated thioesters could not be detected among the products, although isomerizations of β,γ-unsaturated esters to α,β-unsaturated isomers occurs readily.[197] An isomeric mixture of β,γ-unsaturated thioesters were obtained when some alcohols were employed as substrates. To prove the question of double bond integrity of the product, the thiocarbonylations of (*E*)- and (*Z*)-2-hexen-1-ol (**2.21** and **2.17**) have been examined under the standard conditions (Table 2-4, entries 13 and 14). **2.21** and **2.17** can be converted into a mixture of (*E*)- and (*Z*)-phenyl-3-heptenethioate (**2.51**) in the same ratio (4:1), irrespective of the stereochemistry of the starting alcohol. Loss of the stereochemistry of the carbon-carbon double bond should be due to π–σ–π-isomerization of the intermediate π–allylpalladium complexes (Scheme 2-7).[198] Thermodynamically more stable (*E*)-isomers are obtained preferentially. As Murahashi[198a] observed in the alkoxycarbonylation of diethyl cinnamyl phosphate and diethyl geranyl phosphate,

cinnamyl alcohol (**2.54**) and geraniol (**2.62**) undergo the thiocarbonylation to afford stereoselectively (*E*)-phenyl-4-phenyl-3-butenethioate (**2.55**) and (*E*)-phenyl-4,8-dimethyl-3-nonenethioate ((*E*)-**2.57**), respectively (Table 2-4, entries 15 and 19).

Table 2-4. Palladium-Catalyzed Thiocarbonylation of Acyclic Allylic Alcohols with Thiols and Carbon Monoxide[a]

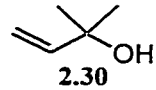
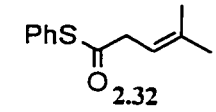
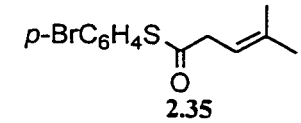
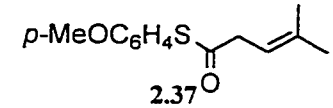
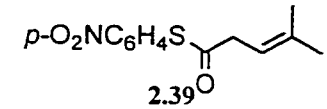
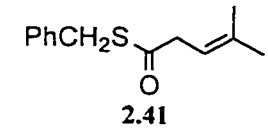
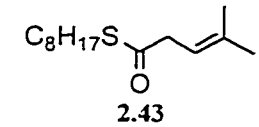
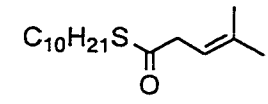
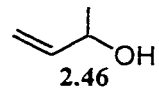
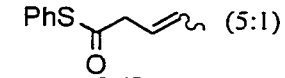
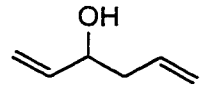
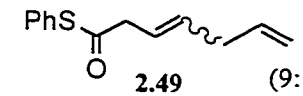
entry	alcohol	thiol	product (E/Z)[b]	yield (%)[c]
1	 **2.30**	PhSH **2.31**	 **2.32**	93
2	**2.30**	*p*-BrC_6H_4SH **2.34**	 **2.35**	88
3	**2.30**	*p*-$MeOC_6H_4SH$ **2.36**	 **2.37**	90
4	**2.30**	*p*-$NO_2C_6H_4SH$ **2.38**	 **2.39**	92
5	**2.30**	$PhCH_2SH$ **2.40**	 **2.41**	84
6	**2.30**	$C_8H_{17}SH$ **2.42**	 **2.43**	87
7	**2.30**	$C_{10}H_{21}SH$ **2.44**	 **2.45**	86
8	 **2.46**	**2.31**	 (5:1) **2.47**	94
9	 **2.48**	**2.31**	 **2.49** (9:1)	78

Table 2-4. (continued)

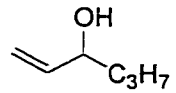
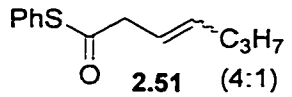
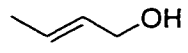
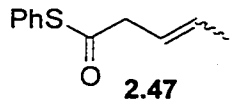
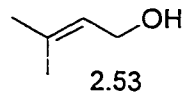
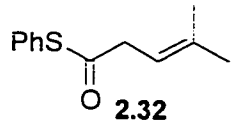
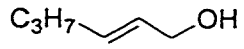
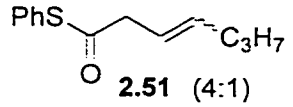
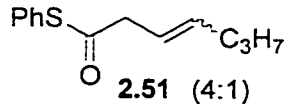
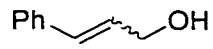
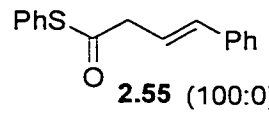
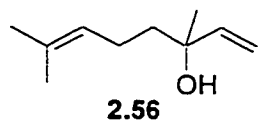
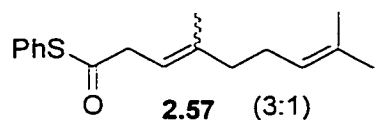
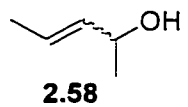
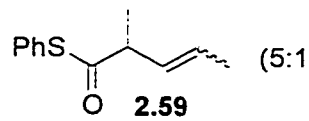
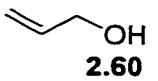
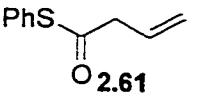
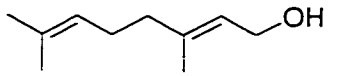
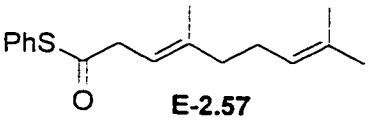
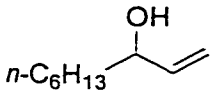
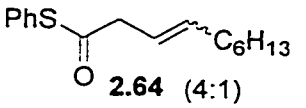
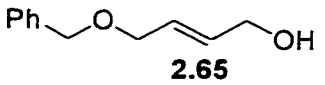
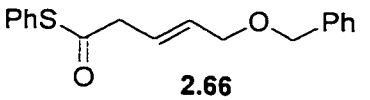
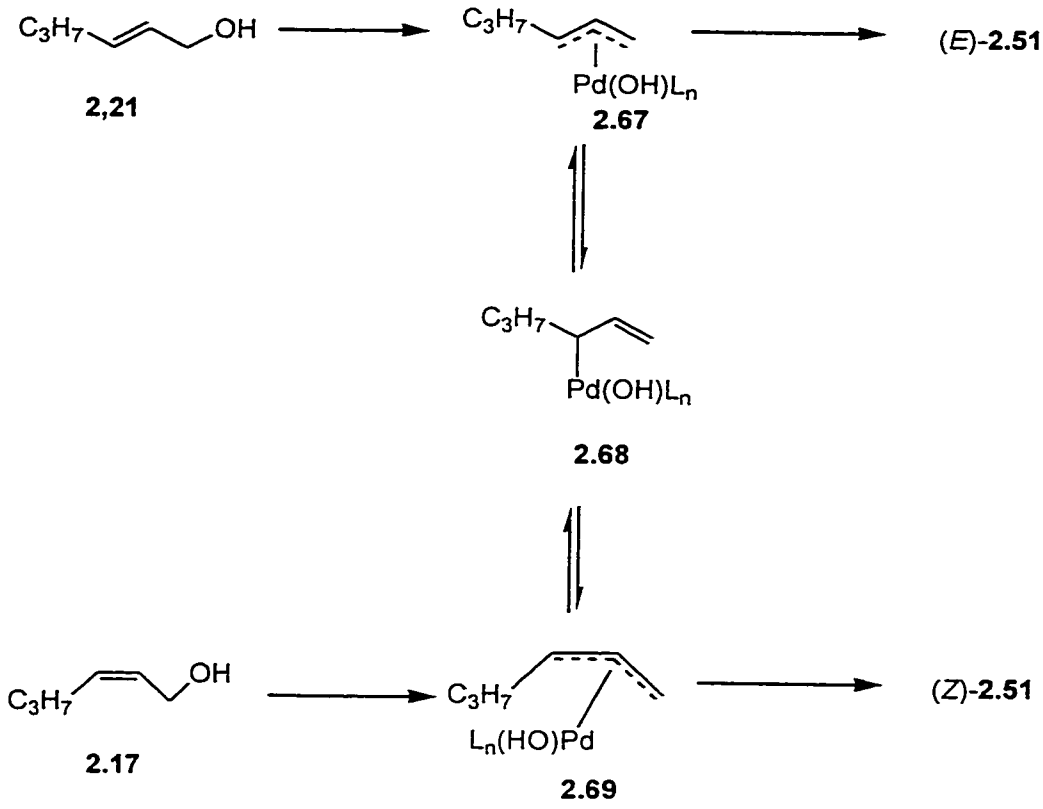
entry	alcohol	thiol	product (*E*/*Z*)	yield (%)
10	 **2.50**	**2.31**	 **2.51** (4:1)	92
11	 **2.52**	**2.31**	 (2:1) **2.47**	89
12	 2.53	**2.31**	 **2.32**	93
13	 **2.21**	**2.31**	 **2.51** (4:1)	87
14	 **2.17**	**2.31**	 **2.51** (4:1)	85
15	 **2.54**	**2.31**	 **2.55** (100:0)	76
16	 **2.56**	**2.31**	 **2.57** (3:1)	91
17	 **2.58**	**2.31**	 (5:1) **2.59**	92

Table 2-4. (continued)

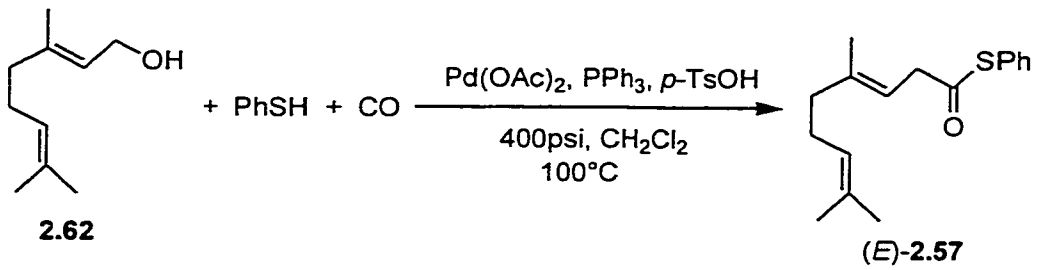
entry	alcohol	thiol	product (*E*/*Z*)	yield (%)
18	 **2.60**	**2.31**	 **2.61**	56
19	 **2.62**	**2.31**	 **E-2.57**	84
20	 **2.63**	**2.31**	 **2.64** (4:1)	93
21	 **2.65**	**2.31**	 **2.66**	87

[a] Reaction conditions: alcohol (2 mmol), thiol (2 mmol), CO 400 psi, $Pd(OAc)_2$ (0.06 mmol),PPh_3 (0.24 mmol), *p*-TsOH (0.1 mmol), CH_2Cl_2 (10 ml), 100°C, 48 h. [b] The ratio of *E* to *Z* is measured by ^1H NMR. [c] Isolated yield based on the thiol employed.

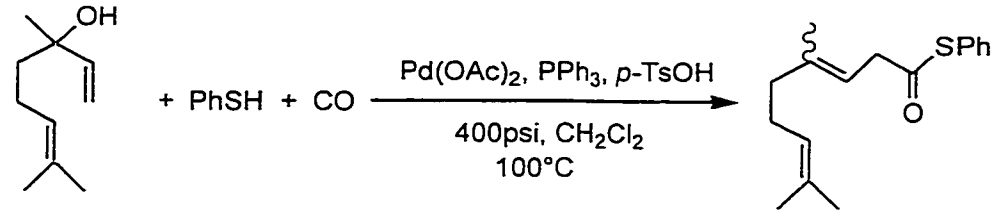
Scheme 2-7. η^3-η^1-η^3 Isomerization of π-Allylpalladium Complexes



In order to further demonstrate the regioselectivity of the reaction, the reactions of linalool (**2.56**) and geraniol (**2.62**) were examined. Both reactions gave the same product, **2.57**, irrespective of the positions of the OH groups in the substrates (Eqs. 2-6 and 2-7).

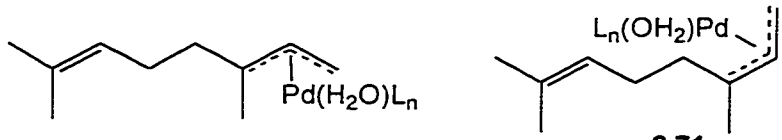


2.62 (*E*)-**2.57** (2-6)



2.56 (*E*)-and (*Z*)-**2.57** (2-7)

This indicates that both reactions pass through the same kind of π-allylpalladium



2.70 **2.71**

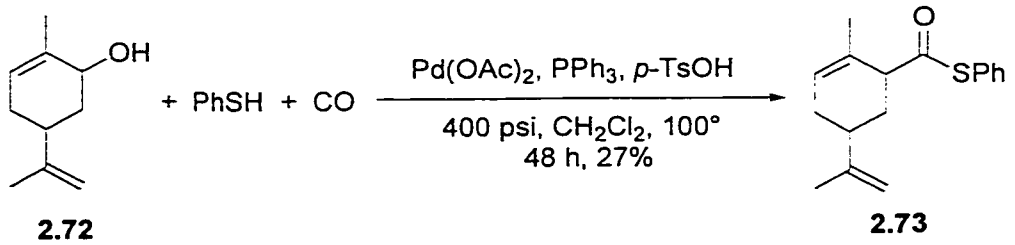
complex,**2.70** and **2.71**, and the phenylthiocarbonyl group adds to the less hindered terminal position of π-allylpalladium complex to give **2.57** as the sole product.

It is noteworthy that the thiocarbonylation of **2.56** under the standard conditions gave a 3:1 mixture of (*E*)- and (*Z*)-isomers of **2.57** , while the reaction of **2.62** under the same conditions gave (*E*)-**2.57** stereoselectively. In these reactions, the oxidative addition of protonated allylic alcohols to palladium(0) complexes occurs in an S_{N2}'-fashion at the γ–position.[199] The expected isomerization between (*E*)- and (*Z*)-isomers

during the course of the reaction is not observed.[193] The *E/Z* ratio may be governed by the relative stability of **2.70** and **2.71**[200] as well as the relative rate of CO insertion into the π-allylpalladium intermediate, and that of the isomerization (π–σ–π mechanism) between **2.70** and **2.71**.[198]

2.3.4. Thiocarbonylation of Thiophenol to Cyclic Allylic Alcohols

Although acyclic allylic alcohols undergo thiocarbonylation readily under mild conditions, cyclic allylic alcohols show quite low reactivity toward carbonylative coupling reactions with thiophenol and carbon monoxide. When carveol (**2.72**) was treated under the optimized conditions for the thiocarbonylation of acyclic substrates, the phenyl *p*-mentha-6,8-dienyl formthioate (**2.73**) was obtained in only 27% yield, with recovery of 52% of the substrate (Eq. 2-8).



2.72 **2.73** (2-8)

The optimization of the reaction conditions resulted in the thiocarbonylation reaction proceeding to afford thioesters in higher yield at 120°C for 3 to 7 days (other conditions are the same as ones for acyclic substrates).[201]

The scope and limitations of the palladium-catalyzed carbonylative coupling reaction of cyclic allylic alcohols with thiophenol and CO are summarized in Table 2-5. When 2-cyclohexen-1-ol (**2.74**) was allowed to react under the optimal conditions,

phenyl 2-cyclohexenyl formthioate (**2.75**) was formed in 84% yield (Table 2-5, entry 2); but under the same reaction conditions, thiocarbonylation of myrtenol (**2.76**) was unsuccessful (Table 2-5, entry 3). In most cases, the reactions were clean and no by-product was formed (except entry 5).[202] Carvyl carbonate (**2.81**) was thiocarbonylated smoothly to give the corresponding β,γ–unsaturated thioester in excellent yield after reaction for 48h (Table 2-5, entry 6), while the same reaction of carveol (**2.72**) needed a longer reaction time (Table 2-5, entry 1). Some functional groups, such as hydroxyl (Table 2-5, entries 7 to 9), trimethylsilyl (Table 2-5, entry 9), and vinyl (Table 2-5, entries 1, 4, and 6) groups, did not affect the thiocarbonylation reactions. The reaction proceeded regioselectively. Substituted cyclic alcohols with unsymmetrical allylic species, such as **2.79**, **2.23**, and **2.29**, undergo thiocarbonylation exclusively at the less substituted allylic positions (Table 2-5, entries 5, 8, and 9), while the substrates with symmetrical allylic species can, of course, only afford one product (Table 2-5, entries 1, 2, 4, 6, and 7).

Table 2-5. Palladium-Catalyzed Thiocarbonylation of Cyclic Allylic Alcohols with Thiophenol and Carbon Monoxide[a]

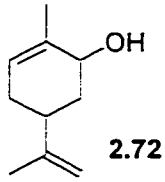
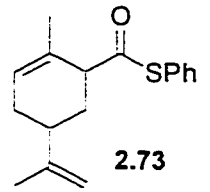
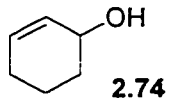
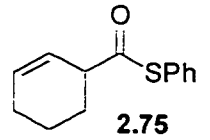
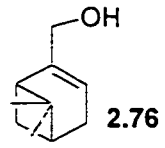
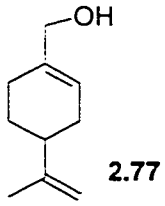
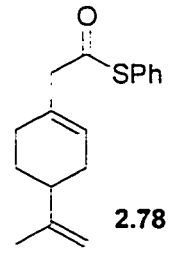
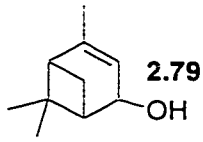
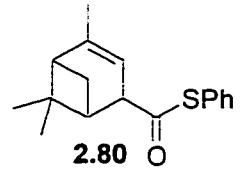
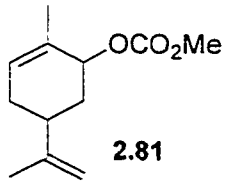
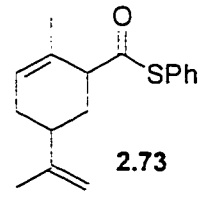
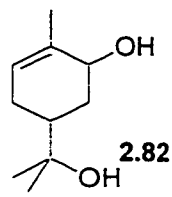
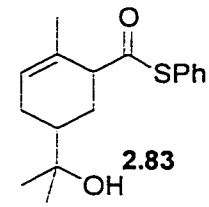
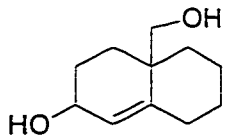
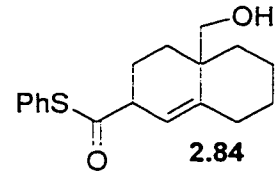
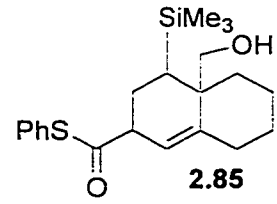
entry	alcohol	reaction time (day)	product	yield (%)[b]
1	 **2.72**	5	 **2.73**	72
2	 **2.74**	3	 **2.75**	84
3	 **2.76**	7	no reaction	0
4	 **2.77**	5	 **2.78**	64
5	 **2.79**	7	 **2.80**	18
6	 **2.81**	2	 **2.73**	86

Table 2-5. (continued)

entry	alcohol	reaction time (day)	product	yield (%)[b]
7	 **2.82**	7	 **2.83**	27
8	 **2.23**	7	 **2.84**	63
9	 **2.29**	7	 **2.85**	54

[a] Reaction conditions: alcohol (2 mmol), thiophenol (2 mmol), CO 400 psi, $Pd(OAc)_2$ (0.06 mmol), PPh_3 (0.24 mmol), p-TsOH (0.1 mmol), CH_2Cl_2 (10 ml), 120°C.

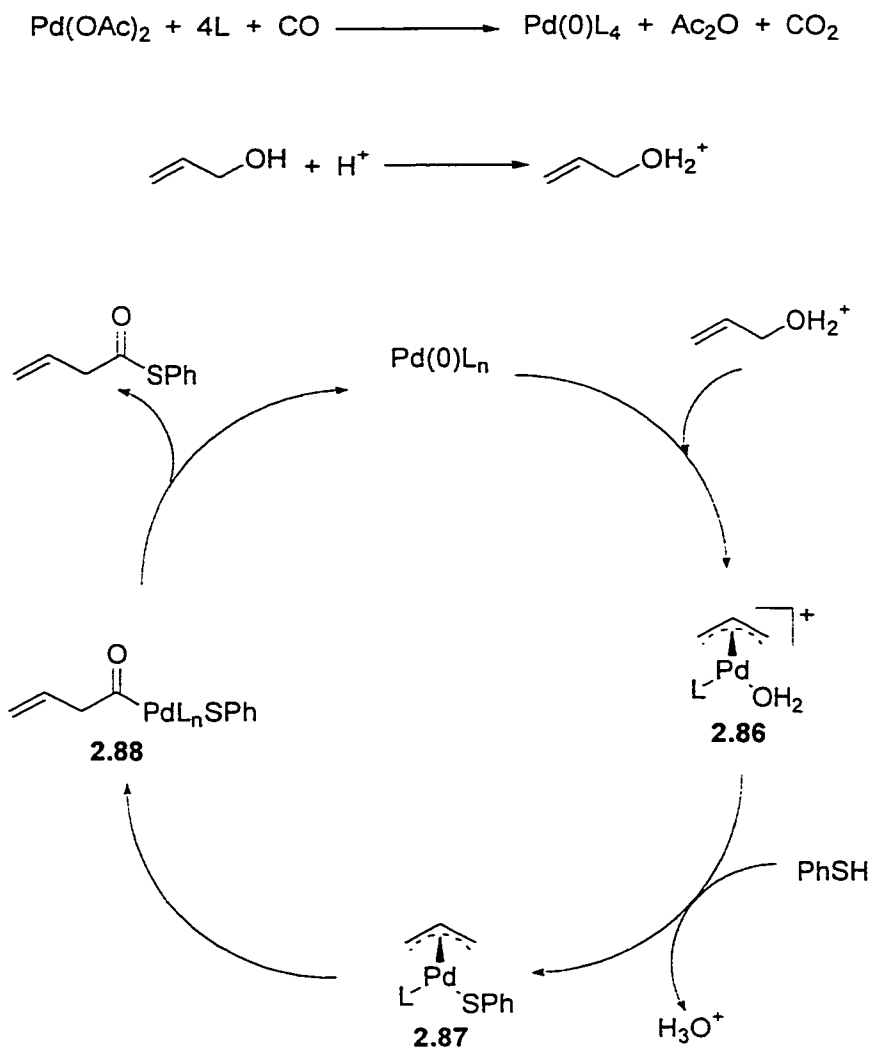
[b] Isolated yield based on thiophenol employed.

2.3.5. Mechanistic Aspects

A probable mechanism for the thiocarbonylation is illustrated in Scheme 2-8, in which the substituent on the allyl alcohol is omitted. It is well known that $Pd(OAc)_2$ is easily reduced to Pd(0) complexes *in situ* in the presence of phosphine ligands with carbon monoxide.[203] Oxidative addition of protonated allylic alcohol to Pd(0) species gives the π-allylpalladium complex **2.86**,[106] which undergoes substitution of H_2O with

PhSH to form the π-allylpalladium sulfide complex **2.87**. Insertion of CO to **2.87** gives acylpalladium complex **2.89**. Reductive elimination of Pd(0) would form the β,γ–unsaturated thioesters and palladium(0) species to complete the catalytic cycle.

Scheme 2-8. A Mechanism of the Thiocarbonylation of Allylic Alcohols



2.4. Conclusions

Palladium complexes such as $Pd(OAc)_2$, $Pd(PPh_3)_4$, and $Pd_2(dba)_3 \bullet CHCl_3$ with added phosphine ligands and *p*-TsOH are effective for the thiocarbonylation of acyclic and cyclic allyl alcohols with thiols and carbon monoxide. These reactions occur highly regioselectively at the less hindered allylic terminal carbon of the substrate to give the corresponding thioesters. Not only is this methodology attractive for the preparation of thioesters and the direct carbonylation of allyl alcohols, but it also demonstrates the utility of transition metal catalysts in the synthetic reactions of chalcogen compounds.

CHAPTER 3

PALLADIUM-CATALYZED THIOLACTONIZATION OF PROPARGYLIC ALCOHOLS AND DITHIOCARBONYLATION OF PROPARGYLIC MESYLATES

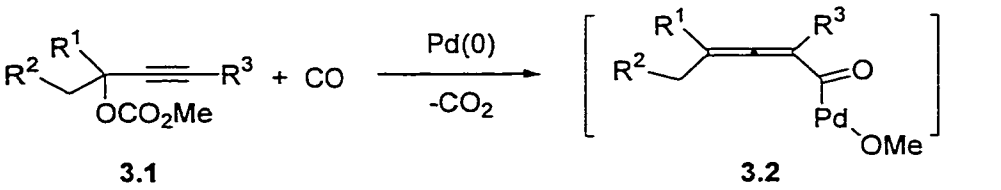
3.1 Introduction: Carbonylation of Propargylic Compounds

3.1.1 General Features and Mechanisms

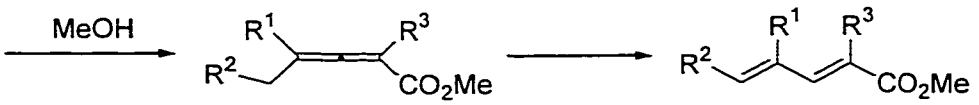
The first examples of the palladium-catalyzed carbonylation of propargylic compounds were published in 1966,[204] and described the conversion to dicarbonylation products. Later it was found that, under similar conditions, propargylic carbonates undergo facile monocarbonylation.[205] The mono- and di-carbonylation of propargylic compounds, when an alcohol is used as the solvent, can be explained by the following mechanism. Initially, insertion of carbon monoxide into an allenylpalladium intermediate may generate an acylpalladium complex (**3.2**), which could then react with methanol to give the 2,3-dienoate (**3.3**). Under certain reaction conditions, **3.3** could then isomerize to the 2,4-dienoate (**3.4**) (Scheme 3-1). The mono-carbonylation product is obtained for the carbonylation of propargylic carbonates under mild conditions; however, under a high pressure of carbon monoxide, or in the presence of an activating group (e.g. R^3=CO_2R),

further attack of carbon monoxide at the central *sp* carbon of the allenyl intermediate (**3.3**) takes place to afford the diester (**3.5**) (Scheme 3-2).

Scheme 3-1. Monocarbonylation of Propargylic Carbonates



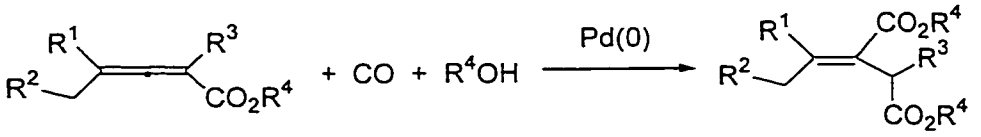
3.1 **3.2**



3.3 **3.4**

R^1, R^2, R^3 = alkyl or aryl

Scheme 3-2. Further Carbonylation of 2,3-Dienoates

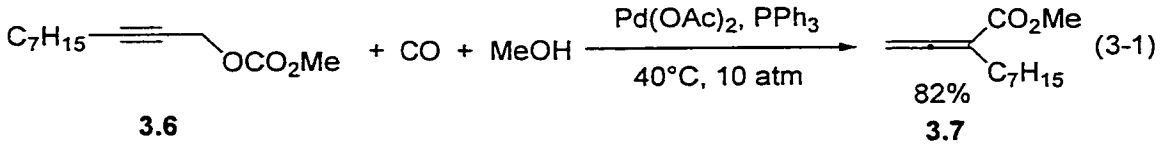


3.3 **3.5**

R^1, R^2, R^3 = alkyl or aryl
R^4 = alkyl

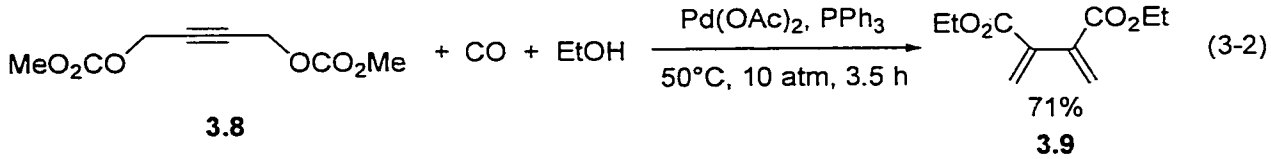
3.1.2 Mono- and Di-carbonylations

Propargylic compounds can be carbonylated in the presence of nucleophiles to give mono- or di-carbonylation products.[56c] Decarboxylation-carbonylation of propargylic carbonate (**3.6**) with methanol as a nucleophile gives the terminal allenic ester (**3.7**) under mild neutral conditions (Eq. 3-1).[206]



3.6 **3.7** (3-1)

Bis(methylene)butanedioate (**3.9**) can be prepared in good yield by the carbonylation of the dicarbonate of butynediol (**3.8**) (Eq. 3-2).[207]

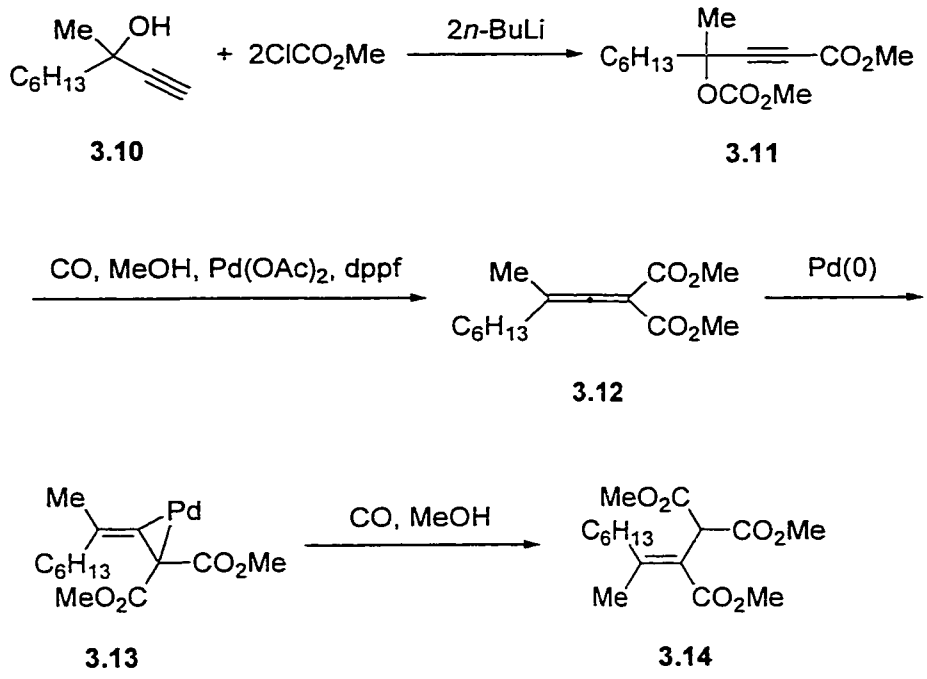


3.8 **3.9** (3-2)

Facile dicarbonylation becomes the main pathway when an ester group is introduced on to the terminal acetylenic carbon atom of propargylic carbonates.[57d] The dicarbonylation of **3.11** takes place at room temperature, without stopping at the stage of the monocarbonylation to form **3.12**. Bidentate ligands such as dppp and 1,1'-*bis*(diphenylphosphino)ferrocene (dppf) are the most effective for the dicarbonylation. The allenyl geminal diester **3.12** is susceptible to Michael-type addition of $L_nPd(0)$ to the

central *sp* carbon, resulting in the formation of the palladacyclopropane **3.13**. Insertion of carbon monoxide to **3.13** and methanolysis afford the triester **3.14** (Scheme 3-3).[208]

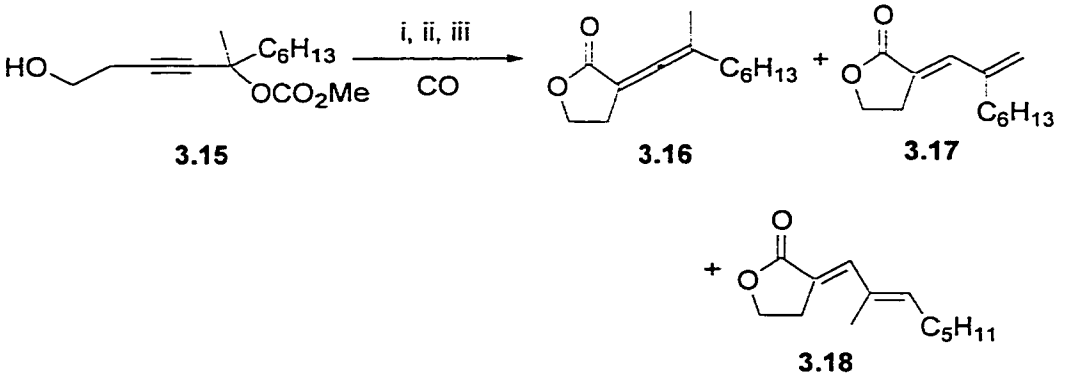
Scheme 3-3. Dicarbonylation to Form Triesters



3.10 **3.11** **3.12** **3.13** **3.14**

3.1.3 Carbonylation to Form Lactones

The carbonylation of hydroxyl-alkynyl methyl carbonate gives α-alkenylidene-γ-lactones in good yields, under mild conditions. As a typical example, carbonylation of **3.15** afforded the products **3.16-3.18**. in ratios dependent on the reaction conditions (Eq. 3-3).[209]



(3-3)

	3.16 : 3.17 : 3.18
(i) $Pd(OAc)_2$, dppp, 1h, 70%	97 : 3 : 0
(ii) $Pd(OAc)_2$, dppp, 14h, 81%	0 : 73 : 27
(iii) $Pd(OAc)_2$, dppf, 14h, 84%	100 : 0 : 0

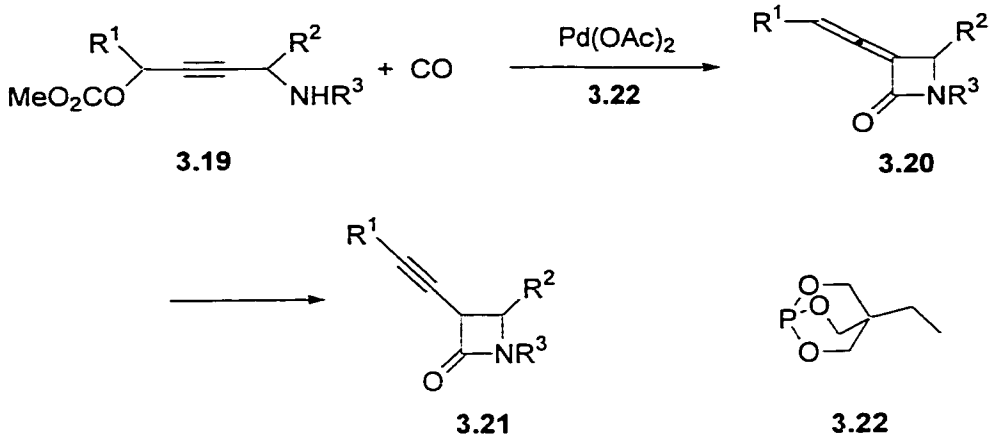
Propargylic alcohols are less reactive than their esters, and their lactonization requires more severe conditions.[196, 210]

3.1.4 Carbonylation to Form β-Lactams

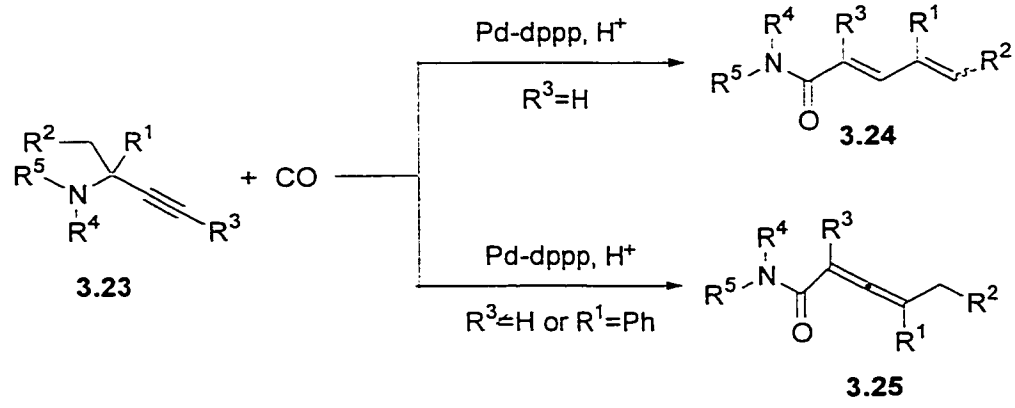
In addition to alcohols, other nucleophiles can trap the acylpalladium intermediate (**3.2**) as well. α-Alkenylidene-β-lactams (**3.20**) could be prepared by the carbonylation of 4-amino-2-alkynyl methyl carbonates (**3.19**) (Scheme 3-4).[211]

Carbonylation in the presence of amines yields amides. For example, $Pd_2(dba)_3 \bullet CHCl_3$, together with dppp and *p*-TsOH, catalyzes the regioselective carbonylation of propargylamines to 2,4- or 2,3-dienamides (Scheme 3-5).[212]

Scheme 3-4. Preparation of α-Alkenylidene-β-Lactams by Carbonylation Reactions



Scheme 3-5. Carbonylation of Propargylamines



3.2. Aim of the Research

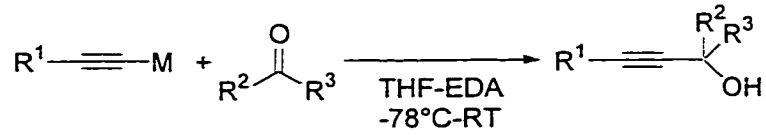
Since propargylic alcohols are easily prepared by the reaction of terminal alkynes with carbonyl compounds, the palladium-catalyzed transformation of various propargylic compounds has synthetic value. Although the carbonylation of propargylic derivatives in the presence of nucleophiles such as alcohols, amines, active methylene compounds and water (phase transfer conditions) has been the subject of many investigations, the carbonylation of those compounds with thiols as nucleophiles has not been reported in the literature. As mentioned already, perhaps the widespread belief that organosulfur compounds are poisons to catalysts has precluded intensive research in this area. On the contrary, we have developed a regioselective thiocarbonylation of allylic alcohols with various thiols (see Chapter 2). The aim of this work is to further demonstrate the efficacy of palladium catalysts in synthetic reactions of thiols and to explore the thiocarbonylation of propargylic compounds, leading to the formation of highly functionalized unsaturated compounds and to oxygen heterocycles.

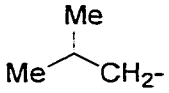
3.3 Results and Discussion

3.3.1 Synthesis of Starting Materials

Propargylic Alcohols. Some propargylic alcohols were prepared by the reaction of metal acetylides with ketones in this study (Table 3-1).[213]

Table 3-1. Synthesis of Propargylic Alcohols

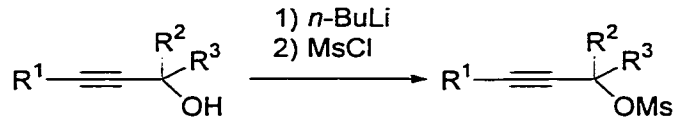


entry	R^1	R^2	R^3	yield(%)[a]
1[b]	CH_3	cyclohexyl		67
2[c]	H	Ph	H	58
3[c]	H	CH_3		73

[a] Isolated yield. [b] 1-Propynylmagnesium bromide (0.5 M solution in THF) was used. [c] Lithium acetylide-ethylenediamine (EDA) complex (90%) was used.

Propargylic Mesylates. All propargylic mesylates were preparaed from the corresponding alcohols by a modification of a published procedure.[214] Using *n*-BuLi as the base, in place of triethylamine, increased the yields greatly. The results are summarized in Table 3-2.

Table 3-2. Preparation of Propargylic Mesylates



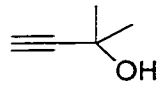
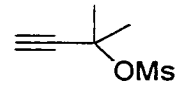
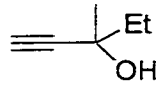
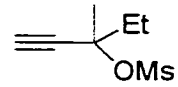
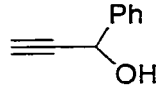
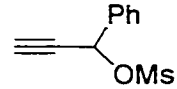
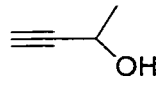
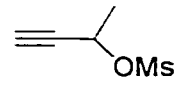
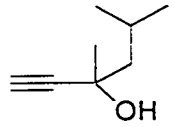
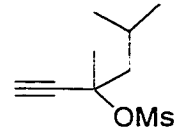
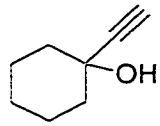
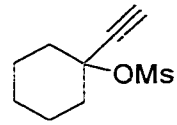
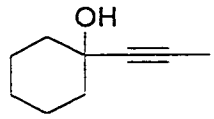
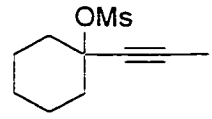
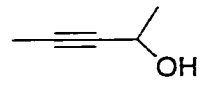
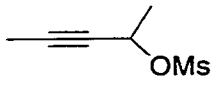
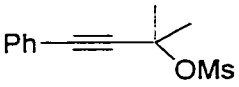
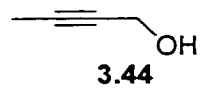
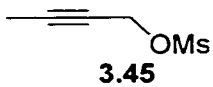
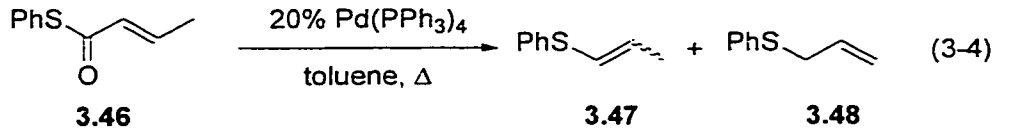
entry	propargylic alcohol	propargylic mesylate	isolated yield(%)
1	 **3.26**	 **3.27**	89
2	 **3.28**	 **3.29**	92
3	 **3.30**	 **3.31**	80
4	 **3.32**	 **3.33**	90
5	 **3.34**	 **3.35**	72
6	 **3.36**	 **3.37**	83
7	 **3.38**	 **3.39**	74

Table 3-2. (continued)

entry	propargylic alcohol	propargylic mesylate	isolated yield(%)
8	 **3.40**	 **3.41**	87
9	 **3.42**	 **3.43**	68
10	 **3.44**	 **3.45**	86

3.3.2 Reaction of 2-Methyl-3-butyn-2-ol with Thiophenol and Carbon Monoxide. Demonstration of Process

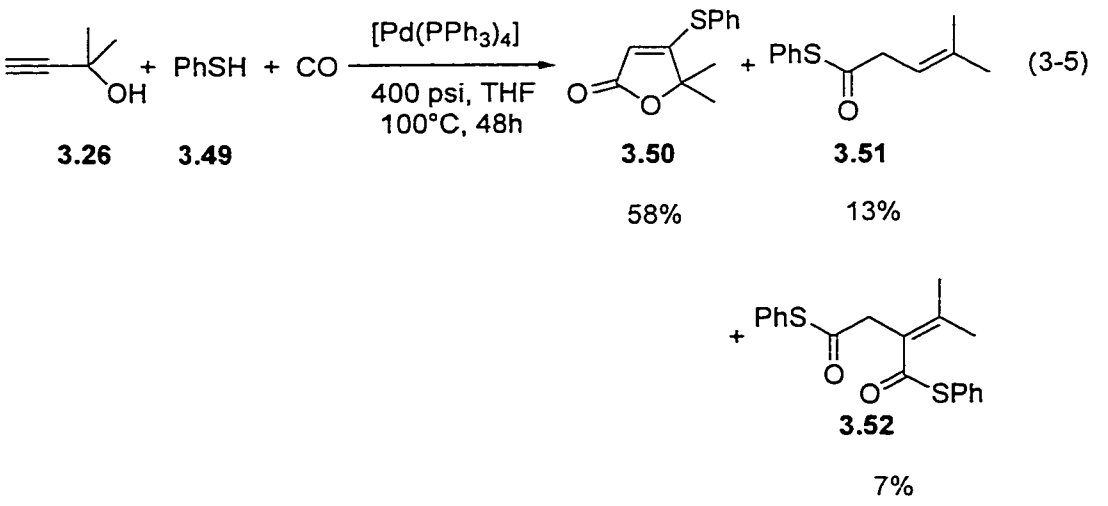
As a model substrate, we chose 2-methyl-3-butyn-2-ol (**3.26**) and examined its reaction with catalytic amounts of a variety of metal complexes. The first system we studied was the same as the one employed for the carbonylation of 2-alkoxytetrahydrothiophenes and 2-benzylthiotetrahydrofuran,[181h] namely $[Rh(COD)Cl]_2$ in benzene at 60 atm of carbon monoxide. Under these conditions we obtained a very complicated mixture and therefore turned our attention to other systems. For instance, *tetrakis*(triphenylphosphine)palladium was used by Yamamoto and co-workers[215] for the decarbonylation of thioesters, as shown in equation 3-4.



3.46 **3.47** **3.48** (3-4)

They also reported that simple diaryl thioesters could be decarbonylated using catalytic amounts of $[Pd(PCy_3)_2]$. It was envisaged that these catalytic systems might also be used to carry out the thiocarbonylation of propargylic compounds.

Initially, we examined the reaction of 2-methyl-3-butyn-2-ol (**3.26**) with thiophenol (**3.49**) and carbon monoxide, in anhydrous THF, in the presence of 3 mol% $[Pd(PPh_3)_4]$ at 100°C under 400 psi for 48 h (Eq. 3-5).



3.26 **3.49** **3.50** **3.51** (3-5)

58% 13%

3.52

7%

Indeed, the reaction gave thiofuranone (**3.50**), monothioester (**3.51**), as well as the dithioester (**3.52**) in 58, 13, and 7% isolated yields, respectively (Table 3-3, entry 1). Thus, the influence of palladium complexes was then investigated in detail.

Table 3-3. Palladium-Catalyzed Reaction of 3.26 With PhSH and CO With or Without *p*-TsOH in THF[a]

entry	catalyst system	isolated yield(%)		
		3.50	**3.51**	**3.52**
1	$Pd(PPh_3)_4$	58	13	7
2	$Pd(PPh_3)_4$ + *p*-TsOH	trace	74	9
3	$Pd(OAc)_2$	23	18	14
4	$Pd(OAc)_2 + PPh_3$	56	16	8
5	$Pd(OAc)_2 + PPh_3$ + *p*-TsOH	trace	82	trace
6	$Pd(OAc)_2$ + dppp	64	16	5
7	$Pd(OAc)_2$ + dppp + *p*-TsOH	12	68	trace
8[b]	$Pd(dba)_2$	36	13	trace
9[c]	$Pd(dba)_2$ + *p*-TsOH	16	29	trace
10	$Pd(dba)_2 + PPh_3$	63	7	5
11[c]	$Pd_2(dba)_3{\cdot}CHCl_3 + PPh_3$ + *p*–TsOH	8	38	5

[a] Reaction conditions: **3.26** (2 mmol), **3.49** (2 mmol), palladium complex (0.06 mmol), ligand PPh_3 (0.24 mmol) or dppp (0.12 mmol), *p*-TsOH (0.1 mmol) (if used), THF (5 ml), 400 psi of carbon monoxide, 100°C, 48 h. [b] 14% of substrate was recovered. [c] Some catalyst decomposition was observed.

Table 3-3 shows the results of carbonylation reactions of 2-methyl-3-butyn-2-ol (**3.26**) with thiophenol and carbon monoxide using several palladium catalysts. Initial catalyst screening indicated that use of palladium(0) or palladium(II) complexes with added phosphine ligands displayed the highest catalytic activity toward the formation of **3.50** and **3.51** in THF. In particular, the use of 3 mol% palladium acetate with 4 equiv of triphenylphosphine and 5 mol% of *p*-toluenesulfonic acid (*p*-TsOH) was the most effective catalyst system for the selective formation of **3.51**, which was isolated in 82% yield (Table 3-3, entry 5), while use of $Pd(dba)_2$, with triphenylphosphine, but in the absence of *p*-TsOH, afforded **3.50** in 63% isolated yield (Table 3-3, entry 10).

$Pd(PPh_3)_4$ is also an excellent catalyst for this reaction (Table 3-3, entries 1 and 2). However, other palladium complexes, such as $Pd(dba)_2$ (Table 3-3, entries 8 and 9), $Pd_2(dba)_3 \bullet CHCl_3$ (Table 3-3, entry 11), and $Pd(OAc)_2$, without added phosphine ligand (Table 3-3, entry 3), were less effective for this transformation. The bidentate phosphine, 1,3-*bis*(diphenylphosphino)propane (dppp), was also effective as an added ligand for the $Pd(OAc)_2$-catalyzed reaction, and good yields of **3.50** and **3.51** resulted in the absence and presence of *p*-TsOH (Table 3-3, entries 6 and 7).

We also examined other metal complexes known to be effective for the carbonylation of sulfides. Some nickel complexes which were known to catalyze the cross coupling of allyl sulfides and Grignard reagents,[216] namely $Ni(PPh_3)_2(CO)_2$ and $NiCl_2(DPPE)_2$, did not promote the thiocarbonylation even when stoichiometric amounts were used. Molybdenum carbonyl, which is known to form π-allyl complexes and to desulfurize organic sulfides did not effect any reaction.[217] It was found that a mixture of dicobalt octacarbonyl and ruthenium carbonyl, which were previously used in the

carbonylation of thietanes,[129b] afforded complicated mixtures of products, none of which were **3.50**, **3.51**, or **3.52**.

3.3.3. Palladium-Catalyzed Thiocarbonylation of 3.26. Optimization of Reaction Conditions

The optimization of reaction conditions was effected using **3.26** as the model substrate and *tetrakis*(triphenylphosphine)palladium as the catalyst. The influence of solvents, CO pressure, reaction temperature, and the mole ratio of **3.26** to thiophenol was then investigated. Some representative results are shown in Table 3-4.

The thiocarbonylation reaction can selectively afford **3.50**, **3.51** and **3.52** as the principal product (Table 3-4), depending on the reaction conditions. Basically, the reaction gave mono- and di-thioesters under relatively severe conditions (i.e. higher temperature and pressure), while thiofuranone would be formed preferentially under milder conditions (i.e. lower temperature and pressure). The presence of *p*-toluenesulfonic acid promoted the preferential formation of thioesters (Table 3-4, entries 2-3, and 7-11). Without *p*-TsOH, thiofuranone **3.50** would be formed preferentially (Table 3-4, entries 1 and 4-6). The function of *p*-TsOH is presumably to protonate the hydroxyl group of propargylic alcohol so as to eliminate H_2O to form an allenylpalladium intermediate **3.2**, which results in the formation of **3.51** and **3.52**. The ratio of **3.26** to **3.49** had a significant influence on the reaction. When 2 equivalents of thiophenol was used, the reaction afforded dithioester **3.52** predominantly (Table 3-4, entries 7-11).

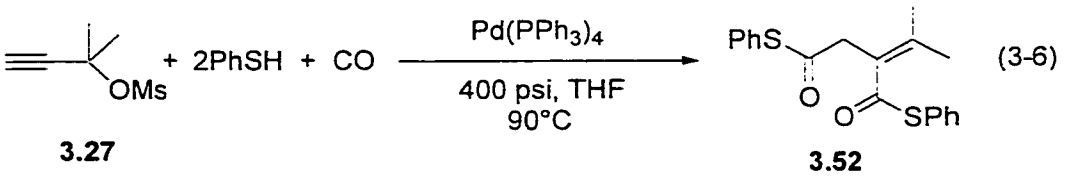
Table 3-4. Palladium-Catalyzed Thiocarbonylation of 3.26. Optimization of Reaction Conditions[a]

entry	**3.26**[b]**/3.49**	P_{CO} (psi)	solvent	temp.(°C)	isolated yield(%)		
					3.50	**3.51**	**3.52**
1	2/2	400	THF	100	58	13	7
2[c]	2/2	400	THF	100	trace	74	9
3[c,d]	2/2	400	THF	110	0	72	6
4	2/2	400	DME	100	67	5	4
5	2/2	250	DME	90	74	trace	0
6[e]	2/2	250	DME	90	82	0	0
7[c]	2/4	400	THF	110	0	12	52
8[c]	2/4	400	toluene	110	0	8	63
9[c]	2/4	600	toluene	110	0	trace	76
10[c,d]	2/4	600	toluene	150	0	trace	78
11[c]	2/4	800	toluene	150	0	0	76

[a] Reaction conditions: **3.26** (2 mmol), **3.49** (2-4 mmol), $Pd(PPh_3)_4$ (0.06 mmol), dppp (0.12 mmol, if used), *p*-TsOH (0.1 mmol, if used), solvent (5 ml). [b] The mole ratio of 2-methyl-3-butyn-2-ol to thiophenol (mmol/mmol). [c] *p*-TsOH was used. [d] Palladium acetate with 4 equivalents of triphenylphosphine was used instead of $Pd(PPh_3)_4$. [e] DPPB was used as an additional ligand.

In particular, using 2 equivalents of thiophenol with 5 mol% of *p*-TsOH at 150°C under 800 psi of carbon monoxide in toluene, the reaction afforded **3.52** as the sole product in 76% isolated yield (Table 3-4, entry 11). With 1,4-bis(diphenylphosphino)butane (dppb) as the additional ligand, the reaction in DME at 90°C under 250 psi of carbon monoxide only gave **3.50** in 82% yield (Table 3-4, entry 6).

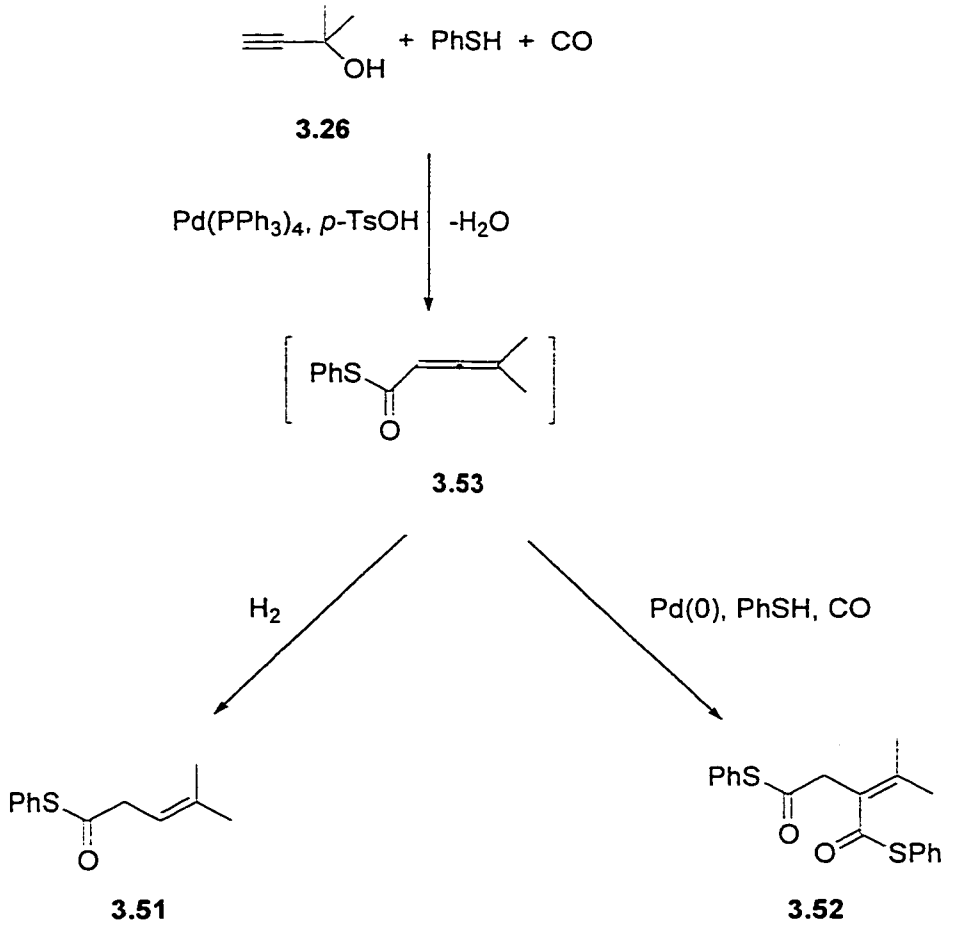
Importantly, tertiary propargylic mesylates with a terminal triple bond are very reactive and give a high yield of the dithioester under very mild conditions (Eq. 3-6).



3.27 **3.52** (3-6)

Note that the thiocarbonylation of propargylic alcohol does not stop at the stage of the 2,3-alkadienoate **3.53**, the latter reacting further with either thiophenol and carbon monoxide to form the dithiocarbonylation product **3.52**, or hydrogen to afford the reduction product **3.51** (Scheme 3-6).

Scheme 3-6. Thiocarbonylation of Propargylic Alcohol to Mono- and Dithioesters



The hydrogen gas for the reduction process might be generated by the water-gas-shift-reaction (Eq. 3-7),[51, 218] although neither this possibility, nor the mechanism for the formation of **3.51**, was investigated. Another possibility of the formation of **3.51** may arise from the protonation of **3.102** in the presence of *p*-TsOH.

$$CO + H_2O \xrightarrow{\text{Metal catalyst}} CO_2 + H_2 \qquad (3\text{-}7)$$

3.3.4 Palladium-Catalyzed Thiolactonization of Propargylic Alcohols to 2(5H)-Furanones

Thiolactonization. Table 3-5 presents the results of $Pd(PPh_3)_4$/dppb-catalyzed thiolactonization of a series of propargylic alcohols with thiols and carbon monoxide. In all cases, propargylic alcohols were completely consumed, and the corresponding β-thio-γ-lactones were obtained in good to excellent isolated yields. Various thiols, such as aromatic thiols (Table 3-5, entries 2 and 3), an aliphatic thiol (**3.58**, Table 3-5, entry 4), and a heteroaromatic thiol (**3.60**, Table 3-5, entry 5), were used in the present thiolactonization with similar efficiency. The procedure can also be applied to a series of propargylic alcohols, and unlike the previously published procedure,[196] both internal and terminal alkynols could be smoothly thiolactonized under reaction conditions employed here (Table 3-5, entries 1 and 15). Primary, secondary, and tertiary propargyl alcohols can be converted to the corresponding 4-thio-2(*5H*)-furanones in reasonable yields (Table 3-5, entries 6-7 and 11-14). It is noteworthy that spirocyclic lactones with a β-thiophenyl group (**3.66-3.68**) can be prepared by similar treatment of internal as well as terminal cyclic alkynols (Table 3-5, entries 8, 9, and 10). In addition to alkyl-substituted propargyl alcohols, aryl-substituted alcohols could also undertake thiolactonization cleanly (Table 3-5, entries 11 and 14).

Table 3-5. Palladium-Catalyzed Thiolactonization of Propargylic Alcohols to 4-Thio-2(*5H*)-Furanones[a]

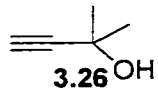
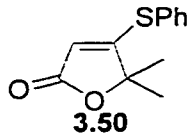
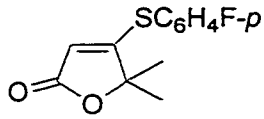
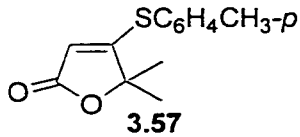
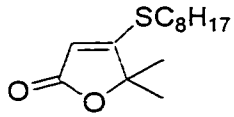
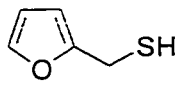
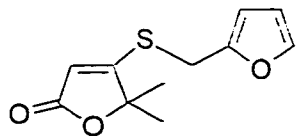
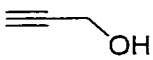
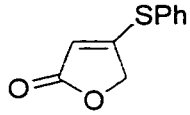
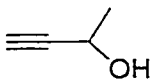
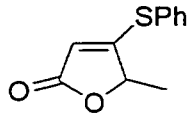
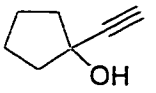
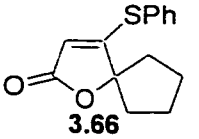
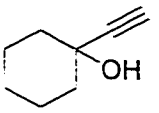
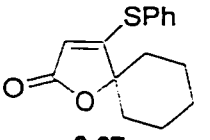
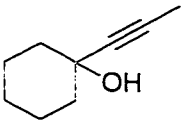
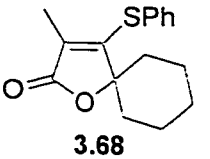
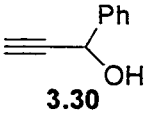
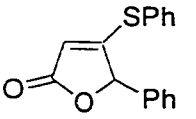
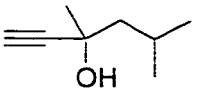
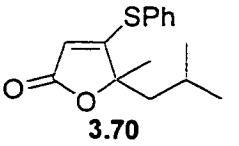
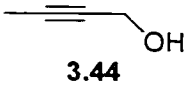
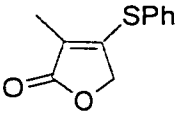
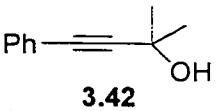
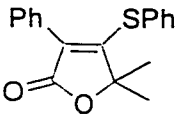
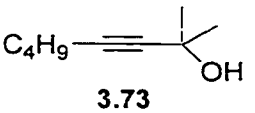
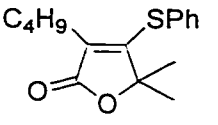
entry	alcohol	thiol	product	yield(%)[b]
1	 **3.26**	PhSH **3.49**	 **3.50**	67
2	**3.26**	*p*-FC_6H_4SH **3.54**	 **3.55**	82
3	**3.26**	*p*-$CH_3C_6H_4SH$ **3.56**	 **3.57**	64
4	**3.26**	$C_8H_{17}SH$ **3.58**	 **3.59**	74
5	**3.26**	 **3.60**	 **3.61**	76
6	 **3.62**	**3.49**	 **3.63**	58
7	 **3.32**	**3.49**	 **3.64**	88

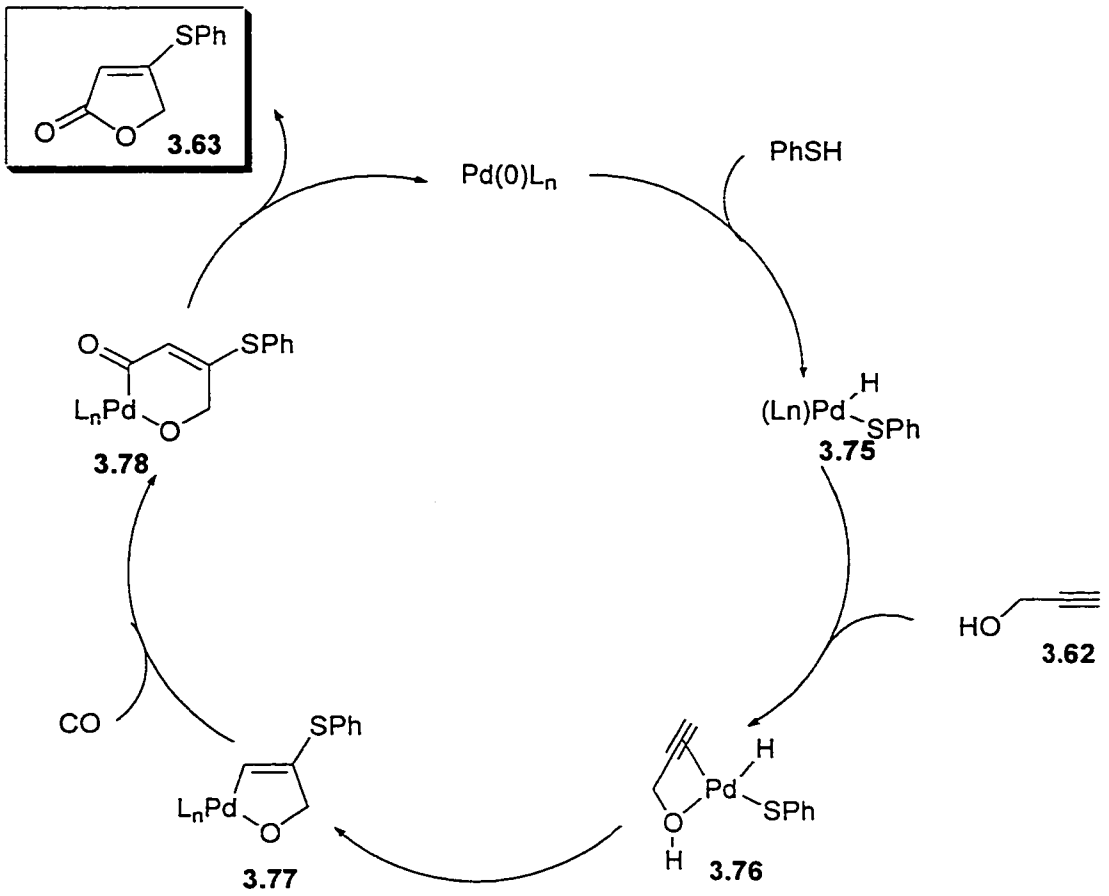
Table 3-5. (continued)

entry	alcohol	thiol	product	yield(%)[b]
8	 **3.65**	PhSH **3.49**	 **3.66**	85
9	 **3.36**	**3.49**	 **3.67**	82
10	 **3.38**	**3.49**	 **3.68**	73
11	 **3.30**	**3.49**	 **3.69**	81
12	 **3.34**	**3.49**	 **3.70**	75
13	 **3.44**	**3.49**	 **3.71**	72
14	 **3.42**	**3.49**	 **3.72**	63
15	 **3.73**	**3.49**	 **3.74**	70

[a] Reaction conditions: propargylic alcohols (2 mmol), thiol (2 mmol), $Pd(PPh_3)_4$ (0.06 mmol), dppb (0.12 mmol), 250 psi of CO, DME (5 ml), 90 °C, 48 h. [b] Isolated yield.

Proposed Mechanism. A possible mechanism for the thiolactonization of propargylic alcohols is outlined in Scheme 3-7.

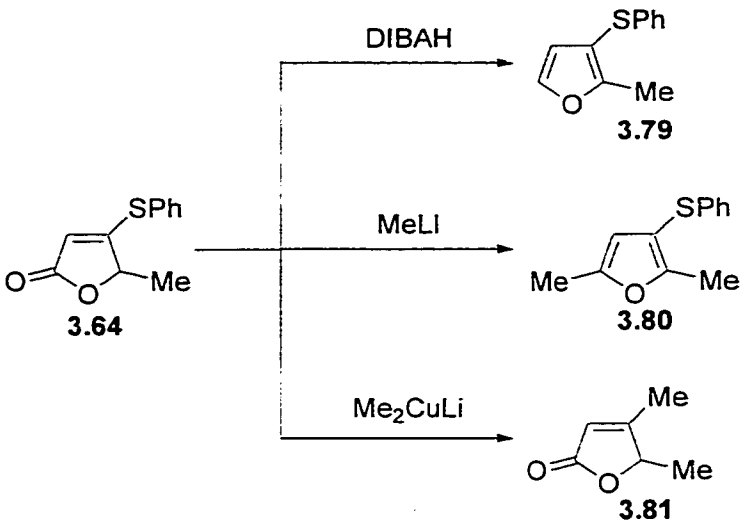
Scheme 3-7. A Possible Mechanism for the Thiolactonization Reaction



Similar to the hydrothiolation of rhodium[219] and platinum[220] complexes, the thiolactonization may also start from the oxidative addition of thiophenol to Pd(0) to form the phenylthiopalladium complex **3.75**, which then coordinates with the electron-rich carbon-carbon triple bond and hydroxyl group of the propargylic alcohol to form the complex **3.76**. Subsequent insertion of the triple bond into the Pd-S bond (intramolecular cyclization) or intermolecular attack of another thiophenol to **3.76** would form a cyclic palladium complex **3.77**. The introduction of carbon monoxide into either the palladium-carbon bond or palladium-oxygen bond could give the acylpalladium intermediate **3.78** and then reductive elimination would afford the β-phenylthio-γ-lactone (**3.63**) as well as regenerate the active species.

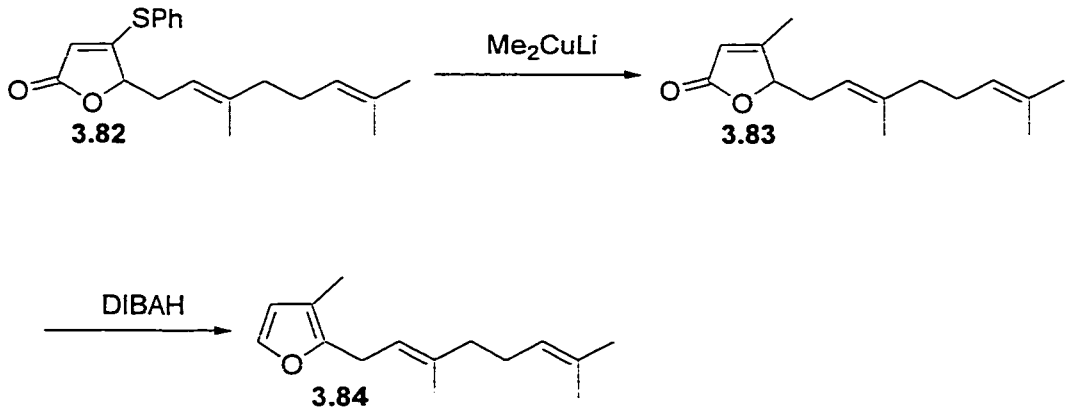
Synthetic Applications. The present procedure allows for the preparation of a number of 4-phenylthio-2(*5H*)-furanones. In view of their unique functionality, these compounds could serve as useful precursors towards complex organic compounds or natural products.[221] Typical reactions of furanones are shown in Scheme 3-8.

Scheme 3-8. Some Typical Reactions of 2(*5H*)-Furanones



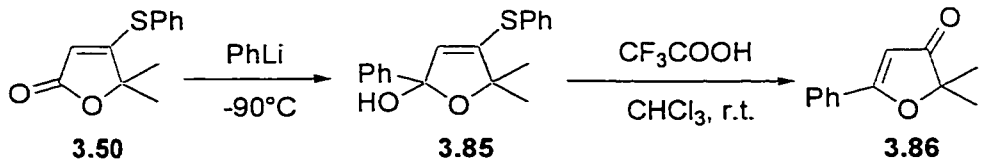
Combination of the conjugate addition of lithium dimethylcuprate with DIBAH reduction could provide a strategy for the synthesis of sesquirose furan (**3.84**), one of the constituents of the leaf oil of *Actinodaphne Longifolia* (Baribari) (Scheme 3-9).[222]

Scheme 3-9. Synthesis of Sesquirose Furan from 4-Phenylthio-2(*5H*)-Furanone 3.82



Bullatenone (**3.86**) is a 3-furanone derivative isolated from the blistered-leaf myrtle *Myrtus Bullate*,[223] which can be easily synthesized from the 4-phenylthio-2(*5H*)-furanone **3.50** (Scheme 3-10).[224] Moreover, 4-tributylstannylfuran-2(*5H*)-ones, which are

Scheme 3-10. Synthesis of Bullatenone from 4-Phenylthio-2(*5H*)-Furanone 3.50



versatile intermediates to many nature products containing a furanone ring, [225] can be readily prepared by ipso radical desulfurative stannylation of 4-phenylthio-2(*5H*)-furanones.[226]

3.3.5. Palladium-Catalyzed Dithiocarbonylation of Propargylic Alcohols to Dithioesters

Dithiocarbonylation. Results of the dithiocarbonylation of various propargylic mesylates are shown in Table 3-6. Aliphatic or aromatic thiols with an electron-donating, or an electron-withdrawing group, readily undergo this transformation (Table 3-6, entries 1-4). Propargylic mesylates of primary, secondary or tertiary alcohols, in the presence of 2 equivalents of thiols, and under a 400 psi atmosphere of CO react cleanly to give the corresponding dithioesters in good yields (Table 3-6, entries 5-13). For some secondary and tertiary propargylic mesylates, with a terminal or internal triple bond, the reaction stereoselectively afforded *E*-dithioesters as products (Table 3-6, entries 5-8, and 11).

Table 3-6. Palladium-Catalyzed Dithiocarbonylation of Propargylic Mesylates[a]

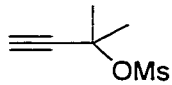
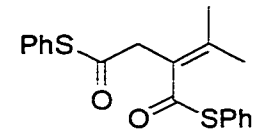
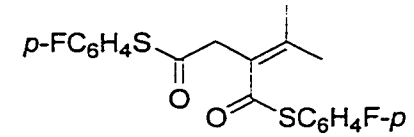
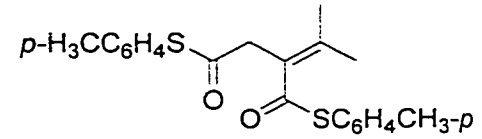
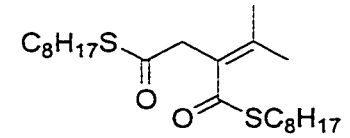
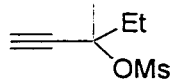
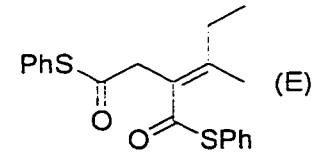
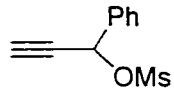
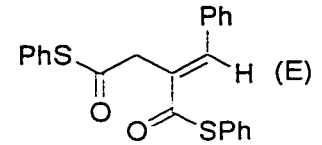
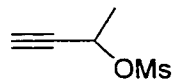
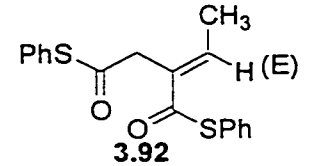
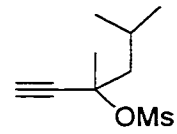
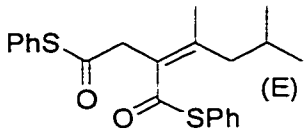
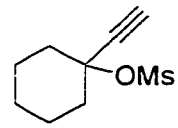
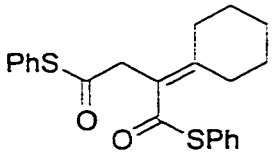
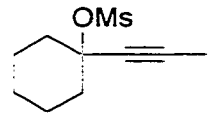
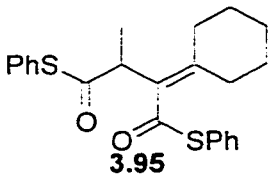
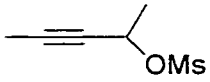
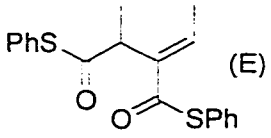
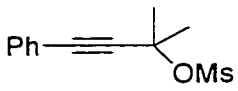
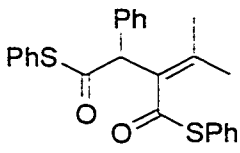
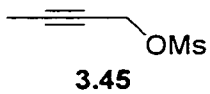
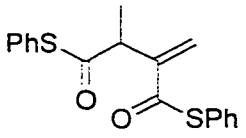
entry	alcohol	thiol	product	yield(%)[b]
1	 **3.27**	PhSH **3.49**	 **3.52**	66
2	**3.27**	*p*-FC_6H_4SH **3.54**	 **3.87**	74
3	**3.27**	*p*-$CH_3C_6H_4SH$ **3.56**	 **3.88**	65
4	**3.27**	$C_8H_{17}SH$ **3.58**	 **3.89**	60
5[c]	 **3.29**	**3.49**	 **3.90**	72
6[c]	 **3.31**	**3.49**	 **3.91**	63
7[c]	 **3.33**	**3.49**	 **3.92**	88

Table 3-6. (continued)

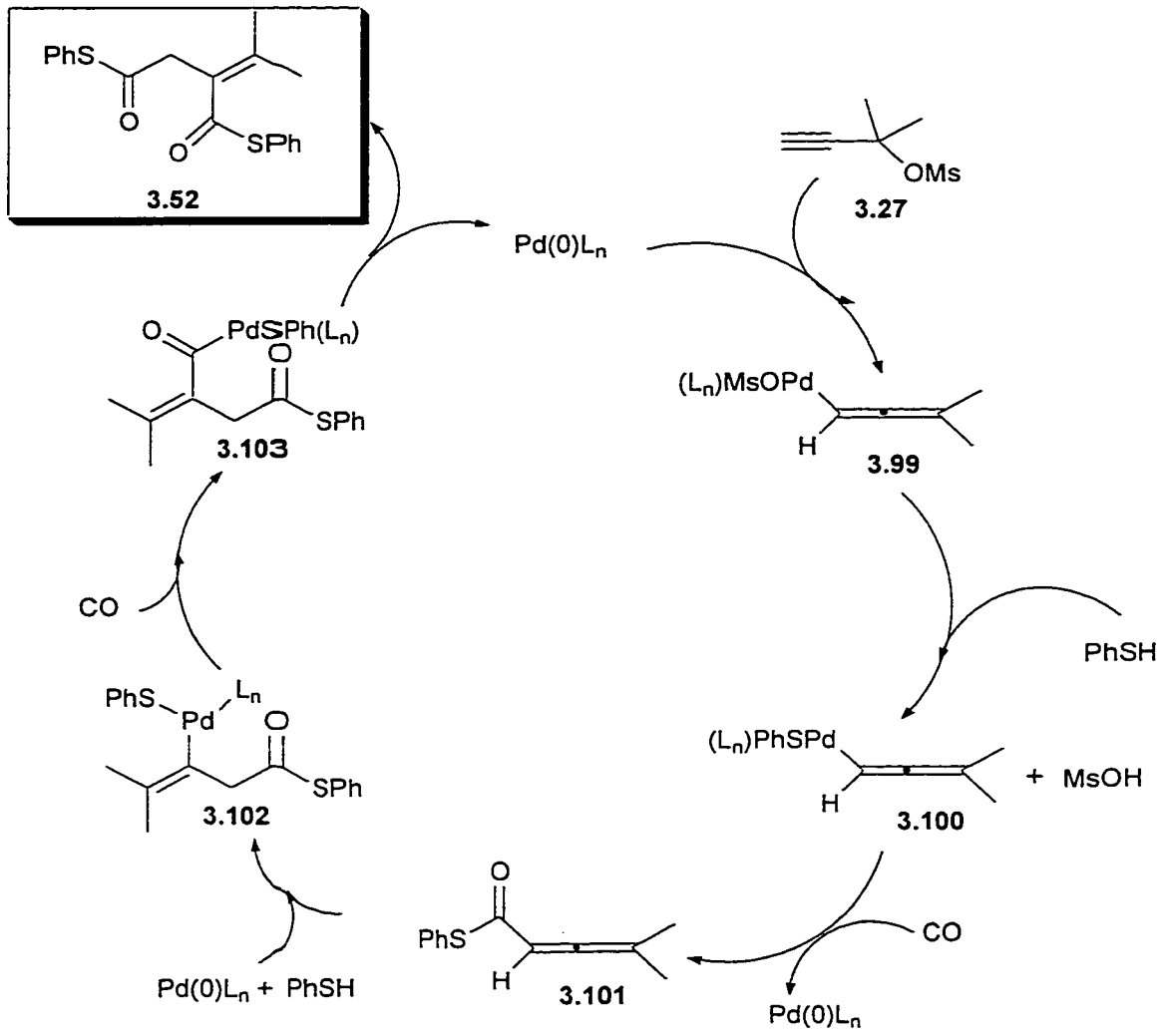
entry	alcohol	thiol	product	yield(%)[b]
8	 **3.35**	PhSH **3.49**	 **3.93**	76
9	 **3.37**	**3.49**	 **3.94**	57
10	 **3.39**	**3.49**	 **3.95**	64
11	 **3.41**	**3.49**	 **3.96**	70
12	 **3.43**	**3.49**	 **3.97**	67
13	 **3.45**	**3.49**	 **3.98**	62

[a] Reaction conditions: propargylic mesylate (2 mmol), thiol (4 mmol), $Pd(PPh_3)_4$ (0.06 mmol), 400 psi of CO, THF (5 ml), 90 °C. [b] Isolated yield. [c] The stereochemistry was assigned as *E* by NOE experiments.

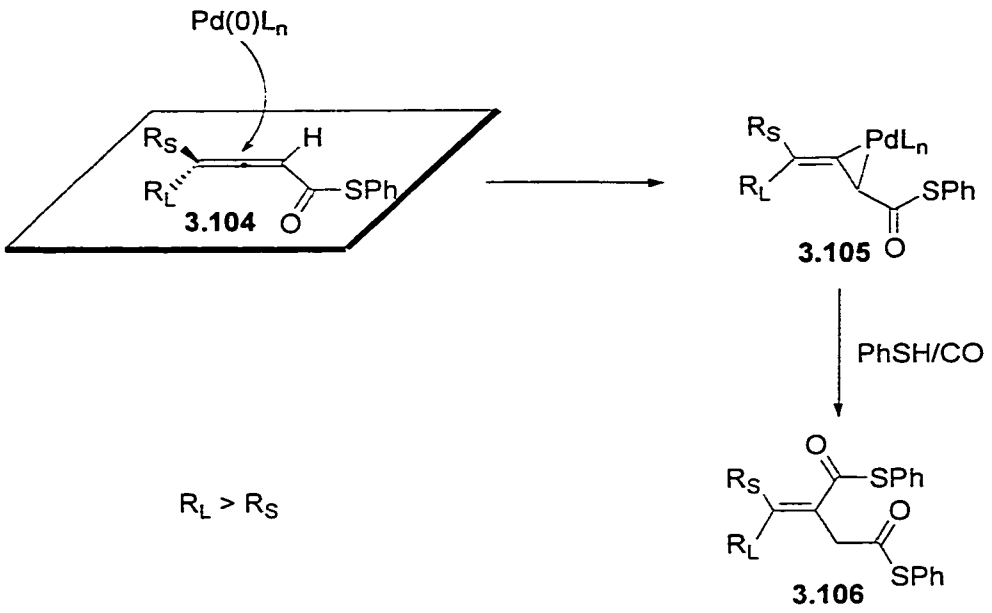
Mechanism. The reaction may proceed by the mechanism which is proposed in Scheme 3-11. The first step of the catalytic reaction may be the oxidative addition of propargylic mesylate (**3.27**) to the Pd(0) species to form a coordinatively unsaturated Pd(II) intermediate (**3.99**).[227] Ligand exchange would afford a thiopalladium complex (**3.100**). The allenyl ester, **3.101**, may be formed *via* insertion of carbon monoxide into complex **3.100**, followed by reductive elimination. It is expected that compound **3.101** would be susceptible to Michael type addition of $Pd(0)L_n$ to its allenyl *sp* carbon[56c] followed by the reaction with thiophenol, resulting in the formation of **3.102**. Finally, dithioester resulted by the second CO insertion into **3.102**, and subsequent the reductive elimination of Pd(0).

The formation of **3.101**, although not detected directly, could be supported by the observation that *E* geometry was accomplished with high stereoselectivity as shown in entries 5-8 and 11 of Table 3-6, respectively. Such high stereoselectivity might be rationalized by a mechanism where nucleophilic attack of a $Pd(0)L_n$ species on the allenyl *sp* carbon occurs from the less hindered side of an alkyl substituted (R_s) (Scheme 3-12).

Scheme 3-11. A Possible Mechanism for the Dithiocarbonylation of Propargylic Mesylates



Scheme 3-12. A Possible Mechanism for the Formation of *E*-Dithioesters



3.4 Conclusions

We have found that palladium complexes exhibit excellent catalytic activity toward the thiocarbonylation of propargylic compounds, affording 4-phenylthio-2(*5H*)-furanones, monothioesters, and dithioesters, respectively, depending on the reaction conditions. Reactions of propargylic alcohols with thiols and carbon monoxide gave 4-phenylthio-2(*5H*)-furanones as the principal products, using $Pd(PPh_3)_4$/dppb as the catalyst at 90°C under 250 psi in DME. In the presence of *p*-TsOH, the reaction with 1 equivalent of thiols afforded monothioesters in excellent yields when $Pd(OAc)_2$ with 4 equivalent of PPh_3 was used as the catalyst system under 400 psi of carbon monoxide at

100°C in THF. Dithioesters could be formed from the corresponding alcohols when 2 equivalents of thiols were employed and $Pd(PPh_3)_4$ was used as the catalyst in the presence of *p*-TsOH under 800 psi of carbon monoxide at 150°C in toluene. However, compared to the reaction of propargylic alcohols, the dithiocarbonylation could be carried out under much milder conditions (400 psi, 90°C) to give the corresponding dithioesters in good yields.

In general, not only is this methodology attractive for the preparation of thioesters and 4-phenylthio-2(*5H*)-furanones, but it also further demonstrates the utility of transition-metal complexes as catalysts for the transformation of organosulfur compounds. To our knowledge, these are the first examples of transition-metal-catalyzed thiocarbonylations of propargylic compounds with various thiols and carbon monoxide.

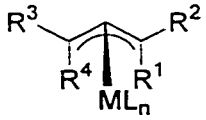
CHAPTER 4

HIGHLY REGIOSELECTIVE PALLADIUM-CATALYZED THIOCARBONYLATION OF ALLENES WITH THIOLS AND CARBON MONOXIDE

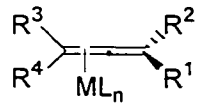
4.1. Introduction

Because of the presence of the cumulative bond, transition metal-catalyzed reactions of allenes are often quite different from those of other unsaturated compounds.[228] Usually, allenes react with transition metal complexes to form π-allyl (**4.1**), π-η^2-allenyl (**4.2**) or σ-η^1-allenyl (**4.3**) complexes (Scheme 4-1).[229]

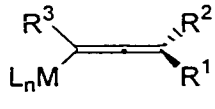
Scheme 4-1 Various Allene-Metal Complexes



4.1



4.2



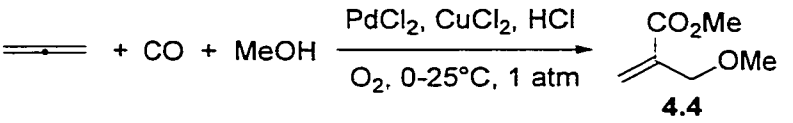
4.3

These complexes have been proposed as intermediates in the transition metal catalyzed reactions of allenes. In recent years a range of processes which employ allenes and

substituted allenes as substrates have been developed.[230-232] Among these processes, transition-metal catalyzed carbonylation of allenes has been the subject of relatively few investigations and thus not achieved their full potential. Here, a brief introduction of carbonylation chemistry of allenes will be given.

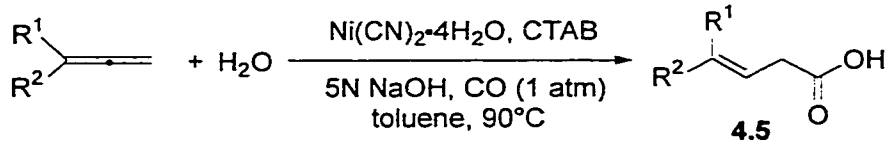
4.1.1. Transition Metal-Catalyzed Carbonylation of Allenes

During the 1960's several reports appeared on the carbonylation of allenes catalyzed by various metal complexes.[56b] These reactions afford unsaturated carboxylic esters and acids in low to moderate yields, and usually require drastic conditions.[233] Later on, much milder procedures has been found for the carbonylation of allenes. For example, allenes underwent alkoxy-alkoxycarbonylation to give 2-methoxymethylacrylates (**4.4**) in good yields when treated with carbon monoxide, oxygen, palladium and copper (II) chloride as well as hydorchloric acid in methanol (Eq. 4-1).[234]



4.4 (4-1)

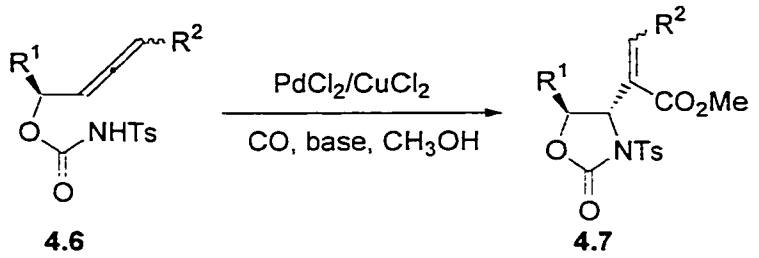
Very mild reaction conditions were used for the carbonylation of allenes under phase transfer catalysis (PTC). A nickel cyanide phase transfer system was developed for the regiospecific carbonylation of allenes to afford unsaturated carboxylic acids (**4.5**) (Eq. 4-2).[235]



(4-2)

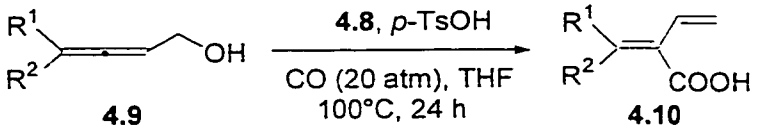
The use of $Mn_2(CO)_{10}$ and $Co_2(CO)_8$ for the acylation of allenes under PTC conditions has also been developed.[236]

When allenes bear tethered nucleophiles, intramolecular nucleophilic attack takes place, allowing the preparation of heterocyclic compounds.[237] For example, five membered heterocycles **4.7** could be prepared by the aminocarbonylation of allenes **4.6** using the $PdCl_2/CuCl_2$ system, in the presence of base (Eq. 4-3).[238]



(4-3)

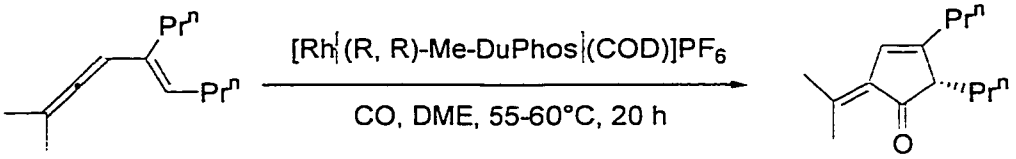
When hydridoaquopalladium complex, *trans*-$[(Cy_3P)_2Pd(H)(H_2O)]BF_4$ (**4.8**),[239] was used as the catalyst in the presence of *p*-TsOH, the carbonylation of α-allenic alcohols (**4.9**) afforded α-vinylacrylic acids (**4.10**) in 43-74% yields (Eq. 4-4).[240]



(4-4)

Similar to this transformation, the carbonylation of α-allenylamines to vinylacrylic amides could be carried out using Pd-dppp and *p*-TsOH as the catalytic system.[212a]

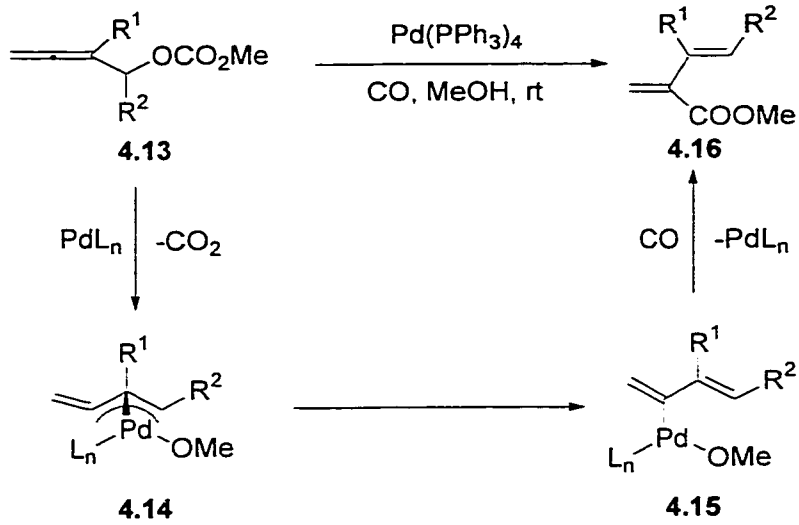
Vinyl allene **4.11** underwent carbonylative [4+1] cycloaddition when treated with Rh(I) complexes and carbon monoxide.[241] When the reaction was carried out in the presence of a chiral phosphine ligand, asymmetric induction took place and the unsaturated cyclopentanone **4.12** was formed in moderate ee's, 41-64% (Eq. 4-5).[242]



4.11 **4.12** (4-5)

Reaction of α-allenyl carbonates **4.13** with carbon monoxide catalyzed by Pd(0) complexes involved the S_N2' attack of Pd(0) species at the central carbon of the allene, the carbonate being the leaving group (Scheme 4-2).[243]

Scheme 4-2 Palladium-Catalyzed Carbonylation of α-Allenyl Carbonates



The release of carbon dioxide might be the driving force for the reaction. The allylpalladium complex **4.14** may be an the intermediate. Carbon monoxide insertion and reductive elimination could then give the methyl 1,3-dien-2-carboxylate **4.16**.

Recently, Rh-complex catalyzed copolymerization of allene with carbon monoxide has been reported.[244] Linear and branched polyketones can be easily synthesized by this methodology.

4.2 Aim of the Research

The versatility of allenes as substrates in palladium-catalyzed processes has been demonstrated by a substantial number of publications. As noted in the introduction,

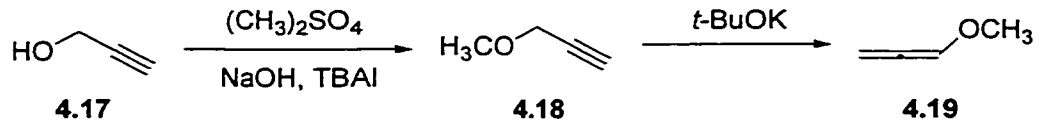
attention has been recently focused on the palladium-catalyzed carbonylative coupling reaction of nucleophiles to allenes. These reactions make it possible to synthesize the targeted compounds directly in a few steps, and therefore are very efficient and useful from the standpoint of organic synthesis. Although there are numerous publications concerning the carbonylation of allenes with oxo-, nitro-, and carbo-nucleophiles, the use of palladium complexes as homogeneous catalysts in the coupling reaction[245] of thiols and allenes as well as its carbonylative version has been the subject of very few investigations. In Chapter 3, we found that a palladium-catalyzed dithiocarbonylative reaction of propargylic mesylates with thiols might involve an allene species as a possible intermediate. In our continuing study on the thiocarbonylation of unsaturated substrates to develop new carbonylation chemistry, as well as to further demonstrate the mechanism for the dithiocarbonylation of propargylic compounds, we concentrated on the palladium-catalyzed reactions of allenes with thiols and carbon monoxide.

4.3 Results and Discussion

4.3.1 Synthesis of Allenes

A number of satisfactory methods are known for the preparation of allenes,[246] and all of the starting allenes (except 3-methyl-1,2-butadiene) were prepared through the application of known procedures. Thus, methoxyallene (**4.19**) was prepared by the base-catalyzed isomerization of propargyl methyl ether (Scheme 4-3).[247]

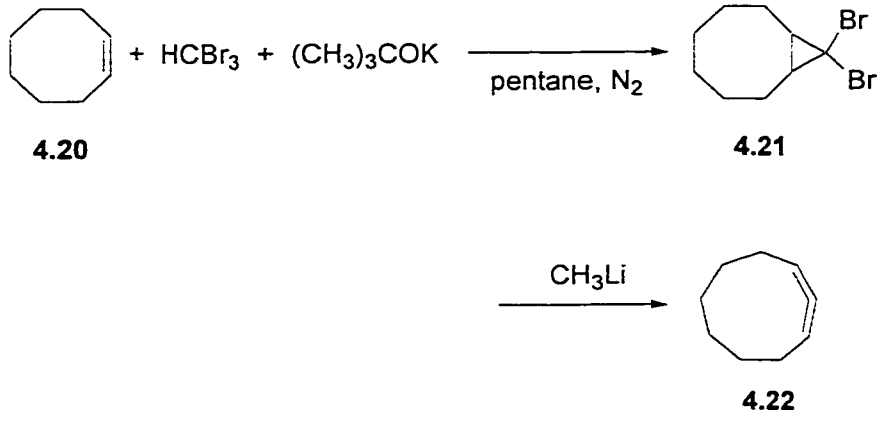
Scheme 4-3 Preparation of Methoxyallene



4.17 **4.18** **4.19**

1,2-Cyclononadiene (**4.22**) was prepared by successive treatment of *cis*-cyclooctene (**4.20**) with bromoform as well as potassium *tert*-butoxide and then methyllithium (Scheme 4-4).[248]

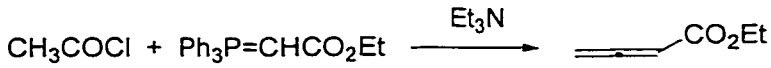
Scheme 4-4 Preparation of 1,2-Cyclononadiene



4.20 **4.21**

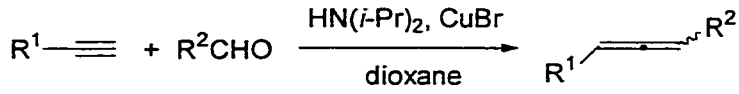
4.22

Ethyl 1,2-butadienoate (**4.25**) was prepared by the Wittig reaction of α-phosphoranylidene ester (**4.24**) and acetyl chloride (Eq. 4-6).[249]



4.23 **4.24** **4.25** (4-6)

Finally, other allenes, i.e., **4.26-4.29**, were prepared by a one-step reaction of acetylenic compounds with aldehydes in the presence of base and copper (I) bromide (Eq. 4-7).[250]



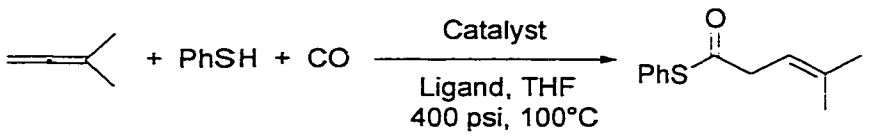
(4-7)

4.26	R^1=*n*-Pr	R^2=*n*-Pr	yield: 54%
4.27	R^1=CH_2Ph	R^2=CH_3	yield: 63%
4.28	R^1=Ph	R^2=Et	yield: 48%
4.29	R^1=C_6H_{13}	R^2=H	yield: 57%

4.3.2 Palladium-Catalyzed Thiocarbonylation of Allenes

We chose 3-methyl-1,2-butadiene (**4.30**) as a model substrate and investigated its reaction with thiophenol (**4.31**), carbon monoxide, and catalytic quantities of a variety of metal complexes. The results are summarized in Table 4-1.

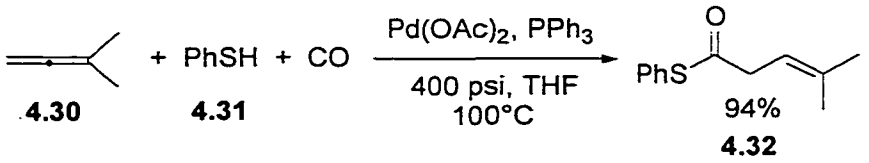
Table 4-1 Thiocarbonylation of 3-Methyl-1,2-Butadiene with Thiophenol and CO Effected by Various Transition-Metal Complexes[a]



entry	catalyst	additive	time (h)	isolated yield (%)
1	none	none	48	0
2	$Pd(PPh_3)_4$	none	48	67
3	$Pd(OAc)_2$	none	60	37
4	$Pd(OAc)_2$	4 equiv of PPh_3	48	94
5	$Pd(OAc)_2$	2 equiv of dppp	48	88
6	$Pd(OAc)_2$	2 equiv of dppb	48	72
7	$Pd(dba)_2$	none	48	52
8	$Pd_2(dba)_3 \cdot CHCl_3$	none	48	56
9	$Pd_2(dba)_3 \cdot CHCl_3$	4 equiv of PPh_3	48	90
10	$[RhCl(COD)]_2$	none	48	13
11	$RhCl(PPh_3)_3$	none	48	5
12	$Co_2(CO)_8$	none	60	3
13	$NiCl_2(PPh_3)_2$	none	48	0
14	$RuCl_2(PPh_3)_3$	2 equiv of PPh_3	48	21

[a] Reaction conditions: 3-methyl-1,2-butadiene (3 mmol), thiophenol (2 mmol), catalyst (0.06 mmol), PPh_3 (0.24 mmol, if used), dppp or dppb (0.12 mmol, if used), 400 psi of CO, 100°C, THF (7 ml).

Initial catalyst screening indicated that use of palladium (0) and palladium (II) complexes with added phosphine ligands displayed the highest catalytic activity toward the formation of the thiocarbonylation product, phenyl 4-methyl-3-pentenethioate (**4.32**) in THF (Table 4-1, entries 4-6 and 9). In particular, the use of 3 mol% palladium acetate (relative to thiophenol) with 4 equivalents of triphenylphosphine was the most effective catalyst system for the formation of **4.32** in 94% yield (Eq. 4-8).



4.30 **4.31** **4.32** (4-8)

Tetrakis(triphenylphosphine)palladium (0) is also a good catalyst for this reaction (Table 4-1, entry 2). However, other palladium (0) catalysts without added phosphine ligands, such as bis(dibenzylideneacetone)palladium(0) (Table 4-2, entry 7) and tris(dibenzylideneacetone)-dipalladium(0)-chloroform adduct (Table 4-2, entry 8), were less effective for this transformation. Although palladium acetate did catalyze the thiocarbonylation in the absence of a phosphine ligand, the reaction afforded **4.32** in low yield (Table 4-1, entry 3). In addition to triphenylphosphine, the bidentate phosphine, 1,3-bis(diphenylphosphino)propane (dppp) and 1,4-bis(diphenylphosphino)butane (dppb), were also effective as added ligands for the $Pd(OAc)_2$-catalyzed reaction (Table 4-1, entries 5 and 6).

Other metal systems which are known to insert into carbon-sulfur bonds were examined as well. $[Rh(COD)Cl]_2$, which is active for the carbonylation of sulfur-substituted heterocycles,[181h] and $RuCl_2(PPh_3)_3$, which can catalyze the insertion of carbon

monoxide into allylic carbon-sulfur bonds,[181g] were ineffective catalysts for the present carbonylation reaction (Table 4-1, entries 10 and 14). $NiCl_2(PPh_3)_2$, which has been reported to catalyze the cross coupling of allyl sulfides and Grignard reagents,[216a] did not promote the thiocarbonylation (Table 4-1, entry 13). In addition, $RhCl(PPh_3)_3$ and $Co_2(CO)_8$ were also ineffective in this case even using stoichiometric amounts of the transition-metal complexes (Table 4-1, entries 11 and 12). Starting material was recovered when the reaction was performed in the absence of the catalyst (Table 4-1, entry 1).

The effect of the solvent on the carbonylative coupling reaction of **4.30** with thiophenol and carbon monoxide was also studied, and the results are presented in Table 4-2.

Table 4-2 Solvent Effect for Palladium-Catalyzed Thiocarbonylation of 3-Methyl-1,2-Butadiene with Thiophenol

entry	solvent	time (h)	isolated yield (%)
1	THF	48	94
2	DME	60	83
3	CH_2Cl_2	48	92
4	benzene	72	76

[a] Reaction conditions: 3-methyl-1,2-butadiene (3 mmol), thiophenol (2 mmol), $Pd(OAc)_2$ (0.06 mmol), PPh_3 (0.24 mmol), 400 psi of carbon monoxide, 100°C, solvent (7 ml).

Using the palladium acetate-triphenylphosphine catalyst system, we found that the reaction works very well in THF, 1,2-dimethoxyethane (DME), or dichloromethane but less so in benzene (Table 4-2). Also, the pressures of carbon monoxide between 400 to 800 psi gave the thioester **4.32** in similar yields. Prolonged heating did not increase the reaction yield (76 h versus 48 h), while a decrease (to 50°C) or increase (to 150°C) in the reaction temperature resulted in a reduction of the yield of **4.32**.

The carbonylative coupling reaction of a series of allenes (**4.19**, **4.22**, and **4.25-4.30**) was effected using 1 equivalent of thiol or mercaptan, 3 mol% of palladium acetate, and 12 mol% of triphenylphosphine, in THF at 400 psi of carbon monoxide for 48 hours at 100°C. The β, γ-unsaturated thioesters were isolated in 73-94% yields (Table 4-3). The reaction exhibits highly regioselectivity. The 1,1-disubstituted allene, **4.30**, and monosubstituted allenes, **4.19**, **4.25**, and **4.29**, reacted with thiols and carbon monoxide affording β, γ-unsaturated thioesters as the sole product, in which the phenylthiocarbonyl group added to the unsubstituted part of the allene (Table 4-3, entries 1-7, 9, and 13). The reaction was slower when the allene contained an electron-withdrawing group, but the regioselectivity is unaffected in this case (Table 4-3, entry 9). 1,3-Disubstituted unsymmetrical allenes such as **4.27** and **4.28** underwent thiocarbonylation preferentially at the less bulkier of the two double bonds (Table 4-3, entries 11 and 12), while symmetric internal allenes (i.e., **4.22** and **4.26**) can, of course, only afford one product (Table 4-3, entries 8 and 10). Note that monosubstituted and 1,3-disubstituted allenes reacted with thiophenol and carbon monoxide to give a mixture of *E* and *Z* thioesters (Table 4-3, entries 7 and 9-13), in which the *E* isomers predominate.

Table 4-3 Palladium-Catalyzed Thiocarbonylation of Allenes with Thiols[a]

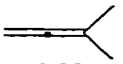
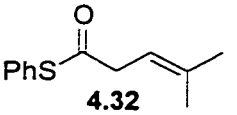
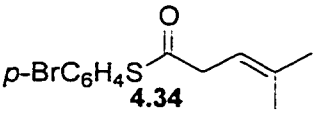
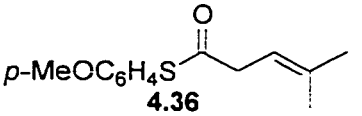
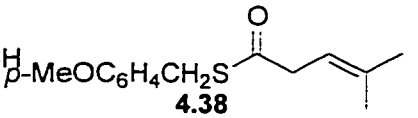
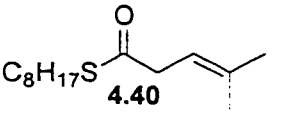
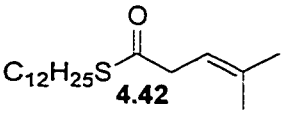
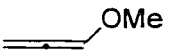
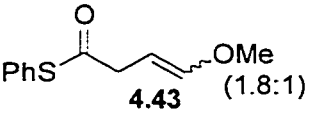
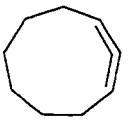
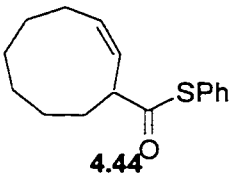
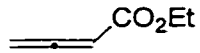
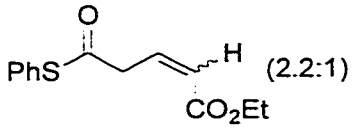
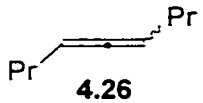
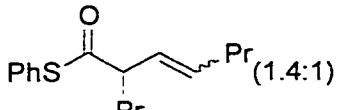
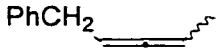
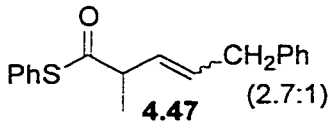
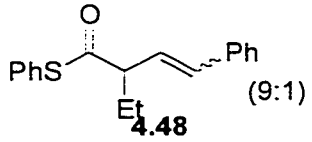
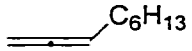
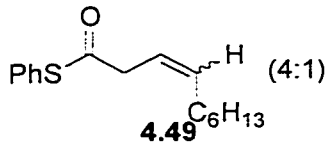
entry	allene	thiol	product (*E*/*Z*)[b]	isolated yield (%)[c]
1[d]	 **4.30**	C_6H_5SH **4.31**	 **4.32**	94
2	**4.30**	*p*-BrC_6H_4SH **4.33**	 **4.34**	73
3	**4.30**	*p*-$MeOC_6H_4SH$ **4.35**	 **4.36**	76
4	**4.30**	*p*-$MeOC_6H_4CH_2SH$ **4.37**	 **4.38**	83
5	**4.30**	$C_8H_{17}SH$ **4.39**	 **4.40**	77
6	**4.30**	$C_{12}H_{25}SH$ **4.41**	 **4.42**	92
7	 **4.19**	PhSH **4.31**	 **4.43** (1.8:1)	83
8	 **4.22**	**4.31**	 **4.44**	92

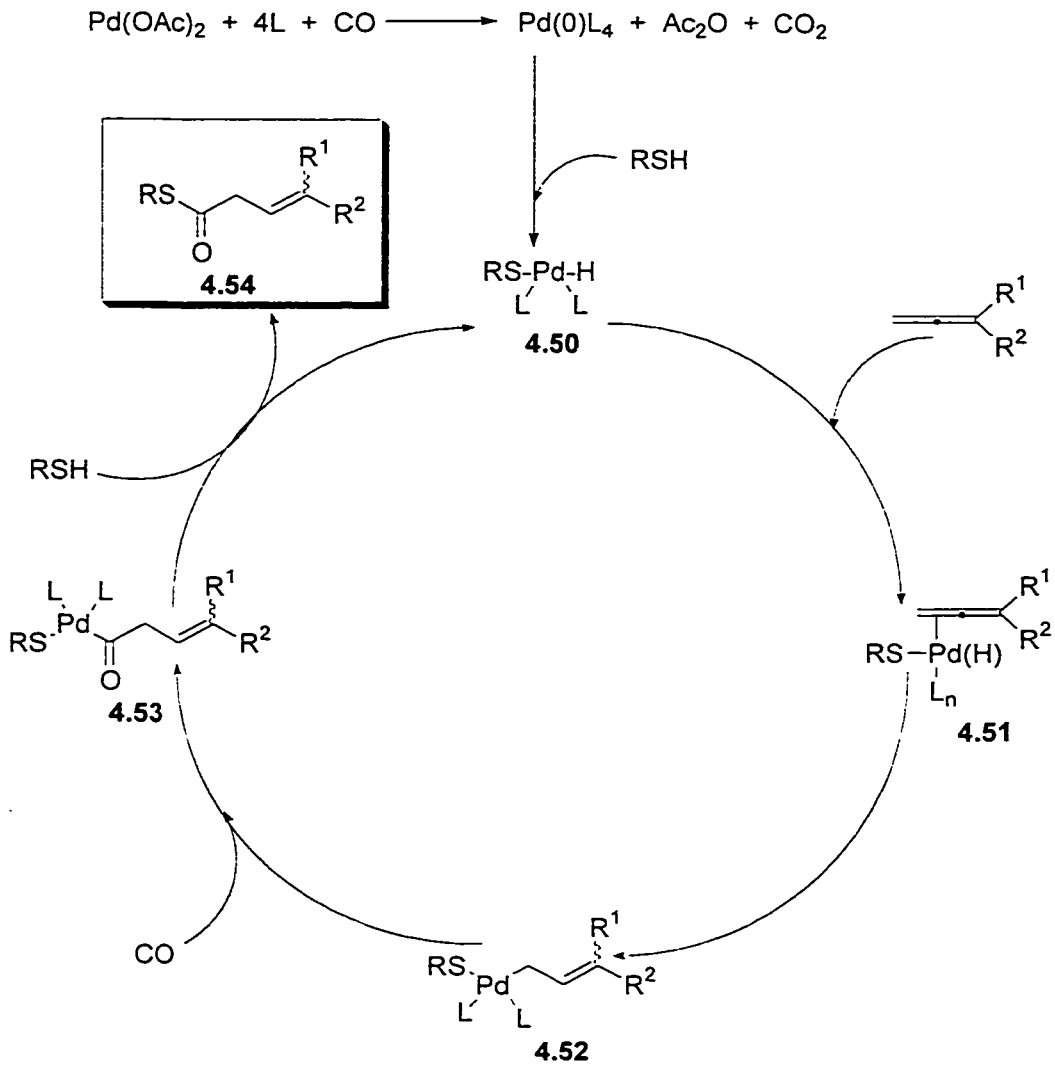
Table 4-3 (continued)

entry	allene	thiol	product (*E*/*Z*)[b]	isolated yield (%)[c]
9[e]	 **4.25**	**4.31**	 (2.2:1) **4.45**	88
10	 **4.26**	**4.31**	 (1.4:1) **4.46**	86
11	 **4.27**	**4.31**	 (2.7:1) **4.47**	83
12	 **4.28**	**4.31**	 (9:1) **4.48**	87
13	 **4.29**	**4.31**	 (4:1) **4.49**	80

[a] Reaction conditions: allene (2 mmol), thiol (2 mmol),$Pd(OAc)_2$ (0.06 mmol), PPh_3 (0.24 mmol), 400 psi of CO, 100°C, THF (7 ml), 48 h. [b] The ratio of *E* to *Z* was measured by ^1H NMR. [c] Based on the thiol employed. [d] The mole ratio of **4.30** to thiophenol was 3:2. [e] Reaction time: 60 h.

A possible pathway for the thiocarbonylation of allenes with thiols and carbon monoxide may include the formation of an H-Pd(L_n)-SR species *via* oxidative addition of RSH to Pd(0)L_n.[251] The mechanism outlined in Scheme 4-5 merits consideration and comprises the following steps:

Scheme 4-5 A Mechanism for Palladium-Catalyzed Thiocarbonylation of Allenes



(1) formation of a palladium (0) species as the active catalyst ($Pd(OAc)_2$, which is easy reduced to Pd(0) in the presence of phosphine ligands with carbon monoxide);[56b]

(2) oxidative addition of palladium (0) by the thiol to give H-Pd-SR;

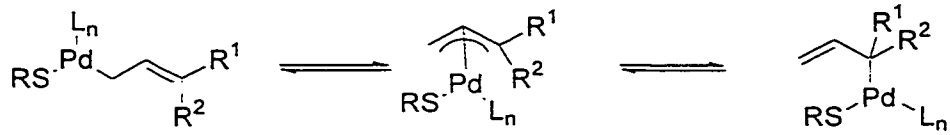
(3) coordination of the allene double bond and subsequent insertion into a Pd-H bond to form a σ-thiopalladium intermediate (**4.52**);

(4) coordination and CO insertion resulting in the formation of a carbonylthio species (**4.53**);

(5) quenching the carbonylthiopalladium complex by RSH to afford the thioester (**5.54**) and regeneration of the active species.

An equilibrium between two σ-allylthiopalladium species (which could be formed when the thiocarbonylation took place to the external or the internal double bond) might occur under the reaction conditions (Scheme 4-6). However, other isomers were not observed in the reaction.

Scheme 4-6 Isomerization of Allylthiopalladium Complexes



4.52 **4.55** **4.56**

4.4. Conclusions

Palladium catalyst systems such as $Pd(OAc)_2$-PPh_3, $Pd(PPh_3)_4$, and $Pd_2(dba)_3 \cdot CHCl_3$-PPh_3 are very effective for the carbonylative coupling reaction of allenes with thiols and carbon monoxide. The reaction is completely regioselective, in which the thiophenyl group adds to the less substituted double bond of the allene to afford the corresponding β, γ-unsaturated thioester. These reactions indirectly demonstrate our hypothesis in Chapter 3 that an allene species can be an intermediate in the thiocarbonylation of proprgylic mesylates.

CHAPTER 5

HIGHLY CHEMO- AND REGIOSELECTIVE THIOCARBONYLATION OF CONJUGATED ENYNES WITH THIOLS AND CARBON MONOXIDE CATALYZED BY PALLADIUM COMPLEXES: AN EFFICIENT AND ATOM-ECONOMICAL ACCESS TO 2-(PHENYLTHIOCARBONYL)-1,3-DIENES

5.1 Introduction

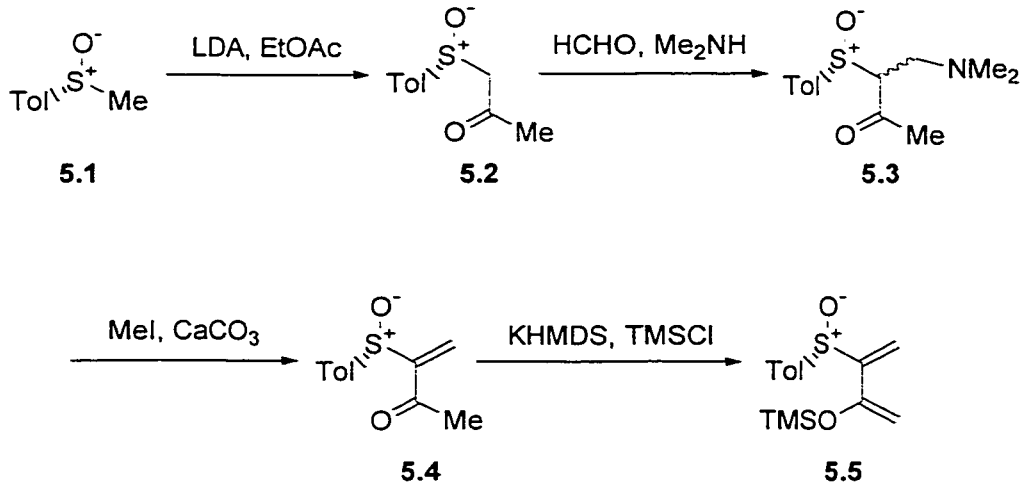
Electron-deficient conjugated dienes have recently attracted considerable interest as useful building blocks in organic synthesis.[252] The electron-withdrawing group not only increases the reactivity of such dienes as well as the chemo-and stereoselectivity of the reaction but also acts as a handle for further functional group transformations. Among the best known examples of this chemistry are Michael-type additions,[253] Diels-Alder reactions,[254], additive Pummerer reactions,[255] and transition metal catalyzed coupling reactions.[256]

The introductory section of the present chapter will give some typical preparations of several representive electron-deficient conjugated dienes.

Sulfur-substituted dienes have proved to be versatile intermediates and a number of synthetic procedures have been reported in the literature. Examples include oxidation[257] and condensation[258] reactions of the corresponding sulfur-containing compounds as well as palladium-catalyzed addition[259] and elimination[260-261] reactions.

The synthesis of optically active 1,3-dienes has recently been described.[254a, 256c] For example, the synthesis of chiral 2-(*p*-tolylsulfinyl)-3-trimethylsilyloxybuta-1,3-diene **5.5** was accomplished starting from commercially available *R*-methyl *p*-tolylsulfoxide **5.1** (Scheme 5-1).[254a]

Scheme 5-1 Preparation of Chiral p-Tolylsulfinyl-1,3-Diene



5.1 **5.2** **5.3** **5.4** **5.5**

Condensation of **5.1** with ethyl acetate gave sulfinylketone **5.2**, which reacted with formaldehyde and dimethylamine to afford **5.3** as a mixture of epimers. Enantiopure ketosulfoxide **5.4** was generated *via* Hofmann degradation, which was then subjected to enolization to form enantiopure diene **5.5**.

The synthesis of other important electron-deficient dienes, such as nitro-dienes[262-263] and phosphorus-substituted dienes,[264-265] has been well documented in the literature as well.

5.2 Aims of Research

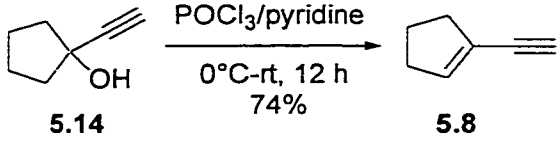
Due to the significance of electron-deficient 1,3-dienes in organic synthesis, it is not surprising that considerable effort has been directed toward the development of efficient synthesis protocols to such compounds. From a synthetic point of view, controlling regio- and chemoselectivity, as well as atom economy, is of great importance.[4] Our goal is to develop a new route to access 2-(phenylthiocarbonyl)-1,3-dienes with fine synthetic efficiency.

As part of our program to develop the thiocarbonylation of unsaturated substrates, conjugated enynes became attractive targets since they are readily available and reactive. In view of the palladium-catalyzed addition of aromatic thiols to acetylenes,[181l, 245] we believe that the thiocarbonylation of conjugated enynes should occur and allow a one-pot synthesis of phenylthiocarbonyl dienes.

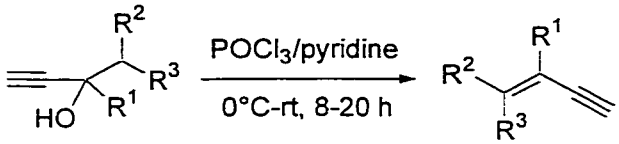
5.3 Results and Discussion

5.3.1 Synthesis of Starting Materials

Except 1-ethynylcyclohexene (**5.6**) and 2-methyl-1-buten-3-yne (**5.7**), which are commercially available, other enynes employed in this study were prepared according to the procedures shown in Eq. 5-1 to 5-4. For example, 1-ethynylcyclopentene (**5.8**), 3.5-dimethyl-3-hexen-1-yne (**5.9**), 3-methyl-3-penten-1-yne (**5.10**), and 3-ethyl-3-penten-1-yne (**5.11**) were prepared by treating the corresponding propargylic alcohols with $POCl_3$ in pyridine (Eq. 5-1 and 5-2).[266]



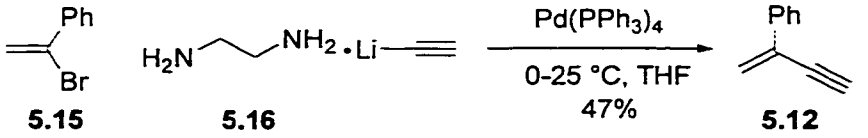
5.14 **5.8** (5-1)



(5-2)

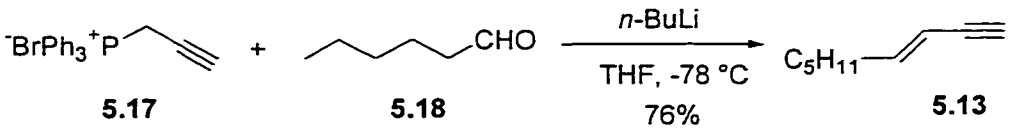
5.9 $R^1=R^2=R^3=CH_3$	67%
5.10 $R^1=R^2=CH_3$, $R^3=H$	58%
5.11 $R^1=CH_2CH_3$, $R^2=CH_3$, $R^3=H$	64%

2-Phenyl-1-buten-3-yne (**5.12**) was prepared by the palladium-catalyzed reaction of lithium acetylide with alkenyl halide (Eq. 5-3).[267]



5.15 **5.16** **5.12** (5-3)

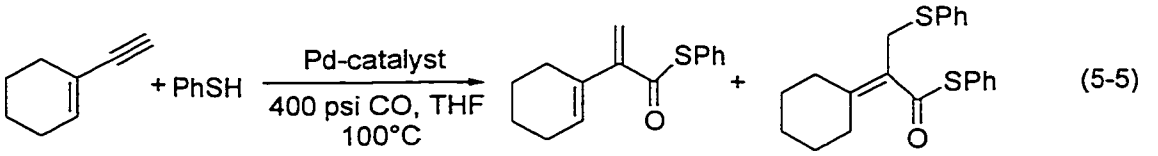
3-Nonen-1-yne (**5.13**) was obtained by the Wittig reaction of propargyl triphenylphosphonium bromide with hexanal using n-BuLi as the base (Eq. 5-4).[268]



5.17 **5.18** **5.13** (5-4)

5.3.2 Reaction of 1-Ethynylcyclohexene with Thiophenol. Demonstration of Process and Yield Optimization

The palladium-catalyzed reaction of 1-ethynylcyclohexene (**5.6**) with thiophenol (**5.19**) and carbon monoxide was chosen as a model reaction to determine the viability of the process and the optimum reaction conditions (Eq. 5-5).

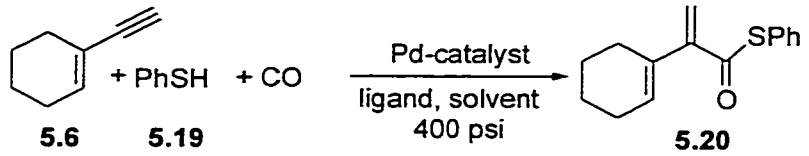


5.6 **5.19** **5.20** **5.21** (5-5)

The reaction conditions previously used for the thiocarbonylation of allenes (see Chapter 4) were initially applied to the reaction of **5.6**, **5.19**, and carbon monoxide (CO) [1 equiv of enyne, 1 equiv of thiophenol, 3 mol% $Pd(OAc)_2$, 12 mol% PPh_3, 400 psi of CO, THF

(3.5 ml per 1 mmol of thiophenol), and 100°C]. Two products, **5.20** and **5.21,** were obtained in 18% and 7% yield, respectively. By-product **5.21** may arise by 1, 4-addition of thiophenol to **5.20** and, in that event, it should be possible to control the consecutive reaction by increasing the mole ratio of **5.6** to **5.19** and decreasing the concentrations of the reactants. Indeed, treatment of **5.6** (3 mmol) with **5.19** (1 mmol) in the presence of $Pd(OAc)_2$ (0.03 mmol) and PPh_3 (0.12 mmol) in THF (15 ml) at 100°C under 400 psi of carbon monoxide gave exclusively **5.20** in 38% yield (no **5.21** was formed). The effect of varying the catalyst, ligand, solvent, reaction temperature, and reaction time on the yield of **5.20** was examined, and the results are summarized in Table 5-1.

Table 5-1 Optimization of Reaction Conditions (eq 5-6)[a]



5.6 **5.19** **5.20** (5-6)

entry	catalyst	ligand	solvent	temp.(°C)	time (h)	**5.20**(%)[b]
1	$Pd(OAc)_2$	none	THF	100	24	0[c]
2	$Pd(PPh_3)_4$	none	THF	100	24	20
3	$Pt(PPh_3)_4$	none	THF	100	24	47
4	$Pd_2(dba)_3 \cdot CHCl_3$[d]	none	THF	100	24	12
5	$Pd(OAc)_2$	PPh_3	THF	100	24	38
6	$Pd(OAc)_2$	dppb	THF	100	12	62
7	$Pd(OAc)_2$	dppe	THF	100	24	0
8	$Pd(OAc)_2$	dppp	THF	100	8	70
9	$Pd(OAc)_2$	dppp	THF	110	6	76
10	$Pd(OAc)_2$	dppp	CH_2Cl_2	110	6	43
11	$Pd(OAc)_2$	dppp	DME	110	6	8[e]
12	$Pd(OAc)_2$	dppp	C_6H_6	110	6	62
13	$Pd(OAc)_2$	dppp	CH_3CN	110	6	37
14	$Pd(OAc)_2$	dppp	THF	130	6	36
15	$Pd(OAc)_2$	dppp	THF	140	24	7
16	$Pd(OAc)_2$	dppp	THF	110	60	trace

[a]Reaction conditions: 1-ethynylcyclohexene (3 mmol), thiophenol (1 mmol), catalyst (0.03 mmol), PPh_3 (0.12 mmol, if used), bidentate phosphine (0.06 mmol, if used), 400 psi CO, solvent (15 ml). [b]Isolated yield based on the amount of thiophenol employed. [c]The decarbonylation product, phenyl 2-(1'-cyclohexenyl)-ethenyl sulfide, was isolated in 53% yield. [d]0.015 mmol of the catalyst was used. [e]27% of thiophenol was recovered, and polymerization of the enyne was observed.

A series of reactions between **5.6** and **5.19** were carried out under various conditions to optimize the reaction yield. It was shown that $Pd(OAc)_2$ with 1,3-bis(diphenylphosphino)propane (dppp) was the best catalyst system among those examined and the reaction proceeded efficiently in THF as the solvent (Table 5-1, entry 8). Increasing the reaction temperature to 110°C and decreasing the reaction time to 6 h further improved the yield to 76% (Table 5-1, entry 9). $Pd(OAc)_2$ with 1,4-bis(diphenylphosphino)butane (dppb) is also a good catalytic system for this reaction (Table 5-1, entry 6); however, $Pd(OAc)_2$ with 1, 2-bis(diphenylphosphino)ethane (dppe) was ineffective here (Table 5-1, entry 7). Other palladium catalysts, such as $Pd(PPh_3)_4$ and $Pd_2(dba)_3 \cdot CHCl_3$, without an added phosphine ligand, were not useful for this transformation (Table 5-1, entries 2 and 4). While $Pd(OAc)_2$ with 4 equiv. of PPh_3 was found to be an excellent catalyst system for the thiocarbonylation of allenes (see Chapter 4), it was not of genuine value for this carbonylative coupling reaction. The reaction of **5.6** and **5.19** catalyzed by $Pd(OAc)_2$ with PPh_3 afforded **5.20** in 38% yield (Table 5-1, entry 5), whereas using $Pd(OAc)_2$ without any ligand only gave the decarbonylation

product (Table 5-1, entry 1). Tetrakis(triphenylphosphine)platinum(0), which was very effective for the regioselective hydrothiocarbonylation of acetylenes with thiols,[181d] does catalyze this thiocarbonylation, but in appreciably lower yield of **5.20** when compared with $Pd(OAc)_2$ and dppp (Table 5-1, entry 3).

The nature of the solvent, and the reaction time, greatly affected the yield of **5.20** in the model reaction. Using the $Pd(OAc)_2$-dppp catalyst system, THF was found to be the best solvent for the reaction, whereas **5.20** was only obtained in 8% yield when 1, 2-dimethoxyethane (DME) was the reaction solvent (compare entries 9 to 13 in Table 5-1). The reaction works well at 110°C in THF and is complete in 6 h. Raising the reaction temperature to 140°C resulted in decomposition of the catalyst, and prolonged heating proved detrimental for the reaction (Table 5-1, entries 14-16), probably because of the facile polymerization of the product.[269]

5.3.3 Scope of the Thiocarbonylation of Enynes

The thiocarbonylation reaction of a series of enynes (**5.6-5.13**) with thiols (**5.19, 5.22, 5.24,** and **5.26**) were performed using 3 mol% of $Pd(OAc)_2$ and 6 mol% of dppp in THF (15 mL per 1 mmol of thiol) at 400 psi of carbon monoxide for 8-15 h at 110°C, and the results are summarized in Table 5-2.

Table 5-2. Palladium-Catalyzed Thiocarbonylation of Enynes with Thiols and CO[a]

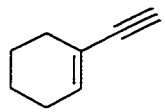
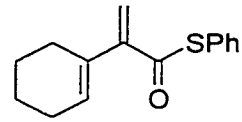
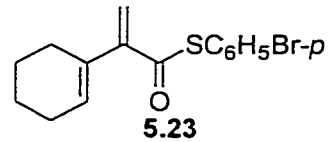
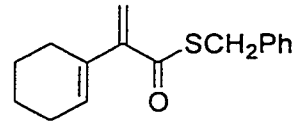
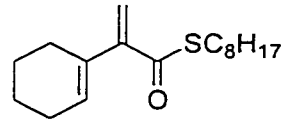
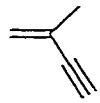
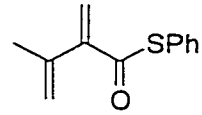
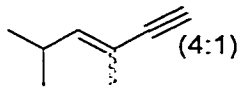
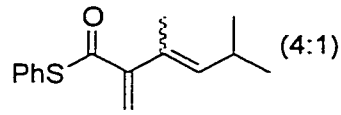
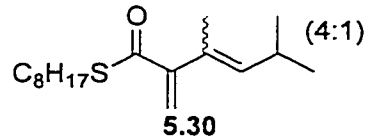
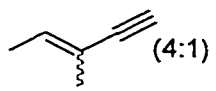
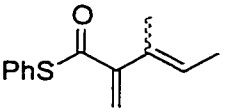
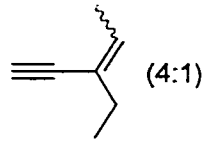
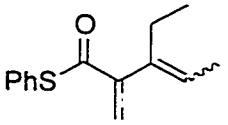
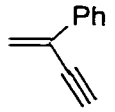
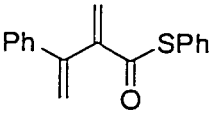
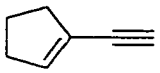
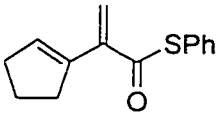
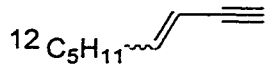
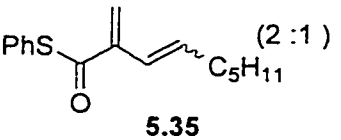
entry	enyne	thiol	time (h)	product (E/Z)[b]	yield(%)[c]
1	 **5.6**	PhSH **5.19**	10	 **5.20**	76
2	**5.6**	*p*-BrC_6H_4SH **5.22**	8	 **5.23**	70
3	**5.6**	$C_6H_5CH_2SH$ **5.24**	12	 **5.25**	73
4	**5.6**	$C_8H_{17}SH$ **5.26**	15	 **5.27**	73
5[d]	 **5.7**	**5.19**	8	 **5.28**	54
6	 **5.9**	**5.19**	8	 **5.29**	52
7	**5.9**	**5.26**	12	 **5.30**	72

Table 5-2. (continued)

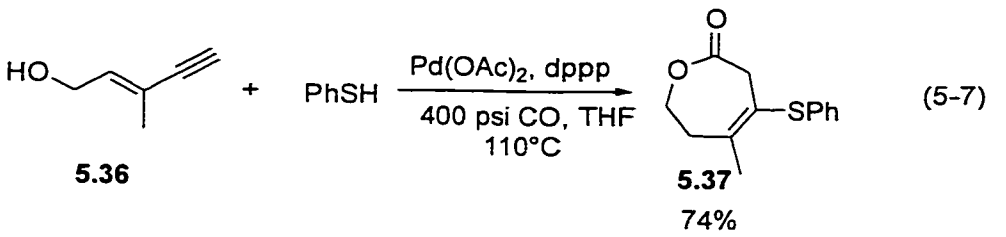
entry	enyne	thiol	time (h)	product (E/Z)[b]	yield(%)[c]
8[e]	 (4:1) **5.10**	**5.19**	8	 (4:1) **5.31**	33
9	 (4:1) **5.11**	**5.19**	8	 (4:1) **5.32**	56
10[f]	 **5.12**	**5.19**	8	 **5.33**	51
11	 **5.8**	**5.19**	12	 **5.34**	67
12  (2 :1) **5.13**		**5.19**	12	 (2 :1) **5.35**	74

[a]Reaction conditions: enyne (3.0-6.0 mmol), thiol (1.0 mmol), CO (400 psi), $Pd(OAc)_2$ (0.03 mmol), dppp (0.06 mmol), THF (15 mL), 110°C. [b]The *E/Z* ratio was determined by ^1H NMR. [c]Isolated yield based on the reactant thiol. [d]**5.7** (6.0 mmol) was used. [e]**5.10** (5.0 mmol) was used. [f]**5.12** (6.0 mmol) was used.

The thiocarbonylation of enynes was highly chemoselective, and only the triple bond was attacked by the sulfur nucleophile (Table 5-2). Such behaviour was observed for palladium-catalyzed chloropalladation[270a], and for the hydropalladation of nonconjugated enynes.[270b] Importantly, only one regioisomer was formed in these reactions, by selective attack of the phenylthiocarbonyl group at carbon-2 of the 1, 3-conjugated enyne (Table 5-2). Both cyclic and acyclic conjugated enynes can be smoothly and regioselectively transformed into the corresponding 2-(phenylthiocarbonyl)-1, 3-dienes in moderate to good yields of isolated pure products via the palladium-catalyzed carbonylative coupling reactions with thiols (Table 5-2). This regiochemical outcome is in excellent accord with the related transition metal-catalyzed addition reactions of alkynes[181k, 181l] and enynes.[245] Note that the stereochemical characteristics of the products were the same as those of the substrates when 1, 2-disubstituted enynes were employed as the starting materials (Table 5-2, entries 6-9 and 12). It further demonstrates that the double bond of the enyne is not affected by the reaction.

The yields and selectivities using arenethiols or alkanethiols as reactants are similar, although the reaction time for arenethiols is less than that for alkanethiols in these carbonylative coupling reactions (Table 5-2, entries 1-4). The higher acidity of aromatic thiols may contribute to this difference in reactivity. Unlike the palladium catalyzed addition of thiols to acetylenes,[181l] attempts to thiocarbonylate enynes with internal triple bonds were unsuccessful (e.g. 2-methyl-1-hepten-3-yne and 3-octen-5-yne were recovered using the standard reaction conditions for 48 h). An enyne bearing a hydroxyl group (**5.36**) in the allylic position afforded a sulfur-substituted lactone (**5.37**) in

74% yield instead of an α,β-unsaturated thioester on reaction with thiophenol and CO (Eq. 5-7).

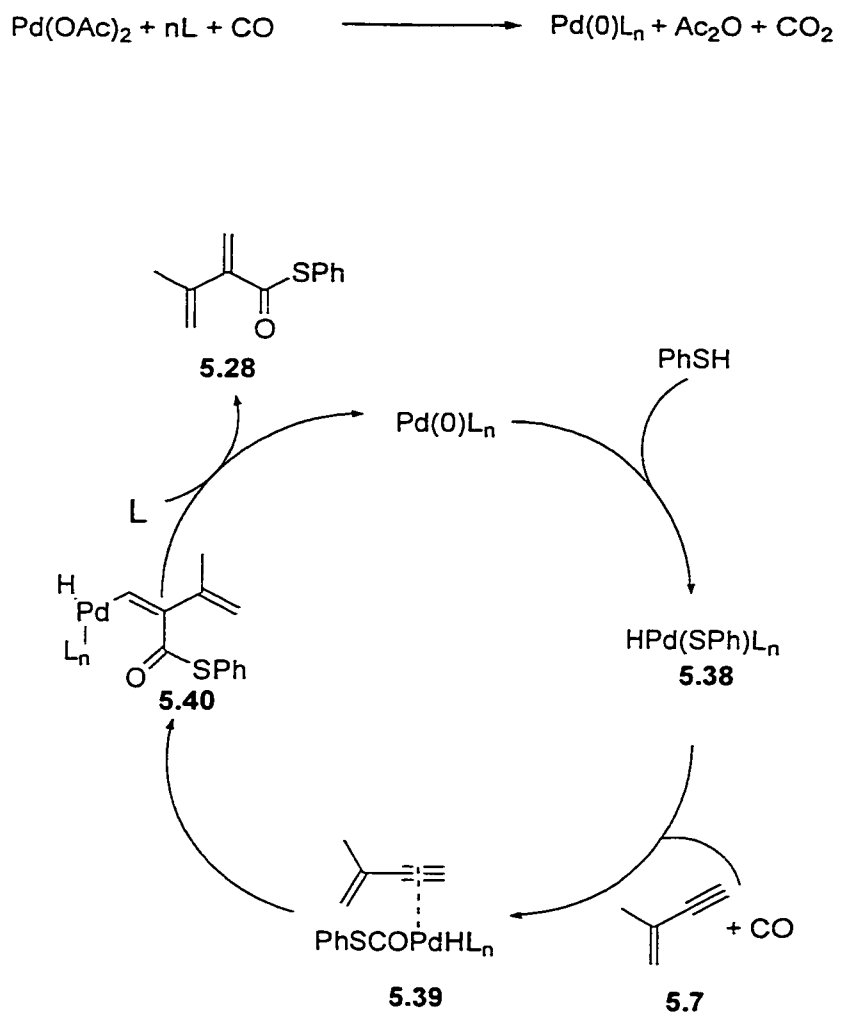


5.36 **5.37** 74% (5-7)

5.3.4 Mechanism

Scheme 5-2 outlines a possible pathway for the palladium-catalyzed thiocarbonylation of conjugated enynes (**5.7** as the example) with thiophenol (**5.19**).

Scheme 5-2. Proposed Mechanism for the Pd-Catalyzed Thiocarbonylation of Enynes



The reaction may proceed by initial palladium acetate reduction to palladium(0),[271] followed by oxidative addition of **5.19** to the palladium(0) complex to form the PhSPdH species **5.38**, which undergoes coordination to the triple bond of the enyne and then insertion of carbon monoxide to form **5.39**. Regioselective intramolecular

acylpalladation of the latter would give complex **5.40**[272] and subsequent reductive elimination would produce the observed 2-(phenylthiocarbonyl) 1, 3-diene and regenerate the palladium(0) catalyst.

5.4 Conclusions

In summary, this research has resulted in the first chemo- and regioselective thiocarbonylation of enynes bearing a terminal triple bond with thiols and carbon monoxide catalyzed by $Pd(OAc)_2$ and dppp to form α,β-unsaturated thioesters in moderate to good yields. This methodology is particularly impressive as a one pot, atom-economical synthesis of 2-(phenylthiocarbonyl) 1, 3-dienes, which are versatile and useful reagents in organic synthesis. For example, they are of genuine value in cycloaddition and Michael addition reactions.

CHAPTER 6

AN ATOM-ECONOMICAL SYNTHESIS OF β,γ-UNSATURATED THIOESTERS: HIGHLY REGIOSELECTIVE THIOCARBONYLATION OF CONJUGATED DIENES VIA PALLADIUM-CATALYZED THREE-COMPONENT COUPLING REACTIONS

6.1 Introduction

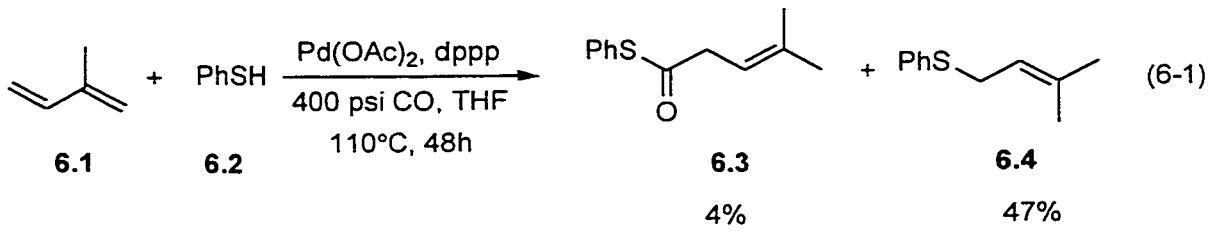
With the assistance of palladium complexes, 1,3-conjugated dienes may be capable of undergoing the reaction with a thiol and carbon monoxide *via* η^3-allylpalladium complexes.[56b] Our interest in the development of palladium-catalyzed thiocarbonylation and atom-economical reactions led us to explore the reaction of dienes, thiols, and carbon monoxide. The main intent here was to extend the thiocarbonylation chemistry, and to provide a convenient one-pot regio- and stereoselective synthesis of β,γ-unsaturated thiol esters.

In addition, the importance and practicality of asymmetric synthesis as a tool to obtain enantiomerically pure or enriched compounds has been fully acknowledged by chemists. Another goal of this research is to develop the first example of asymmetric thiocarbonylation and give a general method to optically active thiol esters.

6.2 Results and Discussion

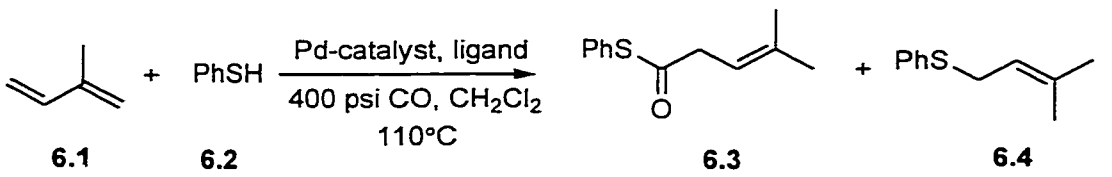
6.2.1 Reaction Conditions for the Thiocarbonylation of 2-Methyl-1,3-Butadiene. Influence of the Catalyst System on the Reaction

Initially, the reaction of 2-methyl-1, 3-butadiene(**6.1**) with thiophenol and carbon monoxide was investigated. The optimal reaction conditions [5 equiv of diene, 1 equiv of thiophenol, 3 mol% [$Pd(OAc)_2$], 6 mol% 1,3-bis(diphenylphosphino)propane (dppp), 400 psi of carbon monoxide, and THF(15 ml per mmol of thiophenol)] employed previously for the thiocarbonylation of conjugated enynes (see Chapter 5) were used to determine the feasibility of the process (Eq. 6-1).



The reaction gave two products **6.3** and **6.4** in yields of 4% and 47%, respectively, with 16% recovery of unreacted thiophenol after 48 hours. Although the yield of the desired product **6.3** was low, we were nevertheless encouraged and examined the reaction in detail under a variety of conditions in an attempt to increase the yield. Several palladium complexes and phosphine ligands were examined as catalytic systems, and the results are summarized in Table 6.1.

Table 6.1. Optimization of Catalyst Systems for the Palladium Catalyzed Thiocarbonylation of Conjugated Dienes.[a]



6.1 **6.2** **6.3** **6.4**

entry	catalyst	ligand	time(h)	yield(%)[b]	
				6.3	**6.4**
1	$Pd(OAc)_2$	dppb	60	12	66
2	$Pd(OAc)_2$	dppp	60	8	74
3	$Pd(OAc)_2$	dppe	72	trace[c]	52
4	$Pd(OAc)_2$	dppf	60	trace[c]	90
5	$Pd(OAc)_2$	PPh_3	60	83	0
6	$Pd(OAc)_2$	PCy_3	48	70	0
7	$Pd(OAc)_2$	PBu_3	48	72	0
8	$Pd(PPh_3)_4$	PPh_3	48	58	0
9	$Pd_2(dba)_3 \cdot CHCl_3$	PPh_3	48	64	0
10[d]	$Pd(OAc)_2$	none	48	0	0

[a] Reaction conditions: thiophenol (1 mmol), 2-methyl-1, 3-butadiene (5 mmol), catalyst (0.05 mmol), Ph_3P, PCy_3, or PBu_3 (0.2 mmol, if used), 1,4-bis(diphenylphosphino)butane (dppb), 1,3-bis(diphenylphosphino)propane (dppp), 1,2-bis(diphenylphosphino)ethane (dppe), or 1,1'-bis(diphenylphosphino)ferrocene (dppf) (0.1 mmol, if used), CH_2Cl_2 (5

mL), 110°C. [b] isolated yield. [c] The presence of the phenylthiocarbonyl group was indicated by an IR of the crude product, but attempts to isolate the carbonylation product were unsuccessful. [d] The reaction gave a deep red and very insoluble solid, which might be a polymer.[181]

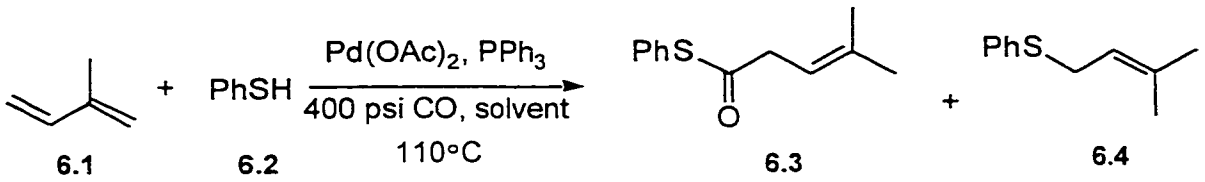
Among the catalysts examined, $[Pd(OAc)_2]$, with 4 equivalents of PPh_3 showed high activity for the catalytic thiocarbonylation reaction (Table 6.1, entry 5), while $[Pd(OAc)_2]$ with dppf (2 equiv) as the added ligand resulted in the 1,4-addition of thiophenol to 2-methyl-1,3-butadiene (Table 6.1, entry 4). Palladium(0) complexes, such as $[Pd(PPh_3)_4]$ and $[Pd_2(dba)_3 \cdot CHCl_3]$, with added triphenylphosphine, were also good catalysts for the thiocarbonylation reaction (Table 6.1, entries 8 and 9). It was observed that the ligands employed played an important role in the selectivity of the reaction (Table 6.1, entries 1-7 and 10). For example, using $[Pd(OAc)_2]$ as the catalyst precursor in the presence of bidentate phosphines gave 1,4-addition as the sole or major pathway (Table 6.1, entries 1-4), while only carbonylative 1, 4-adducts were isolated in the case of monodentate phosphines (Table 6.1, entries 5-7). Under the same conditions, the yield of **6.3** increased by changing the ligand from dppe to dppp or dppb. These results are in accord with the observation by van Leeuwen and co-workers that the rate of carbon monoxide insertion into a Pd-C bond is faster for alkylpalladium bisphosphine complexes containing a flexible metal ligand chelate ring.[195] In addition to triphenylphosphine, PCy_3 and PBu_3 can also be used for this reaction, but they are inferior to PPh_3 (Table 6.1, entries 5-7). When the reaction was performed without any ligand, a deep red precipitate

was formed, and there was 68% and 47% recovery of 2-methyl-butadiene and thiophenol, respectively.[181]

6.2.2 Solvent Optimization

The reaction is sensitive to the solvent as shown by the results in Table 6.2. As noted already, THF was not an ideal solvent for the thiocarbonylation of **6.1** (Eq. 6-1).

Table 6.2. Solvent Effects on the Palladium-Catalyzed Reaction of 2-Methyl-butadiene with Thiophenol and Carbon Monoxide[a]



6.1 6.2 6.3 6.4

entry	solvent	time(h)	isolated yield(%)	
			6.3	**6.4**
1	THF	48	27	52
2	CH_3CN	60	0	78
3	Benzene	60	trace[b]	64[c]
4	DME	48	47	18
5	Et_2O	48	64	20
6	CH_2Cl_2	60	83	0

[a] Reaction conditions: 2-Methyl-1,3-butadiene (5 mmol), Thiophenol (1 mmol), $[Pd(OAc)_2]$ (0.05 mmol), PPh_3 (0.2 mmol), 400 psi of carbon monoxide, solvent (5 mL), 110°C. [b] Phenylthiocarbonyl group was identified by IR of the crude product, but attempts to isolate the carbonylation product were unsuccessful. [c] 15% of thiophenol was recovered.

When $[Pd(OAc)_2]$ with PPh_3 was used as the catalyst precursor, the reaction in THF gave the thioester (**6.3**) and sulfide (**6.4**) in 27% and 52% yield, respectively (Table 6.2, entry 1). The reaction worked very well in CH_2Cl_2, and afforded **6.3** as the sole product in 83% isolated yield (Table 6.2, entry 6); however, under the same conditions, using CH_3CN or benzene as the solvent, **6.4** was formed as the major or the sole product (Table 6.2, entries 2 and 3). Reactions in 1,2-dimethoxyethane (DME) and diethyl ether gave a mixture of **6.3** and **6.4** (Table 6.2, entries 4 and 5).

On the basis of these results, the reaction of a variety of conjugated dienes and thiols were performed and the results are summarized in Tables 6.3, 6.4, and 6.5.

6.2.3 Thiocarbonylation of 2-Methyl-1,3-Butadiene (6.1) Using Various Thiols

The results in Table 6.3 indicate the scope and limitations of the palladium-catalyzed carbonylative coupling reaction of **6.1** and representative thiols.

Table 6.3. Palladium-Catalyzed Reaction of Isoprene with Thiols and Carbon Monoxide[a]

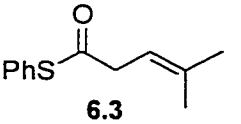
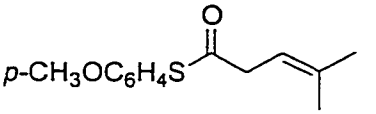
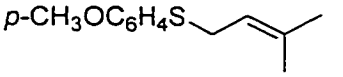
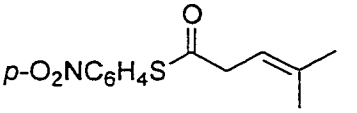
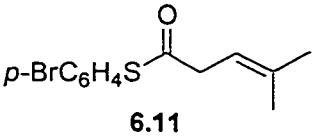
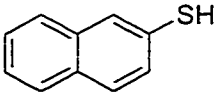
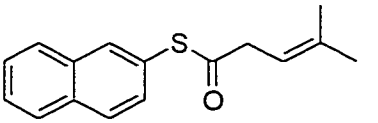
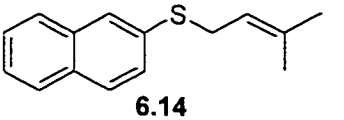
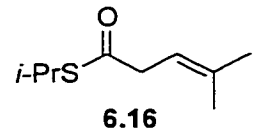
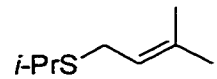
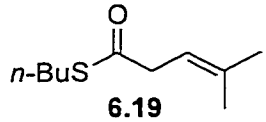
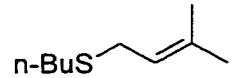
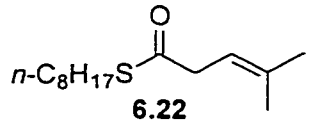
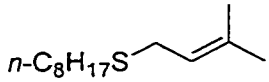
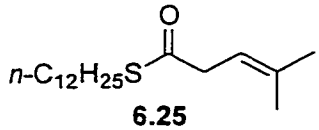
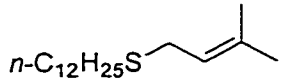
entry	thiol	time(h)	product	isolated yield(%)
1	PhSH **6.2**	60	 **6.3**	83
2	*p*-CH_3O-C_6H_4SH **6.5**	72	 **6.6**	60
			 **6.7**	18
3	*p*-O_2N-C_6H_4SH **6.8**	48	 **6.9**	84
4	*p*-Br-C_6H_4SH **6.10**	60	 **6.11**	80
5	 **6.12**	60	 **6.13**	18
			 **6.14**	20

Table 6.3. (continued)

entry	thiol	time(h)	product	isolated yield(%)
6	*i*-PrSH **6.15**	84	 **6.16**	42
			 **6.17**	36
7	*n*-BuSH **6.18**	84	 **6.19**	45
			 **6.20**	23
8	n-$C_8H_{17}SH$ **6.21**	120	 **6.22**	17
			 **6.23**	54
9	n-$C_{12}H_{25}SH$ **6.24**	128	 **6.25**	trace
			 **6.26**	58

[a] Reaction conditions: 2-Methyl-1, 3-butadiene (10 mmol), thiol (2 mmol), $[Pd(OAc)_2]$ (0.1 mmol), PPh_3 (0.4 mmol), 400 psi of carbon monoxide, CH_2Cl_2 (10 mL).

In most cases, thiophenols were found to work more effectively than alkanethiols. For example, **6.1** reacted with thiophenol (**6.2**), *p*-nitrobenzenethiol (**6.5**), and *p*-bromobenzenethiol (**6.10**), repectively, only affording the carbonylative 1,4-addition products **6.3**, **6.9**, and **6.11** in similar yields (Table 6.3, entries 1, 3, and 4); however, the corresponding reaction with alkanethiols always gave mixtures of thiocarbonylation and simple 1,4-addition products (Table 6.3, entries 6-9). Reactions involving alkanethiols took longer to complete than those with arenethiols. The reaction was rather sensitive to both the acidity and the effective bulk (steric factors) of the thiols. For example, **6.5** (*p*-methoxybenzenethiol), an arenethiol with an electron-donating *p*-methoxy group, and **6.8** (*p*-nitrobenzenethiol), an arenethiol with an electron-withdrawing group show somewhat different behaviour in this reaction. Using **6.5** as the substrate gives a mixture of **6.6** (60%yield) and **6.7** (18% yield) after a period of 72h (Table 6.3, entry 2), whereas **6.8** gives only the carbonylative 1,4-addition product in 80% yield (Table 6.3, entry 3) after a period of 48h. Reactions with arenethiols, such as 2-naphthalenethiol (**6.12**), gave an approximately 1:1 mixture of the carbonylation **6.13** and 1,4-addition products (**6.14**) (Table 6.3, entry 5). In the case of alkanethiols, it was observed that increasing the length of the alkyl group caused the thiols to become less reactive, with a mixture of addition and carbonylative addition products formed in all the cases (Table 6.3, entries 7-9). When cyclohexyl mercaptan was employed as the substrate, no products were obtained at all.

6.2.4 Thiocarbonylation of Acyclic Conjugated Dienes Using Thiophenol(6.2)

A series of acyclic conjugated dienes were thiocarbonylated smoothly by $[Pd(OAc)_2]$ and PPh_3 to give the corresponding β, γ-unsaturated thioesters in good to excellent yields (Table 6.4).

Table 6.4. Palladium-Catalyzed Thiocarbonylation of Acyclic Conjugated Dienes with Thiophenol and CO[a]

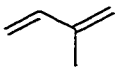
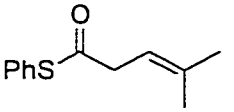
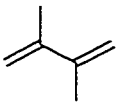
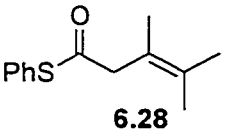
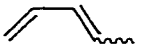
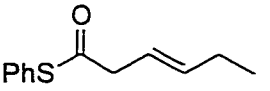
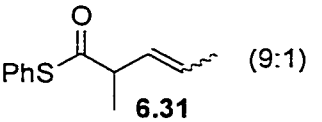
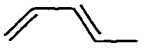
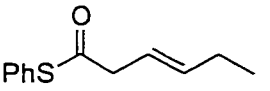
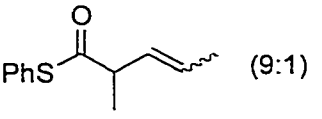
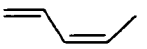
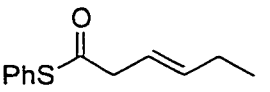
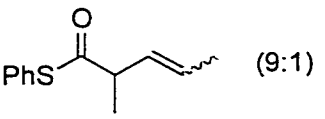
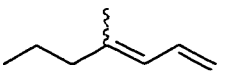
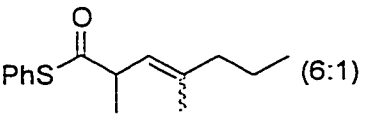
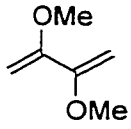
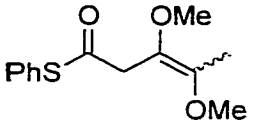
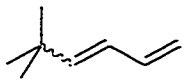
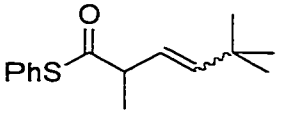
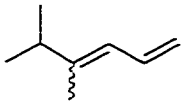
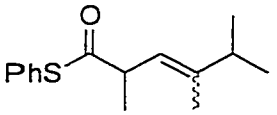
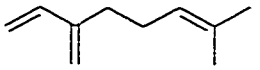
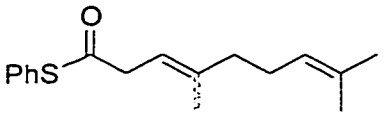
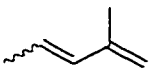
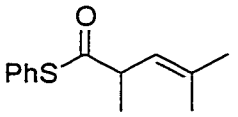
entry	diene	product (*E*/*Z*)[b]	isolated yield(%)
1	 **6.1**	 **6.3**	83
2	 **6.27**	 **6.28**	94
3	 **6.29**	 **6.30**	15
		 (9:1) **6.31**	64
4	 **6.32**	 **6.30**	22
		 (9:1) **6.31**	59
5	 **6.33**	 **6.30**	17
		 (9:1) **6.31**	65
6	 **6.34**	 (6:1) **6.35**	69

Table 6.4. (continued)

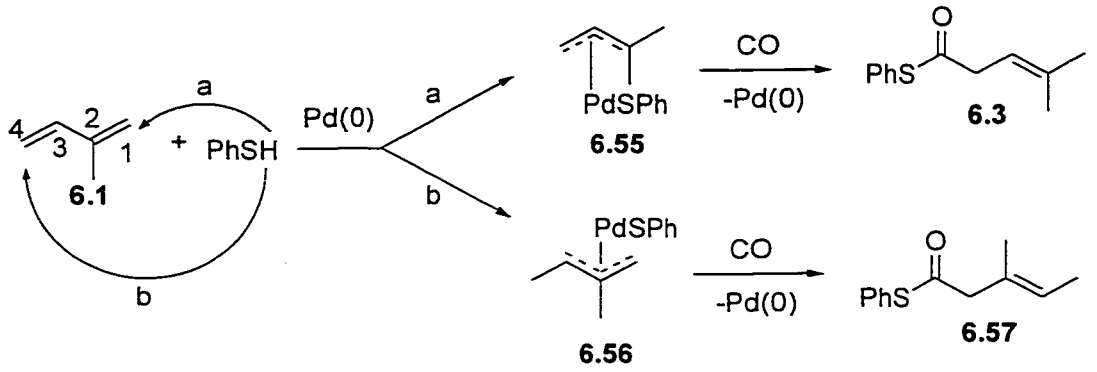
entry	diene	product (*E*/*Z*)[b]	isolated yield(%)
7	 **6.36**	 (11:1) **6.37**	58
8	 **6.38**	 (9:1) **6.39**	89
9	 **6.40**	 (10:1) **6.41**	70
10	 **6.42**	 (19:1) **6.43**	91
11	 **6.44**	 **6.45**	86

[a] Reaction conditions: Diene (10 mmol), thiophenol (2 mmol), [$Pd(OAc)_2$] (0.1 mmol), PPh_3 (0.4 mmol), CO (400 psi), CH_2Cl_2 (10 mL), reaction time (60h), reaction temperature (110 °C). [b] The ratio of *E* to *Z* was determined by ^1H NMR.

α, β-Unsaturated thioesters were not detected among the products either before or after purification, although it is well known that isomerizations of β, γ-unsaturated thioesters to α, β-unsaturated isomers might occur.[197] Importantly, the reaction exhibits excellent regioselectivity in all cases. Depending on the structural characteristics of the

dienes employed, the reaction could selectively afford carbonylative 1,4- or 1,2- addition products. Usually, the monosubstituted and 2,3-substituted dienes reacted with thiophenol (**6.2**) and CO to afford carbonylative 1,4-addition products (Table 6.4, entries 1-5, 7, 10, and 11), while 1,1-disubstituted dienes such as **6.34** and **6.40,** as well as 1-*t*-butyl-substituted butadiene (**6.38**) underwent thiocarbonylation to form products of carbonylative 1,2-addition (Table 6.4, entries 6, 8, and 9). A substitutent at the C-2 position of the dienes was found to direct the H of **6.2** exclusively to the C-1 position, and the phenylthiocarbonyl group to the C-4 position of the molecule, although the reaction might give two isomeric carbonylative 1,4- adducts. The regioselectivity can be explained by the nature of the diene, and the stability of the η^3-allylpalladium complex. For example, in the case of **6.1** (Scheme 6-1), the H of **6.2** can attack either at C-1 or C-4 to form two isomeric π-allylpalladium complexes **6.55** or **6.56**,

Scheme 6-1 Palladium(0)-Catalyzed Thiocarbonylation of 6.1

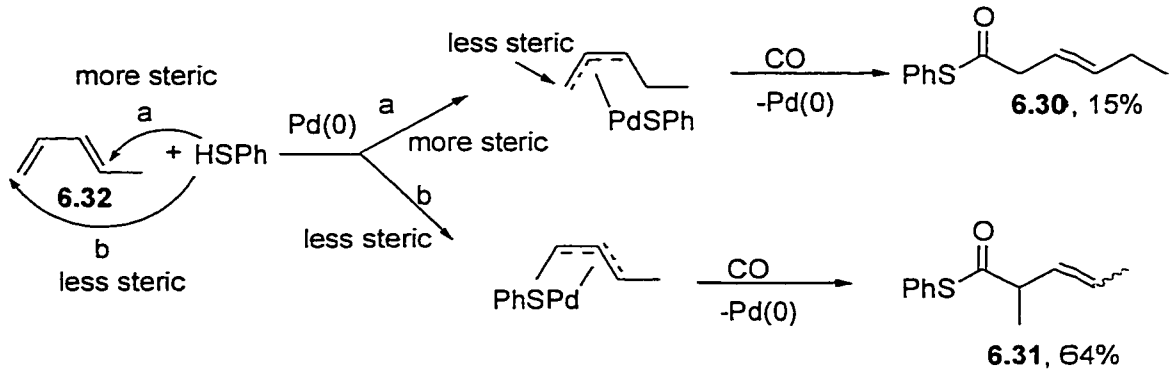


which would then give thioester **6.3** or **6.57**, respectively. With an electron-donating group in the C-2 position, C-1 is more protophilic than C-4.[273] Furthermore, η^3-

allylpalladium complex **6.55** is known to be more stable than **6.56**.[274] Therefore, it can be envisaged that the reaction of **6.1** with **6.2** and CO can only occur by path (a) to give the thioester **6.3** as the sole product.

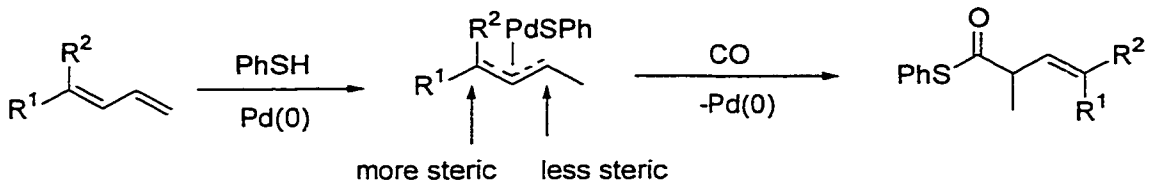
It was observed that the regioselectivity decreased when a substrate with a substituent at C-1 of the diene was employed in this reaction (Table 6.4, entries 3-5). It is probable, therefore, that during the reaction, two isomeric η^3-allylpalladium complexes were formed (Scheme 6-2, illustrated for piperylene). The ratio of the two products (**6.30** and **6.31**) may depend on steric factors.

Scheme 6-2 Palladium(0)-Catalyzed Thiocarbonylation of 6.32



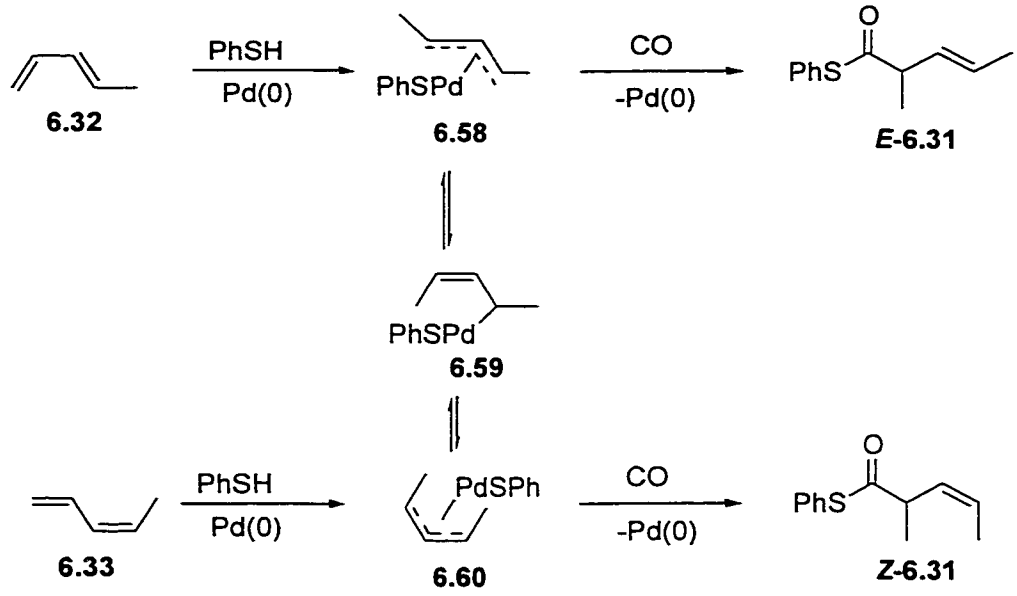
For 1,1-disubstituted dienes, the phenylthiocarbonyl group exclusively attacked the least substituted terminal allylic carbon of the η^3-allylpalladium complexes, affording the carbonylative 1,2-addition products (Scheme 6-3).

Scheme 6-3 Palladium(0)-Catalyzed Thiocarbonylation of a 1,1-Disubstituted Butadiene



Fine stereoselectivity for the β,γ-unsaturated thioesters resulted using some dienes as substrates. The thermodynamically more stable (*E*)-isomers were obtained preferentially, irrespective of the stereochemistry of the starting reactants (Table 6.4, entries 3-10). For example, homogeranic acid, which is a precursor of tetrahydroastinidiolides,[275] can be obtained in 19:1 *E*/*Z* stereoselectivity from myrcene (**6.42**) (Table 6.4, entry 10). Note that double thiocarbonylation of the triene did not occur. It is interesting to note that the thiocarbonylation reactions of (*E*)- and (*Z*)-piperylene (**6.32** and **6.33**) afford a 9:1 mixture of (*E*)- and (*Z*)-phenyl 2-methyl-3-pentenethioate (**6.31**), independent of the stereochemistry of the starting dienes (Table 6.4, entries 4 and 5). It is likely that the variation of the stereochemistry is due to the η^3-η^1-η^3 isomerization of the intermediate π-allylpalladium complexes **6.58** and **6.60** (Scheme 6-4),[198b] with preference for the thermodynamically more stable (*E*)-isomer product.

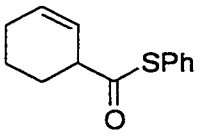
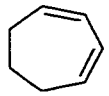
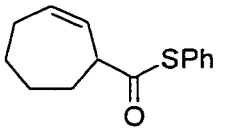
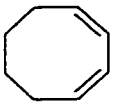
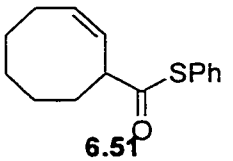
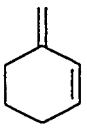
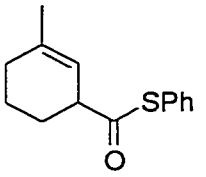
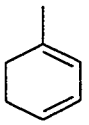
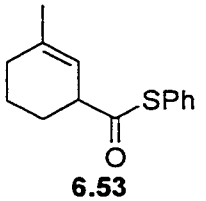
Scheme 6-4 Palladium(0)-Catalyzed Thiocarbonylation of 6.32



6.2.5 Thiocarbonylation of Cyclic Dienes Using Thiophenol (6.2)

Table 6.5 shows the results of the $[Pd(OAc)_2]/PPh_3$ catalyzed thiocarbonylation of PhSH with several cyclic conjugated dienes.

Table 6.5. Palladium-catalyzed Thiocarbonylation of Cyclic Conjugated Dienes[a]

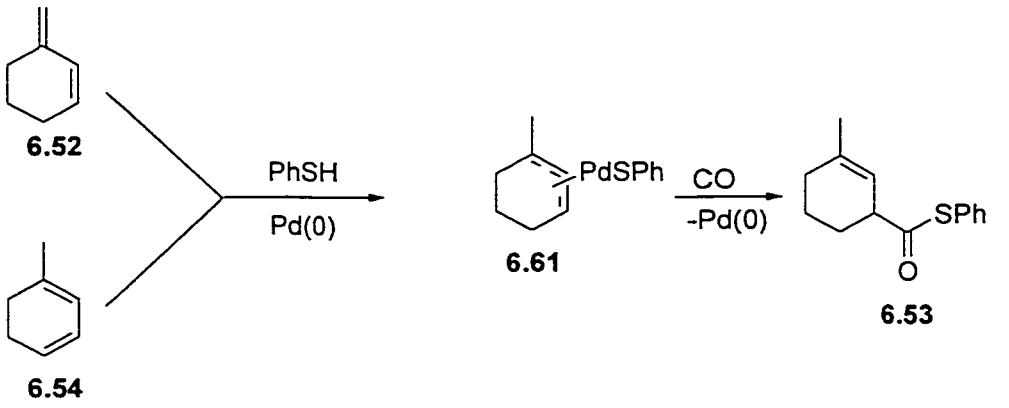
entry	diene	reaction time(h)	product	isolated yield(%)
1	 **6.46**	48	 **6.47**	84
2	 **6.48**	72	 **6.49**	86
3	 **6.50**	144	 **6.51**	61
4	 **6.52**	48	 **6.53**	75
5	 **6.54**	48	 **6.53**	67

[a] Reaction conditions: Cyclic diene (10 mmol), thiophenol (2 mmol), $Pd(OAc)_2$ (0.1 mmol), PPh_3 (0.4 mmol), reaction temperature 110 °C, CH_2Cl_2 (10 mL).

Consistent with the pattern found for acyclic analogues, the regioselectivity of the reaction employing cyclic dienes was high. While 1,4- and 1,2-thiocarbonylative adducts are structurally identical when unsubstituted cyclic dienes were used as substrates (Table

6.5, entries 1-3), the substituted cyclic dienes afford 1,4- or 1,2-products, depending on the substrates. For example, only the 1,4-product was formed when *exo*-methylene cyclohexene (**6.52**) was the reactant (Table 6.5, entry 4). In contrast, the 1,2-product was obtained in the case of 1-methyl-1,3-cyclohexadiene (**6.54**) (Table 6.5, entry 5). It is conceivable that the reactions of **6.52** and **6.54** proceed through the same intermediate (Scheme 6-5), and this could be the reason why both reactions gave identical products.

Scheme 6-5 Palladium(0)-Catalyzed Thiocarbonylation of 6.52 and 6.54



6.2.6 Asymmetric Thiocarbonylation of Conjugated Dienes

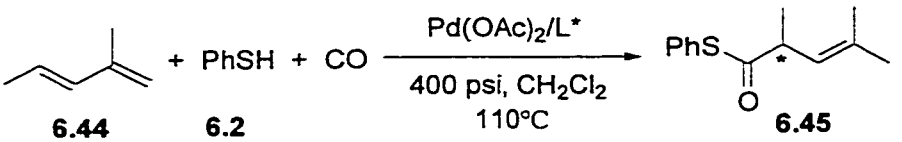
Despite the great potential of asymmetric carbonylation reactions and the extensive effort devoted to this transformation in recent years,[7, 276] the asymmetric version of thiocarbonylation has never been reported, and the development of efficient asymmetric carbonylation reactions is still viewed as one of the most challenging problems in asymmetric catalysis. We reasoned that the addition of appropriate chiral ligands could, in principle, lead to the formation of optically active thiol esters (Figure 6-

1) in reasonable enantiomeric excess. We also recognized the challenge having the chirality created at a center which is both allylic and alpha to the thiol ester functionality.

Figure 6-1 Optically Active Thioesters

Enantiometrically enriched unsaturated thiol esters should be interesting synthetic building blocks. For example, utilization of **A** and **B** in asymmetric cycloaddition,[166] peptide synthesis,[264] and natural product synthesis[153c] can be envisioned. In this section, we describe the first examples of asymmetric thiocarbonylation of dienes.

Table 6-6 Palladium-Catalyzed Asymmetric Thiocarbonylation of 6.44 with 6.2 and CO Using Various Chiral Phosphine Ligands[a]



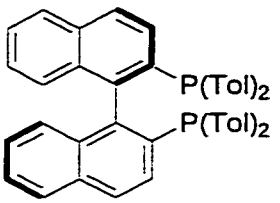
6.44 **6.2** **6.45**

entry	ligand	yield (%)	e.e (%)[b]	$[\alpha]^{22}_D$ in $CHCl_3$[c]
1	*R*-Tol-BINAP	77	47	-19.8 (c 1.92)
2	*R*-BINAP	56	42	-18.2 (c 2.03)
3	*R*-PROPHOS	12	17	-14.6 (c 2.06)
4	*S,S*-BDPP	31	76	+35.7 (c 1.68)
5	*R,R*-DIOP	71	89	-48.3 (c 1.06)
6	*S,S*-DIOP	67	87	+44.4 (c 1.12)
7	*R,R*-Boc-PYRPHOS	18	56	-24.2 (c 2.01)
8	(-)-Me-DuPHOS	7	43	-18.7 (c 1.97)

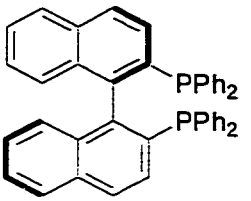
[a] Reaction conditions: thiophenol (1 mmol), 2-methyl-1,3-pentadiene (2 mmol), $Pd(OAc)_2$ (0.05 mmol), ligand (0.1 mmol), CH_2Cl_2 (5 mL), 400 psi of CO, 110°C.

[b] Determined by chiral GC installed with Supelco β-Dex 120 column (30 m).

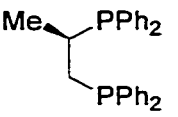
[c] Measured on a Perkin-Elmer polarimeter in a 10 cm cell at 22°C.



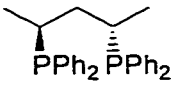
(*R*)-Tol-BINAP



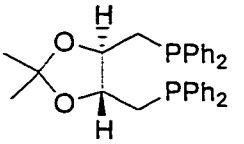
(*R*)-BINAP



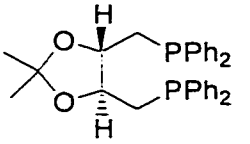
(*R*)-PROPHOS



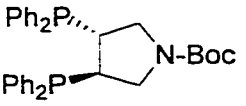
(*S*, *S*)-BDPP



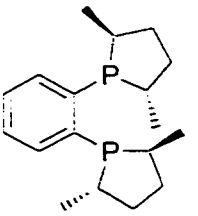
(*R*, *R*)-DIOP



(*S*, *S*)-DIOP

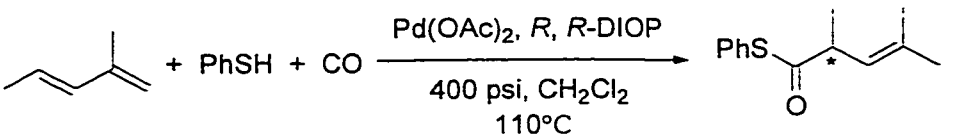


(*R*, *R*)-Boc-PYRPHOS



(-)-Me-DuPHOS

We started our investigation by performing the thiocarbonylation reaction of **6.44** and **6.2** under 400 psi of carbon monoxide in CH_2Cl_2 in the presence of $Pd(OAc)_2$ and (*R*, *R*)-DIOP. After 60 hours of the reaction at 110°C, *S*-phenyl 2,4-dimethyl-3-pentenethioate (**6.45**) was isolated in 71% yield and in 89% ee as determined by chiral GC (Eq. 6-2).



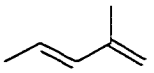
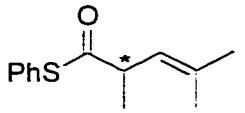
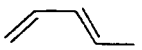
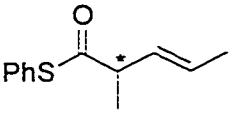
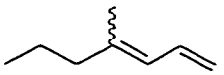
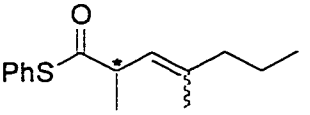
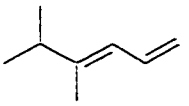
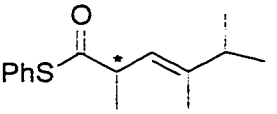
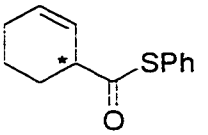
(6-2)

6.44 **6.2** **6.45**

Other commercially available chiral ligands such as R-Tol-BINAP (72% yield, 47% ee), *R*-BINAP (56% yield, 42% ee), *R*-PROPHOS (12% yield, 17% ee), *S*, *S*-BDPP (31% yield, 76% ee), *R*, *R*-Boc-PYRPHOS (18% yield, 56% ee), and (-)-Me-DuPHOS (7% yield, 43% ee) were less effective in terms of asymmetric induction, whereas *S*, *S*-DIOP (67% yield, 87% ee) gave almost the same yield and %ee as that obtained by using *R*, *R*-DIOP but, as anticipated, for the other enantiomer (Table 6-6). The effect of varying solvents has been examined as well. The reaction works well in CH_2Cl_2 (71% yield, 89% ee) and THF (63% yield, 85% ee), but less so in benzene (34% yield, 67% ee) and diethyl ether (47% yield, 54% ee).

A series of β,γ-unsaturated thiol esters were similarly synthesized, usually in good optical purity, using the Pd(0)-DIOP catalyst system which was generated *in situ* by the reaction of 5 mol% of $Pd(OAc)_2$ with 2 equiv of bidentate ligand [(R, R)-DIOP] relative to palladium. The results are shown in Table 6-7.

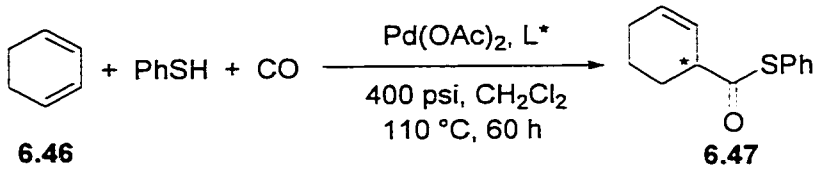
Table 6-7 Asymmetric Thiocarbonylation of Various 1, 3-Conjugated Dienes with Thiophenol and CO in the Presence of $Pd(OAc)_2$-(R, R)-DIOP as the Catalyst[a]

entry	diene	product (*E*/*Z*)	yield (%)	ee (%)	$[a]^{22}_D$ in $CHCl_3$
1	 **6.44**	 **6.45**	71	89	-48.37 (c 1.06)
2	 **6.29**	 (14:1) **6.31**	38	6	-3.78 (c 1.38)
3	 **6.34**	 (19:1) **6.35**	72	82	-53.31 (c 1.42)
4	 **6.40**	 (16:1) **6.41**	46	84	-53.08 (c 1.18)
5	 **6.46**	 **6.47**	64	10	-12.24 (c 1.52)

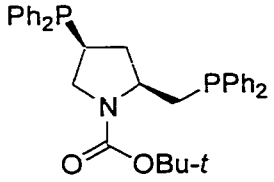
[a] Reaction conditions: Thiophenol (1 mmol), diene (2 mmol), $Pd(OAc)_2$ (0.05 mmol), (R, R)-DIOP (0.1 mmol), 400 psi of carbon monoxide, CH_2Cl_2 (5 mL), 110 °C, 60 h.

Steric factors may play a key role in the asymmetric thiocarbonylation reaction. The monosubstituted diene 1,3-pentadiene (**6.29**), which has a methyl group at C-1, underwent carbonylative coupling in 6% ee (Table 6-7, entry 2), while reactions of disubstituted dienes such as the 1,1-disubstituted dienes **6.34** (82% ee, entry 3 in Table 6-

7) and **6.40** (84% ee, entry 4 in Table 6-6) as well as 1,3-disubstituted diene **6.44** (89% ee, entry 1 in Table 6-7) gave higher %enantiomeric excess. Although the asymmetric thiocarbonylation of acyclic dienes works well, extension of the reaction to the cyclic substrate **6.46** gives very poor results (only 10% ee, entry 5 in Table 6-7). Attempts to improve the stereoselectivity of the reaction of cyclohexadiene by changing chiral ligands were met with no success (Eq. 6-3).



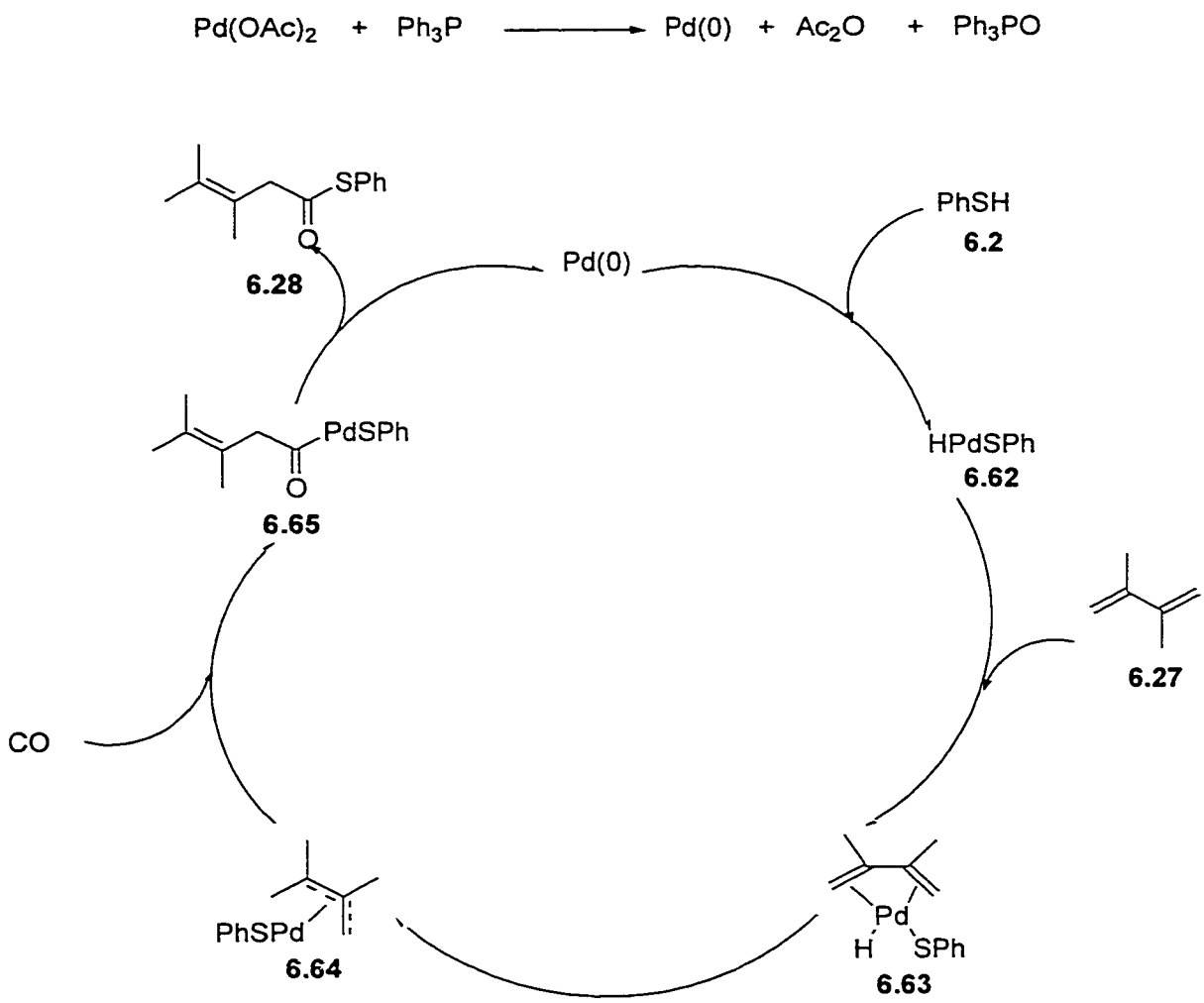
6.46 **6.47** (6-3)

chiral ligand	yield (%)	ee (%)
R, *R*-BDPP	23	0
R-BINAP	69	7
R-PROPHOS	14	2
 (-)-BPPM	64	6

6.2.7 Mechanistic Aspects

A possible pathway for the palladium-catalyzed thiocarbonylation of 1,3-conjugated dienes (using **6.27** as the example) with thiophenol (**6.2**) is outlined in Scheme 6-6.

Scheme 6-6 A Possible Mechanism for the Thiocarbonylation of Dienes



It is well known that Pd(0) is readily formed *in situ* by the reduction of [$Pd(OAc)_2$] in the presence of phosphine ligands.[271] Oxidative addition of **6.2** to palladium(0) can then give the thiopalladium complex (**6.62**),[181d] which can coordinate with the diene to form a Pd-η^4-diene complex **6.63**.[277] Intramolecular hydropalladation would afford the η^3-allylpalladium complex **6.64**. Insertion of CO into the Pd-S bond of **6.64** or into the Pd-C bond of the σ-allyl analog of **6.64,** followed by regioselective intramolecular transfer would afford the acylpalladium complex **6.65**.[272] Reductive elimination of **6.65** would form the thioester (**6.28**), with regeneration of the palladium catalyst.

6.2.8 A Possible Explanation for the Enantioselectivity of the Asymmetric Thiocarbonylation Reactions

Although the source of the enantioselectivity is complicated by the possibility that one or more steps in the catalytic cycle may be the enantiodiscriminating step(s),[278] it is generally accepted that in the attack of CO on the intermediate cationic (η^3-allyl)Pd(II) complex,[279] the repulsive interactions in the transition states[280] between the chiral ligand and the organic entity bound to the Pd center are an important factor which can largely determine the selectivity.

The working and cartoon models for *R,R*-DIOP utilized herein are depicted in Figure 6-2, which derive from the ground-state structure of the ligand-palladium-π-allyl complex and Trost's hypothesis regarding the structural features required for creating chiral space and molecular modeling.[281]

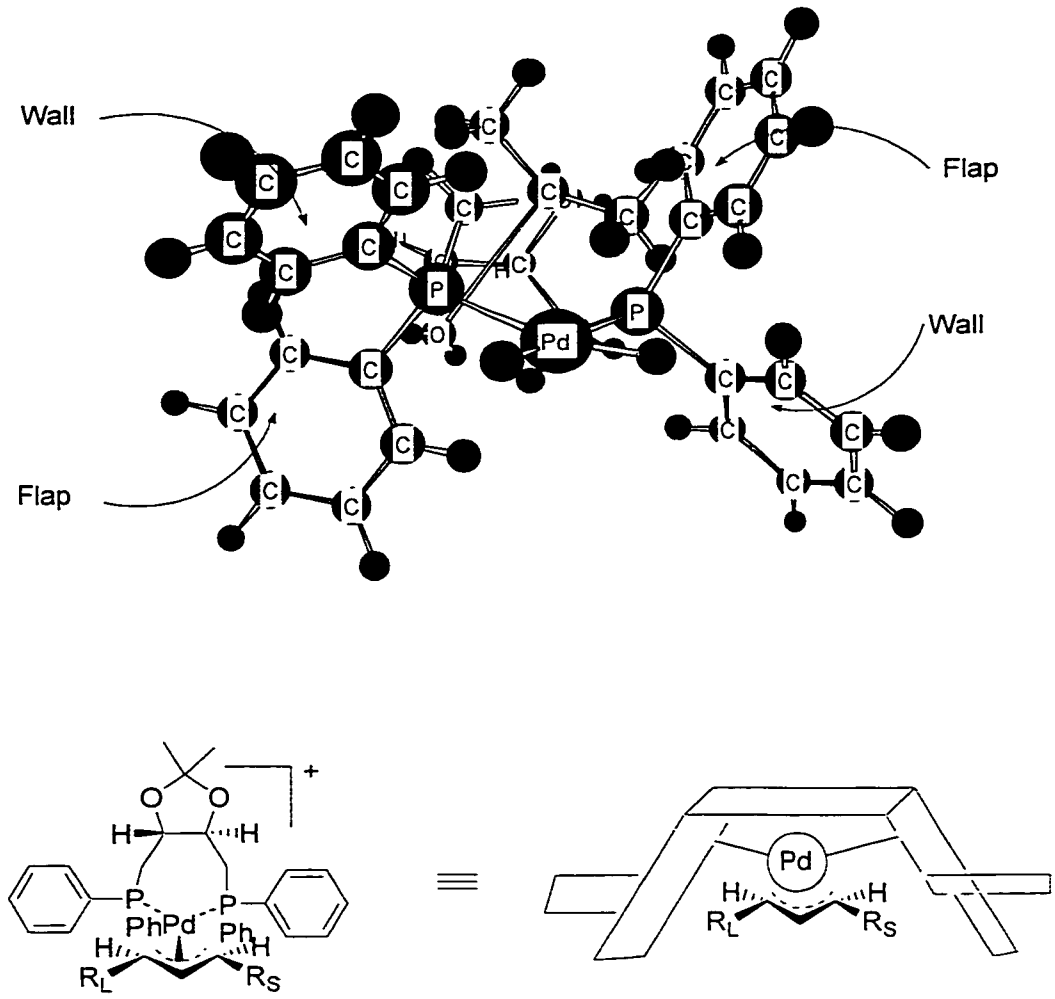


Figure 6-2. Trost's Model of Chiral Pocket and Cartoon Representation of Complex Derived from R, R-DIOP

In this model, the walls represent the chiral space created by the propeller-like array of the phenyl rings; the raised flaps represent the phenyls which lie in a plane approximately perpendicurar to the allyl, while the lowered flaps represent phenyls which are somewhat parallel to the allyl.[181e]

When a prochiral diene was employed, intermediates **6.67** and **6.68** could be formed, which could rapidly racemize *via* π-σ-π mechanism.[198] Insertion of CO into both intermediates resulted in the formation of both stereoisomers, respectively (Figure 6-3).

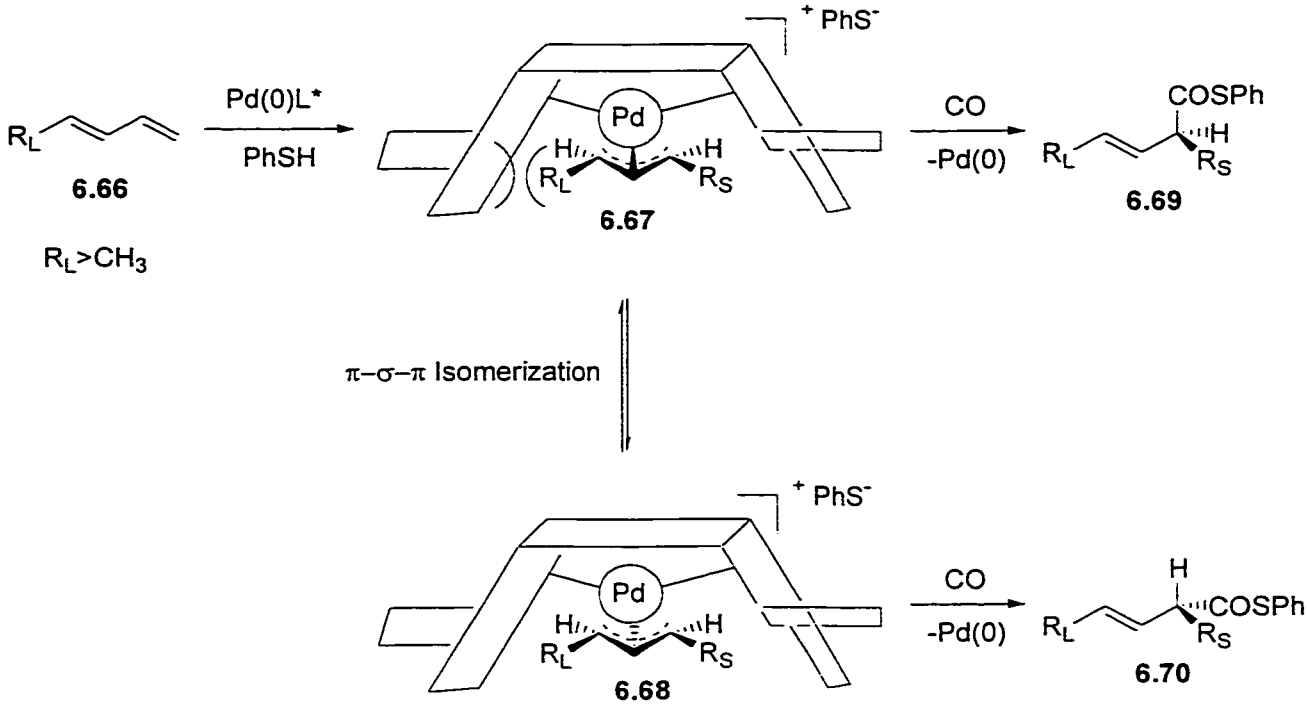


Figure 6-3. Predicted Path for Asymmetric Thiocarbonylation of Chiral Precursor for Reaction Using R, R-DIOP

The enantiodifferentiation step in this asymmetric thiocarbonylation was presumed to be the CO insertion step. Good enantioselectivity was presumably attributed to the differentiation of allyl complexes. Molecular modeling calculations indicate that the difference between these two π-allyl complexes, **6.67** and **6.68**, is approximately 3.1 kcal/mol,[281e, 282] which might be due to greater steric interaction between the "wall" and

the sunstitutent, R_L. To some extent that the transition-state energy for the insertion of CO into **6.68** is lower than that for CO insertion into **6.67**, thus, one of the intermediates reacted significantly faster than the other and consequently gave the major enantiomer. The magnitude of the %ee might depend on the relative rate of the CO insertion and π-σ-π isomerization.

In the case of cyclohexadiene as the substrate, the stereoselectivity of the reaction was dramatically decreased, presumably because of the symmetric structure of the possible intermediate. In this case, the R_L and R_S are exactly the same and carbon monoxide can insert from both sides to result in decreasing the enantioselectivity of the reaction.

6.3 Conclusions

In summary, a highly effective catalytic system ([$Pd(OAc)_2$]-PPh_3) has been developed for the carbonylative coupling reaction of conjugated dienes, thiols, and carbon monoxide to form the corresponding β,γ-unsaturated thioesters. These reactions take place in a highly regioselective manner, depending on the steric characteristics and stability of the proposed η^3-allylpalladium complex. Furthermore, the reactions exhibit good to excellent stereoselectivity.

In addition, we developed the first asymmetric thiocarbonylation of prochiral 1,3-conjugated dienes with thiophenol and CO for the synthesis of optically active thiol

esters. Employing *R*,*R*-DIOP as the ligand, the catalytic asymmetric protocol occurred in up to 89% ee.

CHAPTER 7

REGIOSELECTIVE CARBONYLATIVE HETEROANNULATION OF *O*-IODOTHIOPHENOLS WITH ALLENES AND CARBON MONOXIDE CATALYZED BY A PALLADIUM COMPLEX: A NOVEL AND EFFICIENT ACCESS TO THIOCHROMAN-4-ONE DERIVATIVES

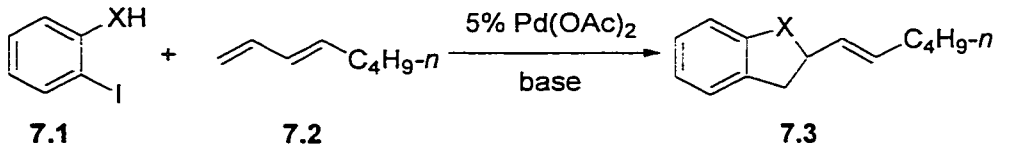
7.1 Introduction: Palladium-Catalyzed Synthesis of Heterocycles

Palladium-catalyzed heteroannulations are now emerging as a unique, powerful, and versatile synthetic approach toward a variety of heterocycles. An advantage of this methodology is the ability to modulate selectivity for ring formation. Reducing the number of steps in the preparation of useful heterocycles can be easily achieved as well as good stereo- and regio-control. The reaction can be carried out under milder conditions when compared with conventional methods. Moreover, the palladium catalyst provides accessibility to some heterocycles which cannot be synthesized by other methods.

Here, we wish to give some examples including the palladium-catalyzed intra- and intermolecular cyclization of unsaturated substrates such as 1,3- and 1,2-dienes and alkynes with functionally substituted aromatic or vinyl iodides or bromides.

7.1.1 Heteroannulation of 1,3-Dienes

Larock and co-workers have extensively studied the heteroannulation of a wide range of cyclic and acyclic 1,3-dienes using appropriately functionalized aryl iodides and 5% of a suitable palladium catalyst (Eq. 7-1).[283]



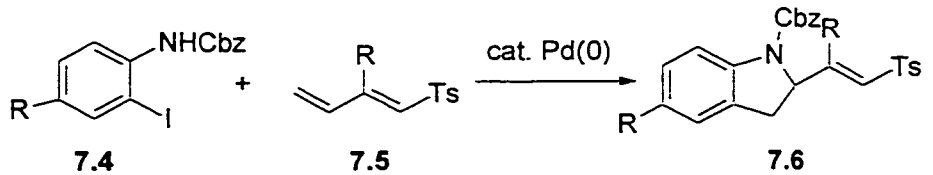
(7-1)

7.1 **7.2** **7.3**

X	yield (%)
O	75
CH_2O	56
NAc	63
NTs	84
CH_2NTs	81

o-Iodophenols afford 2,3-dihydrobenzofuranes, *o*-iodobenzylic alcohols produce benzopyrans, and *o*-iodoaniline as well as *o*-benzylic amine derivatives generate the corresponding nitrogen-containing heterocycles.

Recently this chemistry has been developed into a convenient approach to sulfone-substituted indolines (**7.6**) (Eq. 7-2).[284]

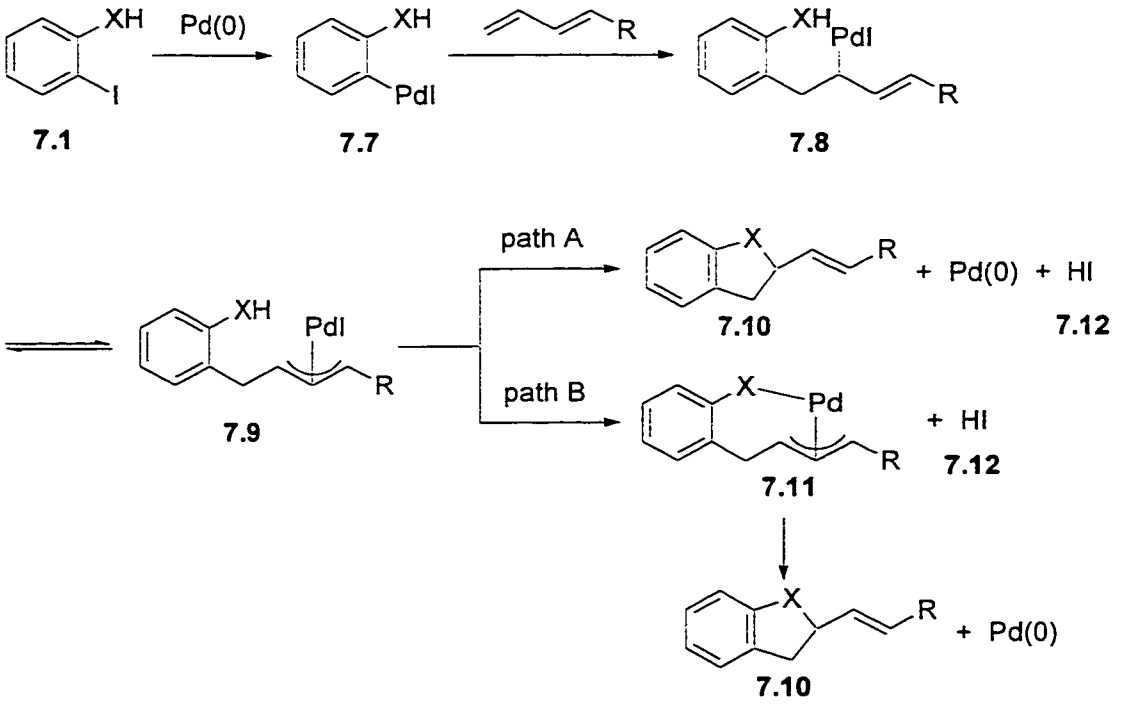


(7-2)

7.4 **7.5** **7.6**

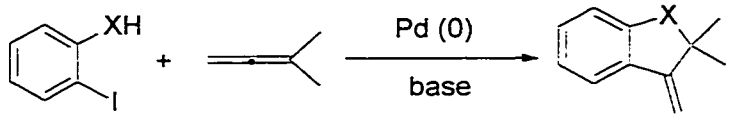
The annulation of 1,3-dienes is believed to proceed by (1) reduction of the palladium(II) to Pd(0), which is the actual catalyst, (2) oxidative addition of aryl halide (**7.1**) to Pd(0), (3) arylpalladation of the carbon-carbon double bond to initially produce a σ-allylpalladium intermediate (**7.8**), which is converted to the more stable η^3-allylpalladium complex (**7.9**), and (4) nucleophilic displacement of palladium by the internal nucleophile (Scheme 7-1).[285]

Scheme 7-1 The Annulation of 1,3-Dienes



7.1.2 Heteroannulation of 1,2-Dienes

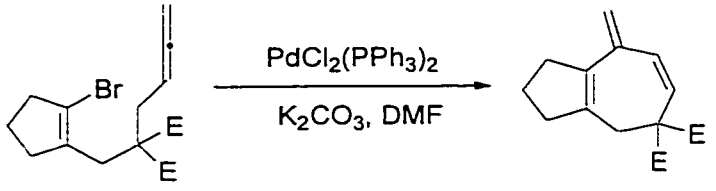
1,2-Dienes have been found to be more easily annulated by a wider variety of nucleophiles than 1,3-dienes. For example, phenols, alcohols, tosylamides and carbanions have been all successfully employed for the heteroannulation of 1,2-dienes to afford the corresponding products in good yield (Eq. 7-3).[286]



7.1 **7.13** **7.14** (7-3)

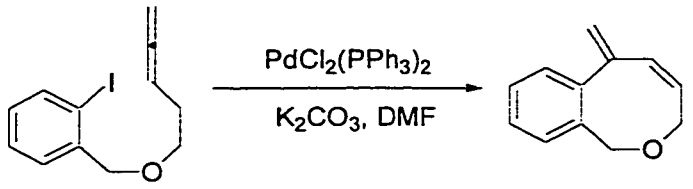
X	yield (%)
NTs	83
CH_2O	63
$C(CO_2Et)_2$	82
O	89

Intramolecular reactions of aryl and alkenyl halides bearing an allene moiety give seven- and eight-membered *exo*-methylene cycloalkenes in good yields (Eq. 7-4 and 7-5).[287]



7.15 **7.16** (7-4)

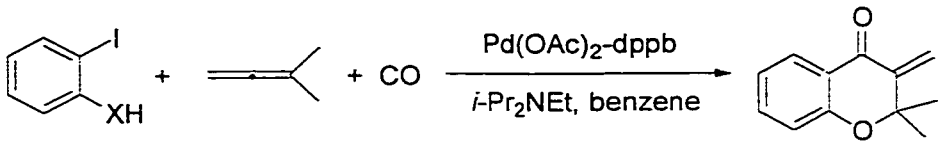
E = COOEt 58%



(7-5)

7.17 **7.18**

Recently, Alper and co-workers reported a one-pot procedure to *4H*-benzopyran-4-ones by treatment of *o*-iodophenol with allenes using a catalyst system consisting of $Pd(OAc)_2$-dppb in the presence of *i*-Pr_2NEt in benzene at 100°C under 20 atm CO (Eq. 7-6).[87]

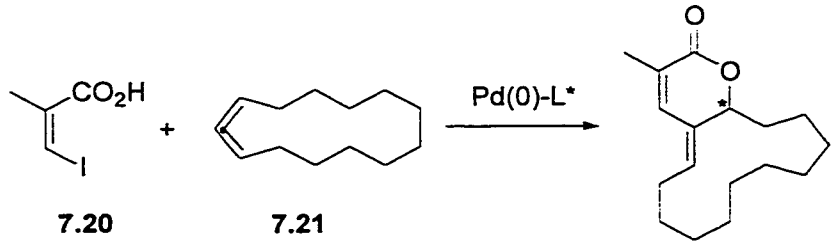


(7-6)

7.1, X=O **7.13** **7.19**

This carbonylative heteroannulation is highly regioselective, in particular when terminal allenes are used, and the regioselectivity is apparently controlled by electronic effects.[286f]

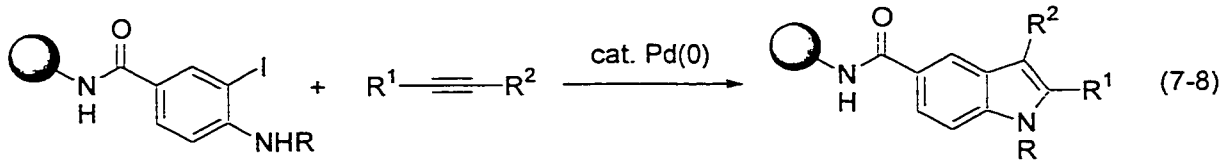
Asymmetric heteroannulation of 1,2-dienes has recently been developed as a powerful method for the enantioselective synthesis of heterocycles by modifying the usual allene reaction conditions to include silver salts, and catalytic amounts of a chiral bis(oxazoline) ligand (Eq. 7-7).[286e]



7.20 7.21 7.22 (7-7)

7.1.3 Heteroannulation of Alkynes

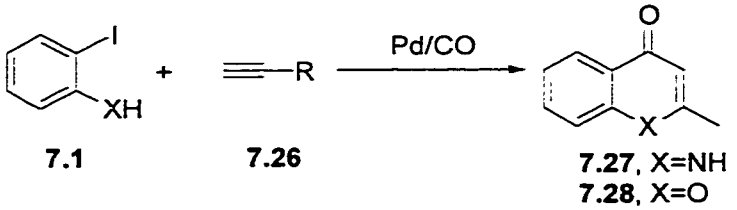
There are a lot of examples which involve heteroannulation of alkynes in the literature, and this chemistry can be efficiently used in the synthesis of a wide variety of heterocycles.[288] The great current interest in the pharmaceutically important indole ring system has resulted in the development of solid phase resin-bound versions of this chemistry (Eq. 7-8)[289] and the synthesis of tryptophan derivatives.[290]



7.23 2.24 7.25 (7-8)

R=H, Ac; 72-94%

The carbonylation version of this chemistry has also been developed.[79b, 83, 291] 4-Quinolones (**7.27**) and chromone (**7.28**) can be easily prepared by palladium-catalyzed intermolecular cyclocarbonylation of terminal alkynes with *o*-iodoanilines (**7.1**, X=NH) or *o*-iodophenols (**7.1**, X=O) respectively (Eq. 7-9).

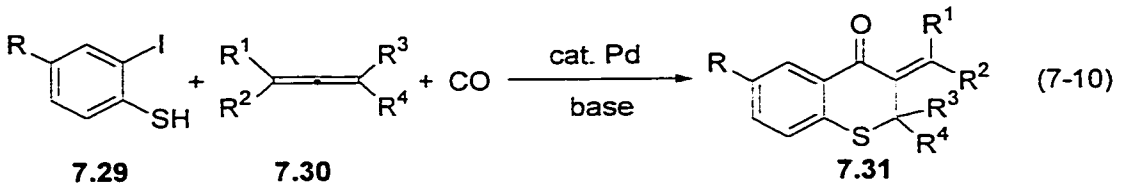


7.1 7.26 **7.27**, X=NH **7.28**, X=O (7-9)

7.2 Aims of Research

In contrast to the extensive literature on the palladium-catalyzed heteroannulation of unsaturated substrates, much less information is available on the cyclocarbonylation version of such processes although, in principle, acylmetal derivatives can add to π-bonds *via* carbometalation.[3, 4] As part of our continuing studies on the scope of palladium-catalyzed carbonylation methodology, we would like to explore such synthetic methods employing carbon monoxide as a direct C-1 resource and involving insertion of carbon-carbon multiple bonds to acylpalladation derivatives. Furthermore, in sharp contrast with the palladium-catalyzed cyclization of *o*-iodophenols and anilines with unsaturated substrates, application of these methodologies in which *o*-iodothiophenol is employed as a reagent instead of its oxo- and nitrogen analogues, seems to be unexplored. The fact that thiocarbonylation methodology seems to be very broad in scope (Chapters 2-6) encouraged us to examine the possible carbonylative heteroannulation of *o*-iodothiophenols with allenes and carbon monoxide. We envisioned that this carbonylative heteroannulation could lead to the corresponding thiochroman-4-one

derivatives (Eq. 7-10), and to our knowledge, this should be the first entry to employ *o*-iodothiophenol as the substrate in the heteroannulation of unsaturated compounds.



7.29 **7.30** **7.31**

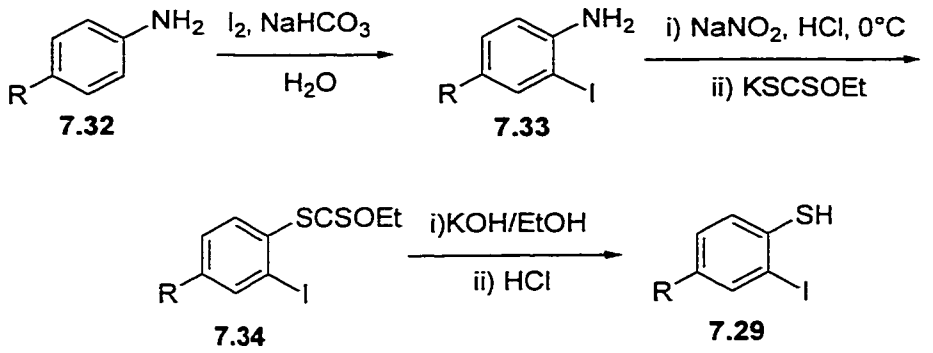
R=H, Me, Cl
R^1, R^2, R^3, or R^4=H, alkyl, -CO2Et, or cycloalkyl

Of particular interest is the fact that some 4-thiochromanone derivatives are potent antifungal agents[292] and very useful precursors[293, 294] of other heterocyclic compounds. Thus, it is not surprising that considerable effort has been expended in the synthesis of such compounds. Our goal is to explore a novel and one-step procedure to make these kind of compounds, using palladium-catalyzed carbonylative heteroannulation of allenes with *o*-iodothiophenols. Of the various routes to their preparation,[295] the methodology we would like to present herein should be one of the most straightforward and efficient ways to synthesize such compounds.

7.3 Results and Discussion

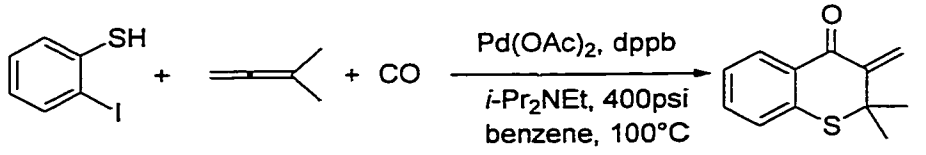
The starting materials were prepared by standard methodology.[296, 297] For example, *o*-iodothiophenols (**7.29a-c**) were prepared by the reactions shown in Scheme 7-2.

Scheme 7-2 Synthesis of *o*-Iodothiophenols



7.29a: R=H
7.29b: R=Me
7.29c: R=Cl

Initial studies were focused on examining the feasibility of the carbonylation annulation and at optimizing reaction conditions which could be applied to a variety of allenes and *o*-iodothiophenol derivatives. The reaction of 2-iodothiophenol (**7.29a**) and 3-methyl-1, 2-butadiene (**7.30a**) with carbon monoxide was chosen as a model reaction. The optimal reaction conditions used previously for the palladium-catalyzed carbonylation of *o*-iodophenols with allenes[87] were initially employed in the present case. This reaction was run on a 1-mmol scale, using 5 mol% $Pd(OAc)_2$ as catalyst, 5 mol% dppb as ligand, 3 equiv of allene, 1.5 equiv of *N*-ethyldiisopropylamine in 5 mL of benzene, at 100°C, under a pressure of 400 psi carbon monoxide for 24 h and gave **7.31a** in 74% isolated yield (Eq. 7-11). The effect of varying the catalyst, ligand, solvent, base, and reaction temperature on the model reaction were then examined.



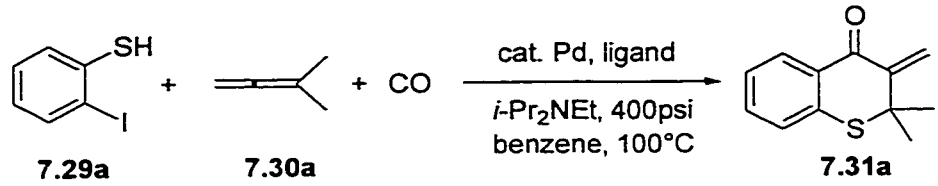
(7-11)

7.29a **7.30a** **7.31a**

74%

Table 7-1 shows the results of the reaction using several palladium catalysts and mono- and bis-phosphine ligands. These results show that both palladium(0) and palladium(II) complexes were excellent catalysts for the carbonylative heteroannulation. The ligands employed played an important role in this transformation, with 1,1'-bis(diphenylphosphino)ferrocene (dppf) being an excellent ligand for both palladium(0) and palladium(II) catalysts (Table 7-1, entries 4, and 7-11). In particular, the use of $Pd(OAc)_2$ with 1 equiv of dppf was the most effective catalyst system for the formation of **7.31a** in 87% yield (Table 7-1, entry 4). Although 1,3-bis(diphenylphosphino)propane (dppp) and 1,4-bis(diphenylphosphino)butane (dppb) were also effective as added ligands for this palladium-catalyzed reaction, the results were generally inferior to those of dppf (Table 7-1, entries 1, 2, and 9). Compared to other bidentate phosphines, 1,2-bis(diphenylphosphino)ethane (dppe) is almost ineffective (Table 7-1, entry 3). This may be due to the fact that the rate of carbon monoxide insertion into a Pd-C bond is faster for those alkylpalladium bisphosphine complexes which contain a more flexible metal ligand chelate ring.[195, 210] The monodentate ligands, like PPh_3 and PCy_3, can be used for this reaction, but they are not as effective as dppf (Table 7-1, entries 5 and 6). Therefore, it was decided to use $Pd(OAc)_2$ with dppf as the catalyst system and examine the effect of different solvents, bases, and reaction temperature on the carbonylative heteroannulation.

Table 7-1 Optimization of Catalysts and Ligands[a]



7.29a **7.30a** **7.31a**

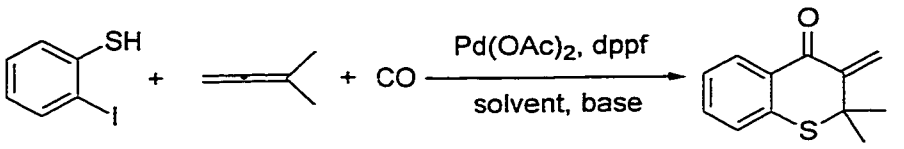
entry	catalyst	Ligand	Time (h)	Yield(%)[b]
1	$Pd(OAc)_2$	dppb	24	74
2	$Pd(OAc)_2$	dppp	24	58
3	$Pd(OAc)_2$	dppe	48	7[c]
4	$Pd(OAc)_2$	dppf	24	87
5	$Pd(OAc)_2$	PPh_3	24	70
6	$Pd(OAc)_2$	PCy_3	24	45
7	$PdCl_2$	dppf	48	77
8	$Pd_2(dba)_3$	dppf	60	80
9	$Pd_2(dba)_3 \cdot CHCl_3$	dppb	60	64
10	$Pd_2(dba)_3 \cdot CHCl_3$	dppf	60	84
11	$Pd(PPh_3)_4$	dppf	60	76

[a] Reaction conditions: 2-iodothiophenol (1 mmol), 3-methyl-1, 2-butadiene (5 mmol), catalyst (0.05 mmol), PPh_3 or PCy_3 (0.1 mmol, if used), dppb, dppp, dppe, or dppf (0.05 mmol, if used), *i*-Pr_2NEt (1.5 mmol), 400 psi, 100 °C, benzene (5 mL). [b] Isolated yield. [c] 38% of **7.29a** was recovered.

It can be concluded from the results summarized in Table 7-2 that the reaction is significantly influenced by the solvent and base employed. For example, when *N*-ethyldiisopropylamine is used as a base, the reaction works very well in benzene and gives the product **7.31a** in 87% isolated yield (Table 7-2, entry 1); however, under the same conditions, using DMF as a solvent, the yield of **7.31a** decreased to 58% (Table 7-2, entry 2). This was of interest, as previous studies noted that DMF was the solvent of choice.[83, 291a] Other solvents, such as THF, DMSO, CH_3CN, and toluene can be employed as the solvent for the reaction, but none appears to be as effective as benzene (compare entries 1-6 in Table 7-2).

In addition to *N*-ethyldiisopropylamine, we have examined a variety of other bases, including inorganic and organic ones, for the reaction (Table 7-2, entries 7-13). These results show that solvents and bases are interdependent. For example, when benzene was employed as the solvent, *N*-ethyldiisopropylamine and triethylamine were observed to be very effective for the reaction. However, the use of K_2CO_3, KOAc, DBU, and DABCO resulted in decreased yields (Table 7-2, entries 7-11). It is worth noting that in DMF, K_2CO_3 is a better base for the model reaction than *i*-Pr_2NEt (Table 7-2, entries 2 and 12), while both benzene/Et_3N and DMF/KOAc systems are similarly effective for this carbonylative heteroannulation (Table 7-2, entries 9 and 13). DBU and DABCO, which were used in the palladium-catalyzed carbonylative coupling of 2-hydroxylaryl iodides with ethynylarenes[291a] and annulation of iodoanilines and ketones,[298] respectively, did not work well in the present reaction (Table 7-2, entries 10 and 11).

Table 7-2. Optimization of Solvents, Bases, and Reaction Temperature[a]



7.29a **7.30a** **7.31a**

entry	solvent	base	temp.(°C)	time (h)	yield (%)[b]
1	benzene	*i*-Pr_2NEt	100	24	87
2	DMF	*i*-Pr_2NEt	100	24	58
3	THF	*i*-Pr_2NEt	100	24	52
4	DMSO	*i*-Pr_2NEt	100	24	33
5	CH_3CN	*i*-Pr_2NEt	100	24	66
6	toluene	*i*-Pr_2NEt	100	24	78
7	benzene	KOAc	100	60	24
8	benzene	K_2CO_3	100	60	29
9	benzene	Et_3N	100	24	64
10	benzene	DBU[c]	100	24	34
11	benzene	DABCO[d]	100	24	37
12	DMF	K_2CO_3	100	48	69
13	DMF	KOAc	100	48	63
14	benzene	*i*-Pr_2NEt	70	36	0[e]
15	benzene	*i*-Pr_2NEt	130	24	70
16	benzene	*i*-Pr_2NEt	150	24	44

[a] Reaction conditions: 2-iodothiophenol (1 mmol), 3-methyl-1,2-butadiene (5 mmol), $Pd(OAc)_2$ (0.05 mmol), dppf (0.05 mmol), *i*-Pr_2Et, Et_3N, DBU, or DABCO (1.5 mmol, if used), K_2CO_3 or KOAc (3 mmol, if used), solvent (5 mL), 400 psi. [b] Isolated yield. [c] 1, 8-Diazabicyclo[5.4.0]under-7-ene.[d]1,4-Diazabicyclo[2.2.2]octane. [e] The decarbonylation product, *o*-iodophenyl 3-methyl-2-butenyl sulfide, was obtained in 74% yield.

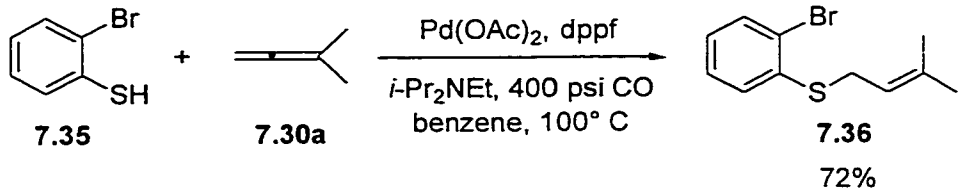
The reaction temperature is another critical factor for the successful carbonylative heteroannulation, with the best result being attained at 100°C. Variations of the temperature from this value have been shown to be detrimental to the reaction. For instance, increasing the temperature to 150°C gave only 44% yield (Table 7-2, entry 16), while decreasing the temperature to 70°C gave exclusively the decarbonylation product in 74% yield (Table 7-2, entry 14).

We did not rigorously examine the effect of CO pressure on the reaction, however, we found that no carbonylation product was formed when the pressure of CO was lower than 100 psi, and when the pressure was raised beyond 1000 psi, a complicated mixture was obtained. In subsequent studies, 400 psi of carbon monoxide was usually used, consistent with our previous experience with other carbonylation reactions.[87]

The heteroannulation of allenes is also sensitive to the concentration of the allene. The reaction gave poor yields when only 1 equivalent of the allene (relative to 2-

iodothiophenol) was used, while 87% yield was attained when 3-5 equivalents of allene was employed.

There has been much interest recently in intramolecular Heck type coupling reactions[299] which employ aromatic chlorides[300] or bromides[301] as substrates. However, the carbonylative reaction of **7.30a** with commercially available 2-bromothiophenol (**7.35**) afforded the bromothioether (**7.36**) rather than thiochroman-4-one (**7.31a**) (Eq. 7-12). The difference in behaviour may be a result of the lower rate of oxidative addition to an Ar-Br moiety, compared with Ar-I.

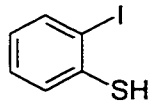
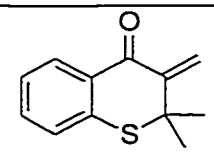
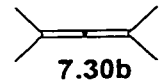
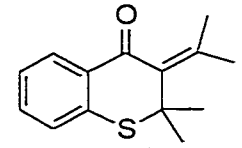
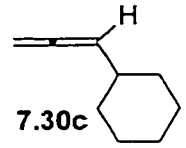
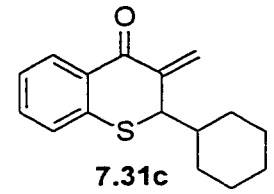
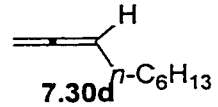
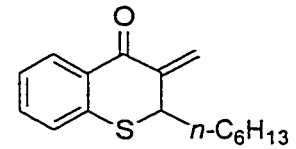
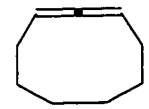
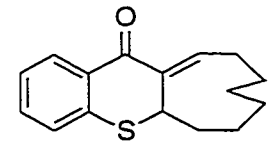
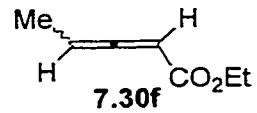
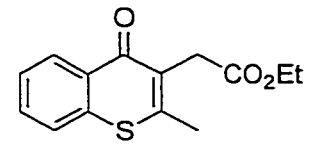


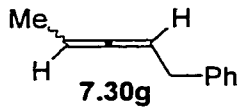
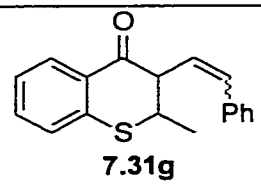
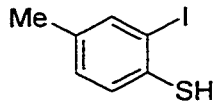
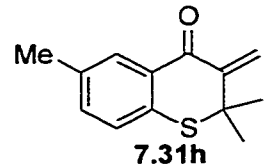
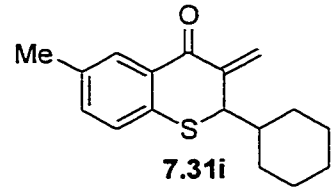
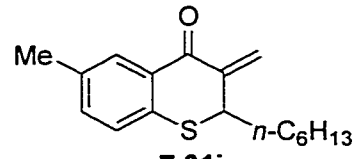
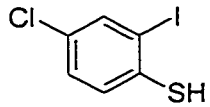
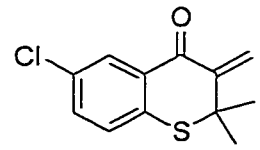
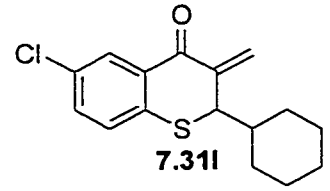
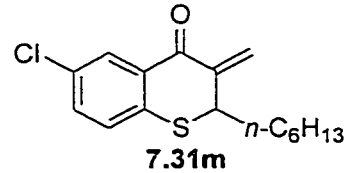
7.35 **7.30a** **7.36** 72% (7-12)

The above experiments indicated that the standard reaction conditions, with substitution of dppf for dppb, gave the best overall yield. Using these reaction conditions, the reactions of a variety of *o*-iodothiophenols and allenes were studied and the results are summarized in Table 7-3.

Acyclic, cyclic, terminal, and internal 1, 2-dienes can be successfully employed in the reaction together with *o*-iodothiophenols containing electron-withdrawing or donating groups (Table 7-3), to give the corresponding thiochromanone derivatives in good to excellent isolated yields. The regioselectivity of this carbonylative heteroannulation methodology is generally quite high. The terminal disubstituted allene, 3-methyl-1, 2-butadiene (**7.30a**), reacted with **7.29a**, **7.29b**, and **7.29c** to give only the *exo*-methylene

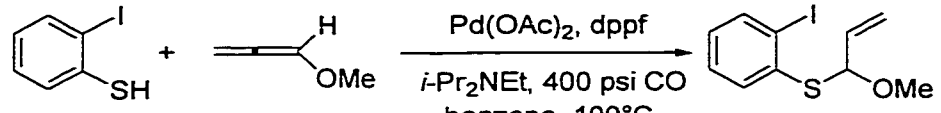
Table 7-3. Palladium-Catalyzed Carbonylative Heteroannulation of Allenes with o-Iodothiophenols and Carbon Monoxide (Eq. 7-10)[a]

entry	iodothiophenol	allene	product	yield(%)[b]
1	 **7.29a**	 **7.30a**	 **7.31a**	87
2	**7.29a**	 **7.30b**	 **7.31b**	84
3[c]	**7.29a**	 **7.30c**	 **7.31c**	76
4	**7.29a**	 **7.30d**	 **7.31d**	68
5	**7.29a**	 **7.30e**	 **7.31e**	72
6[d]	**7.29a**	 **7.30f**	 **7.31f**	72

7[e]	**7.29a**	 **7.30g**	 **7.31g**	90
8	 **7.29b**	**7.30a**	 **7.31h**	92
9	**7.29b**	**7.30c**	 **7.31i**	86
10	**7.29b**	**7.30d**	 **7.31j**	78
11	 **7.29c**	**7.30a**	 **7.31k**	90
12	**7.29c**	**7.30c**	 **7.31l**	77
13	**7.29c**	**7.30d**	 **7.31m**	74

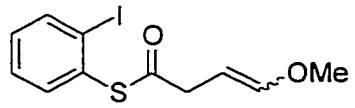
[a] Reaction conditions: *o*-iodothiophenol (1 mmol), allene (2-5 mmol), CO (400 psi), *i*-Pr_2NEt (1.5 mmol), $Pd(OAc)_2$ (0.05 mmol), dppf (0.05 mmol), benzene (5 mL), 100°C. [b] Isolated yield. [c] Reaction time: 36 hrs. [d] Reaction time: 60 hrs. [e] The ratio of *E* to *Z* (*E*/*Z*=1.5:1) was determined by ^{1}HNMR.

products **7.31a**, **7.31h**, and **7.31k** with little variation in yields (Table 7-3, entries 1, 8, and 11). The reactions of monosubstituted allenes, like that of **7.30a**, are regioselective with nucleophilic attack of the –SH group occuring exclusively at the more substituted carbon of the allene unit (Table 7-3, entries 3 and 4). When the cyclic internal allene **7.30e** was employed, the expected product **7.31e** was obtained in 72% yield (Table 7-3, entry 5). When the unsymmetrical acyclic internal allene **7.30g** was employed as the substrate, thiochromanone **7.31g** was isolated in 90% yield as the sole product (Table 7-3, entry 7). The reaction is slower when the allene (**7.30f**) contains an electron-withdrawing group, but the reaction can proceed to completion by prolonging the reaction time to 60 h, affording the corresponding product **7.30f** in 72% yield (Table 7-3, entry 6). The more bulky allene, tetramethylallene (**7.30b**), has been successfully employed in this reaction without any problem and, to our knowledge, this is the first time that it has been used in this type of annulation process (Table 7-3, entry 2). Unlike palladium-catalyzed annulation of allene with functionalized vinylic halides,[286a] attempts to carry out the reaction of methoxyallene (**7.37**) with *o*-iodothiophenol and CO were unsuccessful (Eq. 7-13).



7.29a **7.37** **7.38** 64% (7-13)

Such behaviour was also observed for the palladium-catalyzed carbonylation[87] of *o*-iodophenols with allenes. When the reaction was carried out with 2 equiv of dppf (relative to Pd catalyst) at 110°C, the thiocarbonylation product **7.39** was isolated in 57% yield and no carbonylative heteroannulation product was obtained.



(E/Z=2:1)

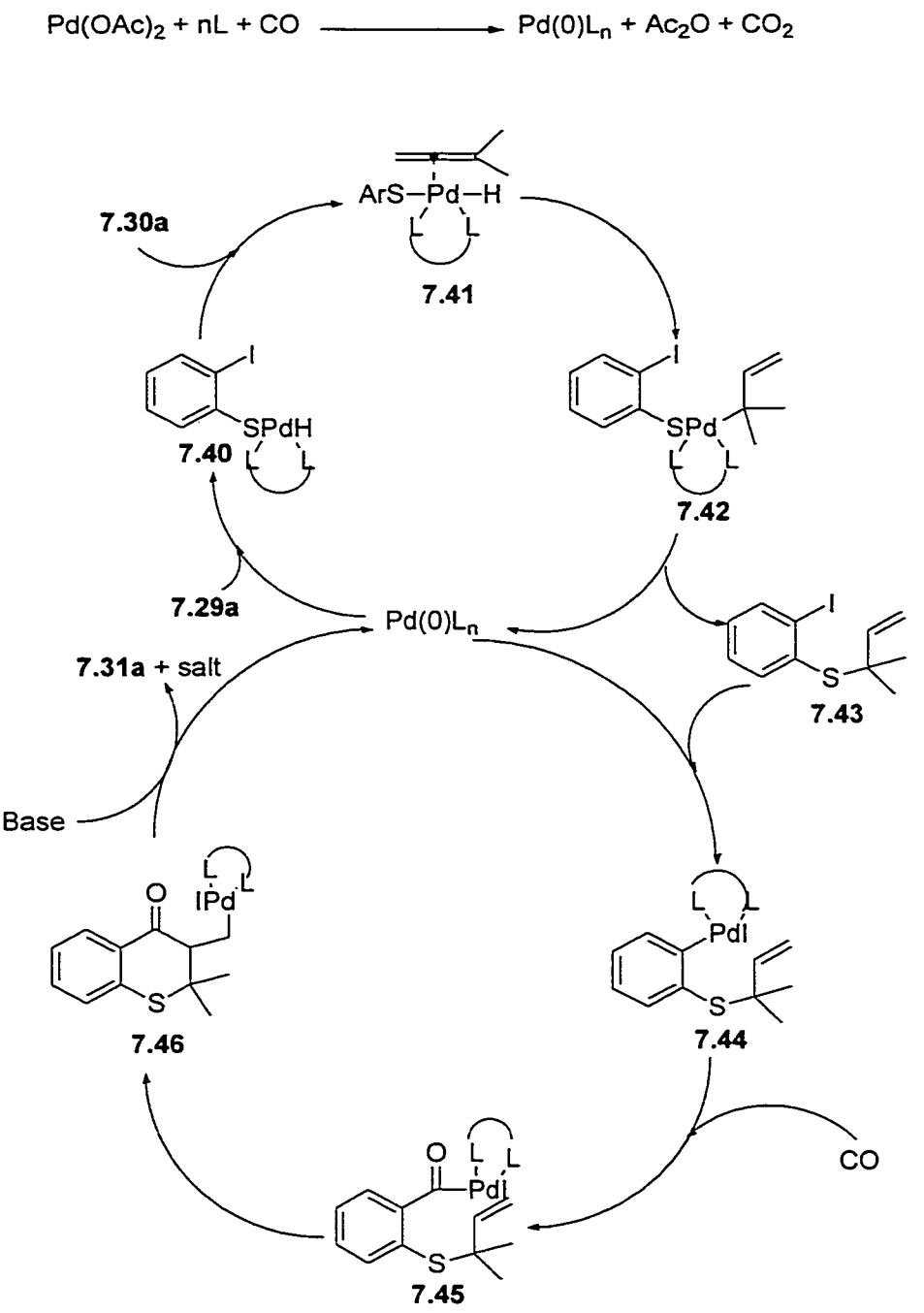
7.39

Note that the regioselectivity of this reaction is consistent with palladium-catalyzed carboannulation of functionally substituted aryl halides with 1, 2-dienes and its asymmetric as well as carbonylative versions,[87, 286e, 286f] and can be explained on the basis of electronic factors.[87, 286e]

A probable mechanism for the carbonylative heteroannulation of 1, 2-dienes with *o*-iodothiophenols is outlined in Scheme 7-3 (illustrated for **7.29a** and **7.30a**). It is conceivable that this reaction may proceed through initial palladium acetate reduction to palladium (0) *in situ*,[271] followed by oxidative addition of the o-iodothiophenol to palladium(0)[219] to form **7.40**, insertion of allene to **7.40** to produce a σ-allylpalladium intermediate **7.42** (*via* **7.41**). Reductive elimination of **7.42** would give the iodothioether (**7.43**). Oxidative addition of the latter to Pd(0) would generate complex **7.44**, which on

subsequent CO insertion and intramolecular cyclization[302] would afford **7.31a** and regenerate the catalyst.

Scheme 7-3. A possible Mechanism of the Carbonylative Heteroannulation of Allenes



7.4 Conclusions

In summary, this research has resulted in the regioselective carbonylative heteroannulation of 1,2-dienes with *o*-iodothiophenols and carbon monoxide catalyzed by palladium acetate and dppf to form thiochroman-4-one derivatives in good to excellent yields. To our knowledge, this is the first example of this type of annulation employing thiophenols as direct reactants. This one-pot procedure, the mild reaction conditions, and the easy access to the starting materials make this methodology of value to the area of thiochromanone chemistry.

CHAPTER 8

EXPERIMENTAL SECTION

8.1. General Experimental

All ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian 200 or 300 MHz Gemini instrument operating at 200 and 300 MHz for ^{1}H and 50 and 75 MHz for ^{13}C, respectively. NMR data are reported in chemical shifts relative to tetramethylsilane as the internal standard, multiplicity (s= singlet, d= doublet, t= triplet, q= quartet, b= broad and m= multiplet), integration and assignment. NMR spectra were run in $CDCl_3$ containing 0.03% TMS or in C_6D_6. Proton spectra were referenced to 7.24 ppm for $CDCl_3$ or 7.16 ppm for C_6D_6 and carbon to 77.0 ppm for $CDCl_3$ or 128.0 ppm for C_6H_6. Infrared data were collected on a Bomem MB-100 FT-IR spectrometer. Liquid samples were run neat using sodium chloride disks. Solid samples were analyzed using fabricated KBr disks. Mass spectra were obtained on a VG 7070 E spectrometer, and the energy of ionization was 70 eV. A Fisher-Johns apparatus was used for melting point determinations. Gas chromatographic analyses were performed on a Varian 3300 using a DB1 capillary column and a Varian 4270 integrator. Chiral chromatographic analyses were performed on a Varian 3300 gas chromatograph installed with a Supelco β-Dex 120 column (30 m)-permethylated β-cyclodextrin fused silica capillary column 0.25 mm i.d.×0.25 μm d_f-

using helium as the carrier gas. Optical rotations were measured on a Perkin-Elmer polarimeter in a 10 cm cell at 22 °C. Elemental analyses were performed by the elemental analysis service of the Department of Chemistry at the University of Ottawa, Canada.

All air and/or moisture sensitive reactions were performed in glassware, flame dried under a purge of dry nitrogen (passed through a drierite tower), or flame dried under vacuum followed by flushing with nitrogen. Solvents, solutions, and liquid reagents were transferred with syrings and double ended needles (cannulae) using standard inert atmosphere techniques. Liquid substrates or reagents for small scale reactions were weighed. Air sensitive solids were handled using standard Schlenk techniques and transferred using a glove bag.

Chromatographic purifications were performed using flash grade silica gel and low pressure was applied to the top of the column using a hand pump. Except for large scale reactions, samples were dissolved in dichloromethane and silica gel added. The volatiles were removed *in vacuo* and the resulting solid pumped on for 5 minutes at high vacuum to remove most of the dichloromethane. The solid was then added to the top of the prepacked column. HPLC purifications were performed using a JAI recycling semi-prep HPLC and columns packed JAIGEL (polystyrene). Chloroform (Omnisolv) was used as the eluant and an RI detector used to observed the peaks. An Aldrich brand Kugelrohr was used for small scale distillations and sublimations.

Solvents were dried using the drying agents listed and distilled under a dry atmosphere: benzene, toluene, diethyl ether, tetrahydrofuran and DME from sodium metal/benzophenone ketyl over nitrogen; dichloromethane, chloroform and triethylamine from calcium hydride under under nitrogen. Carbon monoxide, hydrogen, helium and argon were supplied by Air Products.

Chemicals were purchased from Aldrich, Lancaster, Fluka and Strem Chemicals, and were used as received unless otherwise noted.

Autoclaves, gauges and gauge block assemblies were purchased from Parr Instrument Co..

8.2. Experimental for Chapter 2

8.2.1. Synthesis of Starting Materials

8.2.1.1. Synthesis of cis-2-Hexen-1-ol (2.17)

2-Hexyn-1-ol (2.16). To a solution of propargylic alcohol (**2.15**; 11.6 g, 0.21 mol) in 50 ml of dry THF was added *n*-BuLi (2.0 M solution in cyclohexane, 210 ml, 0.42 mol) at -78°C, and the mixture was stirred for 1h. A solution of *n*-PrBr (14.0 g, 0.11 mol) in 50 ml of THF was then added to the mixture at -78°C. The reaction mixture was stirred at room temperature for 3h. The mixture was left overnight at room temperature

and then diluted with 10% HCl and extracted with diethyl ether. The combined ether solution was washed with brine and dried with $MgSO_4$. Filtration and concentration of the filtrate *in vacuo* was followed by distillation to give 10.9g of **2.17** in 84% yield. ^1H NMR (200 MHz, $CDCl_3$) δ 0.96 (t, 3H, *J*=7.0 Hz), 1.50 (tq, 2H, *J*=6.2 and 7.0 Hz), 2.17 (m, 2H), 2.44 (s, 1H), 4.25 (t, 2H, *J*=1.8 Hz).

cis-2-Hexen-1-ol (2.17). To a suspension of Pd-$BaSO_4$ (1g) in n-hexane (100 ml) was added **2.16** (10.0g, 0.60 mol) and quinoline (0.5 ml). The mixture was stirred under H_2 (1 atm) for 6h. The catalyst was then filtered off, and the filtrate was respectively washed with 10% HCl and brine, dried with $MgSO_4$, and concentrated. The residue was distilled to give 7.2g of **2.17** in 71% yield as colorless oil. ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (t, 3H, *J*=7.2 Hz), 1.20-1.64 (m, 2H), 2.12 (dt, 2H, *J*=6.2 and 6.0 Hz), 2.40 (s, 1H), 4.13 (d, 2H, *J*=6.0 Hz), 5.44-5.86 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.33, 23.68, 30.04, 58.48, 126.44, 134.58.

8.2.1.2. Synthesis of trans-2-Hexen-1-ol (2.21)

A 100 ml flask fitted with a relux condenser and magnetic stirring bar was flushed with nitrogen and charged with 50 ml of 0.5 M 9-BBN (0.025 mol) in THF. To the solution was added 1-pentyne (**2.18**; 1.70g, 0.025 mol), and the solution was stirred overnight to ensure complete hydroboration. Paraformaldehyde (1.5g, 0.05 mol) was added, and the solution was heated under reflux for 16h. After cooling to room temperature, 15 ml of 3N sodium hydroxide and 15 ml of 30% hydrogen peroxide were added to the mixture. The solution was maintained at 50°C for 4h. The aqueous layer

was saturated with potassium carbonate, separated, and extracted with hexane. The combined organic layer was dried over anhydrous magnesium sulfate and analyzed by GC, which indicated a 87% yield of 2-hexen-1-ol with 100% E-selectivity. Distillation provided 1.35g of trans-2-hexen-1-ol in 54% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.9 (t, 3H, *J*=7.0 Hz), 1.32-1.46 (m, 2H), 2.06 (dt, 2H, *J*=6.2 and 6.0 Hz), 2.18 (s, 1H), 4.08 (d, 2H, *J*=6.4 Hz), 5.56-5.74 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.54, 22.08, 35.57, 64.84, 129.76, 134.55.

*8.2.1.3. Synthesis of 10-Hydroxymethyl-$\Delta^{1,9}$-2-octalol (**2.23**)*

To a solution of $LiAlH_4$ (2.85g, 0.075 mol) in 70 ml of diethyl ether was added anhydrous $AlCl_3$ powder (3.34g, 0.025 mol) at 0°C under nitrogen, and the mixture was stirred for 45 min. at room temperature. 10-Carbethoxy-$\Delta^{1,9}$-2-octalone (**2.22**; 10.0g, 0.045 mol) in 50 ml of ether was added to the mixture at 0°C with vigorous stirring. After the addition, the reaction mixture was maintained at room temperature for 1h with stirring. Then 25 ml of 20% sulfuric acid was carefully added to destroy excess AlH_3, and the reaction mixture was kept stirring for another 45 min. The organic layer was separated and the aqueous layer was extracted with ether 3 times. The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. After the solvent was removed, the crude product was purified by flash column (eluant: EtOAc:hexane=9:1) to afford 7.0g (85%) of **2.23**. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.30-2.27 (m, 14H), 3.28-3.32 (m, 1H), 3.65-3.78 (m, 1H), 4.06-4.23 (m, 1H), 5.48 (d, 1H, *J*=6.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.08, 26.36, 28.04, 31.03, 32.00, 36.72, 41.02, 63.88, 67.24, 120.89, 142.76; MS (EI) *m/z* 182.1 (M^+); HRMS calcd for $C_{11}H_{18}O_2$ 182.1307, found 182.1312.

8.2.1.4. Synthesis of 6-(Hydroxymethyl)-5-(Trimethylsilyl)bicyclo[4.4.0]dec-en-3-ol (2.29)

3-(Trimethylsilyl)-2-propyn-1-ol. Magnesium turnings (3.43g, 0.14 mmol) were placed in a dry, three-necked, 500-ml, round-bottomed flask equipped with a condenser, a dropping funnel, and a stirring bar. Anhydrous diethyl ether (100 ml) and a crystal of iodine were added into the flask. Bromoethane (14.3g, 0.13 mol) was added dropwise over a 25-min period while the reaction mixture was kept refluxing. After 20 min of stirring, the solution was cooled to 0°C and propargyl alcohol (**2.15**; 2.53g, 0.045 mol) in anhydrous diethyl ether (5 ml) was added dropwise over a 10-min period. The reaction mixture was warmed to room temperature while stirring continued for 45 min. Chlorotrimethylsilane (11.2g, 0.103 mol) was added into the flask and stirring continued under an atmosphere of nitrogen for 15 h. The reaction was quenched at 0°C with aqueous H_2SO_4 (3.0 M, 100 ml) and the solution was extracted with diethyl ether. The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to give 5.73g of 3-(trimethylsilyl)-2-propyn-1-ol as a yellow oil in 99% crude yield. The compound was used in next step without further purification.

(*E*)-3-(Trimethylsilyl)-2-propen-1-ol. 3-(Trimethylsilyl)-2-propyn-1-ol (5.73g, 0.045 mol) in anhydrous diethyl ether (100 ml) was cooled to 0°C in a 500-ml, round-bottomed flask equipped with a dropping funnel and a stirring bar. Sodium bis(2-methoxyethoxy)aluminum hydride (3.4 M solution in toluene, 18.4 ml, 0.062 mol) in anhydrous diethyl ether (20 ml) was added into the flask over a 15-min period. The

solution was warmed to room temperature and stirred for 2h. The reaction mixture was cooled to 0°C and quenched by the addition of water (20 ml) and then aqueous H_2SO_4 (10%, 100 ml). The solution was extracted with diethyl ether. The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to a yellow oil. The crude product was purified by flash column chromatography (eluant: EtOAc: hexane=1 :9) to give expected product as a colorless oil in 84% yield (4.94g). ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.06 (s, 9H), 1.52 (s, 1H), 4.17 (dd, 2H, *J*=4.0 and 1.0 Hz), 5.79 (dt, 1H, *J*=17.6 and 1.0 Hz), 6.33 (dt, 1H, *J*=17.6 and 4.0 Hz), which is consistent with those reported in the literature.[303]

(*E*)-3-(Trimethylsilyl)-2-propen-1-al. Solid pyridinium chlorochromate (9.73g, 0.042 mol) was added to a stirring solution of (*E*)-3-(trimethylsilyl)-2-propen-1-ol (4.94g, 0.038 mol) in dichloromethane (100 ml). Stirring continued for 4 h. The solution was filtered through a pad of Celite, and the remaining black precipitant in the flask was rinsed with diethyl ether followed by filtration. The filtrates were combined and washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated to give the crude product. The crude product was then purified by flash column chromatography under nitrogen (eluant: EtOAc: hexane=1:9) to give the aldehyde in 78% yield (3.802g). IR (neat) ν 1674 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.13 (s, 9H), 6.32 (dd, 1H, *J*=18.0 and 7.0 Hz), 7.18 (d, 1H, *J*=18.0 Hz), 9.48 (d, 1H, *J*=7.0 Hz). The spectroscopic data were consistent with ones reported in the literature.[191a]

(*E*)-4-(Trimethylsilyl)-3-buten-2-ol. Magnesium turnings (2.087g, 0.086 mol) were placed in a dry, three-necked, 250-ml, round-bottomed flask equipped with a condenser and a stirring bar. Anhydrous diethyl ether (50 ml) and a crystal of iodine were added into the flask. Iodomethane (5.4 ml, 12.212g, 0.086 mol) was added dropwise over a 10-min period while the reaction mixture was kept refluxing. After 30 min of stirring, the solution was cooled to 0°C. A solution of (E)-3-(trimethylsilyl)-2-propen-1-al (3.72g, 0.029 mol) in anhydrous diethyl ether (4.0 ml) was added into the flask over 5 min. The reaction mixture was warmed to room temperature and stirring continued for half an hour under nitrogen. The solution was cooled to 0°C and the reaction was quenched by adding water and dilute H_2SO_4. The reaction mixture was extracted with diethyl ether. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to give an oil. The crude product was purified by column chromatography (eluant: EtOAc:hexane=1:9) to give the alcohol as a light yellow oil in 91% yield (3.81g). IR (neat) ν 3340 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.07 (s, 9H), 1.23(d, 3H, *J*=6.0 Hz), 1.55 (s, 1H), 4.08-4.22(m, 1H), 5.68 (dd, 1H, *J*=18.0 and 0.5 Hz), 6.22 (dd, 1H, *J*=18.0 and 4.0 Hz).

(*E*)-4-(Trimethylsilyl)-3-buten-2-one (2.25). To a stirred solution of (*E*)-4-(trimethylsilyl)-3-buten-2-ol (3.80g, 0.026 mol) in acetone (15 ml) at 0°C was slowly added Jones reagent (2.5 M CrO_3 solution in 4M H_2SO_4, 11.45 ml, 0.029 mol). After 15 min of stirring at 0°C, the reaction mixture was quenched with 2-propanol (3.5g, 0.058 mol). The reaction mixture was diluted with diethyl ether (50 ml) and water (25 ml); the organic layer was separated and washed with water, saturated aqueous $NaHCO_3$, and

brine. The organic layer was dried over $MgSO_4$, filtered and concentrated to give enone **2.25** (3.7g) as a yellow oil in 100% crude yield. The product was directly used in the next synthesis without further purification.

Ethyl 5-(Trimethylsilyl)bicyclo[4.4.0]dec-en-3-one-6-carboxylate (2.28). Sodium ethoxide in ethanol (1.5 M, 13.3 ml, 0.02 mol) was added slowly to a stirred mixture of ethyl 2-cyclohexanonecarboxylate (**2.26**; 3.41g, 0.02 mol) and enone **2.25** (2.88g, 0.02 mol) at 0°C. After 5h, the reaction mixture was heated to 80°C in a preheated oil bath for 24 h. The reaction was quenched with saturated aqueous NH_4Cl (4 ml) and the solution was extracted with diethyl ether. The organic layer was washed with 10% H_2SO_4, saturated aqueous $NaHCO_3$, and brine, dried over anhydrous $MgSO_4$, filtered, and then concentrated to give an oil. The crude product was purified by flash column chromatography (eluant: EtOAc:hexane=1:9) to give **2.28** in 52% yield (3.06g). IR (neat) ν 1720 and 1675 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.04 (s, 9H), 0.78-2.64 (m, 14H), 4.02 (q, 2H, J=7.0 Hz), 5.98 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ -3.73, 11.07, 18.34, 24.96, 25.38, 34.90, 38.63, 46.54, 55.43, 61.72, 119.63, 124.87, 177.14, 196.23; MS (EI) *m/z* 294.1 (M^+); HRMS calcd for $C_{16}H_{26}O_3Si$ 294.1651, found 294.1662.

6-(Hydromethyl)-5-(trimethylsilyl)bicyclo[4.4.0]dec-1-en-3-ol (2.29). $LiAlH_4$ (1.52g, 0.04 mol) and $AlCl_3$ (1.78g, 0.0133 mol) was added to a stirred solution of ester **2.28** (1.53g, 0.0052 mol) in anhydrous diethyl ether (75 ml) at 0°C. The reaction mixture was stirred at room temperature for overnight. The reaction was then quenched at 0°C with EtOAc and saturated aqueous Na_2SO_4. The resulting slurry was filtered and the

precipitate was washed with EtOAc followed by filtration. The crude product was purified by small column chromatography (eluant: EtOAc:hexane=3:7) to give pure **2.29** (0.96g) 73% yield. m.p. 167-171°C; IR (KBr) ν 3340 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.07(s, 9H), 0.62-2.55 (m, 13H), 3.33 (d, 1/3H, J=11.0 Hz), 3.58(d, 2/3H, J=11.5 Hz), 3.78-4.22 (m, 2H), 5.61-5.72 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -3.71, 22.38, 26.45, 28.03, 31.90, 34.27, 45.63, 64.25, 71.13, 128.95, 137.42; MS (CI) *m/z* 254.2 (M^+); Anal. Calcd for $C_{14}H_{26}O_2Si$: H, 10.31, C, 66.10; found H, 10.24, C, 66.31.

8.2.1.5. Synthesis of Allylic Carbonates

To a cooled (0°C) and stirred solution of allyl alcohol (0.1 mol) and dry pyridine (7.9g, 0.1 mol) in 50 ml of dry diethyl ether was added methyl chloroformate (9.45g, 0.1 mol) over 10 min. The mixture was stirred at room temperature for 3 h and then 10% HCl was added. After extraction with ether, the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Following evaporation of the solvent, the allyl carbonate was isolated by column chromatography.

Methyl 2-Methyl-3-butenyl carbonate (2.33a). Eluant, EtOAc:hexane=5:95. 84% yield. ^1H NMR (200 MHz, $CDCl_3$) δ 1.40 (s, 6H), 3.62 (s, 3H), 4.97 (d, 1H, *J*=12.0 Hz), 5.34 (d, 1H, *J*=8.0 Hz), 5.88 (dd, 1H, *J*=8.0 and 12.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.44, 48.67, 74.23, 119.24, 138.97, 164.52.

Methyl 5-Isopropenyl-2-methyl-cyclohex-2-enyl carbonate (2.81). Eluant: EtOAc: hexane=1:9. 73% yield. ^1H NMR (200 MHz, $CDCl_3$) δ 1.26-2.58 (m, 11H), 3.64 (s, 3H), 4.06 (d, 1H, *J*=7.0 Hz), 4.78-5.02 (m, 2H), 5.64 (t, 1H, *J*=7.0 Hz); ^{13}C NMR (50

MHz, $CDCl_3$) δ 14.15, 19.40, 28.03, 31.44, 37.28, 56.14, 75.36, 117.42, 130.17, 131.18, 144.42, 162.76; MS (EI) *m/z* 210.1; Anal. calcd for $C_{12}H_{18}O_3$: H, 8.63, C, 68.53; found H, 8.58, C, 68.62.

*8.2.1.6. Synthesis of O,O-dimethyl 2-methyl-3-butenyl Phosphonate (**2.33b**)*

Dimethyl chlorophosphate (7.225g, 0.05 mol) was added to the solution of 2-methyl-3-buten-2-ol (**2.30**; 3.876g, 0.045 mol) and pyridine (4.0 ml) in dichloromethane (50 ml) at 0°C for 5 min. The resulting white slurry was stirred for 6 h at room temperature. The reaction mixture was diluted with diethyl ether and was washed successively with a 10% HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over anhydrous $MgSO_4$. After removal of the solvent in vacuo, the crude product was purified by column chromatography (eluant: EtOAc:hexane=5:95) to give **2.33b** (6.63g, 76%). IR (neat) 1270, 1000 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.33 (s, 6H), 3.58 (s, 3H), 3.63 (s, 3H), 5.14 (d, 1H, *J*=12.4 Hz), 5.33 (d, 1H, *J*=8.0 Hz), 5.86-6.20 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 27.18, 28.32, 50.49, 51.26, 74.88, 115.55, 140.78.

8.2.2. Optimization of Reaction Conditions

8.2.2.1. Influence of Catalyst

In a 45-ml stainless-steel autoclave were placed the palladium complex (0.06 mmol), triphenylphosphine (0.0629g, 0.24 mmol, if used) or bidentate phosphine (e.g. dppe, dppp, or dppb; 0.12 mmol, if used), *p*-TsOH (0.0190g, 0.1 mmol) or HCl (4 μl) (if

used), 2-methyl-3-buten-2-ol (**2.30**; 0.1723g, 2 mmol), thiophenol (**2.31**; 0.2204g, 2 mmol),and dichloromethane (10 ml). After carbon monoxide was introduced up to 400 psi, the mixture was stirred at 100-120°C for 48-72 h. The results are listed in Table 2-2.

8.2.2.2. Influence of Solvents

A solution of $Pd(OAc)_2$ (0.0135g, 0.06 mmol), PPh_3 (0.0629g, 0.24 mmol), *p*-TsOH (0.0190g, 0.1 mmol), **2.30** (0.1723g, 2 mmol), and **2.31** (0.2204g, 2 mmol) in solvent (10 ml) was stirred under CO (400 psi) at 100°C for 48 h. The results are listed in Table 2-3.

8.2.2.3. Influence of Reaction Temperature

A solution of $Pd(OAc)_2$ (0.0135g, 0.06 mmol), PPh_3 (0.0629g, 0.24 mmol), *p*-TsOH (0.0190g, 0.1 mmol), **2.30** (0.1723g, 2 mmol), and **2.31** (0.2204g, 2 mmol) in CH_2Cl_2 (10 ml) was stirred under CO (400 psi) at 50 (reaction time 48 h), 100 (reaction 48 and 80 h, respectively), and 150°C (reaction time 48 h), respectively. The results are listed in Table 2-3.

8.2.2.4. Influence of CO Pressure

A solution of $Pd(OAc)_2$ (0.0135g, 0.06 mmol), PPh_3 (0.0629g, 0.24 mmol), *p*-TsOH (0.0190g, 0.1 mmol), **2.30** (0.1723g, 2 mmol), and **2.31** (0.2204g, 2 mmol) in CH_2Cl_2 (10 ml) was stirred under CO (100, 400, 800 psi, respectively) at 100°C for 48 h. The results are listed in Table 2-3.

8.2.3. Palladium-Catalyzed Carbonylative Reaction of Methyl 2-methyl-3-butenyl carbonate (2.33a) with Thiophenol (2.31) and Carbon Monoxide

To a 45-ml Parr autoclave fitted with a glass liner and stirring bar were added $Pd(OAc)_2$ (0.0135g, 0.06 mmol), PPh_3 (0.0629g, 0.24 mmol), methyl 2-methyl-3-butenyl carbonate (**2.33a**; 0.288g, 2 mmol), thiophenol (**2.31**; 0.2204g, 2 mmol) and CH_2Cl_2 (10 ml). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 400 psi. The mixture was stirred in the autoclave at 100°C (oil bath temperature) for 6 h. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation under reduced pressure. The subsequent purification by preparative TLC (silica gel F_{254}, eluant: n-hexane/ethyl acetate 10:1) gave *S*-phenyl 4-methyl-3-pentenethioate (0.3749g, 91%).

8.2.4. Palladium-Catalyzed Carbonylative Reaction of O,O-Dimethyl 2-Methyl-3-butenyl Phosphonate (2.33b) with Thiophenol (2.31) and Carbon Monoxide

To a 45-ml Parr autoclave fitted with a glass liner and stirring bar were added $Pd(OAc)_2$ (0.0135g, 0.06 mmol), PPh_3 (0.0629g, 0.24 mmol), *O*, *O*-dimethyl 2-methyl-3-butenyl phosphonate (**2.33b**; 0.388g, 2 mmol), thiophenol (**2.31**; 0.2204g, 2 mmol) and CH_2Cl_2 (10 ml). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 400 psi. The mixture was stirred in the autoclave at 100°C (oil bath

temperature) for 8 h. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation under reduced pressure. The subsequent purification by preparative TLC (silica gel F_{254}, eluant: n-hexane/ethyl acetate 10:1) gave *S*-phenyl 4-methyl-3-pentenethioate (0.3832g, 93%).

8.2.5. Palladium-Catalyzed Carbonylative Reaction of Methyl 5-Isopropenyl-2-methyl-cyclohex-2-enyl Carbonate (2.81) with Thiophenol (2.31) and Carbon Monoxide

To a 45-ml Parr autoclave fitted with a glass liner and stirring bar were added $Pd(OAc)_2$ (0.0135g, 0.06 mmol), PPh_3 (0.0629g, 0.24 mmol), methyl 5-isopropenyl-2-methyl-cyclohex-2-enyl carbonate (**2.81**; 0.4200g, 2 mmol), thiophenol (**2.31**; 0.2204g, 2 mmol) and CH_2Cl_2 (10 ml). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 400 psi. The mixture was stirred in the autoclave at 120°C (oil bath temperature) for 48 h. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation under reduced pressure. The subsequent purification by preparative TLC (silica gel F_{254}, eluant: n-hexane/ethyl acetate 10:1) gave *S*-phenyl 5-isopropenyl-2-methyl-2cyclohexene-1-carbothioate (0.4681g, 86%).

8.2.6. Palladium-Catalyzed Thiocarbonylation of Allylic Alcohols with Thiols and Carbon Monoxide

General Procedure: To a 45-ml Parr autoclave fitted with a glass liner and stirring bar were added $Pd(OAc)_2$ (0.0135g, 0.06 mmol), PPh_3 (0.0629g, 0.24 mmol), p-TsOH (0.0190g, 0.1 mmol), allylic alcohol (2 mmol), thiol (2 mmol) and CH_2Cl_2 (10 ml). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 400 psi. The mixture was stirred in the autoclave at 100-120°C (oil bath temperature) for 2 to 7 days. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation under reduced pressure. The residue was separated by preparative TLC (silica gel F_{254}, eluant: n-hexane/ethyl acetate 10:1). The yields and stereochemistry of the products are presented list in Table 2-4 and 2-5. The characterization data of the thiocarbonylation products are as follows:

***S*-Phenyl 4-methyl-3-pentenethioate (2.32)**: oil; IR (neat) 1708 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.70 (s, 3H), 1.78 (s, 3H), 3.35 (d, 2H, *J*=7.4 Hz), 5.36 (t, 1H, *J*=7.4 Hz), 7.40 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.10, 25.76, 43.10, 115.10, 127.76, 128.68, 129.07, 133.27, 137.82, 196.36; MS (EI) *m/z* 206 (M^+); HRMS calcd for $C_{12}H_{14}OS$ 206.0765, found 206.0790.

***S*-(4'-Bromophenyl) 4-methyl-3-pentenethioate (2.35)**: m.p.=74-75 °C; IR (KBr) 1708 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.68 (s, 3H), 1.78 (s, 3H), 3.32 (d, 2H, *J*=7.6 Hz), 5.32 (t, 1H, *J*=7.6 Hz), 7.25-7.50 (dd, 4H, *J*=8.5Hz, *J'*=2.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.14, 25.80, 43.14, 114.81, 123.88, 127.18, 132.14, 132.29, 135.91, 195.77; MS (EI) m/z 284 (M^+), 286 (M^++2); HRMS Calcd for $C_{12}H_{13}BrOS$:

283.9870. Found: 283.9867. Anal. Calcd for $C_{12}H_{13}BrOS$: C, 50.54, H, 4.59. Found: C, 50.60, H. 4.64.

***S*-(4'-Methoxyphenyl) 4-methyl-3-pentenethioate (2.37)**: oil; IR (neat) 1712 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.68 (s, 3H), 1.77 (s, 3H), 3.30 (d, 2H, J=7.5 Hz), 3.80 (s, 3H), 5.34 (t, 1H, J=7.5 Hz), 7.29-7.33 (dd, 4H, J=8.4 Hz, J'=2.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.09, 25.74, 42.92, 55.32, 114.82, 122.26, 129.24, 136.06, 136.33, 139.65, 197.30; MS (EI) m/z 236 (M^+); HRMS Calcd for $C_{13}H_{16}O_2S$: 236.0871. Found: 236.0862. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07, H, 6.82. Found: C, 65.98, H. 6.88.

***S*-(4'-Nitrophenyl) 4-methyl-3-pentenethioate (2.39)**: oil; IR (neat) 1706 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.78 (s, 3H), 1.81 (s, 3H), 3.33 (d, 2H, *J*=7.4 Hz), 5.34 (t, 1H, *J*=7.4 Hz), 7.15-7.40 (dd, 4H, *J*=8.5 Hz, *J'*=2.0 Hz); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 18.11, 25.77, 43.03, 114.95, 116.51, 136.47, 136.97, 137.93, 138.08, 196.40; MS (EI) m/z 251 (M^+); HRMS Calcd for $C_{12}H_{13}NO_3S$: 251.0633. Found: 251.0624; Anal. Calcd for $C_{12}H_{13}NO_3S$: C, 57.35; H, 5.21. Found: C, 57.42; H, 5.26.

***S*-Benzyl 4-methyl-3-pentenethioate (2.41)**: oil; IR (neat) 1704 cm^{-1} (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.80 (s, 3H), 1.84 (s, 3H), 3.40 (d, 2H, *J*=7.0 Hz), 4.13 (s, 2H), 5.38 (t, 1H, J=7.0 Hz), 7.34 (s, 5H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 17.03, 24.53, 33.63, 44.42, 113.90, 116.10, 126.25, 130.60, 132.27, 137.98, 198.27; MS (EI) m/z 220.1 (M^+); HRMS Calcd for $C_{13}H_{16}OS$: 220.0922. Found: 220.0931; Anal. Calcd for

$C_{13}H_{16}OS$: C, 70.88; H, 7.33. Found: C, 71.03; H, 7.62.

***S*-Octyl 4-methyl-3-pentenethioate (2.43)**: oil; IR (neat) 1711 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ 0.84 (t, 3H, *J*=6.9 Hz), 1.23-1.51 (m, 12H), 1.63 (s, 3H), 1.73 (s, 3H), 2.82 (t, 2H, *J*=7.4 Hz), 3.20 (d, 2H, *J*=7.4 Hz), 5.26 (t, 1H, *J*=7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.02, 17.97, 22.59, 25.68, 28.83, 28.90, 29.04, 29.10, 29.48, 31.75, 43.46, 115.65, 136.95, 198.47; MS (EI) m/z 242.1 (M+); HRMS Calcd. for C14H26OS: 242.1704. Found: 242.1708.

***S*-Decyl 4-methyl-3-pentenethioate (2.45)**: oil; IR (neat) 1709 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J*=6.2 Hz), 1.25-1.57 (m, 16H), 1.63 (s, 3H), 1.75 (s, 3H), 2.85 (t, 2H, *J*=6.0 Hz), 3.20 (d, 2H, *J*=8.0 Hz), 5.26 (t, 1H, *J*=8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.07, 17.95, 22.65, 25.68, 28.83, 29.09, 29.32, 29.46, 29.60, 30.76, 31.87, 42.42, 43.37, 115.58, 136.91, 198.44; MS (EI) m/z 270.2 (M^+); HRMS Calcd for $C_{16}H_{30}OS$: 270.2017. Found: 270.2021; Anal. Calcd for $C_{16}H_{30}OS$: C, 71.06; H, 11.19. Found: C, 71.26; H, 11.38.

***S*-Phenyl 3-pentenethioate (2.47)** (a mixture of stereoisomers): oil; IR (neat) 1710 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.67 (d, 1/6×3H, J=6.8 Hz), 1.74 (d, 5/6×3H, J=6.2 Hz), 3.40 (d, 5/6×2H, J=7.0 Hz), 3.48 (d, 1/6×2H, J=7.5 Hz), 5.50-6.18 (m, 2H), 7.38 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.33, 17.02, 38.20, 45.76, 118.97, 127.15, 130.01, 131.55, 132.59, 136.87, 198.24; MS (EI) m/z 192 (M^+); HRMS Calcd for $C_{11}H_{12}OS$: 192.0609. Found: 192.0623; Anal. Calcd for $C_{11}H_{12}OS$: C, 68.73; H, 6.30.

Found: C, 69.02; H, 6.18.

***S*-Phenyl 3,6-heptadienethioate (2.49)** (a mixture of stereoisomers); oil; IR (neat) 1706 cm^{-1} (C=O); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 2.82 (m, 2H), 3.35 (d, 9/10×2H, *J*=7.5 Hz), 3.40 (d, 1/10×2H, *J*=7.5 Hz), 5.04 (m, 2H), 5.57 (m, 3H), 7.38 (s, 5H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 31.80, 36.58, 42.06, 47.14, 115.73, 121.40, 122.16, 127.80, 129.16, 129.35, 134.03, 134.50, 136.07, 196.00; MS (EI) m/z 218 (M^+); HRMS Calcd for $C_{13}H_{14}OS$: 218.0782. Found: 218.0784; Anal. Calcd for $C_{13}H_{14}OS$: C, 71.52; H, 6.46. Found: C, 71.56; H, 6.44.

***S*-Phenyl 3-heptenethioate (2.51)** (a mixture of stereoisomers): oil; IR (neat) 1708 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.87 (t, 3H, J=7.5 Hz), 1.29-1.39 (m, 2H), 2.10-2.19 (m, 2H), 3.33 (d, 4/5×2H, J=7.0 Hz), 3.44 (d, 1/5×2H, J=7.2 Hz), 5.17-5.19 (m, 1/5×1H), 5.46-5.51 (m, 4/5×1H), 5.88-6.10 (m, 1H), 7.40 (s, 5H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.33, 23.10, 28.67, 32.18, 37.34, 44.12, 118.98, 129.23, 131.07, 131.24, 133.08, 136.21, 196.89; MS (EI) m/z 220.1 (M^+); HRMS Calcd for $C_{13}H_{16}OS$: 220.0922. Found: 220.0928; Anal. Calcd for $C_{13}H_{16}OS$: C, 70.88; H, 7.33. Found: C, 70.37; H, 7.54.

***S*-Phenyl 4-phenyl-3-butenethioate (2.55)**: oil; IR (neat) 1711 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.55 (d, 2H, *J*=7.0 Hz), 5.92-6.18 (m, 1H), 6.32 (d, 1H, *J*=15.0 Hz), 7.18-7.36 (m, 10H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 46.42, 124.79, 126.67,

126.98, 127.00, 127.14, 127.35, 127.89, 128.24, 128.43, 128.74, 128.82, 128.90, 128.95, 197.66; MS (EI) m/z 254 (M^+); HRMS Calcd for $C_{16}H_{14}OS$: 254.3460. Found: 254.3398; Anal. Calcd for $C_{16}H_{14}OS$: C, 75.56; H, 5.55. Found: C, 75.62; H, 5.59.

***S*-Phenyl 4, 8-dimethyl-3, 7-nonadienethioate (2.57)** (a mixture of stereoisomers); oil; IR (neat) 1707 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.64 (s, 3H), 1.72 (s, 3H), 1.81 (s, 3/4×3H), 1.84 (s, 1/4×3H), 2.12-2.13 (m, 4H), 3.38 (d, 3/4×2H, *J*=7.0 Hz), 3.40 (d, 1/4×2H, *J*=7.0 Hz), 5.14-5.20 (m, 1H), 5.39 (t, 1H, *J*=7.0 Hz), 7.41 (s, 5H). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 16.50, 17.71, 22.37, 25.57, 25.73, 26.32, 39.04, 39.64, 43.07, 114.96, 115.64, 123.71, 123.87, 128.03, 129.10, 129.21, 131.71, 134.47, 141.41, 196.40; MS (EI) m/z 274 (M^+); HRMS Calcd for $C_{17}H_{22}OS$: 274.1408. Found: 274.1413; Anal. Calcd for $C_{17}H_{22}OS$: C, 74.41; H, 8.08. Found: C, 74.49; H, 8.14.

***S*-Phenyl 2-methyl-3-pentenethioate (2.59)** (a mixture of stereoisomers); oil; IR (neat) 1703 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.32 (d, 3H, *J*=7.0 Hz), 1.76 (m, 3H), 3.37 (m, 5/6×1H), 3.75 (m, 1/6×1H), 5.50-5.78 (m, 2H), 7.40 (s, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 17.56, 17.78, 18.00, 46.45, 51.66, 119.68, 127.72, 128.01, 128.85, 129.01, 129.11, 129.23, 131.47, 134.47, 199.61; MS (EI) m/z 206 (M^+); HRMS Calcd for $C_{12}H_{14}OS$: 206.0765. Found: 206.0758. Anal. Calcd for $C_{12}H_{14}OS$: C, 69.86; H, 6.84. Found: C, 69.92, H, 6.90.

***S*-Phenyl 3-butenethioate (2.61)**: oil; IR (neat) 1704 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.31 (dt, 2H, J=7.0 Hz, J'=1.3 Hz), 5.13-5.22 (m, 2H), 5.77-5.98 (m,

1H), 7.33 (s, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 48.18, 120.21, 129.35, 129.43, 129.68, 130.11, 134.52, 195.18; MS (EI) m/z 178 (M^+); HRMS Calcd for $C_{10}H_{10}OS$: 178.0452. Found: 178.0458. Anal. Calcd for $C_{10}H_{10}OS$: C, 67.42; H, 5.62. Found: C, 67.56, H, 5.31.

S-Phenyl 3-decenethioate (2.64): oil; IR (neat) 1710 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.1 Hz), 1.26-1.34 (m, 8H), 2.05-2.11 (m, 1H), 2.23-2.26 (m, 1H), 3.32 (dd, 2H, J=7.0 Hz, J'=1.0 Hz), 5.55-5.70 (m, 2H), 7.45 (s, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 14.03, 22.58, 28.43, 28.91, 28.94, 32.51, 47.25, 120.71, 127.97, 129.26, 134.47, 135.07, 135.68, 136.98, 142.24, 196.03; MS (EI) m/z 262 (M^+); HRMS Calcd for $C_{16}H_{22}OS$: 262.1391. Found: 262.1381. Anal. Calcd for $C_{16}H_{22}OS$: C, 73.24; H, 8.46. Found: C, 73.31, H, 8.52.

***S*-Phenyl 5-benzyloxy-3-pentenethioate (2.66)** (a mixture of stereoisomers); oil; IR (neat) 1710 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.47 (d, 6/7×2H, *J*=7.0 Hz), 3.50 (d, 1/7×2H, *J*=7.0 Hz), 4.14 (d, 2H, *J*=7.0 Hz), 4.22 (s, 2H), 5.54-5.60 (m, 2H), 7.36-7.54 (m, 10H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 43.27, 45.36, 51.60, 52.78, 54.95, 115.17, 117.82, 121.44, 123.65, 123.78, 124.76, 125.02, 127.76, 127.85, 128.43, 133.08, 197.04; MS (EI) m/z 298 (M^+); HRMS Calcd for $C_{18}H_{18}O_2S$: 298.1044. Found: 298.1032. Anal. Calcd for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08. Found: C, 72.47; H, 6.12.

***S*-Phenyl 5-(2'-propenyl)-2-methyl-2-cyclohexene-1-carbothioate (2.73)**; oil; IR (neat) 1703 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.43-1.58 (m, 2H), 1.72 (s, 3H), 1.76 (s, 3H), 1.88-2.37 (m, 4H), 4.72 (s, 2H), 5.70 (t, 1H, *J*=7.4 Hz); 7.36-7.40 (m,

5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.11, 28.07, 29.27, 32.90, 48.44, 50.98, 125.75, 126.79, 128.56, 128.81, 128.95, 129.14, 129.29, 131.66, 134.44, 197.23; MS (EI) m/z 272 (M^+); HRMS Calcd for $C_{17}H_{20}OS$: 272.1252. Found: 272.1246. Anal. Calcd for $C_{17}H_{20}OS$: C, 74.96; H, 7.40. Found: C, 74.98; H, 7.46.

***S*-Phenyl 2-cyclohexene-1-carbothioate (2.75)**; oil; IR (neat) 1701 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.92-2.08 (m, 6H), 3.30-3.38 (m, 1H), 5.78-5.84 (m, 1H), 5.94-6.02 (m, 1H), 7.38 (s, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 20.44, 24.70, 26.27, 49.92, 123.36, 127.98, 129.09, 129.18, 131.50, 134.55, 199.77; MS (EI) m/z 218 (M^+); HRMS Calcd for $C_{13}H_{14}OS$: 218.0782. Found: 218.0764. Anal. Calcd for $C_{13}H_{14}OS$: C, 71.52; H, 6.46. Found: C, 71.44; H, 6.50.

***S*-Phenyl 2-[4-(2'-propenyl)-1-cyclohexene]-acethioate (2.78)**; oil; IR (neat) 1708 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.05-1.12 (m, 2H), 1.26 (s, 3H), 2.08-2.26 (m, 5H), 3.30 (s, 2H), 4.74 (br. s, 2H), 5.74 (t, 1H, *J*=7.4 Hz), 7.35-7.43 (m, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 20.77, 27.62, 28.96, 30.90, 40.49, 52.11, 108.76, 127.33, 129.10, 129.24, 130.46, 134.43, 149.55, 195.96; MS (EI) m/z 272 (M^+); HRMS Calcd for $C_{17}H_{20}OS$: 272.1252. Found: 272.1255. Anal. Calcd for $C_{17}H_{20}OS$: C, 74.96; H, 7.40. Found: C, 74.98; H, 7.46.

***S*-Phenyl 6,6-dimethylbicyclo[3,1,1]hept-3-ene-2-carbothioate (2.80)**; oil; IR (neat) 1707 cm^{-1} (C=O); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.92 (s, 3H), 1.30 (s, 3H), 1.50 (t, 1H, *J*=7.0 Hz), 1.75 (s, 3H), 2.05 (t, 1H, *J*=7.0 Hz), 2.25-2.40 (m, 2H), 4.02(m, 1H), 5.33

(d, 1H, *J*=7.5 Hz), 7.26-7.45 (m, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 20.53, 22.88, 26.44, 29.01, 42.34, 45.58, 47.38, 50.55, 116.40, 126.30, 128.77, 130.93, 136.22, 147.64, 197.88; MS (EI) m/z 272 (M^+); HRMS Calcd for $C_{17}H_{20}OS$: 272.1252. Found: 272.1247. Anal. Calcd for $C_{17}H_{20}OS$: C, 74.96; H, 7.40. Found: C, 74.88; H, 7.48.

***S*-Phenyl 5-(2'-hydroxy-2'-propyl)-2-methyl-2-cyclohexene-1-carbothioate (2.83)**; m.p.64.5-66°C; IR (KBr) 1713 cm^{-1} (C=O), 3300-3500 cm^{-1} (OH); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.08 (s, 6H), 1.22-1.32 (m, 1H), 1.68-1.76 (m, 5H), 1.86-1.92 (m, 1H), 1.94-2.06 (m, 1H), 3.74 (m, 1H), 3.83 (br. s, 1H), 5.48 (t, 1H, *J*=7.50 Hz), 7.27-7.30 (m, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 21.78, 26.13, 26.27, 33.00, 38.02, 47.10, 66.82, 115.10, 123.98, 127.76, 128.69, 129.07, 134.27, 199.04; MS (EI) m/z 290 (M^+); HRMS Calcd for $C_{17}H_{22}O_2S$: 290.1357. Found: 290.1348. Anal. Calcd for $C_{17}H_{22}O_2S$: C, 70.31; H, 7.64. Found: C, 70.27; H, 7.68.

***S*-Phenyl 4a-hydroxymethyl-2,3,4,4a,5,6,7,8-octahydronaphthalene-2-carbothioate (2.84)**; m.p. 102-104°C; IR (KBr) 1710 cm^{-1} (C=O), 3300-3500 cm^{-1} (OH); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.80-2.20 (m, 12H), 1.54 (s, 1H), 3.25-3.36 (m, 1H), 3.36 (s, 2H), 5.60 (d, *J*=7.0 Hz, 1H), 7.35-7.43 (m, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.66, 28.12, 33.94, 34.08, 34.42, 37.43, 43.44, 64.27, 68.86, 117.61, 124.01, 128.87, 129.14, 130.88, 143.55, 196.95; MS (EI) m/z 302 (M^+); HRMS Calcd for $C_{18}H_{22}O_2S$: 302.1357. Found: 302.1352. Anal. Calcd for $C_{18}H_{22}O_2S$: C, 71.49; H, 7.33. Found: C, 71.52; H, 7.37.

***S*-Phenyl 4-trimethylsilyl-4a-hydroxymethyl-2,3,4,4a,5,6,7,8-octahydronaphthalene-2-carbothioate (2.85)**; m.p. 137-139°C; IR (KBr) 1713 cm^{-1} (C=O), 3300-3500 cm^{-1} (OH); ^{1}H-NMR (200 MHz, $CDCl_3$) δ 0.09 (s, 9H), 0.86-2.50 (m, 11H), 1.52 (s, 1H), 3.33-3.44 (m, 1H), 3.66 (s, 2H), 5.66 (d, *J*=7.0 Hz, 1H), 7.36-7.42 (m, 5H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ -0.14, 21.98, 25.09, 28.09, 31.76, 32.49, 33.76, 45.23, 64.72, 68.78, 126.91, 128.38, 129.08, 134.14, 135.14, 141.86, 142.71, 199.20; MS (EI) m/z 374 (M^+); HRMS Calcd for $C_{21}H_{30}O_2SSi$: 374.1753. Found: 374.1748. Anal. Calcd for $C_{21}H_{30}O_2SSi$: C, 67.33; H, 8.07. Found: C, 67.35; H, 8.11.

8.3. Experimental for Chapter 3

8.3.1. Synthesis of Starting Materials

8.3.1.1. Synthesis of Propargylic Alcohols

1-(1-Propynyl)cyclohexanol. A 500-ml flask was charged with 120 ml of THF-EDA (3:1) and 140 ml of 1-propynylmagnesium bromide (0.5 M, 0.07 mol). Cyclohexanone (6.6 ml, 0.064 mol) was added over 30 min at room temperature. The mixture was stirred for an additional hour and then hydrolyzed with excess water. The aqueous solution was extracted with diethyl ether three times. The organic phase was dried over anhydrous Na_2SO_4, filtered, and the solvent was removed using a rotary evaporator. Distillation of the crude product gave 5.92g of the title compound, 67% yield, mp 47-49 °C (lit.[183] value 49.5 °C). IR (neat) 3300-3500 cm^{-1} (OH); ^{1}H-NMR (200

MHz, $CDCl_3$) δ 1.22-1.44 (m, 6H), 1.82 (s, 3H), 2.47 (s, 1H), 2.78-3.05 (m, 4H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 12.73, 22.54, 26.05, 44.17, 68.33, 87.93, 92.12; MS (EI) m/z 138.1 (M^+).

1-Phenyl-prop-2-yn-1-ol. Following the known procedure,[213] reaction of benzaldehyde (10.6g, 0.1 mol) and the lithium acetylide-ethylenediamine (EDA) complex (11.05g, 90%, 0.12 mol) in THF at -78 °C gave 7.66g of 1-phenyl-prop-2-yn-1-ol, 58% yield. IR (neat) 3300-3500 cm^{-1} (OH); ^1H NMR (200 MHz, $CDCl_3$) δ 2.67 (d, 1H, J=1.2 Hz), 2.71 (s, 1H), 5.44 (d, 1H, J=1.2 Hz), 7.34-7.42 (m, 3H), 7.53-7.57 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 64.21, 74.80, 83.43, 126.56, 128.44, 128.58, 139.91; MS (EI) m/z 132 (M^+).

3,5-Dimethyl-1-hexyn-3-ol. Following the known procedure,[183] reaction of 4-methyl-2-pentanone (10.01g, 0.1 mol) and the lithium acetylide-ethylenediamine (EDA) complex (11.05g, 90%, 0.12 mol) in THF at -78 °C to room temperature gave 9.21g of 3,5-Dimethyl-1-hexyn-3-ol in 73% yield. IR (neat) 3300-3500 cm^{-1} (OH); ^1H-NMR (200 MHz, $CDCl_3$) δ 1.03 (d, 6H, J=7.2 Hz), 1.51 (s, 3H), 1.60 (d, 2H, J=8.0 Hz), 1.90-1.98 (m, 1H), 2.22 (s, 1H), 2.46 (s, 1H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 23.98, 24.02, 25.78, 32.00, 51.87, 67.98, 71.74, 88.23; MS (EI) m/z 126.1 (M^+).

8.3.1.2. Synthesis of Propargylic Mesylates

General Procedure: To a solution of the propargylic alcohol (0.05 mol) in 50 ml of THF at -78 °C was added 25 ml of butyllithium in cyclohexane (2.0 M) and

methanesulfonyl chloride (4.0 ml, 0.052 mol). After 30 min, the mixture was stirred at room temperature for another 30 min. Then water was added and the organic layer was extracted with ether. Drying, concentration, and chromatographic separation (10% ethyl acetate in hexane as eluant) gave the corresponding propargylic mesylate. The yields of products were list in Table 3-2. The characterization data of the mesylates are as follows:

1,1-Dimethyl-prop-2-ynyl methanesulfonate (3.27): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.54 (s, 6H), 2.44 (s, 1H), 2.81 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 32.71, 41.63, 65.23, 71.71, 86.39; MS (EI) m/z 162 (M^+).

1-Ethyl-1-methyl-prop-2-ynyl methanesulfonate (3.29): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.14 (t, 3H, J=7.5 Hz), 1.57 (s, 3H), 1.70 (q, 2H, J=7.5 Hz), 2.44 (s, 1H), 2.83 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 8.84, 29.52, 36.17, 41.43, 68.83, 72.00, 87.36; MS (EI) m/z 176.1 (M^+).

1-Phenyl-prop-2-ynyl methanesulfonate (3.31): ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.67 (s, 1H), 2.88 (s, 3H), 5.53 (s, 1H), 7.44-7.56 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 46.37, 69.02, 78.91, 82.76, 124.42, 126.78, 130.05, 144.29; MS (EI) m/z 210.0 (M^+); HRMS Calcd for $C_{10}H_{10}O_3S$: 210.0351. Found: 210.0357.

1-Methyl-prop-2-ynyl methanesulfonate (3.33): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.46 (d, 3H, J=7.0 Hz), 2.49 (s, 1H), 2.83 (s, 3H), 4.56 (q, 1H, J=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.01, 41.76, 58.31, 72.10, 86.13; MS (EI) m/z 148.0 (M^+).

1-Isobutyl-1-methyl-prop-2-ynyl methanesulfonate (3.35): ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.99 (d, 6H, J=7.0 Hz), 1.53 (s, 3H), 1.61 (d, 2H, J=7.5), 1.92-1.98 (m, 1H), 2.45 (s, 1H), 2.84 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.17, 25.47, 30.99, 41.69, 51.87, 68.03, 71.44, 88.34; MS (EI) m/z 204.1 (M^+).

1-Ethynyl-cyclohexyl methanesulfonate (3.37): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.28-1.54 (m, 8H), 1.61-1.87 (m, 2H), 2.68 (s, 1H), 2.89 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.38, 25.57, 44.86, 68.39, 74.97, 87.08; MS (EI) m/z 202.1 (M^+).

1-Prop-1-ynyl-cyclohexyl methanesulfonate (3.39): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.26-1.49 (m, 8H), 1.60-1.96 (m, 2H), 1.87 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 7.08, 22.57, 24.89, 38.07, 41.24, 75.39, 82.44, 85.63; MS (EI) m/z 216.3 (M^+).

1-Methyl-but-2-ynyl methanesulfonate (3.41): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.38 (d, 3H, J=7.0 Hz), 1.84 (s, 3H), 2.86 (s, 3H), 4.76 (q, 1H, J=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 6.27, 21.38, 42.95, 67.31, 74.52, 81.37; MS (EI) m/z 162.0 (M^+).

1,1-Dimethyl-3-phenyl-prop-2-ynyl methanesulfonate (3.43): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.63 (s, 3H), 1.72 (s, 3H), 2.92 (s, 3H), 7.27-7.33 (m, 3H), 7.48-7.64 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.03, 29.47, 40.99, 70.32, 83.77, 89.18, 123.57,

125.90, 127.45, 130.01; MS (EI) m/z 238.1 (M^+).

But-2-ynyl methanesulfonate (3.45): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.64 (s, 3H), 2.84 (s, 3H), 4.87 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 5.78, 41.38, 58.02, 79.14, 82.18; MS (EI) m/z 148.0 (M^+).

8.3.2 Reaction of 2-Methyl-3-Butyn-2-ol (3.26) with Thiophenol and CO. Demonstration of Process

In a 45-ml stainless-steel autoclave were placed palladium complex (0.06 mmol), triphenylphosphine (0.0629g, 0.24 mmol, if used) or dppp (0.12 mmol, if used), *p*-TsOH (0.0190g, 0.1 mmol, if used), 2-methyl-3-butyn-2-ol (**3.26**; 0.1717g, 98%, 2 mmol), thiophenol (**3.49**; 0.2204g, 2 mmol),and THF (5 ml). After carbon monoxide was introduced up to 400 psi, the mixture was stirred at 100 °C for 48 h. The results are given in Table 3-3.

8.3.3 Palladium-Catalyzed Thiocarbonylation of 3.26. Optimization of Reaction Conditions

*8.3.3.1 Thiocarbonylation of **3.26** with [$Pd(PPh_3)_4$]*

In a 45-ml stainless-steel autoclave were placed [$Pd(PPh_3)_4$] (0.0693g, 0.06 mmol), 2-methyl-3-butyn-2-ol (**3.26**; 0.1717g, 98%, 2 mmol), thiophenol (**3.49**; 0.2204g, 2 mmol),and THF (5 ml). After carbon monoxide was introduced up to 400 psi, the

mixture was stirred at 100 °C for 48 h. The result is listed in entry 1 of Table 3-4.

*8.3.3.2 Thiocarbonylation of **3.26** with Pd-Complexes and p-TsOH*

In a 45-ml stainless-steel autoclave were placed [$Pd(PPh_3)_4$] (0.0693g, 0.06 mmol) or $Pd(OAc)_2$ (0.0135g, 0.06 mmol) with PPh_3 (0.0629g, 0.24 mmol), *p*-TsOH (0.0190g, 0.1 mmol), 2-methyl-3-butyn-2-ol (**3.26**; 0.1717g, 98%, 2 mmol), thiophenol (**3.49**; 0.2204g, 2 mmol),and THF (5 ml). After carbon monoxide was introduced up to 400 psi, the mixture was stirred at 100 °C for 48 h. The results are listed in entries 2 and 3 of Table 3-4.

*8.3.3.3 Thiocarbonylation of **3.26** with [$Pd(PPh_3)_4$] in DME*

In a 45-ml stainless-steel autoclave were placed [$Pd(PPh_3)_4$] (0.0693g, 0.06 mmol) with dppb (0.0512g, 0.12 mmol, if used), 2-methyl-3-butyn-2-ol (**3.26**; 0.1717g, 98%, 2 mmol), thiophenol (**3.49**; 0.2204g, 2 mmol),and THF (5 ml). After carbon monoxide was introduced up to 400 or 250 psi, the mixture was stirred at 90 or 100 °C for 48 h. The results are listed in entries 4 to 6 of Table 3-4.

*8.3.3.4 Thiocarbonylation of **3.26** with Two Equivalents of **3.49***

In a 45-ml stainless-steel autoclave were placed [$Pd(PPh_3)_4$] (0.0693g, 0.06 mmol) or $Pd(OAc)_2$ (0.0135g, 0.06 mmol) with PPh_3 (0.0629g, 0.24 mmol), *p*-TsOH (0.0190g, 0.1 mmol), 2-methyl-3-butyn-2-ol (**3.26**; 0.1717g, 98%, 2 mmol), thiophenol (**3.49**; 0.4408g, 4 mmol),and solvent (THF or toluene, 5 ml). After carbon monoxide was gradually introduced up to the desired pressure level (400, 600, or 800 psi), the mixture

was stirred at the appropriate temperature (110 or 150 °C) for 48 h. The results are listed in entries 7-11 of Table 3-4.

8.3.4 Palladium-Catalyzed Thiolactonization of Propargylic Alcohols to Thio-2(5H)-Furanones

General Procedure: An autoclave, its glass liner and a magnetic stirring bar were dried in an oven and cooled in a dry box. The liner was charged with $[Pd(PPh_3)_4]$ (0.0693g, 0.06 mmol) and dppb (0.0512g, 0.12 mmol). The propargylic alcohol (2 mmol), thiol (2 mmol) and 5 ml of DME were then added to the liner. An additional amount of DME (from 1-2 ml) was placed in the autoclave prior to insertion of the liner. The gauge and gauge block assembly were attached. The CO line was flushed 3 times with CO and the system was also pressurized and flushed 3 times with CO, gradually increasing the pressure to 250 psi. The autoclave was then placed in the center of an oil bath on a heater stirrer preset to 90 °C. After 48 hours, the autoclave was removed from the oil bath and allowed to cool to room temperature. The excess gas was discharged and the system disassembled. The reaction mixture was filtered through Florisil and washed with diethyl ether. The solvent was removed by rotary evaporation under reduced pressure. The residue was separated by preparative TLC or HPLC. The results are listed in Table 3-5. The characterization data of the 2(*5H*)-furanones are as follows:

5,5-Dimethyl-4-phenylthio-2(*5H*)-furanone (3.50): oil; IR (neat) 1759 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.58 (s, 6H), 5.12 (s, 1H), 7.42-7.60 (m, 5H); ^{13}C NMR (125

MHz, $CDCl_3$) δ 26.54, 86.23, 109.54, 127.89, 129.33, 130.38, 134.51, 169.95, 177.93; MS (EI) m/z 220 (M^+); HRMS Calcd for $C_{12}H_{12}O_2S$: 220.0558. Found: 220.0563. Anal. Calcd for $C_{12}H_{12}O_2S$: C, 65.44; H, 5.50. Found: C, 65.71; H, 5.38.

4-(4-Fluoro-phenylthio)-5,5-dimethyl-2(*5H*)-furanone (3.55): oil; IR (neat) 1762 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.57 (s, 6H), 5.13 (s, 1H), 7.5 (dd, 4H, J=8.0 Hz, J'=1.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.51, 86.21, 109.84, 125.20, 126.92, 133.35, 135.99, 169.62, 176.96; MS (EI) m/z 238 (M^+); HRMS Calcd for $C_{12}H_{11}FO_2S$: 238.0464. Found: 238.0473. Anal. Calcd for $C_{12}H_{11}FO_2S$: C, 60.49; H, 4.66. Found: C, 60.71; H, 4.39.

5,5-Dimethyl-4-p-tolylthio-2(*5H*)-furanone (3.57): oil; IR (neat) 1758 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.58 (s, 6H), 2.12 (s, 3H), 5.16 (s, 1H), 7.23-7.30 (m, 2H), 7.38-7.46 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.03, 28.76, 86.23, 110.54, 127.89, 130.01, 130.44, 135.07, 167.37, 178.24; MS (EI) m/z 234 (M^+); HRMS Calcd for $C_{13}H_{14}O_2S$: 234.0715. Found: 234.0721. Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.65; H, 6.03. Found: C, 66.72; H, 6.10.

5,5-Dimethyl-4-octylthio-2(*5H*)-furanone (3.59): oil; IR (neat) 1759 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, 3H, J=7.0 Hz), 1.22-1.34 (m, 10 H), 1.48 (s, 6H), 1.73 (q, 2H, J=7.0 Hz), 2.87 (t, 2H, J=7.0 Hz), 5.56 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.67, 23.20, 27.06, 27.28, 28.49, 29.21, 29.43, 29.60, 29.65, 32.30, 33.53, 87.38, 108.44, 177.69; MS (EI) m/z 256 (M^+); HRMS Calcd for $C_{14}H_{24}O_2S$: 256.1497. Found:

256.1492. Anal. Calcd for $C_{14}H_{24}O_2S$: C, 65.59; H, 9.44. Found: C, 65.78; H, 9.60.

5,5-Dimethyl-4-furfurylthio-2(*5H*)-furanone (3.61): oil; IR (neat) 1761 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.47 (s, 6H), 4.16 (s, 2H), 5.74 (s, 1H), 6.33 (dd, 2H, J=7.6 Hz, J'=1.8 Hz), 7.38 (d, 1H, J=1.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.34, 29.63, 87.00, 108.36, 108.94, 110.12, 143.18, 148.02, 169.98, 175.18; MS (EI) m/z 224 (M^+); HRMS Calcd for $C_{11}H_{12}O_3S$: 224.0507. Found: 224.0518. Anal. Calcd for $C_{11}H_{12}O_3S$: C, 58.92; H, 5.40. Found: C, 56.07; H, 5.38.

4-Phenylthio-2(*5H*)-furanone (3.63): oil; IR (neat) 1759 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.72 (s, 2H), 5.76 (s, 1H), 7.39-7.48 (m, 3H), 7.63-7.66 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 73.51, 115.60, 123.32, 130.01, 130.10, 136.00, 164.50, 171.87; MS (EI) m/z 192.0 (M^+); HRMS Calcd for $C_{10}H_8O_2S$: 192.0245. Found: 192.0253. Anal. Calcd for $C_{10}H_8O_2S$: C, 62.49; H, 4.20. Found: C, 62.57; H, 4.08.

5-Methyl-4-phenylthio-2(*5H*)-furanone (3.64): oil; IR (neat) 1758 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.55 (d, 3H, J=7.2 Hz), 5.06 (q, 1H, J=7.2 Hz), 5.26 (s, 1H), 7.45-7.55 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.93, 79.20, 110.75, 127.86, 130.15, 130.48, 134.48, 163.42, 173.73; MS (EI) m/z 206 (M^+); HRMS Calcd for $C_{11}H_{10}O_2S$: 206.0402. Found: 206.0431. Anal. Calcd for $C_{11}H_{10}O_2S$: C, 64.07; H, 4.89. Found: C, 64.11; H, 4.67.

4-Phenylthio-1-oxaspiro[4.4]-3-nonen-2-one (3.66): mp 59-61 °C (a white

solid); IR (KBr) 2966, 1754 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.90-2.10 (m, 8H), 5.14 (s, 1H), 7.40-7.60 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.97, 38.49, 96.19, 110.41, 127.88, 130.03, 134.57, 170.14, 175.32; MS (EI) m/z 246 (M^+); HRMS Calcd for $C_{14}H_{14}O_2S$: 246.0715. Found: 246.0718. Anal. Calcd for $C_{14}H_{14}O_2S$: C, 68.27; H, 5.73. Found: C, 68.33; H, 5.69.

4-Phentlthio-1-oxaspiro[4.5]-3-decen-2-one (3.67): mp 71-74 °C; IR (KBr) 1740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.65-2.05 (m, 8H), 2.07-2.26 (m, 2H), 5.28 (s, 1H), 7.35-7.51 (m, 3H), 7.61-7.64 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.06, 24.46, 36.21, 89.27, 114.36, 124.73, 130.08, 130.22, 136.11, 170.36, 176.22; MS (EI) m/z 260.1 (M^+); HRMS Calcd for $C_{15}H_{16}O_2S$: 260.0871. Found: 260.0873. Anal. Calcd for $C_{15}H_{16}O_2S$: C, 69.21; H, 6.20. Found: C, 69.42; H, 6.08.

3-Methyl-4-phentlthio-1-oxaspiro[4.5]-3-decen-2-one (3.68): mp 101-103 °C; IR (KBr) 1747 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.65-2.05 (m, 10 H), 2.13 (s, 3H), 7.24-7.68 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.24, 22.32, 25.00, 36.44, 88.91, 114.67, 124.54, 130.03, 130.97, 136.85, 169.72, 177.36; MS (EI) m/z 274.1 (M^+); HRMS Calcd for $C_{16}H_{18}O_2S$: 274.1028. Found: 274.1013. Anal. Calcd for $C_{16}H_{18}O_2S$: C, 70.05; H, 6.62. Found: C, 70.21; H, 6.48.

5-Phenyl-4-phenylthio-2(*5H*)-furanone (3.69): oil; IR (neat) 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.43 (s, 1H), 6.04 (s, 1H), 7.33-7.52 (m, 10 H); ^{13}C NMR (50

MHz, $CDCl_3$) δ 86.28, 111.27, 123.98, 126.90,127.03, 127.44, 128.67, 132.54, 137.18, 169.21, 179.55; MS (EI) m/z 268 (M^+); HRMS Calcd for $C_{16}H_{12}O_2S$: 268.0559. Found: 268.0563. Anal. Calcd for $C_{16}H_{12}O_2S$: C, 71.63; H, 4.51. Found: C, 71.79; H, 4.38.

5-Isobutyl-5-methyl-4-phenylthio-2(*5H*)-furanone (3.70): oil; IR (neat) 1759 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.96 (d, 6H, J=6.5 Hz), 1.58 (s, 3H), 1.73-1.79 (m, 1H), 2.87 (d, 2H, J=7.0 Hz), 6.28 (s, 1H), 7.36-7.48 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.18, 24.41, 25.97. 48.12, 83.37, 109.12, 125.78, 127.01, 127.56, 135.28, 171.54, 179.41; MS (EI) m/z 262.1 (M^+); HRMS Calcd for $C_{15}H_{18}O_2S$: 262.1028. Found: 262.1017. Anal. Calcd for $C_{15}H_{18}O_2S$: C, 68.68; H, 6.92. Found: C, 69.03; H, 6.68.

3-Methyl-4-phenylthio-2(*5H*)-furanone (3.71): oil; IR (neat) 1763 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.97 (s, 3H), 4.12 (s, 2H), 7.34-7.50 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.71, 74.28, 121.00, 123.17, 127.08, 127.31, 135.44, 168.70, 171.73; MS (EI) m/z 206 (M^+); HRMS Calcd for $C_{11}H_{10}O_2S$: 206.0402. Found: 206.0417. Anal. Calcd for $C_{11}H_{10}O_2S$: C, 64.07; H, 4.89. Found: C, 64.27; H, 4.73.

5,5-Dimethyl-3-phenyl-4-phenylthio-2(*5H*)-furanone (3.72): mp 56-59 °C; IR (KBr) 1749 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.58 (s, 3H), 7.24-7.31 (m, 1H), 7.45-7.55 (m, 7H), 7.64-7.70 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.07, 86.52, 123.31, 127.01, 127.36, 127.74, 127.88, 129.23, 129.39, 137.04, 169.05,, 178.73; MS (EI) m/z 296.1 (M^+); HRMS Calcd for $C_{18}H_{16}O_2S$: 296.0871. Found: 296.0877. Anal. Calcd for $C_{18}H_{16}O_2S$: C, 72.95; H, 5.45. Found: C, 73.04; H, 5.68.

3-Butyl-5,5-dimethyl-4-phenylthio-2(*5H*)-furanone (3.74): oil; IR (neat) 1763 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, 3H, J=7.0 Hz), 1.28-1.50 (m, 4H), 1.58 (s, 6H), 2.74 (t, 2H, J=7.2 Hz), 7.45-7.55 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.73, 22.45, 27.68, 30.01, 30.56, 32.00, 86.23, 118.90, 127.04, 126.71, 128.88, 135.42, 168.03, 176.49; MS (EI) m/z 276.1 (M^+); HRMS Calcd for $C_{16}H_{20}O_2S$: 276.1184. Found: 276.1203. Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.54; H, 7.30. Found: C, 69.38; H, 7.51.

8.3.5 Palladium-Catalyzed Dithiocarbonylation of Propargylic Compounds to Dithioesters

8.3.5.1 Palladium-Catalyzed Dithiocarbonylation of Propargylic Alcohols

The general procedure decribed in Section 8.3.4 was followed with propargylic alcohols (2 mmol), thiol (4 mmol), [$Pd(PPh_3)_4$] (0.0693g, 0.06 mmol) and *p*-TsOH (0.0190g, 0.1 mmol) in 5 ml of toluene under 600 psi of carbon monoxide at 110 °C.

8.3.5.2 Palladium-Catalyzed Dithiocarbonylation of Propargylic Mesylates

The general procedure decribed in Section 8.3.4 was followed with propargylic mesylate (2 mmol), thiol (4 mmol) and [$Pd(PPh_3)_4$] (0.0693g, 0.06 mmol) in 5 ml of THF under 400 psi of carbon monoxide at 90 °C. The results are listed in Table 3-6. The structures of the dithioesters obtained were characterized unambiguously on the basis of analytical and spectral data.

2-Isopropylidene-dithiosuccinic acid di-*S*-phenyl ester (3.52): oil; IR (neat) 1703, 1676 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.92 (s, 3H), 2.14 (s, 3H), 3.81 (s, 2H), 7.40-7.55 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.79, 23.90, 45.28, 118.42, 129.67, 129.82, 130.00, 130.08, 132.56, 133.74, 134.76, 134.93, 135.43, 138.45, 148.59, 192.47, 195.17; MS (EI) m/z 342 (M^+); HRMS Calcd for $C_{19}H_{18}O_2S_2$: 342.0748. Found: 342.0741. Anal. Calcd for $C_{19}H_{18}O_2S_2$: C, 66.65; H, 5.30. Found: C, 66.72; H, 5.48.

2-Isopropylidene-dithiosuccinic acid bis-*S*-(4-fluoro-phenyl) ester (3.87): oil; IR (neat) 1707, 1672 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.94 (s, 3H), 2.12 (s, 3H), 3.80 (s, 2H), 7.08-7.44 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.85, 24.19, 45.13, 116.91, 117.35, 127.26, 127.91, 133.42, 134.78, 137.11, 137.28, 137.57, 149.18, 161.64, 166.62, 195.14, 202.99; MS (EI) m/z 378 (M^+); HRMS Calcd for $C_{19}H_{16}F_2O_2S_2$: 378.0560. Found: 378.0554. Anal. Calcd for $C_{19}H_{18}F_2O_2S_2$: C, 60.31; H, 4.27. Found: C, 60.65; H, 4.33.

2-Isopropylidene-dithiosuccinic acid di-*S*-*p*-tolyl ester (3.88): oil; IR (neat) 1711, 1684 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.87 (s, 6H), 1.93 (s, 3H), 2.15 (s, 3H), 3.86 (s, 2H), 7.08-7.17 (m, 4H), 7.35-7.44 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.81, 22.05, 22.31, 45.33, 116.98, 131.04, 131.83, 132.00, 132.78, 136.56, 141.44, 141.85, 154.08, 161.76, 194.67, 199.24; MS (EI) m/z 370.1 (M^+); HRMS Calcd for $C_{21}H_{22}O_2S_2$: 370.1061. Found: 370.1059. Anal. Calcd for $C_{21}H_{22}O_2S_2$: C, 68.09; H, 5.99. Found: C, 68.33; H, 5.68.

2-Isopropylidene-dithiosuccinic acid di-*S*-octyl ester (3.89): oil; IR (neat) 1709, 1688 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 6H, J=6.8 Hz), 1.24-1.55 (m, 24H), 1.84 (s, 3H), 2.12 (s, 3H), 2.68-2.78 (m, 4H), 3.81 (s, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.02, 20.78, 22.37, 27.58, 28.97, 28.99, 29.02, 31.23, 46.71, 134.86, 157.24, 192.05, 198.36; MS (EI) m/z 414.3 (M^+); HRMS Calcd for $C_{23}H_{42}O_2S_2$: 414.2626. Found: 414.2637. Anal. Calcd for $C_{23}H_{42}O_2S_2$: C, 66.62; H, 10.22. Found: C, 66.72; H, 10.38.

2-*sec*-Butylidene-dithiosuccinic acid di-*S*-phenyl ester (3.90): oil; IR (neat) 1705, 1678 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.02(t, 3H, J=7.2 Hz), 1.89 (s, 3H), 2.87 (q, 2H, J=7.2 Hz), 3.74 (s, 2H), 7.33-7.50 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.41, 21.05, 24.78, 45.24, 119.07, 128.05, 129.10, 129.47, 130.51, 131.55, 133.74, 141.17, 152.23, 153.09, 193.17, 198.24; MS (EI) m/z 356.1 (M^+); HRMS Calcd for $C_{20}H_{20}O_2S_2$: 356.0905. Found: 356.0911. Anal. Calcd for $C_{20}H_{20}O_2S_2$: C, 67.40; H, 5.66. Found: C, 67.72; H, 5.30.

2-Benzylidene-dithiosuccinic acid di-*S*-phenyl ester (3.91): oil; IR (neat) 1707, 1684 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.88 (s, 2H), 7.13-7.58 (m, 13H), 7.62-7.78 (m, 2H), 7.88-8.00(m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 49.73, 118.97, 122.45, 126.88, 128.04, 128.31, 129.17, 131.00, 131.25, 133.99, 135.20, 144.31, 149.05, 155.93, 193.24, 196.78; MS (EI) m/z 390.1 (M^+); HRMS Calcd for $C_{23}H_{18}O_2S_2$: 390.0748. Found: 390.0741. Anal. Calcd for $C_{23}H_{18}O_2S_2$: C, 70.76; H, 4.65. Found: C, 70.72; H, 4.39.

2-Ethylidene-dithiosuccinic acid di-*S*-phenyl ester (3.92): oil; IR (neat) 1711,

1681 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.95, (d, 3H, J=7.0 Hz), 3.74 (s, 2H), 7.42-7.48 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.28, 40.87, 114.65, 119.36, 120.54, 127.45, 129.12, 129.38, 129.71, 130.52, 133.14, 134.28, 134.80, 142.06, 190.31, 193.76; MS (EI) m/z 328 (M^+); HRMS Calcd for $C_{18}H_{16}O_2S_2$: 328.0592. Found: 328.0603. Anal. Calcd for $C_{18}H_{16}O_2S_2$: C, 65.84; H, 4.92. Found: C, 65.90; H, 5.08.

2-(1,3-Dimethyl-butylidene)-dithiosuccinic acid di-*S*-phenyl ester (3.93): oil; IR (neat) 1704, 1676 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (d, 6H, J=6.4 Hz), 1.85 (s, 3H), 1.90-2.07(m, 1H), 2.83 (d, 2H, J=7.0 Hz), 3.86 (s, 2H), 7.35-7.47(m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.89, 22.76, 27.91, 37.38, 45.27, 121.88, 127.54, 128.97, 129.10, 130.08, 131.55, 134.12, 139.69, 154.55, 158.73, 193.22, 197.82; MS (EI) m/z 384.1 (M^+); HRMS Calcd for $C_{22}H_{24}O_2S_2$: 384.1218. Found: 384.1223. Anal. Calcd for $C_{22}H_{24}O_2S_2$: C, 68.73; H, 6.30. Found: C, 68.44; H, 6.52.

2-Cyclohexylidene-dithiosuccinic acid di-*S*-phenyl ester (3.94): oil; IR (neat) 1710, 1676 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.33-1.66 (m, 6H), 2.97-3.34 (m, 4H), 3.89 (s, 2H), 7.34-7.50 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.00, 27.76, 31.12, 36.48, 46.52, 122.02, 127.55, 128.88, 129.12, 131.05, 131.71, 134.17, 140.06, 155.31, 161.54, 192.50, 196.84; MS (EI) m/z 382.1 (M^+); HRMS Calcd for $C_{22}H_{22}O_2S_2$: 382.1061. Found: 382.1057. Anal. Calcd for $C_{22}H_{22}O_2S_2$: C, 69.09; H, 5.80. Found: C, 69.17; H, 5.69.

2-Cyclohexylidene-3-methyl-dithiosuccinic acid di-*S*-phenyl ester (3.95): oil;

IR (neat) 1710, 1678 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.26 (d, 3H, J=7.0 Hz), 1.30-1.78 (m, 6H), 3.12-3.34 (m, 4H), 4.03 (q, 1H, J=7.0 Hz), 7.34-7.50 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.22, 25.83, 28.86, 33.23, 36.90, 50.02, 122.77, 126.34, 129.07, 129.18, 130.95, 131.27, 132.60, 140.51, 155.54, 168.72, 192.97, 196.26; MS (EI) m/z 396.1 (M^+); HRMS Calcd for $C_{23}H_{24}O_2S_2$: 396.1218. Found: 396.1227. Anal. Calcd for $C_{23}H_{24}O_2S_2$: C, 69.68; H, 6.11. Found: C, 69.47; H, 5.97.

2-Ethylidene-3-methyl-dithiosuccinic acid di-*S*-phenyl ester (3.96): oil; IR (neat) 1717, 1684 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.27 (d, 3H, J=7.2 Hz), 1.88 (d, 3H, J=7.5 Hz), 4.02 (q, 1H, J=7.2 Hz), 7.34-7.52 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.83, 17.02, 47.82, 122.76, 127.54, 128.61, 129.03, 131.00, 131.52, 133.07, 141.50, 149.47, 162.55, 192.07, 197.25; MS (EI) m/z 342.1 (M^+); HRMS Calcd for $C_{19}H_{18}O_2S_2$: 342.0748. Found: 382.1057. Anal. Calcd for $C_{19}H_{18}O_2S_2$: C, 66.65; H, 5.30. Found: C, 66.17; H, 5.55.

2-Isopropylidene-3-phenyl-dithiosuccinic acid di-*S*-phenyl ester (3.97): oil; IR (neat) 1701, 1669 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.92 (s, 3H), 2.18 (s, 3H), 5.21(s, 1H), 7.34-7.71 (m, 15H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.88, 24.27, 52.00, 117.02, 118.73, 124.79, 126.23, 127.71, 129.04, 133.24, 134.05, 134.21, 137.52, 144.12, 157.27, 162.62 195.51, 199.73; MS (EI) m/z 418.1 (M^+); HRMS Calcd for $C_{25}H_{22}O_2S_2$: 418.1061. Found: 418.1044. Anal. Calcd for $C_{25}H_{22}O_2S_2$: C, 71.75; H, 5.30. Found: C, 71.92; H, 5.07.

2-Methyl-3-methylene-dithiosuccinic acid di-*S*-phenyl ester (3.98): oil; IR (neat) 1712, 1683 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.28 (d, 3H, J=7.0 Hz), 3.84 (q, 1H, J=7.0 Hz), 7.21(s, 1H), 7.33-7.50(m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.14, 53.60, 117.34, 129.65, 129.73, 130.00, 131.17, 132.68, 134.17, 137.16, 138.35, 157.04, 190.07, 196.28; MS (EI) m/z 328 (M^+); HRMS Calcd for $C_{18}H_{16}O_2S_2$: 328.0592. Found: 328.0603. Anal. Calcd for $C_{18}H_{16}O_2S_2$: C, 65.84; H, 4.92. Found: C, 66.07; H, 5.13.

8.4 Experimental for Chapter 4

8.4.1. Synthesis of Starting Materials

8.4.1.1. Synthesis of Methoxyallene (4.19)

Methyl Propargyl Ether (4.18). Synthesis of methyl propargyl ether was accomplished by the literature method of Merz.[217a] The colorless liquid was dried over Na_2SO_4 and distilled (60-65 °C, 1 atm); yield 36%.

1-Methoxy-1,2-propadiene (4.19). Methoxyallene was prepared by the literature procedure.[217b] Thus, methyl propargyl ether (37.14 g, 0.53 mol) was added to 7.32 g (0.065 mol) potassium *tert*-butoxide. The mixture was refluxed for 2 h and distilled (50-53 °C, 1 atm) to give **4.19** (20.803 g, 56%). ^1H NMR (200 MHz, $CDCl_3$) δ 3.33 (s, 3H), 5.42 (d, 2H, J=5.8 Hz), 6.69 (dt, 1H, J=5.8 Hz, J'=0.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 55.60, 90.98, 122.73, 200.99; MS (EI) m/z 70.0; HRMS Calcd for C_4H_6O: 70.0419.

Found: 70.0423.

8.4.1.2. Synthesis of 1,2-Cyclononadiene (4.22)[218]

9,9-Dibromobicyclo[6.1.0]nonane (4.21). A dry 250-ml three-necked flask is quickly charged with cis-cyclooctene (17.8 g, 0.162 mol), potassium *tert*-butoxide (20.98 g, 0.187 mol) and 50 ml of sodium-dried pentane. Bromoform (42 g, 0.166 mol) was then added dropwise to the stirred slurry over a period of 1 hour. When the addition was complete, the reaction mixture was allowed to warm to room temperature and left stirring overnight. Water (50 ml) was added to the reaction mixture followed by enough 10% aqueous hydrochloric acid to neutralize the slightly basic solution. The reaction mixture was extracted with pentane, and the combined pentane solutions are washed with water. The organic solution was dried over anhydrous magnesium sulfate, filtered, and stripped of solvent on a rotary evaporator. Distillation of the residue yields 23.7 g (52%) of **4.21**, bp 60-64 °C/0.04 mm (literature value 62 °C/0.04mmHg[218]).

1,2-Cyclononadiene (4.22). To a 250-ml three-necked flask are added **4.21** (18.7 g, 0.066 mol) and 50 ml of anhydrous ether. The flask was cooled to –78 °C, and methyllithium (45 ml of 1.9 *M* ether solution, 0.085 mol) was added dropwise with stirring during 0.5 hour. After the addition is complete, the reaction mixture was stirred for 15 minutes, and excess lithium reagent was decomposed by addition of 70 ml of water. The ether layer was separated and aqueous layer was extracted with ether. The combined ether solution was washed with water and dried over magnesium sulfate. The latter was filtered and the ether was removed. Distillation of the residue yields 6.6 g

(81%) of **4.22**, bp. 62-65 °C/16 mm. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.27-1.45 (m, 4H), 1.59-1.82 (m, 4H), 2.56-2.76 (m, 4H), 5.18-5.33 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 27.63, 29.01, 33.41, 95.27, 208.92; MS (EI) m/z 122.1; HRMS Calcd for C_9H_{14}: 122.1096. Found: 122.1084.

*8.4.1.3. Synthesis of Ethyl 1,2-Butadienoate (**4.25**)*[249]

A 100-ml, three-necked, round-bottomed flask was charged with 30 ml of dichloromethane and 3.48 g (0.01 mol) of ethyl (triphenylphosphoranylidene)acetate, which was prepared from triphenylphosphine and ethyl bromoacetate by the known procedure.[304] The yellow solution was stirred at 25 °C as a solution of 1.01 g (0.01 mol) of triethylamine in 10 ml of dichloromethane was added dropwise over 5 min. After 10 min, 0.785 g (0.01 mol) of acetyl chloride in 10 ml of dichloromethane was added dropwise to the vigorously stirred solution over 5 min. Stirring was continued for an additional 30 min, after which the clear, yellow-tinted mixture was evaporated on a rotary evaporator at reduced pressure. A 50-ml portion of pentane was added to the semisolid residue, and the slurry was allowed to stand for 2 hr while it was shaken periodically to facilitate solidification and to complete the extraction of the product. The precipitate was removed by filtration and the filtrate was concentrated at reduced pressure. Distillation of the residual liquid afforded 0.78 g (62%) of **4.25**, bp 57-59 °C (12-14 mm). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.22 (t, 3H, J=7.0 Hz), 4.17 (q, 2H, J=7.0 Hz), 5.21 (d, 2H, J=6.5 Hz), 5.72 (t, 1H, J=6.5 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.28, 60.13, 82.72, 94.58, 176.27, 204.65; MS (EI) m/z 112.1; HRMS Calcd for $C_6H_8O_2$: 112.0524. Found: 112.0520.

8.4.1.4. Synthesis of ***4.26-4.29***

General Procedure: In a 100-ml, three-necked flask were placed terminal alkyne (0.01 mol), 25 ml of dioxane, cuprous bromide (0.005 mol), aldehyde (0.02 mol), and 1.85 g (0.018 mol) of diisopropylamine. The resulting mixture was gently refluxed and stirred for 2 hr and then cooled to room temperature and filtered through a Celite plug. The dark-brown filtrate was concentrated under vacuum to a gummy residue and then diluted with 10 ml of water followed by 30 ml of ether and acidified with 6 *N* hydrochloric acid to pH 2. The ether layer was separated, and the aqueous solution was extracted with ether. The organic layer was then washed with saturated sodium chloride solution and dried over anhydrous $MgSO_4$. After removal of ether, the residual liquid was distilled to give the corresponding allene in 48-63% yield.

4,5-Nonadiene (4.26): yield 54%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, 6H, J=7.2 Hz), 1.36-1.58 (m, 4H), 1.87-2.06 (m, 4H), 5.66-5.83 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.17, 19.28, 32.55, 93.52, 201.79; MS (EI) m/z 124.1.

2,3-Pentadienyl-benzene (4.27): yield 63%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.54 (d, 3H, J=6.8 Hz), 3.33 (d, 2H, J=6.2 Hz), 5.18-5.29 (m, 1H), 5.79-6.12 (m, 1H), 7.28-7.34 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.66, 39.72, 88.33, 90.58, 126.54, 128.76, 130.02, 144.83, 193.85; MS (EI) m/z 144.1; HRMS Calcd for $C_{11}H_{12}$: 144.0939. Found: 144.0936.

1,2-Pentadienyl-benzene (4.28): yield 48%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.13 (t, 3H, J=7.5 Hz), 1.85-2.02 (m, 2H), 5.38-5.50 (m, 1H), 6.25-6.33 (m, 1H), 7.27-7.58 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.05, 22.17, 96.59, 98.24, 123.06, 126.55, 127.54, 131.32, 207.26; MS (EI) m/z 144.1.

1,2-Nonadiene (4.29): yield 57%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=6.5 Hz), 1.22-1.54 (m, 8H), 1.88-2.02 (m, 2H), 5.08 (d, 2H, J=5.5 Hz), 5.68 (t, 1H, J=5.5 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.38, 22.02, 28.73, 29.14, 30.05, 31.77, 76.84, 94.27, 206.55; MS (EI) m/z 124.1; HRMS Calcd for C_9H_{16}: 124.1252. Found: 124.1261.

8.4.2 Transition-Metal-Catalyzed Reaction of 4.30 with 4.31 and CO. Optimization of Reaction Conditions

8.4.2.1. The Influence of Catalysts

In a 45-ml stainless-steel autoclave were placed the transition-metal catalyst (0.06 mmol), PPh_3 (0.24 mmol, if used), dppp or dppb (0.12 mmol, if used), 3-methyl-1,2-butadiene (3 mmol), thiophenol (2 mmol), and 7 ml of THF. After carbon monoxide was introduced up to 400 psi, the mixture was stirred at 100 °C for 48-72 h. The results are listed in Table 4-1.

8.4.2.2. The Influence of Solvents

A solution of $Pd(OAc)_2$ (0.0135 g, 0.06 mmol), PPh_3 (0.0629 g, 0.24 mmol), 3-methyl-1,2-butadiene (0.2044 g, 3 mmol), and thiophenol (0.2204 g, 2 mmol) in 7 ml of

the solvent was stirred under 400 psi of CO at 100 °C for 48-72 h. The results are listed in Table 4-2.

8.4.3 Palladium-Catalyzed Thiocarbonylation of Allenes with Thiols

General Procedure: To a 45-ml Parr autoclave fitted with a glass liner and stirring bar were added $Pd(OAc)_2$ (0.0135 g, 0.06 mmol), PPh_3 (0.0629 g, 0.24 mmol), allene (2.0 mmol), thiol (2.0 mmol), and dry THF (7 ml). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 400 psi. The mixture was stirred in the autoclave at 100 °C (oil bath temperature) for 48 h. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation. The residue was separated by PTLC (silica gel, eluant: *n*-hexane/ethyl acetate 10:1). The results are listed in Table 4-3.

S-Phenyl 4-methyl-3-pentenethioate (**4.32**), *S*-(4'-bromophenyl) 4-methyl-3-pentenethioate (**4.34**), *S*-(4'-methoxyphenyl) 4-methyl-3-pentenethioate (**4.36**), and *S*-octyl 4-methyl-3-pentenethioate (**4.40**) show identical spectral characteristics to those reported in Section 8.2.3. The characterization data of other products are as follows:

***S*-(4'-Methoxybenzyl) 4-methyl-3-pentenethioate (4.38):** oil; IR (neat) 1704 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ 1.81 (s, 3H), 1.87 (s, 3H), 3.44 (d, 2H, J=7.4 Hz), 3.72 (s, 3H), 4.13 (s, 2H), 5.30 (t, 1H, J=7.4 Hz), 7.22 (dd, 4H, J=8.5 Hz, J'=2.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.03, 24.68, 33.36, 35.87, 57.42, 113.92, 116.08,

126.25, 132.50, 134.27, 160.50, 198.27; MS (EI) m/z 250.1 (M^+); HRMS Calcd for $C_{14}H_{18}O_2S$: 250.1028. Found: 250.1022; Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.17; H, 7.25. Found: C, 67.22; H, 7.28.

***S*-Dodecyl 4-methyl-3-pentenethioate (4.42):** oil; IR (neat) 1709 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.85 (t, 3H, J=6.8 Hz), 1.18-1.34 (m, 20H), 1.63 (s, 3H), 1.75 (s, 3H), 2.85 (t, 2H, J=7.4 Hz), 3.20 (d, 2H, J=7.4 Hz), 5.26 (t, 1H, J=7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.07, 17.95, 19.14, 22.65, 25.68, 28.83, 29.09, 29.32, 29.46, 29.60, 30.76, 31.87, 42.42, 43.37, 55.74, 115.58, 136.91, 198.44; MS (EI) m/z 298 (M^+); HRMS Calcd for $C_{18}H_{34}OS$: 298.2347. Found: 298.2339; Anal. Calcd for $C_{18}H_{34}OS$: C, 72.43; H, 11.49. Found: C, 72.22; H, 11.28.

***S*-Phenyl 4-methoxyl-3-butenethioate (4.43)** (a mixture of stereoisomers); oil; IR (neat) 1713 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$) **E-4.43** δ 3.23 (dd, 2H, J=6.1 Hz, J'=1.2 Hz), 3.58 (s, 3H), 4.86 (dt, 1H, J=12.7 Hz, J'=7.0 Hz), 6.50 (d, 1H, J=12.7 Hz), 7.43 (s, 5H); **Z-4.43** δ 3.45 (dd, 2H, J=6.1 Hz, J'=1.2 Hz), 3.66 (s, 3H), 4.62 (dt, 1H, J=8.0 Hz, J'=7.0 Hz), 6.13 (d, 1H, J=8.0 Hz), 7.43 (s, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 42.50, 56.03, 94.12, 128.00, 128.14, 134.47, 149.54, 151.25, 196.91; MS (EI) m/z 208 (M^+); HRMS Calcd for $C_{11}H_{12}O_2S$: 208.0575. Found: 208.0576; Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.44; H, 5.81. Found: C, 63.39; H, 5.88.

***S*-Phenyl 2-cyclononenyl-formathioate (4.44)**: oil; IR (neat) 1710 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.25-1.52 (m, 10H), 2.41-2.47 (m, 2H), 3.72-3.86 (m, 1H),

5.65-5.71 (m, 2H), 7.25-7.28 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.57, 25.60, 26.72, 28.44, 28.73, 29.31, 48.52, 119.23, 123.48, 129.57, 129.85, 130.30, 133.92, 135.71, 200.03; MS (EI) m/z 260.1 (M^+); HRMS Calcd for $C_{16}H_{20}OS$: 260.1235. Found: 260.1232; Anal. Calcd for $C_{16}H_{20}OS$: C, 73.81; H, 7.75. Found: C, 73.83; H, 7.80.

Ethyl 4-phenylsulfanylcarbonyl-2-butenoate (4.45) (a mixture of stereoisomers); oil; IR (neat) 1704 (SC=O), 1738 (OC=O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) **E-4.45** δ 1.18 (t, 3H, J=7.0 Hz), 3.48 (dd, 2H, J=7.0 Hz, J'=1.1 Hz), 4.04 (q, 2H, J=7.0 Hz), 6.31 (d, 1H, J=15.6 Hz), 7.13-7.27 (m, 1H), 7.41 (s, 5H); **Z-4.45** δ 1.25 (t, 3H, J=7.0 Hz), 3.53 (dd, 2H, J=7.5 Hz, J'=1.2 Hz), 4.22 (q, 2H, J=7.0 Hz), 6.02 (d, 1H, J=11.5 Hz), 6.98-7.11 (m, 1H), 7.41 (s, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.23, 40.12, 46.53, 60.02, 121.98, 124.85, 128.99, 130.74, 133.88, 144.05, 147.96, 161.47, 198.27; MS (EI) m/z 250 (M^+); HRMS Calcd for $C_{13}H_{14}O_3S$: 250.0664. Found: 250.0662; Anal. Calcd for $C_{13}H_{14}O_3S$: C, 62.38; H, 5.64. Found: C, 62.32; H, 5.68.

***S*-Phenyl 2-propyl-3-heptenethioate (4.46)** (a mixture of stereoisomers); oil; IR (neat) 1705 cm^{-1} (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) **E-4.46** δ 0.90(t, 3H, J=7.5 Hz), 0.98 (t, 3H, J=7.4 Hz), 1.24-1.49 (m, 4H), 1.78-1.90 (m, 2H), 2.17-2.30 (m, 2H), 3.14-3.32 (m, 1H), 5.73-5.90 (m, 2H), 7.43 (s, 5H); **Z-4.46** δ 0.88-1.04 (m, 6H), 1.24-1.49 (m, 4H), 1.78-1.90 (m, 2H), 2.10-2.16 (m, 2H), 3.10-3.24 (m, 1H), 5.44-5.58 (m, 1H), 5.73-5.90 (m, 1H), 7.43 (s, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.75, 14.23, 20.26, 22.58, 29.79, 30.07, 34.55, 57.64, 116.35, 126.91, 128.38, 129.08, 134.15, 135.14, 141.86, 199.20; MS (EI) m/z 262 (M^+); HRMS Calcd for $C_{16}H_{22}OS$: 262.1408. Found: 262.1400;

Anal. Calcd for $C_{16}H_{22}OS$: C, 73.24; H, 8.45. Found: C, 73.32; H, 8.50.

***S*-Phenyl 2-methyl-5-phenyl-3-pentenethioate (4.47)** (a mixture of stereoisomers); oil; IR (neat) 1710 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) **E-4.47** δ 1.35 (d, 3H, J=7.0 Hz), 3.08-3.12 (m, 1H), 3.32 (d, 2H, J=7.0 Hz), 5.47-5.72 (m, 2H), 7.27-7.46 (m, 10H); **Z-4.47** δ 1.35 (d, 3H, J=7.0 Hz), 3.08-3.18 (m, 1H), 3.47 (d, 2H, J=7.0 Hz), 5.77-5.86 (m, 1H), 6.04-6.27 (m, 1H), 7.27-7.46 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.11, 34.28, 38.81, 52.17, 59.72, 126.16, 128.26, 128.32, 128.57, 129.06, 129.10, 129.20, 134.44, 134.53, 135.13, 139.08, 140.61, 198.57; MS (EI) m/z 282.1 (M^+); HRMS Calcd for $C_{18}H_{18}OS$: 282.1078. Found: 282.1105; Anal. Calcd for $C_{18}H_{18}OS$: C, 76.56; H, 6.42. Found: C, 76.60; H, 6.44.

***S*-Phenyl 2-ethyl-4-phenyl-3-butenethioate (4.48)** (a mixture of stereoisomers); oil; IR (neat) 1704 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, 3H, J=7.4 Hz), 1.44-1.83 (m, 2H), 3.12-3.33 (m, 1H), 5.87 (dd, 1/10×H, J=10 Hz, J'=11.5 Hz), 6.33 (d, 9/10×H, J=16.0 Hz), 6.53-6.65 (m, 1H), 7.20-7.46 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.59, 25.97, 59.70, 63.78, 126.43, 126.61, 127.75, 127.86, 128.23, 128.56, 129.09, 129.25, 133.86, 134.46, 135.00, 136.66, 198.55; MS (EI) m/z 282.1 (M^+); HRMS Calcd for $C_{18}H_{18}OS$: 282.1078. Found: 282.1068; Anal. Calcd for $C_{18}H_{18}OS$: C, 76.56; H, 6.42. Found: C, 76.89; H, 6.68.

***S*-Phenyl 3-decenethioate (4.49)** (a mixture of stereoisomers); oil; IR (neat) 1718 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.1 Hz), 1.26-1.44 (m, 8H),

2.05-2.26 (m, 2H),3.32 (dd, 2H, J=7.0 Hz, J'=1.0 Hz), 5.42-5.51 (m, 1/5×H), 5.64-5.75 (m, 4/5×H), 5.77-5.89 (m, 1/5×H), 5.95-6.10 (m, 4/5×H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.03, 22.58, 25.36, 28.43, 28.91, 28.94, 32.51, 38.41, 47.25, 120.71, 127.97, 129.26, 134.47, 135.07, 135.68, 136.98, 142.24, 196.03; MS (EI) m/z 262.1 (M^+); HRMS Calcd for $C_{16}H_{22}OS$: 262.1391. Found: 262.1388; Anal. Calcd for $C_{16}H_{22}OS$: C, 73.24; H, 8.46. Found: C, 73.31; H, 8.52.

8.5. Experimental for Chapter 5

8.5.1 Synthesis of Starting Materials

8.5.1.1. Synthesis of Conjugated enynes ***5.29-5.32***

General Procedure: A solution of the propargylic alcohol (0.010 mol) in pyridine (25 ml) was cooled to 0 °C, and $POCl_3$ (1.535 g, 0.010 mol) was added. The mixture was kept at room temperature overnight and then poured onto crushed ice (100 g). The resultant mixture was extracted with diethyl ether. The organic layer was washed with 10% HCl and brine, dried over Na_2SO_4, and evaporated. The crude product was purified by column or distillation.

1-Ethynyl-cyclopentene (5.29): 74% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 1.72-2.04 (m, 2H), 2.07-2.30 (m, 4H), 2.79 (s, 1H), 6.18-6.22 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22,03, 25.87, 29.10, 74.69, 85.90, 119.89, 136.57; MS (EI) m/z 92.1 (M^+).

3,5-Dimethyl-3-hexen-1-yne (5.30): 67% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.97 (d, 6H, J=7.0 Hz), 1.87 (s, 3H), 2.78-3.03 (m, 2H), 5.47 (d, 1H, J=9.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.89, 24.57, 28.75, 80.26, 83.77, 115.02, 138.55; MS (EI) m/z 108.1 (M^+).

3-Methyl-3-penten-1-yne (5.31): 58% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.86 (s, 3H), 1.93 (d, 3H, J=7.0 Hz), 2.98 (s, 1H), 6.14 (q, 1H, J=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.46, 18.52, 82.39, 85.17, 115.78, 131.00.

3-Ethyl-3-penten-1-yne (5.32): 64% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.98 (t, 3H, J=7.2 Hz), 1.72 (d, 3H, J=6.8 Hz), 2.33 (q, 2H, J=7.2 Hz), 2.84 (s, 1H), 6.25 (q, 1H, J=6.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.11, 13.57, 26.18, 78.00, 83.15, 121.88, 126.54; MS (EI) m/z 94.1 (M^+).

8.5.1.2. Synthesis of 2-Phenyl-1-Buten-3-yne (5.33)

To a 50-ml flask were added α-bromostyrene (1.831 g, 0.01 mol), tetrakis(triphenylphosphine)palladium(0) (0.5778 g, 0.5 mmol), lithium acetylide-ethylenediamine complex (90%, 1.2276 g, 0.012 mol), and 20 ml of dry THF. The mixture was stirred at room temperature under nitrogen for 6 hours, and then treated with 10% aqueous HCl, extracted with pentane, and filtered through a short alumina column. After removal of the solvent and running HPLC, **5.33** (0.602 g) was obtained in 47% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.87 (s, 1H), 5.37 (s, 1H), 5.56 (s, 1H), 7.19-7.34

(m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 76.07, 83.11, 120.52, 123.97, 126.12, 129.55, 129.67, 137.28.

8.5.1.3. Synthesis of 3-Nonen-1-yne ***5.34***

To a 100-ml flask were charged with propargyltriphenylphosphonium bromide (7.645 g, 0.02 mol) and 50 ml of dry THF. 14 ml of butyllithium (1.6 *M* solution in hexane, 0.022 mol) was added into the flask at –78 °C under N_2. After 30 min, hexanal (2 g, 0.02 mol) in THF (10 ml) was added at –78 °C, and the mixture was stirred overnight. The reaction mixture was then treated with 10% aqueous HCl, extracted with pentane, and filtered through a short silica gel column. Purification of the crude product by HPLC afforded 5.34 (1.854 g) in 76% yield. ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, 3H, J=6.2 Hz), 1.23-1.34 (m, 4H), 1.36-1.64 (m, 2H), 2.01-2.23 (m, 2H), 2.85 (s, 1H), 5.63 (d, 1H, J=16.0 Hz), 5.96-6.11 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.73, 23.54, 31.07, 31.84, 32.52, 79.17, 82.33, 112.44, 145.98; MS (EI) m/z 122.1 (M^+).

8.5.2 Reaction of 1-Ethylcyclohexene (5.27) with Thiophenol. Demonstration of the Process

A solution of $Pd(OAc)_2$ (0.0135 g, 0.06 mmol), PPh_3 (0.0629 g, 0.24 mmol), **5.27** (0.212 g, 2 mmol), and thiophenol (0.2204 g, 2 mmol) in 7 ml of the solvent was stirred under 400 psi of CO at 100 °C for 48 h. Two products, **5.41** and **5.42**, were obtained in 18 and 7% yield, respectively.

8.5.3 Palladium-Catalyzed Reaction of 5.27 with Thiophenol. Yield Optimization

In a 45-ml stainless-steel autoclave were placed palladium complex (0.03 mmol), PPh_3 (0.12 mmol, if used), bidentate phosphine ligand (dppb, dppp, or dppe) (0.12 mmol, if used), 1-ethynylcyclohexene (1 mmol), thiophenol (1 mmol), and 15 ml of the solvent. After carbon monoxide was introduced up to 400 psi, the mixture was stirred at 100-140 °C for 6-60 h. The results are listed in Table 5-1.

8.5.4 Palladium-Catalyzed Thiocarbonylation of Enynes with Thiols and Carbon Monoxide

General Procedure: An autoclave, its glass liner and a magnetic stirring bar were dried in an oven and cooled in a dry box. The liner was charged with $Pd(OAc)_2$ (0.0067 g, 0.03 mmol) and dppb (0.0306 g, 0.12 mmol). The enyne (3.0-6.0 mmol), thiol (1 mmol) and 15 ml of THF were then added to the liner. An additional amount of THF (from 1-2 ml) was placed in the autoclave prior to insertion of the liner. The gauge and gauge block assembly were attached. The CO line was flushed 3 times with CO and the system was also pressurized and flushed 3 times with CO, gradually increasing the pressure to 400 psi. The autoclave was then placed in the center of an oil bath on a heater stirrer preset to 110 °C. After 8-15 hours, the autoclave was removed from the oil bath and allowed to cool to room temperature. The excess gas was discharged and the system disassembled. The reaction mixture was filtered through Florisil and washed with diethyl ether. The solvent was removed by rotary evaporation under reduced pressure. The

residue was separated by preparative TLC or HPLC. The results are listed in Table 3-5. Characterization data of the 2(*5H*)-furanones are as follows:

***S*-Phenyl 2-(1'-cyclohexenyl)-3-propenethioate (5.41)**: oil; IR (neat) 1689 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.58-1.72 (m, 4H), 2.14-2.17 (m, 4H), 5.49 (s, 1H), 5.72 (s, 1H), 6.06 (t, 1H, *J*=7.4 Hz), 7.44-7.45 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.71, 22.45, 25.71, 26.00, 116.22, 128.21, 129.10, 129.30, 130.06, 132.01, 134.49, 149.76, 193.20; MS (EI) m/z 244.1 (M^+); HRMS Calcd for $C_{15}H_{16}OS$ 244.0938, found 244.0934. Anal. Calcd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60. Found: C, 73.75; H, 6.58.

***S*-(4'-Bromophenyl) 2-(1'-cyclohexenyl)-3-propenethioate (5.44)**: oil; IR (neat) 1686 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.58-1.71 (m, 4H), 2.15-2.18 (m, 4H), 5.49 (s, 1H), 5.74 (s, 1H), 6.10 (t, 1H, *J*=7.4 Hz), 7.25 (d, 2H, *J*=7.4 Hz), 7.57 (d, 2H, *J*=7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.02, 23.17, 25.68, 26.14, 114.81, 123.88, 127.21, 130.78, 132.14, 135.91, 135.07, 150.04, 189.76; MS (EI) m/z 322 (M^+); HRMS Calcd for $C_{15}H_{15}BrOS$ 322.0027, found 322.0018. Anal. Calcd for $C_{15}H_{15}BrOS$: C, 55.90; H, 4.69. Found: C, 55.96; H, 4.67.

***S*-Benzyl 2-(1'-cyclohexenyl)-3-propenethioate (5.46)**: oil; IR (neat) 1682 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.58-1.70 (m, 4H), 2.12-2.15 (m, 4H), 4.19 (s, 2H), 5.41 (s, 1H), 5.61 (s, 1H), 5.99 (t, 1H, *J*=7.4 Hz), 7.28-7.32 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.71, 22.44, 25.68, 26.09, 33.73, 116.27, 127.17, 128.57, 128.84,

129.88, 132.17, 137.42, 149.93, 194.63; MS (EI) m/z 258.1 (M^+); HRMS Calcd for $C_{16}H_{18}OS$ 258.1098, found 258.1098. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.39; H, 7.03. Found: C, 74.42; H, 7.05.

***S*-Octyl 2-(1'-cyclohexenyl)-3-propenethioate (5.48)**: oil; IR (neat) 1676 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J*=7.0 Hz), 1.25-1.37 (m, 12H), 1.56-1.67 (m, 4H), 2.11-2.15 (m, 4H), 3.14 (t, 2H, *J*=7.0 Hz), 5.36 (s, 1H), 5.54 (s, 1H), 5.95 (t, 1H, *J*=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.74, 21.72, 22.03, 22.50, 24.17, 25.08, 26.00, 28.14, 29.05, 29.11, 31.07, 35.08, 118.02, 128.17, 130.04, 134.08, 192.04; MS (EI) m/z 280.2 (M^+); HRMS Calcd for $C_{17}H_{28}OS$ 280.1861, found 280.1860. Anal. Calcd for $C_{17}H_{28}OS$: C, 72.81; H, 10.07. Found: C, 72.84; H, 10.08.

2-Phenylthiocarbonyl-3-methyl-1, 3-butadiene (5.49): oil; IR (neat) 1684 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ 1.95 (s, 3H), 5.19 (s, 1H), 5.31 (s, 1H), 5.65 (s, 1H), 5.91 (s, 1H), 7.42-7.47 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.99, 117.82, 119.57, 128.03, 129.20, 129.29, 129.45, 134.59, 134.92, 138.26, 149.18, 192.38; MS (EI) m/z 204 (M^+); HRMS Calcd for $C_{12}H_{12}OS$ 204.0609, found 204.0612. Anal. Calcd for $C_{12}H_{12}OS$: C, 70.57; H, 5.93. Found: C, 70.59; H, 5.90.

2-Phenylthiocarbonyl-3, 5-dimethyl-1, 3-hexadiene (5.50): oil; IR (neat) 1675 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.97 (d, 6H, *J*=7.0 Hz), 1.80 (s, 3H), 2.62 (m, 1H), 5.12 (s, 1H), 5.34 (s, 1H), 6.37 (d, 1H, *J*=7.0 Hz), 7.32-7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.42, 22.83, 27.40, 118.51, 122.15, 126.31, 128.67, 129.17, 130.39,

138.93, 141.05, 192.04; MS (EI) m/z 246 (M^+); HRMS Calcd for $C_{15}H_{18}OS$ 246.1078, found 246.1082. Anal. Calcd for $C_{15}H_{18}OS$: C, 73.14; H, 7.37. Found: C, 73.18; H, 7.34.

2-Octylthiocarbonyl-3, 5-dimethyl-1, 3-hexadiene (5.51): oil; IR (neat) 1672 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.88-0.96 (m, 9H), 1.24-1.33 (m, 10H), 1.58-1.64 (m, 2H), 1.82 (s, 3H), 2.62 (m, 1H), 3.10 (t, 2H, *J*=7.0 Hz), 5.16 (s, 1H), 5.40 (s, 1H), 6.42 (d, 1H, *J*=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.11, 13.02, 22.68, 23.17, 25.09, 27.38, 28.07, 28.38, 29.01, 29.04, 33.43, 35.78, 110.07, 124.06, 133.40, 133.56, 135.07, 141.22, 193.00; MS (EI) m/z 282 (M^+); HRMS Calcd for $C_{17}H_{30}OS$ 282.2017, found 282.2009. Anal. Calcd for $C_{17}H_{30}OS$: C, 72.29; H, 10.71. Found: C, 72.28; H, 10.75.

2-Phenylthiocarbonyl-3-methyl-1, 3-pentadiene (5.52): oil; IR (neat) 1672 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.73 (s, 3H), 1.75 (d, 3H, J=7.0 Hz), 4.92 (s, 1H), 5.08 (s, 1H), 6.34 (q, 1H, *J*=7.0 Hz), 7.36-7.42 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.48, 20.22, 118.04, 122.08, 124.98, 126.26, 126.56, 127.62, 128.09, 128.59, 128.64, 129.03, 138.85, 191.23; MS (EI) m/z 218 (M^+); HRMS Calcd for $C_{13}H_{14}OS$ 218.0765, found 218.0769. Anal. Calcd for $C_{13}H_{14}OS$: C, 71.53; H, 6.47. Found: C, 71.55; H, 6.44.

2-Phenylthiocarbonyl-3-ethyl-1, 3-pentadiene (5.53): oil; IR (neat) 1674 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.02 (t, 3H, *J*=7.0 Hz), 1.76 (d, 3H, *J*=7.0 Hz), 2.27-2.36 (m, 2H), 5.07 (s, 1H), 5.57 (s, 1H), 6.45 (q, 1H, *J*=7.0 Hz), 7.08-7.27 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.82, 19.98, 27.04, 118.26, 122.02, 126.81, 127.09,

127.75, 129.28, 130.05, 138.31, 191.87; MS (EI) m/z 232.1 (M^+); HRMS Calcd for $C_{14}H_{16}OS$ 232.0922. found 232.0926. Anal. Calcd for $C_{14}H_{16}OS$: C, 72.39; H, 6.95. Found: C, 72.41; H, 6.92.

2-Phenylthiocarbonyl-3-phenyl-1, 3-butadiene (5.54): oil; IR (neat) 1668 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 5.34 (s, 1H), 5.86 (s, 1H), 6.07 (s, 1H), 6.18 (s, 1H), 7.19-7.42 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 116.03, 123.04, 127.04, 128.30, 128.97, 129.33, 129.90, 132.07, 133.55, 135.37, 136.44, 136.50, 190.88; MS (EI) m/z 266 (M^+); HRMS Calcd for $C_{17}H_{14}OS$ 266.0765, found 266.0763. Anal. Calcd for $C_{17}H_{14}OS$: C, 76.67; H, 5.30. Found: C, 76.69; H, 5.27.

***S*-Phenyl 2-(1'-cyclopentenyl)-3-propenethioate (5.55)**: oil; IR (neat) 1675 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.72-1.80 (m, 2H), 2.40-2.48 (m, 4H), 5.40 (s, 1H), 5,62 (s, 1H), 6.27 (t, 1H, *J*=7.0 Hz), 7.38-7.42 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.03, 31.80, 33.04, 121.87, 124.02, 127.00, 129.13, 129.18, 130.04, 131.53, 131.74, 141.88, 191.84; MS (EI) m/z 230 (M^+); HRMS Calcd for $C_{14}H_{14}OS$ 230.0765, found 230.0760. Anal. Calcd for $C_{14}H_{14}OS$: C, 73.02; H, 6.13. Found: C, 73.07, H, 6.15.

2-Phenylthiocarbonyl-1, 3-nonadiene (5.56): oil; IR (neat) 1668 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J*=7.4 Hz), 1.28-1.47 (m, 6H), 2.24 (t, 2H, *J*=7.4 Hz), 4.92 (s, 1H), 5.10 (s, 1H), 5.68 (m, 1H), 6.15 (m, 1H), 7.26-7.37 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.07, 18.77, 19.59, 22.58, 31.66, 126.47, 126.53, 127.30, 128.64, 128.74, 128.99, 129.72, 129.99, 130.13, 132.60, 135.56, 192.08; MS (EI) m/z

260 (M^+); HRMS Calcd for $C_{16}H_{20}OS$ 260.1235, found 260.1240. Anal. Calcd for $C_{16}H_{20}OS$: C, 73.81; H, 7.75. Found: C, 73.78; H, 7.74.

8.5.5 Palladium-Catalyzed Thiolactonization of 5.57 with Thiophenol and Carbon Monoxide

Following the general procedure for the palladium-catalyzed thiocarbonylation of enynes, **5.57** (0.1923 g, 2 mmol) was reacted under the used conditions to afford 0.3463g of β-Phenylthio-γ-methyl-β,γ-unsaturated-ε-lactone in 74% yield.

β-Phenylthio-γ-methyl-β,γ-unsaturated-ε-lactone (5.58): m.p. 69-71°C; IR (KBr) 1763 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.47(t, 2H, *J*=6.4 Hz), 3.75 (s, 2H), 4.35 (t, 2H, *J*=6.4 Hz), 7.36-7.40 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.80, 30.74, 40.96, 65.04, 120.39, 129.14, 129.40, 134.54, 154.69, 164.69, 194.51; MS (EI) m/z 234 (M^+); HRMS Calcd for $C_{13}H_{14}O_2S$ 234.0715, found 234.0699. Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.65; H, 6.03. Found: C, 66.68; H, 6.04.

8.6. Experimental for Chapter 6

8.6.1 Thiocarbonylation of 1,3-Conjugated Dienes

A 45-ml Parr autoclave fitted with a glass liner and stirring bar was charged with

$Pd(OAc)_2$ (0.0067 g, 0.03 mmol) and dppb (0.0306 g, 0.12 mmol). 2-Methyl-1,3-butadiene (0.34g, 5.0 mmol), thiophenol (0.1102g, 1 mmol) and 15 ml of THF were then added to the liner. An additional amount of THF (from 1-2 ml) was placed in the autoclave prior to insertion of the liner. The CO line was flushed 3 times with CO and the system was also pressurized and flushed 3 times with CO, gradually increasing the pressure to 400 psi. The autoclave was then placed in the center of an oil bath on a heater stirrer preset to 110 °C. After 48 hours, the autoclave was removed from the oil bath and allowed to cool to room temperature. The excess gas was discharged and the system disassembled. The reaction mixture was filtered through Florisil and washed with diethyl ether. The solvent was removed by rotary evaporation under reduced pressure. The residue was separated by preparative TLC. The reaction gave two products, *S*-phenyl 4-methyl-3-pentenethioate (**6.3**) and 1-phenylsulfanyl-3-methyl-2-butene (**6.4**), in yields of 4% and 47%, respectively, with 16% recovery of unreacted thiophenol.

8.6.2 Influence of the Catalyst System on the Thiocarbonylation of 2-Methyl-1,3-Butadiene

In a 45-ml stainless-steel autoclave were placed the palladium complex (0.05 mmol), monodentate phosphine ligand (e.g. PPh_3, PCy_3, or PBu_3, 0.2 mmol, if used) or bidentate phosphine (e.g. dppe, dppf, or dppb; 0.1 mmol, if used), 2-methyl-1,3-butadiene (0.3406g, 5 mmol), thiophenol (0.1102g, 1 mmol),and dichloromethane (5 ml). After carbon monoxide was introduced up to 400 psi, the mixture was stirred at 110 °C for 48-72 h. The results are listed in Table 6-1.

8.6.3 Solvent Optimization for the Thiocarbonylation of 2-Methyl-1,3-butadiene(6.1)

In a 45-ml stainless-steel autoclave were placed palladium acetate (0.0112g, 0.05 mmol), triphenylphosphine (0.0525g, 0.2 mmol), 2-methyl-1,3-butadiene (0.3406g, 5 mmol), thiophenol (0.1102g, 1 mmol),and the solvent (5 ml). After carbon monoxide was introduced up to 400 psi, the mixture was stirred at 110 °C for 48-60 h. After the reaction completed, the reaction mixture was examined by GC-MS first, and then separated by PTLC (silica gel GF_{254}; eluant: n-hexane: ethyl acetate 9:1). The results are listed in Table 6-2.

8.6.4 Palladium-Catalyzed Thiocarbonylation of 6.1 with Various Thiols

General Procedure: To a 45-ml Parr autoclave fitted with a glass liner and stirring bar were added $Pd(OAc)_2$ (0.0224g, 0.1 mmol), triphenylphosphine (0.1050g, 0.4 mmol), 2-methyl-1,3-butadiene (0.6812g, 10 mmol),), thiol (2 mmol) and CH_2Cl_2 (10 ml). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 400 psi. The mixture was stirred in the autoclave at 110 °C (oil bath temperature) for 48-72. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation under reduced pressure. The residue was separated by HPLC or preparative TLC (silica gel F_{254}, eluant: n-hexane/ethyl acetate 10:1). The results are listed in Table 6-3.

The thiocarbonylation products, *S*-Phenyl 4-methyl-3-pentenethioate (**6.3**), *S*-(4'-bromophenyl) 4-methyl-3-pentenethioate (**6.11**), *S*-(4'-methoxyphenyl) 4-methyl-3-pentenethioate (**6.6**), *S*-(4'-nitrophenyl) 4-methyl-3-pentenethioate (**6.9**), *S*-Dodecyl 4-methyl-3-pentenethioate (**6.25**), and *S*-octyl 4-methyl-3-pentenethioate (**6.22**) show identical spectral characteristics to those reported in Section 8.2.3 and Section 8.4.3. The characterization data of the other products are as follows:

***S*-2'-Naphthyl 4-methyl-3-pentenethioate (6.13):** Waxy solid; mp 92.4-93.6 °C; IR (KBr): 1712 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ=1.70 (s, 3H), 1.81 (s, 3H), 3.42 (d, 2H, J=6.9Hz), 5.68 (t, 1H, J=6.9 Hz), 7.45-7.53 (m, 4H), 7.21-7.76 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=16.78, 24.54, 42.54, 123.54, 137.89, 125.25, 126.25, 127.47, 127.64, 128.03, 130.27, 131.43, 135.36, 196.72; MS (70 ev, EI): 256.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{16}H_{16}OS$ 256.0922, found 256.0919; Anal. calcd for $C_{16}H_{16}OS$: C 74.96, H 6.29; found: C 75.06, H 6.34.

2-(3-Methyl-2-butensulfanyl)-naphthalene (6.14): mp 47-49 °C; ^1H NMR (500 MHz, $CDCl_3$): δ=1.62 (s, 3H), 1.78 (s, 3H), 3.45 (d, 2H, J=7.5 Hz), 5.25 (t, 1H, J=7.5 Hz), 7.36-7.85 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=17.60, 25.70, 31.44, 112.88, 126.25, 127.43, 127.60, 127.61, 129.13, 131.13, 131.89, 135.21, 138.39; MS (70 ev, EI): 228.1 [M^+]; HRMS (70 ev, EI): Calcd for $C_{15}H_{16}S$: 228.0973, found: 228.0958.

***S*-*i*-Propyl 4-methyl-3-pentenethioate (6.16):** Colorless oil; IR (neat): 1702 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ 1.04 (d, 6H, *J*=6.8 Hz), 1.74 (s, 3H), 1.82 (s, 3H),

3.36 (d, 2H, *J*=6.9 Hz), 3.54 (q, 1H, *J*=6.8 Hz), 5.43 (t, 1H, *J*=6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ=16.78, 22.32, 24.54, 34.64, 43.93, 120.03, 133.87, 198.95; MS (70 ev, EI): 172.1 [M^+]; HRMS (70 ev, EI): calcd for $C_9H_{16}OS$ 172.0922, found 172.0926; Anal. calcd for $C_9H_{16}OS$: C 62.74, H 9.36; found: C 62.82, H 9.44.

1-Isopropylsulfanyl-3-methyl-2-butene (6.17): oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.13 (d, 6H, *J*=6.8 Hz), 1.70 (s, 3H), 1.81 (s, 3H), 3.18 (d, 2H, *J*=7.5 Hz), 3.26 (q, 1H, *J*=6.8 Hz), 5.28 (t, 1H, *J*=6.9 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ=17.03, 22.16, 25.09, 25.87, 29.47, 112.05, 131.27; MS (70 ev, EI): 144.1 [M^+]; HRMS (70 ev, EI): calcd for $C_8H_{16}S$ 144.0973, found 144.0981.

***S*-Butyl 4-methyl-3-pentenethioate (6.19):** Colorless oil; IR (neat): 1702 cm^{-1} (C=O); ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.91 (t, 3H, *J*=7.0 Hz), 1.42-1.47 (m, 4H), 1.70 (s, 3H), 1.76 (s, 3H), 3.16 (t, 2H, *J*=7.0 Hz), 3.38 (d, 2H, *J*=6.9 Hz), 5.43 (t, 1H, *J*=6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.43, 16.78, 21.66, 24.54, 28.53, 30.83, 42.85, 120.03, 133.87, 197.79; MS (70 ev, EI): 186.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{10}H_{18}OS$ 186.1078, found 186.1080; Anal. calcd for $C_{10}H_{18}OS$: C 64.46, H 9.78; found: C 64.55, H 9.80.

1-Butylsulfanyl-3-methyl-2-butene (6.20): Colorless oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J*=7.0 Hz), 1.38-1.47 (m, 4H), 1.68 (s, 3H), 1.74 (s, 3H), 2.68 (t, 2H, *J*=7.0 Hz), 3.17 (d, 2H, *J*=7.6 Hz), 5.27 (t, 1H, *J*=7.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 13.68, 17.54, 21.82, 25.73, 29.02, 21.78, 32.86, 113.45, 136.91; MS (70 ev,

EI): 158.1 [M^+]; HRMS (70 ev, EI): calcd for $C_9H_{18}S$ 158.1129, found 158.1137.

3-Methyl-1-octylsulfanyl-2-butene (6.23): Colorless oil; ^1H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J*=6.2 Hz), 1.23-1.51 (m, 12H), 1.68 (s, 3H), 1.76 (s, 3H), 2.42 (t, 2H, *J*=7.0 Hz), 3.13 (d, 2H, *J*=7.6 Hz), 5.26 (t, 1H, *J*=7.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 12.05. 17.24, 22.89, 24.71, 29.08, 29.14, 30.55, 30.82, 32.33, 32.79, 113.54, 137.18; MS (70 ev, EI): 214.2 [M^+]; HRMS (70 ev, EI): calcd for $C_{13}H_{26}S$ 214.1755, found 214.1767.

1-Dodecylsulfanyl-3-methyl-2-butene (6.26): Colorless oil; ^1H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, 3H, J=6.5 Hz), 1.18-1.54 (m, 20H), 1.63 (s, 3H), 1.68 (s, 3H), 2.32 (t, 2H, J=7.0 Hz), 3.11 (d, 2H, J=7.0 Hz), 5.26 (t, 1H, J=7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.22, 17.84, 19.14, 22.65, 25.88, 27.83, 28.04, 28.71, 29.05, 29.73, 30.76, 31.77, 32.00, 33.67, 35.37, 48.74, 115.58, 136.91; MS (70 ev, EI): 270.2 [M^+]; HRMS (70 ev, EI): calcd for $C_{17}H_{34}S$ 270.2381, found 270.2376.

8.6.5 Palladium-Catalyzed Thiocarbonylation of 1,3-Dienes with Thiophenol

General Procedure: To a 45-ml Parr autoclave fitted with a glass liner and stirring bar was added $Pd(OAc)_2$ (0.0224g, 0.1 mmol), triphenylphosphine (0.1050g, 0.4 mmol), 1,3-diene (10 mmol),), thiophenol (0.2204g, 2 mmol) and CH_2Cl_2 (10 ml). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subsequently the pressure was increased to 400 psi. The mixture was

stirred in the autoclave at 110 °C (oil bath temperature) for 60 h. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation under reduced pressure. The residue was separated by HPLC or preparative TLC (silica gel F_{254}, eluant: n-hexane/ethyl acetate 10:1). The results are listed in Table 6-4.

The thiocarbonylation products, *S*-Phenyl 4-methyl-3-pentenethioate (**6.3**), *S*-phenyl) 2-methyl-3-pentenethioate (**6.31**), *S*-Phenyl 4,8-dimethyl-3,7-nonadienethioate (**6.43**), and S-phenyl 2-cyclohexene-1-carbothioate (**6.47**) show identical spectral characteristics to those reported in Section 8.2.3. Characterization data for the other products are as follows:

***S*-Phenyl 3,4-dimethyl-3-pentenethioate (6.28):** Colorless oil; IR (neat): 1705 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 1.76 (s, 3H), 1.79 (s, 6H), 3.34 (s, 2H), 7.40 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.29, 20.82, 21.01, 49.18, 120.36, 128.22, 129.05, 129.13, 130.86, 134.45, 196.37; MS (70 ev, EI): 220.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{13}H_{16}OS$ 220.0922, found 220.0931; Anal. calcd for $C_{13}H_{16}OS$: C 70.88, H 7.33; found: C 70.84, H 7.40.

***S*-Phenyl 3-hexenethioate (6.30):** Colorless oil; IR (neat): 1706 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 1.04 (t, 3H, *J*=7.4 Hz), 2.12 (dq, 2H, *J*=7.4 and 6.8 Hz), 3.44 (d, 2H, *J*=6.8 Hz), 5.50-5.82 (m, 2H), 7.44 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.73, 23.44, 46.75, 121.03, 127.55, 128.04, 130.47, 132.56, 134.02, 196.18; MS (70 ev, EI): 206.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{12}H_{14}OS$ 206.0765, found 206.0760; Anal.

calcd for $C_{12}H_{14}OS$: C 69.88, H 6.85; found: C 69.94, H 6.78.

***S*-Phenyl 2,4-dimethyl-3-heptenethioate (6.35):** Colorless oil; IR (neat): 1707 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ 0.92 (t, 3H, J=6.8 Hz), 1.25 (d, 3H, J=6.8 Hz), 1.43-1.50 (m, 2H), 1.73 (d, 6/7×3H, J=1.4 Hz), 1.75 (d, 1/7×3H, J=1.4 Hz), 2.02-2.15 (m, 2H), 3.55-3.63 (m, 1H), 5.14-5.22 (m, 6/7×1H), 5.44-5.55 (m, 1/7×1H), 7.40 (s, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.60, 14.03, 17.99, 18.39, 20.70, 21.05, 23.44, 40.59, 41.69, 47.37, 47.60, 123.08, 123.59, 127.09, 128.37, 128.98, 129.47, 134.49, 139.83, 200.02; MS (70 ev, EI): 248.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{15}H_{20}OS$ 248.1235, found 248.1235; Anal. calcd for $C_{15}H_{20}OS$: C 72.54, H 8.12; found: C 72.56, H 8.20.

***S*-Phenyl 3,4-dimethoxyl-3-pentenethioate (6.37):** Colorless oil; IR (neat): 1712 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ 1.82 (s, 1/12×3H), 1.87(s, 11/12×3H), 3.61 (s, 3H), 3.66 (s, 1/12×2H), 3.71 (s, 11/12×2H), 3.74 (s, 3H), 7.44 (s, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.27, 16.45, 42.28, 44.35, 56.40, 57.02, 122.50, 129.48, 131.00, 134.22, 142.50, 145.22, 195.38; MS (70 ev, EI): 252.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{13}H_{16}O_3S$ 252.0820, found 252.0826; Anal. calcd for $C_{13}H_{16}O_3S$: C 61.88, H 6.39; found: C 61.85, H 6.47.

***S*-Phenyl 2,5,5-trimethyl-3-hexenethioate (6.39):** Colorless oil; IR (neat): 1708 cm^1 (C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 0.92 (s 3H), 1.05 (s, 6H), 1.32 (d, 3H, J=6.8

Hz), 3.20-3.28 (m, 9/10×1H), 3.34-3.40 (m, 1/10×1H), 5.45 (dd, 1H, J=14.5 and 7.0 Hz), 5.72 (d, 1H, J=14.5 Hz), 7.40 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 17.77, 29.34, 51.76, 122.88, 128.22, 129.06, 129.12, 129.30, 134.26, 134.53, 145.33, 200.06; MS (70 ev, EI): 248.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{15}H_{20}OS$ 248.1235, found 248.1245; Anal. calcd for $C_{15}H_{20}OS$: C 72.54, H 8.12; found: C 72.66, H 8.23.

***S*-Phenyl 2,4,5-trimethyl-3-hexenethioate (6.41):** Colorless oil; IR (neat): 1708 cm^1 (C=O); ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.96 (d, 6H, J=6.8 Hz), 1.22 (d, 3H, J=6.8 Hz), 1.67 (s, 3H), 2.56 (q, 1H, J=6.8 Hz), 3.34 (dq, 1/11×1H, J=6.8 and 9.2 Hz), 3.38 (dq, 10/11×1H, J=7.0 and 9.2 Hz), 5.31 (d, 1H, J=9.2 Hz), 7.40 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.84, 19.97, 22.50, 38.78, 45.78, 47.32, 121.90, 124.84, 128.84, 130.07, 134.19, 137.48, 199.96; MS (70 ev, EI): 248.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{15}H_{20}OS$ 248.1235, found 248.1241; Anal. calcd for $C_{15}H_{20}OS$: C 72.54, H 8.12; found: C 72.58, H 8.07.

***S*-Phenyl 2,4-dimethyl-3-pentenethioate (6.45):** Colorless oil; IR (neat): 1710 cm^1 (C=O); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.22 (dd, 3H, J=7.0 and 1.5 Hz), 1.80 (s, 3H), 1.86 (s, 3H), 3.47 (m, 1H), 5.53 (d, 1H, J=9.2 Hz), 7.44 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 16.43, 18.24, 24.20, 45.78, 121.46, 129.04, 129.40, 131.04, 133.19, 134.28, 199.12; MS (70 ev, EI): 220.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{13}H_{16}OS$ 220.0922, found 220.0924; Anal. calcd for $C_{13}H_{16}OS$: C 70.88, H 7.33; found: C 70.80, H 7.44.

***S*-Phenyl 2-cycloheptene-1-carbothioate (6.49):** Colorless oil; IR (neat): 1706

cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 1.40-1.54 (m, 1H), 1.60-1.86 (m, 3H), 1.93-2.06 (m, 2H), 2.12-2.26 (m, 2H), 3.55-3.61 (m, 1H), 5.94-6.06 (m, 2H), 7.43 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 26.35, 28.45, 29.64, 30.98, 54.63, 127.94, 129.01, 129.08, 129.12, 134.45, 134.75, 199.43; MS (70 ev, EI): 232.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{14}H_{16}OS$ 232.0922, found 232.0936; Anal. calcd for $C_{14}H_{16}OS$: C 72.39, H 6.95; found: C 72.43, H 7.02.

***S*-Phenyl 2-cyclooctene-1-carbothioate (6.51):** Colorless oil; IR (neat): 1708 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 1.30-1.78 (m, 7H), 1.95-2.24 (m, 3H), 3.72-3.84 (m, 1H), 5.65-5.90 (m, 2H), 7.41 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.20, 26.48, 29.16, 33.50, 51.50, 126.84, 127.90, 128.97, 129.10, 129.23, 132.42, 134.54, 199.78; MS (70 ev, EI): 246.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{15}H_{18}OS$ 246.1078, found 246.1075; Anal. calcd for $C_{15}H_{18}OS$: C 73.14, H 7.37; found: C 73.22, H 7.40.

***S*-Phenyl 3-methyl-2-cyclohexene-1-carbothioate (6.53):** Colorless oil; IR (neat): 1704 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 1.58-1.78 (m with a singlet at δ=1.76, 5H), 1.90-2.08 (m, 2H), 2.50-2.67 (m, 2H), 3.26-3.33 (m, 1H), 5.84-5.86 (m, 1H), 7.43 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ 18.04, 22.13, 29.46, 32.04, 53.25, 122.32, 124.18, 129.02, 131.00, 133.29, 136.56, 198.84; MS (70 ev, EI): 232.1 [M^+]; HRMS (70 ev, EI): calcd for $C_{14}H_{16}OS$ 232.0922, found 232.0918; Anal. calcd for $C_{14}H_{16}OS$: C 72.39, H 6.95; found: C 72.46, H 7.04.

8.6.6 General Procedure for Palladium-Catalyzed Asymmetric Thiocarbonylation of

1,3-Dienes with Thiophenol and CO Using Chiral Phosphine Ligands

A mixture of $Pd(OAc)_2$ (0.05 mmol), chiral phosphine ligand (0.1 mmol) and dichloromethane in a 45-ml autoclave was stirred at room temperature under nitrogen for 30 min. 2-Methyl-1,3-pentadiene (5 mmol) and thiophenol (1 mmol) were then added. The reactor was flushed three times with CO and pressurized to 400 psi of CO. The mixture ws stirred at 110 °C (oil bath temperature) for 60 h. After cooling, the excess CO was released. The mixture was filtered through Florisil, and the solvent was removed by rotary evaporation. The residue was purified by preparative silica gel TLC. The purified product was re-chromatographed on preparative HPLC in order to eliminate the rest of the chiral phosphine ligand. The enantiomeric excess was determined by chiral GC installed with Superlco β-Dex 120 column. The results were summarized in Tables 6-5 and 6-6.

8.7. Experimental for Chapter 7

8.7.1 Synthesis of Starting Materials

*8.7.1.1 General Procedure for the Preparation of o-Iodoaniline **7.33b** and **7.33c***

Into a 100 mL beaker was placed 4-methylaniline (2.14g, 0.02 mol) (for **7.33b**) or 4-chloroaniline (2.55g, 0.02 mol) (for **7.33c**), $NaHCO_3$ (2.50g, 0.03 mol) and water (20 mL). The mixture was cooled to 10-15°C by the addition of a little crushed ice. With

stirring, powdered and resublimed iodine (5.08g, 0.02 mol) was introduced in portions of 1g at intervals of 3-5 minutes, after which time the colour of the free iodine in the solution had practically disappeared and the reaction was complete. The organic phase was extracted from the reaction mixture with diethyl ether (3×20 mL). The extracts were combined and dried with $MgSO_4$. Removal of the solvent and recrystallization of the crude product from n-hexane afforded **7.33b** and **7.33c** in 73 and 68% yields, respectively.

4-Methyl-2-iodoaniline (7.33b): needles; m.p.39-40°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.20 (s, 3H), 3.85 (br, s, 2H), 6.66 (d, 1H, *J*=8.1 Hz), 6.90-6.95 (m, 1H), 7.45-7.46 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.83, 84.28, 114.63, 130.00, 133.91, 138.98, 144.25; MS (EI) *m/z* 233 (M^+); HRMS calcd for C_7H_8IN 232.9701, found 232.9686. Anal. Calcd for C_7H_8IN: C, 36.08; H, 3.46. Found: C, 36.16; H, 3.55.

4-Chloro-2-iodoaniline (7.33c): needles; m.p.39.5-42 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.02 (br. s, 2H), 6.60 (d, 1H, J=8.6 Hz), 7.08 (dd, 1H, J=8.6 Hz, J'=2.2 Hz),, 7.57 (d, 1H, J=2.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 83.44, 114.92, 123.00, 129.15, 137.65, 145.45 ; MS (EI) *m/z* 253 (M^+).

8.7.1.2 General Procedure for the Preparation of o-Iodothiophenols ***7.29a-c***

A solution of sodium nitrite (0.704g, 0.01 mol) in water (2 mL) was added during 30 min to an ice –cooled solution of *o*-iodoaniline (0.01 mol) in 35% aqueous HCl (1.67 mL, 0.02 mol) containing ice (2.0g), while potassium ethylxanthate was prepared by rapid

stirring of a mixture of potassium hydroxide (0.796g, 0.012 mol), ethanol (1.34 mL), water (2.5 mL) and carbon disulfide (1.332g, 0.018 mol) for 2.5 h. The first solution of *o*-iodobenzenediazonium salt was added slowly to the prepared potassium ethylxanthate at 0-5°C. After the addition the mixture was heated at 50-55°C for 0.5 h, cooled, and then extracted with ether(3×10 mL). The organic phase was dried ($MgSO_4$) and evaporated to dryness in vacuo. The residue was refluxed with KOH (3.0g, 0.046 mol) in absolute ethanol (10 mL) for 10 h, neutralized with 10% HCl (15 mL), and extracted with ether (3×10 mL). The combined organic phase was dried ($MgSO_4$) and evaporated to afford crude *o*-iodothiophenol, which was purified by chromatography using silica gel (eluant, hexane/ethyl acetate=5:1). The isolated yields of **1a**, **1b**, and **1c** are 63, 54, and 66%, respectively.

2-Iodothiophenol (7.29a): oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.98 (s, 1H), 6.94-6.98 (m, 1H), 7.10-7.16 (m, 1H), 7.32 (d, 1H, *J*=8.6 Hz), 7.50 (d, 1H, *J*=8.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.98, 126.02, 127.84, 129.44, 133.07, 134.12; MS (EI) *m/z* 236.0 (M^+); HRMS calcd for C_5H_5IS 235.9157, found 235.9194.

4-Methyl-2-iodothiophenol (7.29b): oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.27 (s, 3H), 3.97 (s, 1H), 6.70-6.75 (m, 1H), 7.00-7.06 (m, 1H), 7.45 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.90, 85.40, 114.59, 130.75, 131.86, 138.19, 152.53.

4-Chloro-2-iodothiophenol (7.29c): oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.98 (s, 1H), 6.90 (d, 1H, J=8.7 Hz), 7.20 (dd, 1H, J=8.7 Hz, J'=2.5 Hz), 7.60 (d, 1H, J=2.5 Hz);

^{13}C NMR (50 MHz, $CDCl_3$) δ 85.41, 115.62, 126.05, 130.09, 137.06, 153.68.

8.7.1.3 Synthesis of Ethyl 2,3-pentadienoate (7.30f)

A 250-ml flask was charged with 70 ml of dichloromethane and 8.7 g (0.025 mol) of ethyl(triphenylphosphoranylidene)acetate and flushed with nitrogen. The yellow solution was stirred at room temperature as a solution of 2.53g (0.025 mol) of triethylamine in 25 ml of dichloromethane was added dropwise over 5 min. 2.4 g (0.025 mol) of propionyl chloride in 25 ml of dichloromethane was added to the stirred solution. After the reaction was complete, 100-ml portion of pentane was added to the flask. The precipitate was removed, and the filtrates were concentrated. Rapid distillation of the residual liquid in a short-path distillation apparatus under reduced pressure afforded 1.95 g (62%) of 7.30f, bp 57-59 °C (12-14 mmHg). ^1H NMR (200 MHz, $CDCl_3$) δ 1.03 (t, 3H, J=7.0 Hz), 1.96 (d, 3H, J=8.4 Hz), 3.98 (q, 2H, J=7.0 Hz), 5.28-5.42 (m, 1H), 6.22-6.30 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.55, 14.27, 58.72, 84.17, 89.15, 158.03, 200.14; MS (EI) m/z 126.1 (M^+).

8.7.2 Reaction of 7.29a and 7.30a with CO

8.7.2.1 Influence of Catalysts and Ligands

In a 45-ml stainless-steel autoclave were placed palladium catalyst (0.05 mmol), monodentate (PPh_3 or PCy_3, 0.1 mmol, if used) or bidentate phosphine ligand (dppb, dppe, dppf, or dppp, 0.05 mmol, if used), **7.29a** (1 mmol), **7.30a** (5 mmol), *i*-Pr_2NEt (1.5 mmol) and 5 ml of benzene. After carbon monoxide was introduced up to 400 psi, the

mixture was stirred at 100 °C for 24-60 h. The results are listed in Table 7-1.

8.7.2.2 Influence of Solvents, Bases, and Reaction Temperature

A solution of $Pd(OAc)_2$ (0.05 mmol), dppf (0.05 mmol), **7.29a** (1 mmol), **7.30a** (5 mmol), organic base (i-Pr_2NEt, Et_3N, DBU, or DABCO, 1.5 mmol, if used) or inorganic base (K_2CO_3 or KOAc, 3 mmol, if used), and 5 ml of the solvent (benzene, DMF, THF, DMSO, CH_3CN, or toluene) was stirred under CO (100, 400, or 1000 psi) at different temperature (70-150 °C) for 24-60 h. The results are listed in Table 7-2.

8.7.3 Typical Procedure for the Palladium-Catalyzed Carbonylative Heteroannulation of Allenes with o-Iodothiophenols and Carbon Monoxide

A mixture of the allene (2-5 mmol), *o*-iodothiophenol (1 mmol), $Pd(OAc)_2$ (0.05 mmol), dppf (0.05 mmol), *i*-Pr_2NEt (1.5 mmol), and anhydrous benzene (5.0 mL) was heated to 100°C with stirring, under an atmosphere of carbon monoxide (400 psi), in a stainless steel autoclave for 24-60h. After the reaction, the autoclave was cooled to room temperature, excess carbon monoxide was released and the crude reaction mixture was passed through a plug of Florisil, using hexane/ethyl acetate(1:1) as the eluant. The light yellow solution was evaporated to dryness and purified by column chromatography on silica gel using *n*-hexane-ethyl acetate (95:5) as an eluant.

3-Methylene-2, 2-dimethyl-2, 3-dihydro-4H-1-benzothiopyran-4-one (7.31a): oil; IR (neat) 1670 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.60 (s, 6H), 5.46 (d, 1H, *J*= 0.69 Hz), 6.06 (d, 1H, *J*= 0.69 Hz), 7.18-7.19 (m, 2H), 7.22–7.39 (m, 1H), 8.15 (dd, 1H, *J*= 8

and 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.44, 46.73, 118.78, 125.37, 127.83, 129.69, 130.62, 133.52, 140.41, 150.56, 186.84; MS (EI) *m/z* 204.1 (M^+); HRMS calcd for $C_{12}H_{12}OS$ 204.0609, found 204.0598. Anal. Calcd for $C_{12}H_{12}OS$: C, 70.57; H, 5.93. Found: C, 70.62; H, 5.88.

3-(Dimethylmethylene)-2, 2-dimethyl-2, 3-dihydro-4H-1-benzothiopyran-4-one (7.31b): oil; IR (neat) 1671 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.43 (s, 3H), 1.52 (s, 3H), 1.85 (s, 3H), 1.88 (s, 3H), 7.15-7.19 (m, 2H), 7.34-7.38 (m, 1H), 8.09-8.13 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.10, 26.03, 29.82, 29.96, 48.84, 117.47, 124.68, 127.31, 127.43, 128.71, 135.05, 139.70, 141.02, 195.15; MS (EI) *m/z* 232.1 (M^+); HRMS Calcd for $C_{14}H_{16}OS$ 232.0922, found 232.0916; Anal. Calcd for $C_{14}H_{16}OS$: C, 72.39; H, 6.95. Found: C, 72.44; H, 6.88.

2-Cyclohexyl-3-methylene-2, 3-dihydro-4H-1-benzothiopyran-4-one (7.31c): oil; IR (neat) 1670 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.88-1.16 (m, 4H), 1.54-1.74 (m, 6H), 2.16-2.24 (m, 1H), 3.46 (d, 1H, *J*=7.4 Hz), 5.43 (s, 1H), 6.11 (s, 1H), 7.15-7.24 (m, 2H), 7.36-7.42 (m, 1H), 8.14 (d, 1H, *J*=8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.82, 26.60, 27.72, 28.40, 29.72, 32.31, 53.75, 115.55, 123.24, 125.24, 127.44, 128.02, 129.21, 132.96, 143.88, 185.88; MS (EI) *m/z* 258.1 (M^+); HRMS Calcd for $C_{16}H_{18}OS$ 258.1078, found 258.1075. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.39; H, 7.03. Found: C, 74.46; H, 7.10.

2-(*n*-Hexyl)-3-methylene-2, 3-dihydro-4H-1-benzothiopyran-4-one (7.31d):

oil; IR (neat) 1672 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J*=7.0 Hz), 1.13-1.70 (m, 10H), 3.50-3.54 (m, 1H), 5.49 (d, 1H, *J*=0.8 Hz), 6.23 (d, 1H, *J*=0.8 Hz), 6.92-7.04 (m, 2H), 7.33-7.50 (m, 1H), 7.86 (dd, 1H, *J*=8.0 and 1.8 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.07, 22.70, 24.50, 29.47, 31.70, 33.24, 47.76, 118.42, 120.53, 125.78, 127.66, 130.85, 135.40, 139.76, 141.92, 188.51; MS (EI) *m/z* 260 (M^+); HRMS Calcd for $C_{16}H_{20}OS$ 260.1235, found 260.1241. Anal. Calcd for $C_{16}H_{20}OS$: C, 73.81; H, 7.75. Found: C, 73.88; H, 7.75.

2, 3-Dihydro-3'-cyclononena[2,3-b]-4H-1-benzothiopyran-4-one (7.31e): m.p. 57-58°C; IR (KBr) 1672 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.31-1.60 (m, 4H), 2.05-2.42 (m, 8H), 3.95 (t, 1H, *J*=7.4 Hz), 6.24 (t, 1H, *J*=7.0 Hz), 7.14-7.36 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.04, 25.78, 26.93, 27.14, 30.88, 33.04, 58.04, 116.35, 126.34, 126.55, 130.08, 132.33, 135.76, 137.70, 142.36, 184.96; MS (EI) *m/z* 258.1 (M^+); HRMS Calcd for $C_{16}H_{18}OS$ 258.1078, found 258.1080. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.39; H, 7.03. Found: C, 74.46; H, 7.06.

2-Methyl-3-ethoxycarbonylmethyl-4H-1-benzothiopyran-4-one (7.31f): m.p. 71.5-72.0°C; IR (KBr) 1673 cm^{-1} (PhCO-), 1738 cm^{-1} ($-CO_2C_2H_5$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (t, 3H, *J*=7.4 Hz), 2.38 (s, 3H), 3.41 (s, 2H), 4.10 (q, 2H, *J*=7.4 Hz), 7.18-7.20 (m, 2H), 7.22-7.40 (m, 1H), 8.09-8.15 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.12, 20.86, 31.02, 60.89, 114.76, 118.22, 123.30, 125.14, 135.06, 136.12, 153.64, 155.06, 170.78, 186.75; MS (EI) *m/z* 262 (M^+); HRMS Calcd for $C_{14}H_{14}O_3S$ 262.0664, found 262.0670. Anal. Calcd for $C_{14}H_{14}O_3S$: C, 64.11; H, 5.38. Found: C, 64.18, H,

5.44.

2-Methyl-3-(2-phenylvinyl)-2,3-dihydro-4H-1-benzothiopyran-4-one (7.31g) (a mixture of stereoisomers): oil; IR (neat) 1668 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.46-1.53 (m, 3H), 3.24-3.36 (m, 1H), 3.74-3.78 (m, 1H), 6.05-6.22 (m, 1H), 6.52-6.70 (m, 1H), 6.95-7.08 (m, 2H), 7.20-7.52 (m, 6H), 7.85-7.92 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.72, 18.01, 47.36, 48.04, 56.38, 56.76, 116.88, 118.47, 119.50, 119.78, 121.04, 121.49, 126.73, 127.37, 127.62, 127.93, 128.50, 128.59, 128.74, 129.84, 135.90, 135.97, 135.63, 136.26, 136.37, 138.50, 147.62, 148.13, 189.72, 189.85; MS (EI) *m/z* 280.1 (M^+); HRMS Calcd for $C_{18}H_{16}OS$ 280.0922, found 280.0926. Anal. Calcd for $C_{18}H_{16}OS$: C, 77.12; H, 5.76. Found: C, 77.16; H, 5.71.

3-Methylene-2,2,6-trimethyl-2,3-dihydro-4H-1-benzothiopyran-4-one (7.31h): oil; IR (neat) 1666 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 1.60 (s, 6H), 2.34 (s, 3H), 5.45 (d, 1H, *J*=0.8 Hz), 6.06 (d, 1H, *J*=0.8 Hz), 7.13 (d, 1H, *J*=8.0 Hz), 7.25 (d, 1H, *J*=8.0 Hz), 7.97 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.84, 27.43, 46.61, 118.64, 127.78, 129.86, 130.41, 134.67, 135.25, 136.99, 150.80, 187.03; MS (EI) *m/z* 218.1 (M^+); HRMS Calcd for $C_{13}H_{14}OS$ 218.0765, found 218.0751. Anal. Calcd for $C_{13}H_{14}OS$: C, 71.53; H, 6.47. Found: C, 71.62; H, 6.45.

2-Cyclohexyl-6-methyl-3-methylene-2,3-dihydro-4H-1-benzothiopyran-4-one (7.31i): oil; IR (neat) 1670 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.95-1.24 (m, 4H), 1.64-1.78 (m, 6H), 2.12-2.20 (m, 1H), 2.34 (s, 3H), 3.45 (d, 1H, *J*=7.4 Hz), 5.42 (s,

1H), 6.10 (s, 1H), 7.18-7.25 (m, 2H), 7.95 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.84, 25.50, 25.85, 28.03, 31.22, 32.60, 39.39, 53.78, 123.11, 127.71, 128.07, 129.82, 130.47, 131.35, 134.70, 144.18, 186.12; MS (EI) *m/z* 272.1 (M^+); HRMS Calcd for $C_{17}H_{20}OS$ 272.1235, found 272.1229. Anal. Calcd for $C_{17}H_{20}OS$: C, 74.97; H, 7.41. Found: C, 74.88; H, 7.45.

2-(*n*-Hexyl)-6-methyl-3-methylene-2,3-dihydro-4H-1-benzothiopyran-4-one (7.31j): oil; IR (neat) 1669 cm^{-1} (C=O); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, 3H, *J*=7.0 Hz), 1.20-1.88 (m, 10H), 2.36 (s, 3H), 3.88-3.92 (m, 1H), 5.52 (d, 1H, *J*=1.0 Hz), 6.32 (d, 1H, *J*=1.0 Hz), 7.33-7.40 (m, 2H), 7.77 (d, 1H, *J*=0.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.07, 20.38, 23.52, 27.83, 28.90, 31.78, 33.40, 56.68, 119.04, 120.46, 122.05, 127.50, 128.33, 136.37, 139.63, 142.54, 187.60; MS (EI) *m/z* 274.1 (M^+); HRMS Calcd for $C_{17}H_{22}OS$ 274.1391, found 274.1393. Anal. Calcd for $C_{17}H_{22}OS$: C, 74.41; H, 8.09. Found: C, 74.43; H, 8.04.

6-Chloro-2,2-dimethyl-3-methylene-2,3-dihydro-4H-1-benzothiopyran-4-one (7.31k): oil; IR (neat) 1674 cm^{-1} (C=O); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.59 (s, 6H), 5.49 (s, 1H), 6.09 (s, 1H), 7.14 (d, 1H, *J*=8.4 Hz), 7.33 (dd, 1H, *J*=8.4 and 2.0 Hz), 8.10 (d, 1H, *J*=2.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 27.33, 46.80, 119.64, 129.25, 131.51, 131.62, 133.41, 138.74, 149.73, 185.66; MS (EI) *m/z* 238.0 (M^+); HRMS Calcd for $C_{12}H_{11}ClOS$ 238.0219, found 238.0200. Anal. Calcd for $C_{12}H_{11}ClOS$: C, 60.50; H, 4.66. Found: C, 60.58; H, 4.72.

6-Chloro-2-cyclohexyl-3-methylene-2,3-dihydro-4H-1-benzothiopyran-4-one

(7.31l): m.p. 76.5-77°C; IR (KBr) 1674 cm^{-1} (C=O); ^1H NMR (200 MHZ, $CDCl_3$) δ 0.87-1.26 (m, 4H), 1.54-1.78 (m, 6H), 2.14-2.23 (m, 1H), 3.50 (d, 1H, *J*=7.5 Hz), 5.43 (d, 1H, *J*=0.8 Hz), 6.11 (d, 1H, *J*=0.8 Hz), 7.20-7.27 (m, 1H), 7.80-7.84 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.15, 25.23, 27.00, 31.88, 34.02, 39.64, 54.64, 119.84, 122.36, 129.68, 130.60, 133.13, 135.47, 138.37, 139.45, 190.02; MS (EI) *m/z* 292.1 (M^+); HRMS Calcd for $C_{16}H_{17}ClOS$ 292.0689, found 292.0688. Anal. Calcd for $C_{16}H_{17}ClOS$: C, 65.74; H, 5.87. Found: C, 65.78; H, 5.84.

6-Chloro-2-(*n*-hexyl)-3-methylene-2,3-dihydro-4H-1-benzothiopyran-4-one

(7.31m): m.p. 61-62°C; IR (KBr) 1673 cm^{-1} (C=O); ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, 3H, *J*=7.0 Hz), 1.19-1.46 (m, 10H), 3.63-3.70 (m, 1H), 5.53 (d, 1H, *J*=0.8 Hz), 6.32 (d, 1H, *J*=0.8 Hz), 6.90 (d, 1H, *J*=8.5 Hz), 7.24-7.36 (m, 1H), 7.64-7.83 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.07, 22.35, 27.59, 30.42, 31.63, 33.47, 57.35, 119.80, 123.63, 126.88, 133.13, 133.97, 138.42, 139.63, 142.07, 185.04; MS (EI) *m/z* 294.1 (M^+); HRMS Calcd for $C_{16}H_{19}ClOS$ 294.0845, found 294.0851. Anal. Calcd for $C_{16}H_{19}ClOS$: C, 65.29; H, 6.51. Found: C, 65.24; H, 6.56.

References and Notes

1. Roelen, O. *Angew. Chem.* **1948**, *60*, 62.
2. Falbe, J. *New Synthesis with Carbon Monoxide*, Springer, New York, **1980**.
3. Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation: Direct Synthesis of Carbonyl Compounds*, Plenum Press, New York, **1991**.
4. Khumtaveeporn, K.; Alper, H. *Acc. Chem. Res.* **1995**, *28*, 414. (b) El Ali, B.; Alper, H. In *Transition Metals for Organic Synthesis: Building Blocks and Fine Chemicals*, Vol 1: Beller, M. and Bolm, C. Ed. Wiley-VCH, **1998**.
5. Cornils, B.; Herrmann, W. A. *Applied Homogeneous Catalysis with Organometallic Compounds*, VCH: Weinheim, **1996**.
6. Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*, University Science Books, California, **1994**.
7. Yu, W.; Bensimon, C.; Alper, H. *Chem. Eur. J.* **1997**, *3*, 417. (b) Brunner, M.; Alper, H. *J. Org. Chem.* **1997**, *62*, 7565. (c) Cao, P.; Zhang, X. M. *J. Am. Chem. Soc.* **1999**, *121*, 7708. (d) Pamies, O.; Dieguez, M.; Net, G.; Ruiz, A.; Claver, C. *Organometallics* **2000**, *19*, 1488.
8. Mlekuz, M.; Joo, F.; Alper, H. *Organometallics* **1987**, *6*, 1591. (b) Consiglio, G.; Kollar, L.; Kolliker, R. *J. Organomet. Chem.* **1990**, *396*, 375. (c) Chenal, T.; Cipres, I.; Jenck, J.; Kalck, P.; Peres, Y. *J. Mol. Catal.* **1993**, *78*, 351.
9. Lee, C. W.; Alper, H. *J. Org. Chem.* **1995**, *60*, 250.

10.El Ali, B.; Alper, H. *J. Mol. Catal.* **1992**, *77*, 7. (b) El Ali, B.; Alper, H. *J. Org. Chem.* **1993**, *58*, 3595.

11.El Ali, B.; Alper, H. *J. Mol. Catal.* **1993**, *80*, 377. (b) El Ali, B.; Vasapollo, G. Alper, H. *J. Org. Chem.* **1993**, *58*, 4739.

12.Consiglio, G.; Nefkens, S. C. A.; Pisano, C.; Wenzinger, F. *Helv. Chim. Acta* **1991**, *74*, 323.

13.Lin, I. J. B.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1989**, 248.

14.Knifton, J. F. *J. Catal.* **1979**, *60*, 27.

15.Kanzawa, M.; Ishibashi, T.; Kumazawa, T. JP 03255054, **1991**; CA **1992**, 116, 151164w.

16.Vasapollo, G.; Somasunderam, A.; El Ali, B.; Alper, H. *Tetrahedron Lett.* **1994**, *34*, 6203.

17.Xu, Q.; Souma, Y.; Umezawa, J.; Tanaka, M.; Nakatani, H. *J. Org. Chem.* **1999**, *64*, 6306.

18.Nait Ajjou A.; Alper, H. *J. Am. Chem. Soc.* **1998**, *120*, 1466. (b) Bertoux, F.; Monflier, E.; Castanet, Y.; Mortreux, A. *J. Mol. Catal. A-Chem.* **1999**, *143*, 23.

19.Sisak, A.; Ungvary, F.; Marko, L. *J. Org. Chem.* **1990**, *55*, 2508.

20.Nait Ajjou, A.; Alper, H. *Macromolecules* **1996**, *29*, 1784.

21.Drent, E. *Pure Appl. Chem.* **1990**, *62*, 661. (b) Yoneyama, M.; Kakimoto, M.;Imai, Y. *Macromolecules* **1989**, *22*, 2593.

22.Consiglio, G.; Studer, B.; Oldani, F.; Pino, P. *J. Mol. Catal.* **1990**, *58*, L9.

23.Drent, E.; van Broekhooven, J. A. M.; Doyle, M. J. *J. Organomet. Chem.* **1991**, *417*, 235.

24.Batistini, A.; Consiglio, G. *Organometallics* **1992**, *11*, 1766. (b) Panchenko, V. N.; Zakharov, V. A.; Paukshtis, E. A. *J. Mol. Catal. A-Chem.* **1998**, *135*, 115.

25.Brookhart, M.; Rix, F. C.; DeSimone, J. M.; Barborak, J. C. *J. Am. Chem. Soc.* **1992**, *114*, 5894. (b) Meneghetti, S. P.; Lutz, P. J.; Kress, J. *Organometallics* **1999**, *18*, 2734.

26.Sperrle, M.; Consiglio, G. *J. Mol. Catal. A-Chem.* **1999**, *143*, 263.

27.Alper, H.; Woell, J. B.; Despeyroux, B.; Smith, D. J. H. *J. Chem. Soc., Chem. Commun.* **1983**, 1270. Alper, H.; Despeyroux, B.; Woell, J. B. *Tetrahedron Lett.* **1983**, 5691.

28.Alper, H.; Hamel, N. *J. Am. Chem. Soc.* **1990**, *112*, 2803.

29.Brechot, P.; Chauvin, Y.; Commereux, D.; Saussine, L. *Organometallics* **1990**, *9*, 26.

30.Gabriele, B.; Salerno, G.; De Pascali, F.; Costa, M.; Chiusoli, G. P. *J. Org. Chem.* **1999**, *64*, 7693.

31.Morris, G. E.; Oakley, D.; Pippard, D. A.; Smith, D. J. A.; *J. Chem. Soc., Chem. Commun.* **1987**, 410.

32.Nefkens, S. C. A.; Sperrie, M.; Consiglio, G. *Angew. Chem.* **1993**, *105*, 1837.

33.Amer, I.; Alper, H. *J. Organomet. Chem.* **1990**, *383*, 573.

34.Kushino, Y.; Itoh, K.; Miura, M.; Nomura, M. *J. Mol. Catal.* **1994**, *89*, 151. (b) Zargarian, D.; Alper, H. *Organometallics* **1993**, *12*, 712. (c) Ali, B. E.; Alper, H. *J. Mol. Catal.* **1991**, *67*, 29.

35.Torri, S.; Okumoto, H.; Sadakane, M.; Xu, L. H. *Chem. Lett.* **1991**, 1673.

36.Ouerfelli, O.; Ishida, M.; Shinozaki, H.; Nakanishi, K.; Ohfune, Y. *Synlett* **1993**, 409.

37.Lee, J. T.; Alper, H. *Tetrahedron Lett.* **1991**, *32*, 1769.

38.Zargarian, D.; Alper, H. *Organometallics* **1991**, *10*, 2914. (b) Tamaru, Y.; Hojo, M.; Yoshida, Z. *J. Org. Chem.* **1991**, *56*, 1099.

39.Hartstock, F. W.; McMahon, L. B.; Tell, I. P. *Tetrahedron Lett.* **1993**, *34*, 8067.

40.Gabriele, B.; Costa, M.; Salerno, G.; Chiusoli, G. P. *J. Chem. Soc., Chem. Commun.* **1994**, 1429. (b) Gabriele, B.; Costa, M.; Salerno, G.; Chiusoli, G. P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 83.

41.Monteil, F.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1995**, 1601.

42.Matsuda, I.; Ogiso, A.; Sato, S.; Izumi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2332. (b) Ojima, I.; Ingallina, P.; Donovan, R. J.; Clos, N. *Organometallics* **1991**, *10*, 38. (c) Zhou, J. Q.; Alper, H. *Organometallics* **1994**, *13*, 1586.

43.Monteil, F.; Matsuda, I.; Alper, H. *J. Am. Chem. Soc.* **1995**, *117*, 4419. (b) Matsuda, I.; Takeuchi, K.; Itoh, K. *Tetrahedron Lett.* **1999**, *40*, 2553. (c) Sugihara, T.; Okada, Y.; Yamaguchi, M.; Nishizawa, M. *Synlett* **1999**, *6*, 768.

44.Beller, M.; Eckert, M.; Moradi, W. A.; Neumann, H. *Angew. Chem. Int. Ed.* **1999**, *38*, 1454.

45.Xu, W.; Alper, H. *Macromolecules* **1996**, *29*, 6695.

46.Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E. *J. Chem. Soc., Perkin Trans. 1* **1973**, 975. (b) Scheore, N. E. In *Comprehensive Organometallic Chemistry II;* Hegedus, L. S. Ed.; Pergamon: Kidlington, **1995**; Vol. 12, p703. (c) Baxter, R.J.; Knox, G. R.; Pauson, P. L.; Spicer, M. D. *J. Organomet. Chem.* **1999**, *579*, 90.

47.MacWhorter, S. E.; Sampath, V.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1988**, *53*, 203.

48.Joh, T.; Nagata, H.; Takahashi, S. *Inorg. Chim. Acta* **1994**, *220*, 45. (b) Joh, T.; Nagata, H.; Takahashi, S. *Chem. Lett.* **1992**, 1305.

49.Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 5881.

50.Kim, S. -W.; Son, S. U.; Lee, S. I.; Hyeon, T.; Chung, Y. K. *J. Am. Chem. Soc.* **2000**, *122*, 1550.

51.Laine, R. M.; Thomas, D. W.; Cary, L. W.; Buttrill, S. E. *J. Am. Chem. Soc.* **1978**, *100*, 6527.

52.Joh, T.; Doyama, K.; Onitsuka, K.; Shiohara, T.; Takahashi, S. *Organometallics* **1991**, *10*, 2493. (b) Doyama, K.; Joh, T.; Onitsuka, K.; Shiobara, T.; Takahashi, S. *J. Chem. Soc., Chem. Commun.* **1987**, 649.

53.Hong, P.; Mise, T.; Yamazaki, H. *J. Organomet. Chem.* **1991**, *412*, 291.

54.Hong, P.; Mise, T.; Yamazaki, H. *J. Organomet. Chem.* **1987**, *334*, 129.

55.Huh, K. -T.; Orita, A.; Alper, H. *J. Org. Chem.* **1993**, *58*, 6956.

56.For reviews, see: (a) Tsuji, J.; Kiji, J. In *Transition Metals for Organic Synthesis: Building Blocks and Fine Chemicals*, Beller, M. and Bolm, C. Eds., Wiley-VCH, New York, **1998**, Volume 1, p 68. (b) Tsuji, J. *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*, John Wiley, Chichester, **1995**, 1 st ed., p 340. (c) Tsuji, J.; Mandai, T. *Angew. Chem. Int. Ed. Engl.* **1995**, 34, 2589.

57.Satyanarayana, N.; Alper, H. *Organometallics* **1991**, *10*, 804. (b) Matsushita, K.; Komori, T.; Oi, S.; Inoue, Y. *Tetrahedron Lett.* **1994**, *35*, 5889. (c) Arzoumanian, H.; Cochini, F.; Nuel, D.; Rosas, N. *Organometallics* **1993**, *12*, 1871. (d) Mandai, T.; Tsujiguchi, Y.; Matsuoka, S.; Tsuji, J.; Saito, S. *Tetrahedron Lett.* **1994**, *35*, 5697. (e) Marshall, J. A.; Liao, J. L. *J. Org. Chem.* **1998**, *63*, 5962.

58.Murai, S.; Chatani, N.; Fukumoto, Y.; Ida, T. *J. Am. Chem. Soc.* **1993**, *115*, 11614.

59.Takeuchi, R.; Yasue, H. *J. Org. Chem.* **1993**, *58*, 5386.

60.Van den Hoven, B. G.; Alper, H. *J. Org. Chem.* **1999**, *64*, 3964. (b) Van den Hoven, B. G.; Alper, H. *J. Org. Chem.* **1999**, *64*, 9640.

61.Rama, A. D.; Lyengar, D. S.; Pardhasaradhi, M. *Tetrahedron* **1994**, *50*, 2543. (b) Timmermann, P.; Verboom, W.; Reinhoudt, D. N.; Arduini, A.; Grandi, S.; Sicuri, A. R.; Pochini, A.; Ungaro, R. *Synthesis* **1994**, 185.

62.Alper, H.; Amer, I.; Vasapollo, G. *Tetrahedron Lett.* **1989**, *30*, 2615. (b) Amer, I.; Alper, H. *J. Org. Chem.* **1988**, *53*, 5147.

63.Lee, J. T.; Alper, H. *Organometallics* **1990**, *9*, 3064.

64.Foa, M.; Francalani, F.; Gardano, A.; Cainelli, G.; Umani-Ronchi, A. *J. Organomet. Chem.* **1983**, *248*, 225. (b) Bergbreiter, D. E.; Chen, B.; Weatherford, D. *J. Mol. Catal.* **1992**, *74*, 409. (b) Vanderesse, R.; Marchal, J.; Caubere, P.; *Synth. Commun.* **1993**, *23*, 1361.

65.Kobayashi, T.; Tanaka, M. *J. Organomet. Chem.* **1982**, *233*, C64.

66.Okano, T.; Harada, N.; Kiji, J. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1741.

67.Perry, R. J.; Wilson, B. D.; Miller, R. J. *J. Org. Chem.* **1992**, *57*, 2883. (b) Perry, R. J.; Wilson, B. D. *J. Org. Chem.* **1992**, *57*, 6351.

68.Pri-Bar, I.; Alper, H. *J. Org. Chem.* **1989**, *54*, 36.

69.Perry, R. J.; Turner, S. R. *J. Org. Chem.* **1991**, *56*, 6573.

70.Huang, X.; Wu, J. L. *Chem. Ind.* **1990**, 548. (b) Monteil, F.; Kalck, P. *J. Organomet. Chem.* **1994**, *482*, 45.

71.Maeda, K.; Yagita, H.; Omata, K.; Fujimoto, K. *J. Mol. Catal.* **1992**, 347. (b) Grigg, R.; Major, J. P.; Martin, F. M.; Whittaker, M. *Tetrahedron Lett.* **1999**, *40*, 7709.

72.Bertoux, F.; Monflier, E.; Castanet, Y.; Mortreux, A. *J. Mol. Catal. A: Chem.* **1999**, *143*, 11. (b) Choudary, B. M.; Reddy, N. P.; Ashok, B. *Appl. Catal.* **1987**, *32*, 357.

73.Kubota, Y.; Takeuchi, K.; Hanaoka, T.; Sugi, Y. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 563. (b) Perry, R. J.; Turner, S. R.; Blevins, R. W. *Macromolecules* **1993**, *26*, 1509.

74.Kubota, Y.; Takeuchi, K.; Hanaoka, T.; Sugi, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 1553. (b) Kubota, Y.; Takeuchi, K.; Hanaoka, T.; Sugi, Y. *Synlett* **1994**, 515.

75.Watanabe, H.; Hashizume, Y.; Uneyama, K. *Tetrahedron Lett.* **1992**, *33*, 4333.

76.Okano, T.; Harada, N.; Kiji, J. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2329. (b) Misumi, Y.; Ishii, Y.; Hidai, M. *J. Mol. Catal.* **1993**, *78*, 1. (c) Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 452.

77.Ishikura, M.; Terashima, M. *J. Org. Chem.* **1994**, *59*, 2634. (b) Grigg, R.; Redpath, J.; Sridharan, V.; Wilson, D. *Tetrahedron Lett.* **1994**, *35*, 4429. (c) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 1557.

78.Tanaka, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 637.

79.Delaude, L.; Masdeu, A. M.; Alper, H. *Synthesis* **1994**, 1149. (b) Torii, S.; Okumoto, H.; Xu, L. H.; Sadakane, M.; Shostakovsky, M. V.; Ponomaryov, A. B.; Kalinin, V. N. *Tetrahedron* **1993**, *49*, 6773.

80.Nozaki, K.; Sato, N.; Takaya, H. *J. Org. Chem.* **1994**, *59*, 2679.

81.Orito, K.; Miyazawa, M.; Kanbayashi, R.; Tokuda, M.; Suginome, H. *J. Org. Chem.* **1999**, *64*, 6583. (b) Knight, S. D.; Overman, L. E.; Pairaudeau, G. *J. Am. Chem. Soc.*

1993, *115*, 9293. (c) Negishi, E. -I.; Zhang, Y.; Shimoyama, I.; Wu, G. *Tetrahedron Lett.* **1990**, *31*, 2841.

82.Negishi, E. -I.; Zhang, Y.; Shimoyama, I.; Wu, G. *J. Am. Chem. Soc.* **1989**, *111*, 8018.

83.Kalinin, N.; Shostakosky, M. V.; Ponomarjyov, A. B. *Tetrahedron Lett.* **1990**, *31*, 4073.

84.An, Z.; Catallani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1989**, *371*, C51.

85.An, Z.; Catallani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1990**, *397*, C31.

86.Okuro, K.; Furune, M.; Miura, M.; Nomura, M. *J. Org. Chem.* **1992**, *57*, 4754. (b) Inoue, Y.; Taniguchi, M.; Hashimoto, H.; Ohuchi, K.; Imaizumi, S. *Chem. Lett.* **1988**, 81.

87.Okuro, K.; Alper, H. *J. Org. Chem.* **1997**, *62*, 1566.

88.Larksarp, C.; Alper, H. *Org. Lett.* **1999**, *1*, 1619.

89.Larksarp, C.; Alper, H. *J. Org. Chem.* **1999**, *64*, 9194.

90.Arcadi, A.; Cacchi, S.; Carnicelli, V.; Marinelli, F. *Tetrahedron* **1994**, *50*, 437.

91.Amer, I.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 927. (b) Joo, F.; Alper, H. *Organometallics* **1985**, *4*, 1775. (c) Adapa, S. R.; Prasad, C. S. N. *J. Chem. Soc. Perkin Trans.1* **1989**, 1706.

92.Hu, Y.; Wang, J. X.; Cui, W. *Synth. Commun.* **1994**, *24*, 1743. (b) Shim, S. C.; Doh, C. H.; Park, W. H.; Kwon, Y. G.; Lee, H. S. *J. Organomet. Chem.* **1990**, *382*, 419. (c) Galamb, V.; Palyi, G.; Ungvary, F.; Marko, L.; Boese, R.; Schmid, G. *J. Am. Chem. Soc.* **1986**, *108*, 3344.

93.Murahashi, S. -I.; Imada, Y. *Chem. Lett.* **1985**, 1477.

94.Knifton, J. F. *J. Organomet. Chem.* **1980**, *188*, 220.

95.Davies, S. G.; Smallridge, A. J.; Ibbotson, A. *J. Organomet. Chem.* **1990**, *386*, 195. (b) Tanguy, G.; Weinberger, B.; Des Abbayes, H. *Tetrahderon Lett.* **1983**, *24*, 4005.

96.Okano, T.; Okabe, N.; Kiji, J. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2589. (b) Alper, H.; Hashem, K.; Heveling, J. *Organometallics* **1982**, *1*, 775. (c) Takahashi, T.; Ikeda, H.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3885. (d) Kobayashi, T.; Abe, F.; Tanaka, M. *J. Mol. Catal.* **1988**, *45*, 91.

97.Gao, H. R.; Xu, Y.; Liao, S. J.; Yu, D. R. *Chin. Chem. Lett.* **1992**, *3*, 351. (b) Tsuji, J.; Sato, K.; Okumoto, H. *J. Org. Chem.* **1984**, *49*, 1341. (c) Kiji, J.; Okano, T.; Nishiumi, W.; Konishi, H. *Chem. Lett.* **1989**, 957.

98.Brunet, J. -J.; Sidot, C.; Caubere, P. *J. Org. Chem.* **1983**, *48*, 1919.

99.Starks, C. M.; Liotta, C. *Phase Transfer Catalysis: Principles and Techniques*, Academic Press, New York, 1978.

100.Okano, T.; Okabe, N.; Kishi, J. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2589. (b) Okano, T.; Uchida, I.; Nakagaki, T.; Konishi, H.; Kiji, J. *J. Mol. Catal.* **1989**, *54*, 65.

101.Murahashi, S. I.; Imada, Y.; Taniguchi, Y.; Shinya, S. *J. Org. Chem.* **1993**, *58*, 1538. (b) Koyasu, Y.; Matsuzaka, H.; Hiroe, Y.; Uchida, Y.; Hidai, M. *J. Chem. Soc., Chem. Commun.* **1987**, 575.

102.Wang, S. -Z.; Yamamoto, K.; Yamada, H.; Takahashi, T. *Tetrahedron* **1992**, *48*, 2333. (b) Tsuji, J. *Tetrahedron* **1986**, *42*, 4361.

103.Neibecker, D.; Oirier, J.; Tkatchenko, I. *J. Org. Chem.* **1989**, *54*, 2459. (b) Bonnet, M. C.; Neibecker, D.; Stitou, B.; Tkatchenko, I. *J. Organomet. Chem.* **1989**, *366*, C9.

104.Imada, Y.; Shibata, O.; Murahashi, S. -I. *J. Organomet. Chem.* **1993**, *451*, 183.

105.Itoh, K.; Hamaguchi, N.; Miura, M.; Nomura, M. *J. Mol. Catal.* **1992**, *75*, 117. (b) Cavinato, G.; Toniolo, L. *J. Mol. Catal.* **1993**, *78*, 131.

106.Yamamoto, T.; Akimoto, M.; Saito, O.; Yamamoto, A. *Organometallics* **1986**, *5*, 1559.

107.Murahashi, S. -I.; Imada, Y.; Taniguchi, Y.; Higashiura, S. *Tetrahedron Lett.* **1988**, *29*, 4945.

108.Negishi, E. -I.; Wu, G.; Tour, J. M. *Tetrahedron Lett.* **1988**, *29*, 6745. (b) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *107*, 4193. (c) Tamaru, Y.; Bando, T.; Hojo, M.; Yoshida, Z. *Tetrahedron Lett.* **1987**, *28*, 3497.

109.Iwasaki, M.; Kobayashi, Y.; Li, J. -P.; Matsuzaka, H.; Ishii, Y.; Hidai, M. *J. Org. Chem.* **1991**, *56*, 1922. (b) Matsuzaka, H.; Hiroe, Y.; Iwasaki, M.; Ishii, Y.; Koyasu, Y.; Hidai, M. *J. Org. Chem.* **1988**, *53*, 3832.

110.Marchionna, M. In *Oxygenates by Homologenation or CO Hydrogenation with Metal Complexes*, Braca, G. Ed., Kluwer Academic, Dordrecht, **1994**.

111.Drent, E. *Pure Appl. Chem.* **1990**, *62*, 661.

112.Lee, S. Y.; Kim, J. C.; Lee, J. S.; Kim, Y. G. *Ind. Eng. Chem. Res.* **1993**, *32*, 253.

113.Cavinato, G.; Toniolo, L. *J. Mol. Catal.* **1991**, *69*, 283.

114.Kuhlein, K.; Geissler, H. In *Transition Metals for Organic Synthesis: Building Blocks and Fine Chemicals*, Vol 1: Beller, M. and Bolm, C. Ed. Wiley-VCH, **1998**.

115.Wakamatsu, H.; Uda, J.; Zamakami, N. *J. Chem. Soc. Chem. Commun.* **1971**, 1540.

116.Stern, R.; Reffet, D.; Hirschauer, A.; Commereuc, D.; Chauvin, Y. *Synth. Commun.* **1982**, *12*, 1111.

117.Lin, J. J.; Knifton, J. F. *J. Organomet. Chem.* **1991**, *147*, 99.

118.Beller, M.; Eckert, M.; Vollmuller, F.; Geissler, H.; Bogdanovic, S. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1494. (b) Beller, M.; Eckert, M.; Geissler, H.; Napierski, B.; Rebenstock, H. P.; Holla, E. W. *Chem. Eur. J.* **1998**, *4*, 935. (c) Beller, M.; Eckert, M.; Holla, E. W. *J. Org. Chem.* **1998**, *63*, 5658. (d) Beller, M.; Eckert, M.; Moradi, W. A. *Synlett* **1999**, 108. (e) Beller, M.; Eckert, M.; Moradi, W. A.; Neumann, H. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1454. (f) Beller, M.; Moradi, W. A.; Eckert, M.; Neumann, H. *Tetrahedron Lett.* **1999**, *40*, 4523.

119.Jagers, E.; Bohshar, M.; Kleiner, H. -J.; Koll, H. -P. DE 3913891, **1990**. (b) Jagers, E.; Erpenbach, H.; Koll, H. -P. DE 3823885, **1990**.

120.Beller, M.; Eckert, M. K.; Vollmuller, F. *J. Mol. Catal. A: Chem.* **1998**, *135*, 23.

121.Ojima, I.; Okabe, M.; Kato, K.; Kwon, H. B.; Horvath, I. T. *J. Am. Chem. Soc.* **1988**, *110*, 150. (b) Ojima, I.; Hirai, K.; Fujita, M.; Fuchikami, T. *J. Organomet. Chem.* **1985**, *279*, 203.

122.Knifton, J. F.; Lin, J. J.; Storm, D. A.; Wong, S. F. *Catal. Today* **1993**, *18*, 355. (b) Lin, J. J.; Knifton, J. F. *J. Organomet. Chem.* **1991**, *147*, 99.

123.Hirai, K.; Takahashi, Y.; Ojima, I. *Tetrahedron Lett.* **1982**, *23*, 2491. (b) de Vries, J. G.; de Boer, R. P.; Hogeweg, M.; Gielens, E. E. C. G. *J. Org. Chem.* **1996**, *61*, 1842.

124.Izawa, K.; Nishi, S.; Asada, S. *J. Mol. Catal.* **1987**, *41*, 135.

125.Alper, H.; Hamel, N. *Tetrahedron Lett.* **1987**, *28*, 3237.

126.Roberto, D.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 7539.

127.Alper, H.; Arzoumanian, H.; Petrignani, J. F.; Saldana-Maldonado, M. *J. Chem. Soc., Chem. Commun.* **1985**, 340.

128.Calet, S.; Alper, H.; Petrignani, J. F.; Saldana-Maldonado, M. *Organometallics* **1987**, *6*, 1625.

129.Alper, H.; Perera, C. P.; Ahmed, F. R. *J. Am. Chem. Soc.* **1981**, *103*, 1289. (b) Wang, M. D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 20. (c) Wang, M. D.; Alper, H. *J. Am. Chem. Soc.* **1992**, *114*, 7018. (d) Khumtaveeporn, K.; Alper, H. *J. Am. Chem. Soc.* **1994**, *116*, 5662. (e) Calet, S.; Urso, F.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 931. (f) Spears, G. W.; Nakanishi, K.; Ohfune, Y. *Synlett* **1991**, 91. (g) Chamchaang, W.; Pinhas, A. R. *J. Org. Chem.* **1990**, *55*, 2943. (h) Alper, H.; Calet, S. *Tetrahedron Lett.* **1988**, *29*, 1763. (i) Piotti, M. E.; Alper, H. *J. Am. Chem. Soc.* **1996**, *118*, 111. (j) Davoli, P.; Moretti, I.; Prati, F.; Alper, H. *J. Org. Chem.* **1999**, *64*, 518. (k) Tanner, D.; Somfai, P. *Bioorg. Med. Chem. Lett.* **1993**, *3*, 2415.

130.Alper, H. *Pure Appl. Chem.* **1988**, *60*, 35.

131.Chauvel, A.; Delmon, B.; Holderich, W. F. *Appl. Catal.* **1994**, *115*, 173.

132.Lin, M.; Sen, A. *J. Chem. Soc., Chem. Commun.* **1992**, 892. (b) Sen, A.; Lin, M. *J. Chem. Soc., Chem. Commun.* **1992**, 508. (c) Barton, D. H. R.; Doller, D. *Acc. Chem. Res.* **1992**, *25*, 504. (d) Barton, D. H. R.; Csuhai, E.; Doller, D. *Tetrahedron Lett.* **1992**, *33*, 4389. (e) Boese, W. T.; Goldman, A. S. *J. Am. Chem. Soc.* **1992**, *114*, 350.

133.Kunin, A. J.; Eisenberg, R. *Organometallics* **1988**, *7*, 2124.

134.Moore, E. J.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; Labounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888. (b) Tanaka, M.; Sakakaru, T.; Wada, H.; Sasaki, Y. JP 01249741, 1989. Chem. Abstr. 1990, 112: 98197p.

135.Tsunoi, S.; Ryu, I.; Sonada, N. *J. Am. Chem. Soc.* **1994**, *116*, 5473.

136.Ryu, I.; Nagahara, K.; Yamazaki, H.; Tsunoi, S.; Sonuda, N. *Synlett* **1994**, 643. (b) Ryu, I.; Alper, H. *J. Am. Chem. Soc.* **1993**, *115*, 7543. (c) Ryu, I.; Yamazaki, H.; Ogawa, A.; Kambe, N.; Sonuda, N. *J. Am. Chem. Soc.* **1993**, *115*, 1187.

137.Whitham, G. H. *Organosulfur Chemistry*; Oxford University Press: New York, 1995. (b) Page, P. Ed. *Organosulfur Chemistry: Synthetic Aspects*; Academic Press: New York, 1995.

138.Styer, L. *Biochemistry*; W. H. Freeman and Co.: New York, 1988, chapter 20. (b) Halcomb, R. *J. Am. Chem. Soc.* **1995**, *117*, 5720. (c) Corey, E. J.; Reichard, G. *J. Am. Chem. Soc.* **1992**, *114*, 10677.

139.Ashizawa, T.; Kawashima, K.; Kanda, Y.; Gomi, K.; Okabe, M.; Ueda, K.; Tamaoki, T. *Anti-Cancer Drugs* **1999**, *10*, 829. (b) Bolasco, F. *U. S. Patent* No. 4,242,354, 1980.

140.Penn, J.; Owens, W. *Tetrahedron Lett.* **1992**, *33*, 3737.

141.Nagao, Y.; Kawabata, K.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1978**, 330.

142.Fukuyama, T.; Lin, S.; Li, L. *J. Am. Chem. Soc.* **1990**, *112*, 7050.

143.McGarvey, G.; Williams, J. M.; Hiner, R. N.; Matsubara, Y.; Oh, T. *J. Am. Chem. Soc.* **1986**, *108*, 4943.

144.Conrow, R.; Portoghese, P. *J. Org. Chem.* **1986**, *51*, 938.

145.Kawanami, Y.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1983**, *24*, 5131.

146.Liu, H.; Bukownik, R.; Pednekar, P. *Synth. Commun.* **1981**, *11*, 599.

147.Liu, H.; Luo, W. *Synth. Commun.* **1989**, *19*, 387.

148.Chen, C. –Y.; Hart, D. J. *J. Org. Chem.* **1993**, *58*, 3840. (b) Hart, D. J.; Wu, W. –L.; Kozikowski, A. P. *J. Org. Chem.* **1997**, *62*, 5023.

149.Maruoka, K.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1992**, *114*, 1089. (b) Bycon, C. –H.; Chen, C. –Y.; Elis, D. A.; Hart, D. J.; Li, J. *Synlett* **1998**, 596.

150.Hart, D. J.; Wu, W. –L.; Kozikowski, A. P. *J. Am. Chem. Soc.* **1995**, *117*, 9369.

151.Masamune, S.; Bates, G.; Corcoran, J. *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 585. (b) Mohanraj, S.; Ford, W. *J. Org. Chem.* **1985**, *50*, 1616.

152.Baca, M.; Muri, T.; Schnolzer, M.; Kent, S. *J. Am. Chem. Soc.* **1995**, *117*, 1881 and references therein. (b) Beligere, G. B.; Dawson, P. E. *J. Am. Chem. Soc.* **1999**, *121*, 6332.

153.Frykman, H.; Ohrner, N.; Norin, T.; Hult, K. *Tetrahedron Lett.* **1993**, *34*, 1367. (b) Fang, J. Wong, C. *Synlett* **1994**, 393. (c) Um, P. –J.; Drueckhammer, D. G. *J. Am. Chem. Soc.* **1998**, *120*, 5605. (d) White, J. D.; Kim, T. –E.; Nambu, M. *J. Am. Chem. Soc.* **1997**, *119*, 103.

154.Benz, H. *Synthesis* **1994**, 337. (b) Shin, Y.; Winans, K. A.; Backes, B. J.; Kent, S. B. H.; Ellman, J. A.; Bertozzi, C. R. *J. Am. Chem. Soc.* **1999**, *121*, 11684. (c) Kawakami, T.; Yoshimura, S.; Aimoto, S. *Tetrahedron Lett.* **1998**, *39*, 7901. (d) Li, X.; Kamakami, T.; Aimoto, S. *Tetrahedron Lett.* **1998**, *39*, 8669. (e) Nilsson, B. L.; Kiessling, L. L.; Raines, R. *Org. Lett.* **2000**, *2*, 1939.

155.Alpegiani, M. *Eur. J. Med. Chem.* **1992**, *27*, 875.

156.Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F. *Tetrahedron Lett.* **1995**, *36*, 613.

157.Davis, A.; Walsh, J. *Tetrahedron Lett.* **1994**, *35*, 4865. (b) Kataoka, T.; Iwama, T.; Kinoshita, H.; Tsujiyama, S.; Tsurukami, Y.; Iwamura, T.; Watanabe, S. *Synlett* **1999**, 197.

158.Suh, K.; Choo, D. *Tetrahedron Lett.* **1995**, *36*, 6109.

159.Imamoto, T.; Kodera, M.; Yokoyama, M. *Synthesis* **1982**, 134 (Polyphosphate ester). (b) Kim, M.; Patel, D. *Tetrahedron Lett.* **1994**, *35*, 5603 (BOP). (c) Adamczyk, M.; Fishpaugh, J. R. *Tetrahedron Lett.* **1996**, *37*, 4305 (Solid supported synthesis).

160.Spessard, G.; Chan, W.; Masamune, S. *Org. Synth.* **1982**, *61*, 134. (b) Zheng, T. –C.; Burkart, M.; Richardson, D. E. *Tetrahedron Lett.* **1999**, *40*, 603.

161.Ahmad, S.; Iqbal, J. *Tetrahedron Lett.* **1986**, *27*, 3791.

162.Sucheta, K.; Reddy, G.; Ravi, D.; Rao, N. *Tetrahedron Lett.* **1994**, *35*, 4415.

163.Petrillo, G.; Novi, M.; Garbarino, G.; Filiberti, M. *Tetrahedron* **1989**, *45*, 7411.

164.Divekar, S.; Safi, M.; Soufiaoui, M.; Sinou, D. *Tetrahedron* **1999**, *55*, 4369. (b) Harding, R. L.; Bugg, T. D. H. *Tetrahedron Lett.* **2000**, *41*, 2729.

165.Rulev, A. Y.; Larina, L. I.; Keiko, N. A.; Voronkov, M. G. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 1567.

166.Iwama, T.; Kataoka, T.; Muraoka, O.; Tanabe, G. *J. Org. Chem.* **1998**, *63*, 8355.

167.Hegedus, L. L.; McCabe, R. W. *Catalyst Poisoning*; Marcel Dekker: New York, 1984.

168.Chiusoli, G. P. *Chim. Ind.* **1959**, *41*, 503.

169.Tsuji, J.; Kiji, J.; Morikawa, M. *Tetrahedron Lett.* **1963**, *4*, 1811.

170.Kiji, J.; Okano, T.; Higashimate, Y.; Fukui, Y. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1029.

171.Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 433.

172.Murahashi, S. –I.; Imada, Y.; Nishimura, K. *Tetrahedron* **1994**, *50*, 453.

173.Sheffy, F. K.; Gedschalx, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833.

174.Yasui, K.; Fugami, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1995**, *60*, 1365.

175.Tanaka, H.; Hai, A. K. M. A.; Sadakane, M.; Okumoto, H.; Torii, S. *J. Org. Chem.* **1994**, *59*, 3040. (b) Zhou, Z.; Alper, H. *J. Org. Chem.* **1996**, *61*, 1256.

176.Ishii, Y.; Hidai, M. *J. Organomet. Chem.* **1992**, *428*, 279.

177.Ishii, Y.; Gao, C.; Iwasaki, M.; Hidai, M. *J. Org. Chem.* **1993**, *58*, 6818. (b) Duprat, S.; Deweerdt, H.; Jenck, J.; Kalck, P. *J. Mol. Catal.* **1993**, *80*, L9.

178.Zhu, J.; Lu, X. Tetrahedron Lett. **1987**, 28, 1987. (b) Zhu, J.; Lu, X. Chem. Commun. **1987**, 1318.

179.Ito, Y.; Sawamura, M.; Matsuoka, M.; Matsumoto, Y.; Hayashi, T. Tetrahedron Lett. **1987**, 28, 4849. (b) Lu, X.; Jiang, X. J. Organomet. Chem. **1989**, 359, 139.

180.Tamaru, Y.; Yasui, K.; Takanabe, H.; Tanaka, S.; Fugami, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 645.

181.To our knoweldge, there are no reports on the transition metal catalyzed reaction involving a combination of thiols and allylic alcohols. For the transition-metal-catalyzed reactions using organosulfur compounds, see: (a) Ogawa, A.; Obayashi, R.; Ine, H.; Tsuboi, Y.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 881. (b) Ogawa, A.; Kuniyasu, H.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1997**, *62*, 8361. (c) Arterburn, J. B.; Perry, M. C.; Nelson, S. L.; Dible, B. R.; Holguin, M. S. *J. Am. Chem. Soc.* **1997**, *119*, 9309. (d) Ogawa, A.; Kawakami, J.; Mihara, M.; Ikeda, T.; Sonoda, N.; Hirao, T. *J. Am. Chem. Soc.* **1997**, *119*, 12380. (e) Galardon, E.; Maux, P. L.; Simonneaux, G. *J. Chem. Soc., Perkin Trans. 1*, **1997**, 2455. (f) Ogawa, A.; Kawakami, J.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1996**, *61*, 4161. (g) Crudden, C. M.; Alper, H. *J. Org. Chem.* **1995**, *60*, 5579. (h) Khumtaveeporn, K.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1995**, 917. (i) Ogawa, A.; Takeba, M.; Kawakami, J.;

Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1995**, *117*, 7564. (j) Khumtaveeporn, K.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1414. (k) Ishiyama, T.; Nishijima, K.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 7219. (l) Kuniyasu, H.; Ogawa, A.; Sato, K.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 5902. (m) Kuniyasu, H.; Ogawa, A.; Sato, K.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796. (n) Luh, T. Y.; Ni, Z. J. *Synthesis* **1990**, 89. (o) Carpita, A.; Rossi, R.; Scamuzzi, B. *Tetrahedron Lett.* **1989**, *30*, 2699. (p) Osakada, K.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1987**, *28*, 6321. (q) Calet, S.; Alper, H. *Tetrahedron Lett.* **1986**, *27*, 3573. (r) Antebi, S.; Alper, H. *Can. J. Chem.* **1986**, *64*, 2010. (s) Antebi, S.; Alper, H. *Organometallics* **1986**, *5*, 596. (t) Cristau, H. J.; Chabaud, B.; Labaudiniere, R.; Christol, H. *J. Org. Chem.* **1986**, *51*, 875. (u) Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*, 2609. (v) Shim, S. C.; Antebi, S.; Alper, H. *J. Org. Chem.* **1985**, *50*, 147.

182.Dubois, M. R. *Chem. Rev.* **1989**, *89*, 1.

183.Hutton, A. T. In *Comprehensive Coordination Chemistry*; Wilkinson, G.; Gillard, R. D.; McCleverty, J. A. Eds.; Pergamon Press: Oxford, U.K., 1984; Vol. 5, p 1151.

184.Murahashi, S. –I.; Imada, Y.; Nishimura, K. *J. Chem. Soc., Chem. Commun.* **1988**, 1578.

185.Bonnet, M. C.; Coombes, J.; Manzano, B.; Neibecker, D.; Tkatchenko, I. *J. Mol. Catal.* **1989**, *52*, 263.

186.Knifton, J. F. *J. Organometl. Chem.* **1980**, *188*, 223. (b) Tsuji, J.; Kiji, J.; Imamura, S.; Morikawa, M. *J. Am. Chem. Soc.* **1964**, *86*, 4350.

187.Nakagawa, N.; Mori, K. *Agric. Biol. Chem.* **1984**, 48, 2505.

188.Mori, K.; Nakazono, Y. *Tetrahedron Lett.* **1986**, *42*, 6459.

189.Jacob III, P.; Brown, H. C. *J. Org. Chem.* **1977**, *42*, 579.

190.Minckler, L. S.; Hussey, A. S.; Baker, R. H. *J. Am. Chem. Soc.* **1956**, *78*, 1009.

191.Cater, M. J.; Fleming, I.; Percival, A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2415. (b) Hwu, J. R.; Furth, P. S. *J. Am. Chem. Soc.* **1989**, *111*, 8834.

192.Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y.; Sugiura, T.; Takahashi, K. *J. Org. Chem.* **1985**, *50*, 1523.

193.Tsuji, Y.; Yamada, N.; Tanaka, S. *J. Org. Chem.* **1993**, *58*, 16.

194.Tanigawa, Y.; Nishimura, K.; Kawasaki, A.; Murahashi, S. *Tetrahedron Lett.* **1982**, *23*, 5549.

195.Dekker, G. P. C. M.; Elsevier, C. J.; Vrieze, K.; van Leeuwen, P. W. N. M. *Organometallics* **1992**, *11*, 1598. (b) Dekker, G. P. C. M.; Elsevier, C. J.; Vrieze, K.; van Leeuwen, P. W. N. M. *J. Organomet. Chem.* **1992**, *430*, 357.

196.Ali, B. E.; Alper, H. *J. Org. Chem.* **1991**, *56*, 5357.

197.Alcock, S. G.; Baldwin, J. E.; Bohlmann, R.; Harwood, L. M.; Seeman, J. I. *J. Org. Chem.* **1985**, *50*, 3526.

198.Murahashi, S. –I.; Imada, Y.; Taniguchi, Y.; Higashiura, S. *J. Org. Chem.* **1993**, *58*, 1538. (b) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2046. (c) Faller, J. W.; Thomsen, M. E.; Mattina, M. J. *J. Am. Chem. Soc.* **1971**, *93*, 2642.

199.Osakada, K.; Chiba, T.; Nakamura, Y.; Yamamoto, T.; Yamamoto, A. *J. Chem. Soc., Chem. Commun.* **1986**, 1589.

200.Maitlis, P. M.; Espinet, P.; Russell, M. J. H. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; vol. 6, pp385-454.

201.The reaction was monitored by TLC (SiO_2, EtOAc-hexane 1:10) and the reaction time was obtained in this way.

202.The thiocarbonylation of verbenol (**2.79**) gave thioester and sulfide in 18% and 14% yield, respectively, under the reaction conditions.

203.Stromnova, T. A.; Vargaftik, M. N.; Moiseev, I. I. *J. Organomet. Chem.* **1983**, *252*, 113. (b) Grushin, V. V.; Alper, H. *Organometallics* **1993**, *12*, 1890.

204.Tsuji, J.; Nogi, T. *Tetrahedron Lett.* **1966**, 1801. (b) Tsuji, J.; Nogi, T. *J. Am. Chem. Soc.* **1966**, *88*, 1289.

205.Tsuji, J.; Sugiura, T.; Minami, I. *Tetrahedron Lett.* **1986**, *27*, 731.

206.Tsuji, J.; Mandai, T. *J. Organomet. Chem.* **1993**, *451*, 15.

207.Kiji, J.; Okano, T.; Fujii, E.; Tsuji, J. *Synthesis* **1997**, 313.

208.For more examples of dicarbonylation, see: (a) Gabriele, B.; Costa, M.; Salerno, G.; Chiusoli, G. P. *J Chem. Soc., Chem. Commun.* **1992**, 1007. (b) Tsuji, J.; Morikawa, M.; Iwamoto, N. *J. Am. Chem. Soc.* **1964**, *86*, 2095. (c) Kiji, J.; Konishi, H.; Okano, T.; Kometani, S.; Iwasa, A. *Chem. Lett.* **1987**, 313.

209.Mandai, T.; Tsujiguchi, Y.; Matsuoka, S.; Saito, S.; Tsuji, J. *J. Organomet. Chem.* **1995**, *488*, 127.

210.Yu, W. –Y.; Alper, H. *J. Org. Chem.* **1997**, *62*, 5684.

211.Mandai, T.; Ryoden, K.; Kawada, M.; Tsuji, J. *Tetrahedron Lett.* **1991**, *32*, 7683.

212.Imada, Y.; Alper, H. *J. Org. Chem.* **1996**, *61*, 6766. (b) Marshall, J. A.; Wolf, M. A. *J. Org. Chem.* **1996**, *61*, 3238.

213.Mead, K. T. *Tetrahedron Lett.* **1987**, *28*, 1019. (b) Smith, W. N.; Kuehn, E. D. *J. Org. Chem.* **1973**, *38*, 3588.

214.Marshall, J. A.; Xie, S. *J. Org. Chem.* **1995**, *60*, 7230. (b) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1999**, *64*, 5201.

215.Osakada, K.; Yamamoto, T.; Yamamoto, A. *Tetrahedron Lett.* **1987**, *28*, 6321.

216.Okamura, H.; Miura, M.; Takei, H. *Tetrahedron Lett.* **1979**, 43. (b) Okamura, H.; Takei, H. *Tetrahedron Lett.* **1979**, 3425.

217.Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1987**, *109*, 1469.

218.Bunluesin, T.; Gorte, R. J.; Graham, G. W. *Applied Catal. B. Environmental* **1998**, *15*, 107. (b) Bianchini, C.; Lee, H. M.; Meli, A.; Moneti, S.; Patinec, V.; Petrucci, G.; Vizza, F. *Macromolecules* **1999**, *32*, 3859.

219.Ogawa, A.; Ikeda, T.; Kimura, K.; Hirao, T. *J. Am. Chem. Soc.* **1999**, *121*, 5108.

220.Ogawa, A.; Kawabe, K.; Kawakami, J.; Mihara, M.; Hirao, T.; Sonoda, N. *Organometallics* **1998**, *17*, 3111.

221.Corey, E. J.; Cheng, X. M. *The Logic of Chemical Synthesis*; John Wiley & Sons Inc: New York, 1989. (b) Knight, D. W. *Contemp. Org. Synth.* **1994**, *1*, 287. (c) Figadere, D. *Acc. Chem. Res.* **1995**, *28*, 359. (c) Mabon, R.; Richecoeur, A. M. E.; Sweeney, J. B. *J. Org. Chem.* **1999**, *64*, 328. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 3543. Huang, H.; Chen, Q. H. *Chin. Sci. Bull.* **2000**, *45*, 711.

222.Kotake, H.; Inomata, K.; Kinoshita, H.; Aoyama, S.; Sakamoto, Y. *Heterocycles* **1978**, *10*, 105.

223.Brandt, C. W.; Taylor, W. I.; Thomas, B. R. *J. Chem. Soc.* **1954**, 3245. (b) Parker, W.; Raphael, R. A.; Wilkinson, D. I. *J. Chem. Soc.* **1958**, 3871. (c) Smith, A. B.; Jerris, P. J. *Synth. Commun.* **1978**, *8*, 421.

224.Takahashi, Y.; Hagiwara, H.; Uda, H.; Kosugi, H. *Heterocycles* **1981**, *15*, 225.

225.Marshal, P. G. In *Rodd's Chemistry of Carbon Compounds*, 2nd Ed.; Elsevier: New York, 1970, Vol. 2, p 369. (b) Carter, C. A.; Gray, E. A.; Schneider, T. L.; Lovett, C. M.; Scott, L.; Messer, A. C.; Richardson, D. P. *Tetrahedron* **1997**, *46*, 273.

226.Hollingworth, G. J.; Perkins, G.; Sweeney, J. B. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1913. (b) Mabon, R.; Richecoeur, M. E.; Sweeney, J. B. *J. Org. Chem.* **1999**, *64*, 328.

227.Yamamoto, H. In *Comprehensive Organic Synthesis*, Vol. 2 (Eds: Trost, B. M.; Fleming, I.; Heathcock, C. H.), Pergamon, Oxford, 1991, p.81.

228.Doi, T.; Yamamoto, K. *Curr. Org. Chem.* **1997**, *1*, 219. (b) Landor, S. R. *The Chemistry of the Allenes*; Academic Press: London, 1982, Vol. 2.

229.Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; Wiley: New York, 1984.

230.For intermolecular processes, see: (a) Ma, S. M.; Zhang, A. B.; Yu, Y. H.; Xia, W. *J. Org. Chem.* **2000**, *65*, 2287. (b) Arredondo, V. M.; Tian, S.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1999**, *121*, 3633. (c) Wu, M. Y.; Yang, F. Y.; Cheng, C. H. *J. Org. Chem.* **1999**, *64*, 2471. (d) Grigg, R.; Monteith, M.; Sridharan, V.; Terrier, C. *Tetrahedron* **1998**, *54*, 3885 and references cited therein.

231.For cyclisation processes, see: (a) Diederen, J. J. H.; Sinkeldam, R. W.; Fruhauf, H.–W.; Hiemstra, H.; Vrieze, K. *Tetrahedron Lett.* **1999**, *40*, 4255. (b) Meguro, M.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 5421. (c) Grigg, R.; Rasul, R.; Savic, V.

Tetrahedron Lett. **1997**, *38*, 1825. (d) Negishi, E.; Coperet, C.; Ma, S.; Liou, S.-Y.; Liu, F. *Chem. Rev.* **1996**, *96*, 365.

232.For intramolecular processes, see: (a) Karstens, W. F. J.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron Lett.* **1997**, *38*, 6275. (b) Kimura, M.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1995**, *60*, 3764. (c) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett.* **1988**, *29*, 4257.

233.Pino, P.; Piacenti, F.; Bianchi, M. In *Organic Synthesis via Metal Carbonyls*; Wender, I.; Pino, P.; Eds.; Wiley: New York, 1977.

234.Alper, H.; Hartstock, F. W.; Despeyroux, B. *J. Chem. Soc. Chem. Commun.* **1984**, 905.

235.Satyanarayana, N.; Amer, I.; Apler, H. *Organometallics* **1990**, *9*, 284.

236.(a) Gambarotta, S.; Alper, H. *J. Org. Chem.* **1981**, *46*, 2142. (b) Satyanarayana, N.; Alper, H. *J. Chem. Soc. Chem. Commun.* **1991**, 8.

237.Bates, R. W.; Devi, T. R. *Tetrahedron Lett.* **1995**, *36*, 509.

238.Kimura, M.; Saeki, N.; Uchida, S.; Harayama, H.; Tanaka, S.; Fugami, K.; Tamaru, Y. *Tetrahedron Lett.* **1993**, *34*, 7611.

239.Leoni, P.; Sommovigo, M.; Pasquali, M.; Midollini, S.; Braga, D.; Sabatino, P. *Orgnaometallics* **1991**, *10*, 1038.

240.Piotti, M. E.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1956.

241.Murakami, M.; Itami, K.; Ito, Y. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2691.

242.Murakami, M.; Itami, K.; Ito, Y. *J. Am. Chem . Soc.* **1997**, *119*, 2950.

243.Nokami, J.; Maihara, A.; Tsuji, J. *Tetrahedron Lett.* **1990**, *31*, 5629.

244.Osakada, K.; Takenaka, Y.; Choi, J. C.; Yamaguchi, I.; Yamamoto, T. *J. Poly. Sci. A, Pol. Chem.* **2000**, *38*, 1505.

245.Backvall, J. E.; Ericsson, A. *J. Org. Chem.* **1994**, *59*, 5850, and references cited therein.

246.Fischer, H. In *The Chemistry of Alkenes*; Patai, S., Ed.; John Wiley & Sons: London, 1964, p 1015. (b) Patai, S., *The Chemistry of Ketenes, Allenes, and Related Compounds*; Part 1.; New York, 1980, p 157.

247.(a) Merz, A. *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 846. (b) Meyer, A.; McCabe, D. J.; Curtis, M. D. *Organometallics* **1987**, *6*, 1491.

248.Skattebol, L.; Solomon, S. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. V, p 306.

249.Lang, R. W.; Hansen, H.–J. *Helv. Chim. Acta* **1980**, *63*, 438.

250.Crabbe, P.; Nassim, B.; Robert-Lopes, M.–T. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 276.

251.Grushin, V. V. *Chem. Rev.* **1996**, *96*, 2011. (b) Reppe, W. *Liebigs Ann. Chem.* **1953**, *582*, 1. In this paper Reppe reported a similar platinum compound, $HPt(SPh)(PPh_3)_2$.

252.For recent reviews, see: (a) Backvall, J. E.; Chinchilla, R.; Najera, C.; Yus, M. *Chem. Rev.* **1998**, *98*, 2291. (b) Mehta, G.; Uma, R. *Acc. Chem. Res.* **2000**, *33*, 278.

253.For a review, see: Metzner, P. In *Topics in Current Chemistry Vol. 204: Organosulfur Chemistry 1*, Page, P. C. B. Ed.; Springer-Verlag: New York, 1999, p 127-181.

254.Aranda, M. T.; Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Carreno, M. C.; Cid, M. B.; Ruano, J. L. G. *Tetrahedron: Asymmetry* **2000**, *11*, 1217. (b) Adams, H.;

Anderson, J. C.; Bell, R.; Jones, D. N.; Peel, M. R.; Tomkinson, N. C. O. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3967.

255.Marino, J. P. *Pure Appl. Chem.* **1993**, *65*, 667. (b) Marino, J. P.; Bogdan, S.; Kimura, K. *J. Am. Chem. Soc.* **1992**, *114*, 5566.

256.Kimura, M.; Matsuo, S.; Shibata, K.; Tamaru, K. *Angew. Chem. Int. Ed.* **1999**, *38*, 3386. (b) Widenhoefer, R. A.; Stengone, C. N. *J. Org. Chem.* **1999**, *64*, 8681. (c) Paley, R. S.; de Dios, A.; Estroff, C. A.; Lafontaine, J. A.; Montero, C.; McCulley, D. J.; Rubio, M. B.; Ventura, M. P.; Weers, H. L. *J. Org. Chem.* **1997**, *62*, 6326.

257.Aversa, M. C.; Barattucci, A.; Bonacorsi, P.; Giannetto, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1339.

258.Xiao, W. J.; Zhu, J.; Huang, W. F. *Chinese J. Org. Chem.* **1991**, *10*, 66. (b) Masuyama, Y.; Yamazaki, H.; Toyoda, Y.; Kurushu, Y. *Synthesis* **1985**, 964.

259.Backvall, J. E.; Nordberg, R. E.; Nystrom, J. E. *Tetrahedron Lett.* **1982**, *23*, 1617.

260.Akermark, B.; Nystrom, J. E.; Rein, T.; Backvall, J. E.; Helquist, P.; Aslanian, R. *Tetrahedron Lett.* **1984**, *25*, 5719.

261.Padwa, A.; Harrison, B.; Murphree, S. S.; Yeske, P. E. *J. Org. Chem.* **1989**, *54*, 4232.

262.Petrzilka, M. *Synthesis* **1981**, 753.

263.Berestovitskaya, V. M.; Speranskii, E. M.; Perekalin, V. V. *Zh. Org. Khim.* **1979**, *15*, 185; CA 90:203792 (1979).

264.Buchi, G.; Pawlak, M. *J. Org. Chem.* **1975**, *40*, 100.

265.Darling, S. D.; Subramanian, N. *J. Org. Chem.* **1975**, *40*, 2851.

266.Pinault, M.; Frangin, Y.; Genet, J. P.; Zamarlik, H. *Synthesis* **1990**, 935.

267.King, A. O.; Okukado, N.; Negishi, E. *Chem. Commun.* **1977**, 683.

268.Xiao, W. J.; Ding, M. W.; Huang, W. F. *Huazhong Shida Xuebao (Ziran Kexueban)* **1994**, 114. (b) Eiter, K.; Oediger, H. *Liebigs Ann. Chem.* **1965**, 682, 62.

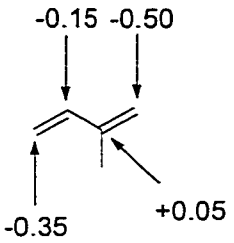
269.Stevens, M. P. *Polymer Chemistry: An Introduction*, 2 nd ed.; Oxford University Press: New York, 1990.

270.Ma, S.; Lu, X. *J. Org. Chem.* **1991**, *56*, 5120. (b) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34.

271.Amatore, C.; Jutand, A.; M'Barki, M. *Organometallics* **1992**, *11*, 3009. (b) Amatore, C.; Carre, E.; Jutand, A.; M'Barki, M. *Organometallics* **1995**, *14*, 1818.

272.A similar mechanism of acetylene insertion into Pd-CO σ bonds was reported. See: Samsel, E. G.; Norton, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 5505.

273.Ab initio calculations showed that the electron distribution of 2-methyl-1,3-butadiene (**6.1**) (after 6-31 G geometry optimization) is as follows:



274.Backvall, J. E.; Nystrom, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3677. (b) Rowe, J. M.; White, D. A. *J. Chem. Soc. A* **1967**, 1451.

275.Kato, T.; Kumazawa, S.; Kitahara, Y. *Synthesis* **1972**, 573. (b) Hoye, T. R.; Caruso, A. J.; Kurth, M. J. *J. Org. Chem.* **1981**, *46*, 3550. (c) Gnonlonfoun, N.; Zamarlik, H. *Tetrahedron Lett.* **1987**, *28*, 4035.

276.For reviews, see: (a) Agbossou, F.; Carpentier, J. –F.; Mortreux, A. Chem. Rev. 1995, 95, 2485. (b) Gladiali, S.; Bayon, J. C.; Claver, C. Tetrahedron: Asymmetry 1995, 6, 1453.

277.Lukas, J.; Kramer, P. A. *J. Organomet. Chem.* **1971**, *31*, 111.

278.Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (b) Trost, B. M. *Acc. Chem. Res.* **1996**, *29*, 355.

279.Dierkes, P.; Ramdeehul, S.; Barloy, L.; Decian, A.; Fischer, J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Osborn, J. A. *Angew. Chem. Int. Ed.* **1998**, *37*, 3116. (b) Ramdeehul, S.; Dierkes, P.; Aguado, R.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Angew. Chem. Int. Ed.* **1998**, *37*, 3118.

280.Both early and late transition states have been proposed. Early transition states: (a) Togni, A.; Burckhardt, U.; Gramlich, V.; Pregosin, P. S.; Salzmann, R. *J. Am. Chem. Soc.* **1996**, *118*, 1031. Late transition states: (b) Brown, J. M.; Hulmes, D. I.; Guiry, P. J. *Tetrahedron* **1994**, *50*, 4493. (c) Steinhagen, H.; Reggelin, M.; Helmchen, G. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2108.

281.Trost, B. M.; Krueger, A. C.; Bunt, R. C.; Zambrano, J. *J. Am. Chem. Soc.* **1996**, *118*, 6520. (b) Trost, B. M.; Breit, B.; Organ, M. G. *Tetrahedron Lett.* **1994**, *35*, 5817. (c) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1994**, *116*, 4089. (d) Trost, B. M.; Vranken, D. L. V.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327. (e) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1999**, *121*, 4545.

282.After 6-31 G geometry optimization, MM2 was used to calculate the ground-state energy of **6.67** and **6.68**. Also see: Akermark, B.; Hansson, S.; Vitagliano, A. *J. Am. Chem. Soc.* **1990**, *112*, 4587.

283.Larock, R. C.; Berrios-Pena, N.; Narayanan, K. *J. Org. Chem.* **1990**, *55*, 3447 and references therein. (b) Larock, R. C.; Guo, L. *Synlett* **1995**, 465.

284.Back, T. G.; Bethell, R. J. *Tetrahedron Lett.* **1998**, *39*, 5463.

285.Trost, B. M.; *Tetrahedron* **1977**, *33*, 2615. (b) Trost, B. M. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259. (c) Larock, R. C. *J. Organomet. Chem.* **1999**, *576*, 111.

286.Larock, R. C.; He, Y.; Leong, W. W.; Han, X.; Refvik, M. D.; Zenner, J. M. *J. Org. Chem.* **1998**, *63*, 2154. (b) Grigg, R.; Sridharan, V.; Terrier, C. *Tetrahedron Lett.* **1996**, *37*, 4221. (c) Ma, S.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 6345. (d) Grigg, R.; Sridharan, V.; Xu, L. –H. *J. Chem. Soc., Chem. Commun.* **1995**, 1903. (e) Larock, R. C.; Zenner, J. M. *J. Org. Chem.* **1995**, *60*, 482. (f) Larock, R. C.; Berrios-Pena, N. G.; Fried, C. A. *J. Org. Chem.* **1991**, *56*, 2615.

287.Ma, S.; Negishi, E. *J. Org. Chem.* **1994**, *59*, 4730. (b) Gandin, J. –M. *Tetrahedron Lett.* **1991**, *32*, 6113.

288.For recent examples, see: (a) Zhang, Q.; Lu, X. *J. Am. Chem. Soc.* **2000**, *122*, 7604. (b) Ma, C.; Liu, X. X.; Yu, S.; Zhao, S.; Cook, J. M. *Tetrahedron Lett.* **1999**, *40*, 657. (c) Larock, R. C.; Yum, E. K.; Refvik, M. D. *J. Org. Chem.* **1998**, *63*, 7652. (d) Chowdhury, C.; Chaudhui, G.; Guha, S.; Mukherjee, A.; Kundu, N. G. *J. Org. Chem.* **1998**, *63*, 1863. (e) Rosech, K. R.; Larock, R. C. *J. Org. Chem.* **1998**, *63*, 5306. (f) Ujjainwalla, F.; Warner, D. *Tetrahedron Lett.* **1998**, *39*, 5355. (g) Kundu, N. G.; Pal, M.; Nandi, B. *J. Chem. Soc., Perkin Trans. 1*, **1998**, 561. (h) Xu, L.; Lewis, I. R.; Davidsen, S. K.; Summers, J. B. *Tetrahedron Lett.* **1998**, *39*, 519. (i) Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. K. C. *J. Org. Chem.* **1995**, *60*, 3270. (j) Fagnola, M. C.; Candiani, I.; Visentin, G.; Bedeschi, A. *Tetrahedron Lett.* **1997**, *38*, 2307. (k)

Zhang, H. C.; Brumfield, K. K.; Jaroskova, L.; Maryanoff. B. E. *Tetrahedron Lett.* **1998**, *39*, 4449.

289.Zhang, H. –C.; Brumfield, K. K.; Maryanoff, B. E. *Tetrahedron Lett.* **1997**, *38*, 2439.

290.Jeschke, T.; Wensbo, D.; Annby, U.; Gronowitz, S.; Cohen, L. A. *Tetrahedron Lett.* **1993**, *34*, 6471.

291.Ciattini, P. G.; Morera, E.; Ortar, G.; Rossi, S. S. *Tetrahedron* **1991**, *47*, 6449. (b) Torii, S.; Okumoto, H.; Xu, L. –H. *Tetrahedron Lett.* **1991**, *32*, 237.

292.Fang, L.; Guo, C.; Zhang, Q. B. *Chin. Chem. Lett.* **1997**, *8*, 939. (b) Fang, L.; Dai, Z.; Zhang, G. *Shengyang Yaoke Daxue Xuebao* **1998**, *15*, 116. (c) Sebok, P.; Levai, A.; Timar, T. *Heterocycl. Commun.* **1998**, *4*, 547. (d) Reddy, D.; Bhaskar, R. M.; Reddy, D. V.; Padmaja, A. *Indian J. Chem., Sect. B*, **1994**, *33B*, 62. (e) Kameo, K.; Hatada, Y.; Takahashi, T.; Tomizawa, K.; Hatayama, K. JP 04059725, 1992; *Chem. Abstr.* **1992**, 117:97317.

293.For reviews, see: (a) Lockhart, I. M. In *Chromenes, Chromanones and Chromones*; Ellis, G. P., Ed.; John Wiley and Sons Ltd.: New York, 1977. (b) Ingall, A. H. In *Comprehensive Heterocyclic Chemistry*; Katritzy, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 3, p885.

294.Metwally, M. A.; Abdel-Mogib, M. *Heterocycl. Commun.* **1999**, *5*, 423. (b) Fisera, L.; Jaroskova, L.; Levai, A.; Jedlovska, E.; Toth, G.; Polakova, M. *Heterocycles* **1997**, *45*, 1651. (c) Gabbutt, C. D.; Hepworth, J. D.; Heron, B. M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3015. (d) Adam, W.; Golsch, D.; Hadjiarapoglou, L.; Levai, A.; Nemes, C.; Patonay, T. *Tetrahedron* **1994**, *50*, 13113. (e) Gabbutt, C. D.; Hepworth, J. D.; Heron, B. M.; Kanjia, M. *Tetrahedron* **1994**, *50*, 827.

295.Ruaro, J. L.; Rumbero, A. *Tetrahedron: Asymmetry* **1999**, *10*, 4427. (b) Clayton, S. E.; Gabbutt, C. D.; Hepworth, J. D.; Heron, B. M. *Tetrahedron* **1993**, *49*, 939. (c) Gabbutt, C. D.; Hepworth, J. D.; Heron, B. M. *Tetrahedron* **1994**, *50*, 5245. (d) Sowmithran, D.; Prasad, R. Synthesis 1985, 545. (e) Arnoldi, A. *Synthesis* **1984**, 856. (f) Yu, X.; Liu, J.; Li, X.; Zhang, G.; Fang, L. *Huaxi Yaoxue Zazhi* **1997**, *12*, 230. (g) Truce, W. E.; Milionis, J. P. *J. Am. Chem. Soc.* **1952**, *74*, 974.

296.Furniss, B. S.; Hannaford, A. T.; Rogers, V.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 4th ed.; Longman: England, 1978; p 676.

297.Arnau, N.; Morenv-Manas, M.; Pleixats, R. *Tetrahedron* **1993**, *49*, 11019.

298.Chen, C.; Lieberman, D. R.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1997**, *62*, 2676.

299.For examples, see: (a) Brown, A.; Grigg, R.; Ravishankar, T.; Thoronton-Pett, M. *Tetrahedron Lett.* **1994**, *35*, 2753. (b) Okita, T.; Isobe, M.; *Tetrahedron* **1994**, *50*, 11143.

300.For examples, see: (a) Wu, G. –Z.; Lamaty, F.; Negishi, E. I. *J. Org. Chem.* **1989**, *54*, 2507. (b) Reetz, M. T.; Lohmer, G.; Schwickardi, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 481.

301.For examples, see: (a) Dankwardt, J. W.; Flippin, L. A. *J. Org. Chem.* **1995**, *60*, 2312. (b) Hong, F.; Xia, J.; Xu, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1665.

302.Negishi, E.; Coperet, C.; Ma, S.; Mita, T.; Sugihara, T.; Tour, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 5904. (b) Negishi, E.; Ma, S.; Amanfu, J.; Coperet, C.; Miller, J. A.; Tour, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 5919.

303.Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595.

304.Isler, O.; Gutmann, H.; Montavon, M.; Ruegg, R.; Ryser, G.; Zeller, P. *Helv. Chim. Acta* **1957**, *40*, 1242.

Claims to Original Research

1. Use of $Pd(PPh_3)_4$ as the catalyst for the thiolactonizatioin of propargylic alcohols to form β-thio-α,β-unsaturated γ-lactones.
2. Use of $Pd(OAc)_2$-PPh_3-*p*-TsOH as the catalyst system for the thiocarbonylation of propargylic alcohols to form monothioesters.
3. Palladium-catalyzed dithiocarbonylation of propargylic mesylates and alcohols to give dithioesters. The reaction was carried out at 90°C in THF, using $Pd(PPh_3)_4$ as the catalyst.
4. Thiocarbonylation of allenes, catalyzed by $Pd(OAc)_2$ with PPh_3, selectively afford thioesters.
5. The palladium-catalyzed regioselective thiocarbonylation of cyclic and acyclic allylic alcohols containing different functional groups led to β,γ-unsaturated thioesters.
6. Chemo- and regio-selective thiocarbonylation of conjugated enynes catalyzed by palladium complexes. This constitutes an efficient and atom-economical access to electron-deficient 1,3-dienes.
7. Atom-economical synthesis of β,γ-unsaturated thiol esters by thiocarbonylaiton of conjugated dienes via palladium-catalyzed three-component coupling reactions.
8. The first asymmetric thiocarbonylation of prochiral dienes was carried out, using $Pd(OAc)_2$ with chiral DIOP as the catalyst system.
9. Carbonylative heteroannulation of *o*-iodothiophenols with allenes providing novel and one-pot access to thiochroman-4-one derivatives.

Publications List

1. W. J. Xiao, H. Alper, Asymmetric Thiocarbonylation of Prochiral 1,3-Conjugated Dienes Catalyzed by Palladium Acetate with Chiral DIOP, *J. Am. Chem. Soc.* In preparation.
2. W. J. Xiao, G. Vasapollo, and H. Alper, Highly Regioselective Thiocarbonylation of Conjugated Dienes via Palladium-Catalyzed Three-Component Coupling Reactions, *J. Org. Chem.* **2000**, *65*, 4138.
3. W. J. Xiao and H. Alper, Regioselective Carbonylative Heteroannulation of *o*-Iodothiophenols with Allenes and Carbon Monoxide Catalyzed by a Palladium Complex: A New and Efficient Access to Thiochroman-4-one Derivatives, *J. Org. Chem.* **1999**, *64*, 9646.
4. W. J. Xiao, G. Vasapollo, and H. Alper, Highly Chemo- and Regioselective Thiocarbonylation of Conjugated Enynes with Thiols and Carbon Monoxide Catalyzed by Palladium Complexes: An Efficient and Atom-Economical Access to 2-(Phenylthiocarbonyl)-1,3-dienes, *J. Org. Chem.* **1999**, *64*, 2080.
5. S. C. Bourque, F. Maltais, W. J. Xiao, O. Tardif, H. Alper, P. Arya, and L. E. Manzer, Hydroformylation Reactions with Rhodium-Complexed Dendrimers on Silica, *J. Am. Chem. Soc.* **1999**, *121*, 3035.
6. W. J. Xiao and H. Alper, Highly Regioselective Thiocarbonylation of Allylic Alcohols with Thiols and Carbon Monoxide Catalyzed by Palladium Complexes: A

New and Efficient Route to β, γ-Unsaturated Thioesters, *J. Org. Chem.* **1998**, *63*, 7939.

7. W. J. Xiao, G. Vasapollo, and H. Alper, Highly Regioselective Palladium-Catalyzed Thiocarbonylation of Allenes with Thiols and Carbon Monoxide, *J. Org. Chem.* **1998**, *63*, 2609.

8. W. J. Xiao and H. Alper, The First Examples of the Palladium-Catalyzed Thiocarbonylation of Propargylic Alcohols with Thiols and Carbon Monoxide, *J. Org. Chem.* **1997**, *62*, 3422.