Pd-Catalyzed Coupling Reactions Involving Propargylic/Allenylic Species

Shengming Ma[a,b]

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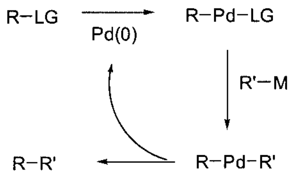
In this review, the Pd-catalyzed coupling reaction involving propargylic/allenylic species is discussed. In these reactions, η^1- and η^3-propargylic/allenylic species have been proposed as the key intermediates for the selective formation of either allenes or alkynes. It should be noted that, in most cases, allenes are formed as the major products. Electronic, steric, and ligand effects have been observed for the control of the regioselectivity.

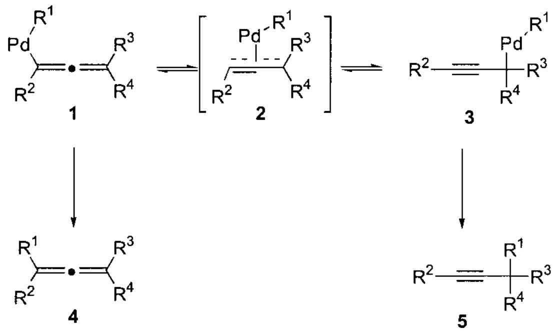
Introduction

Pd^0-catalyzed coupling reactions between a substrate with a leaving group and an organometallic reagent are becoming one of the most powerful pathways for the formation of carbon−carbon bonds (Scheme 1).[1]



Scheme 1

In the chemistry presented in Scheme 1, if R or R′ is a propargylic or allenylic group, there is a regioselectivity issue for this coupling reaction (Scheme 2). The reductive elimination of allenyl Pd species **1** would afford allene **4**, while a similar process with **3** would yield alkyne **5**.



Scheme 2

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[a] Department of Chemistry, Zhejiang University,
Hangzhou 310027, P. R. China
[b] State Key Laboratory of Organometallic Chemistry,
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences,
354 Fenglin Lu, Shanghai 200032, P. R. China

Shengming Ma is originally from Zhejiang Province, China. He received a B.S. degree in Chemistry from Hangzhou University (1986), and an MS (1990) and a Ph.D. (1990) from Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences. After postdoctoral research experience at ETH in Switzerland and Purdue University in USA, he joined the faculty of Shanghai Institute of Organic Chemistry (1997), where he is currently a Professor of Chemistry and the Director of the State Key Laboratory of Organometallic Chemistry. As of February 2003, he is jointly appointed by the Department of Chemistry, Zhejiang University as a Professor of the Cheung Kong Scholars Programme and Shanghai Institute of Organic Chemistry.

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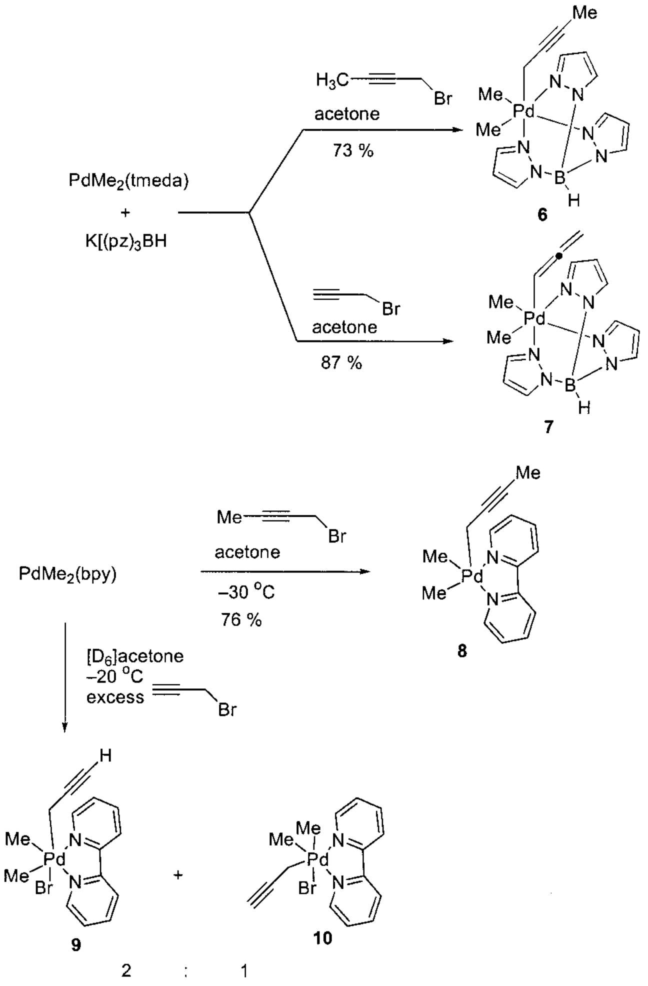
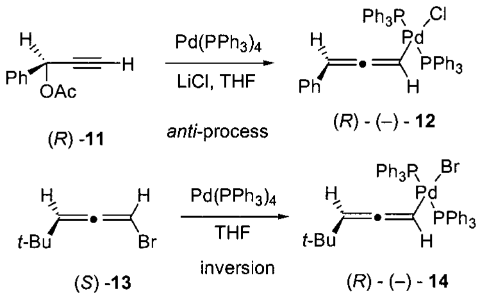
Both allenylic Pd species and propargylic Pd species have been prepared and characterized.[2−4] Canty et al. reported the oxidative addition of 2-propynyl bromide or 2-butynyl bromide with some divalent palladium complexes to afford η^1-allenylic or η^1-propargylic Pd complexes **6−10** depending on the structure of the propargylic bromide and the divalent organometallic complexes (Scheme 3).[3]



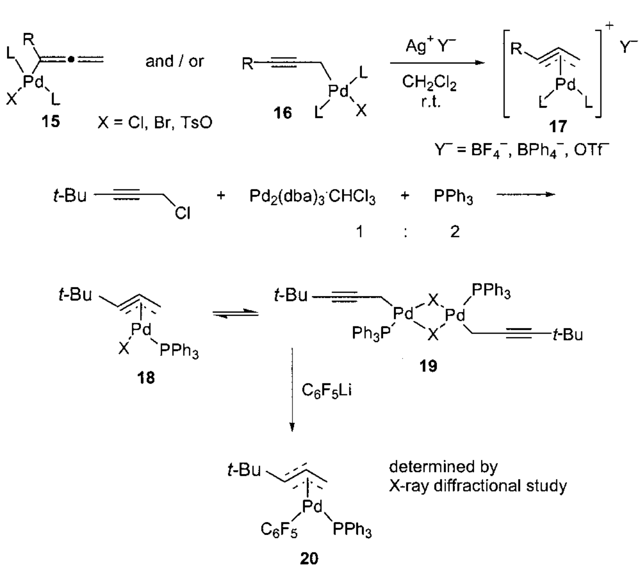
Scheme 3

The stereochemical outcome of the oxidative addition of Pd^0 with propargylic or allenylic halides has also been clearly depicted by Boersma (Scheme 4).[4] The propargylic acetate (*R*)-**11** undergoes an S$_N$2′-type displacement with Pd(PPh$_3$)$_4$ to afford (*R*)-(−)-**12** while the oxidative addition of allenylic bromide (*S*)-**13** with Pd(PPh$_3$)$_4$ follows a similar pathway to give a propargylic Pd intermediate, which then undergoes a suprafacial 1,3-shift of Pd to give *R*-(−)-**14**.



Scheme 4

Besides η^1-allenylic and η^1-propargylic Pd species, the corresponding η^3-Pd complexes, which may be the intermediates in the interconversion of complexes **1** and **3**, have also been prepared and characterized.[5−7] The cationic η^3-allenylic/propargylic palladium complex **17** may be formed by the treatment of η^1-allenylic or η^1-propargylic palladium halides or tosylates **15** or **16** with AgBF$_4$ or NaBPh$_4$,[5,6] while the neutral η^3-allenylic/propargylic palladium complex **20** was prepared by the treatment of the reaction mixture of propargylic chloride and Pd$_2$(dba)$_3$·CHCl$_3$/PPh$_3$ with C$_6$F$_5$Li (Scheme 5).[7]



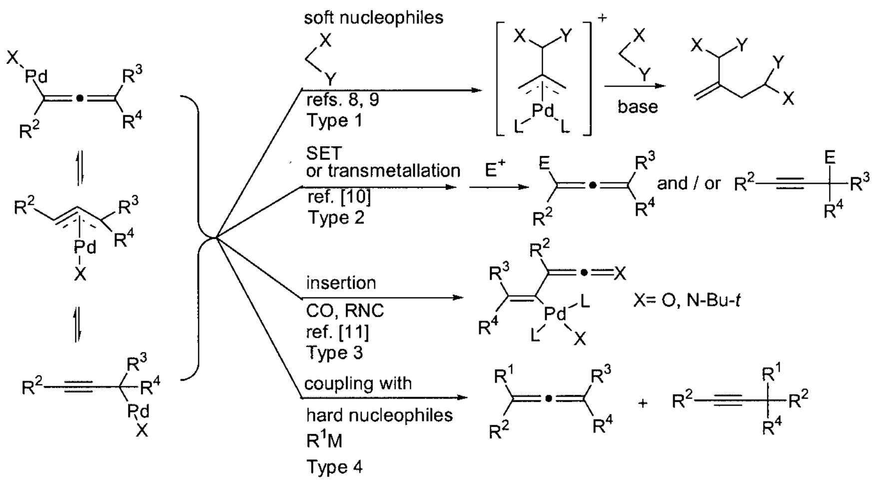
Scheme 5

η^1- or η^3-Allenyl/propargylic palladium species have shown unique reactivity towards different types of nucleophiles and CO/isocyanide, with four typical cases shown in Scheme 6.

Catalytic versions of Types 1 and 2 have been summarized in some excellent reviews and seminal papers.[8−10] In this Microreview, catalytic reactions of Type 4 — the coupling reaction with organometallic reagents — will be described with the emphasis on the control of regioselectivity.

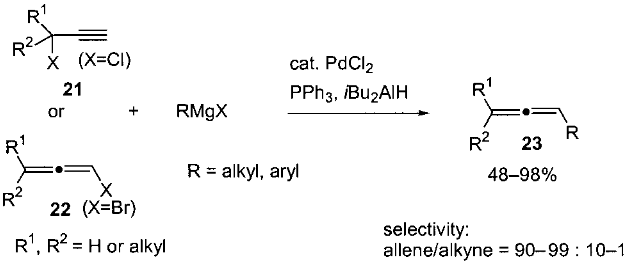
Coupling of Propargylic Halides or 1,2-Allenylic Halides with Grignard Reagents

In 1980, Jeffery-Luong and Linstrumelle reported the coupling reaction of propargylic halides **21** or 1,2-allenylic halides **22** with Grignard reagents, affording trisubstituted allenes **23** highly selectively (Scheme 7).[12]



Scheme 6

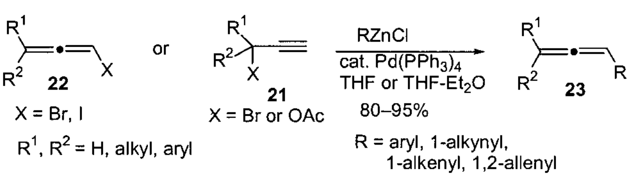
It is interesting to note that the same reaction in the absence of the Pd catalyst resulted in the formation of allene/alkyne mixtures with a low selectivity.



Scheme 7

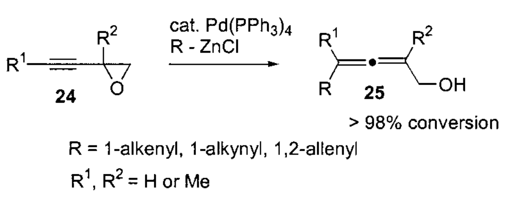
Coupling of Propargylic Halides/Acetates/Carbonates or 1,2-Allenylic Halides with Organozinc Reagents

Since the first report of Pd-catalyzed coupling of propargylic halides/acetates or allenic halides with organozinc reagents in 1981 by Vermeer (Scheme 8),[13] much attention has been paid to this coupling reaction leading to, in most cases, the highly selective formation of allenes.[14–18]



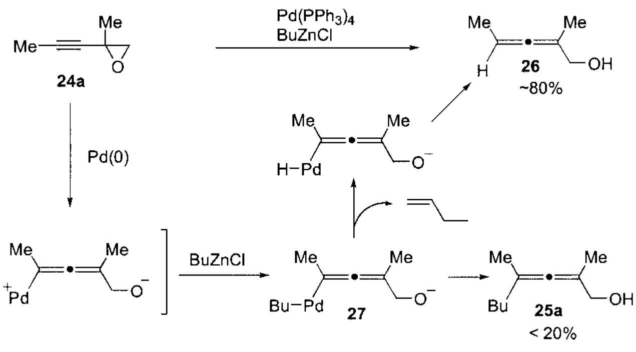
Scheme 8

α-Acetylenic epoxides **24** can also serve as a coupling partner, their coupling with organozinc reagents resulting in the clean formation of 2,3-allenols **25** (Scheme 9).[14] The corresponding reaction of 1-alkynyllithium or -magnesium chloride gives poor results. Only unidentified products were formed when R = Ph.



Scheme 9

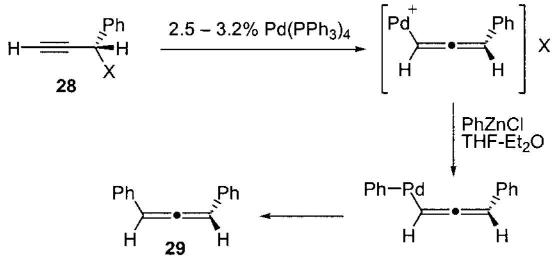
The reaction of 1-methyl-1-(1′-propynyl) epoxide **24a** with BuZnCl yielded 2,4-dimethylocta-2,3-dienol **25a** in a very low yield (<20%). The major product is 2-methyl-2,3-pentadienol **26**, which may be formed via the subsequent β-H elimination and reductive elimination of **27** (Scheme 10).



Scheme 10

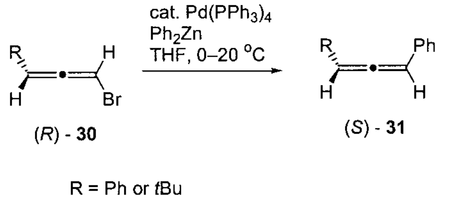
This type of coupling reaction can also be conducted with 1-alkynylmagnesium chloride or lithium di(1-alkynyl)cuprate. For some copper reagents, the reaction can proceed in the absence of a Pd^0 catalyst.[15] For propargylic derivatives, the leaving group can be Br, OAc, O(SO)Me, OSO_2Me or $OP(O)(OEt)_2$.[15]

In 1983, Vermeer et al. reported *anti*-stereoselectivity in the Pd^0-catalyzed coupling of (*R*)-1-phenyl propargyl acetate, trifluoroacetate or sulfate **28** with PhZnCl, affording (*R*)-(−)-1,3-diphenyl allene **29** (Scheme 11). It was observed that the leaving group is not very important for the stereoselectivity. The ratio of *anti*/*syn* 1,3-substitution is ca. 82:18.[16]



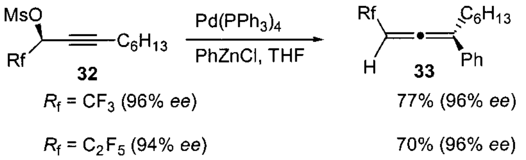
Scheme 11

The $Pd(PPh_3)_4$-catalyzed coupling reaction of optically active allenyl bromide with Ph_2Zn afforded optically active allenes with the configuration inverted (Scheme 12).[17]



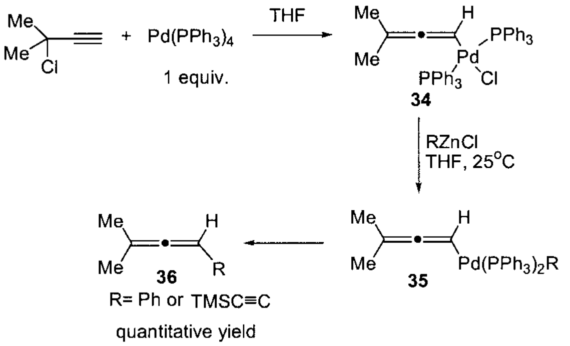
Scheme 12

In 2000, Konno et al. reported the $Pd(PPh_3)_4$-catalyzed coupling reaction of optically active fluorine-containing propargylic mesylates **32** with organozinc reagents, leading to optically active fluorine-containing trisubstituted allenes **33** (Scheme 13).[18]



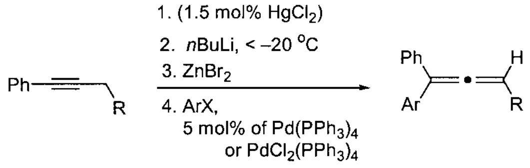
Scheme 13

In order to study the mechanism of this coupling reaction, in 1983 Vermeer studied the formation of the 3-methylbuta-1,2-dienylpalladium complex **34** and its subsequent reaction with PhZnCl, leading to the formation of allene **36** via the intermediacy of the η^1-allenylpalladium complex **35** (Scheme 14).[20]



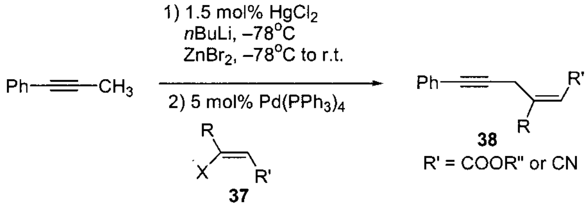
Scheme 14

Ma et al. reported the $Pd(PPh_3)_4$-catalyzed coupling of propargylic/allenyliczinc reagents with aromatic halides. The major product is allene (Scheme 15).[21]



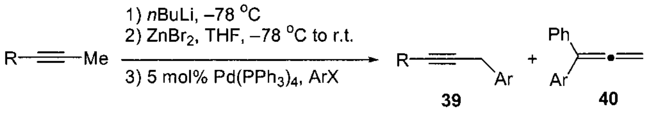
Scheme 15

However, the corresponding coupling reaction with 3-halo-2-alkenoates or 3-iodo-2-alkenenitrile **37** afforded the alkynic products **38** (Scheme 16).[22]



Scheme 16

It was also observed that the regioselectivity of this coupling reaction can be tuned by the steric effect of R and Ar groups (Scheme 17).[22,23] A similar regioselectivity was also observed in the Pd-catalyzed coupling of propargylic carbonates with organozinc reagents.[23]

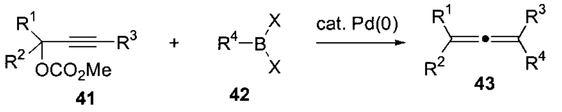


R	Ar	yields (%)	**39**		**40**
Me_3Si	*o*-methylphenyl	52	100	:	0
Ph	phenyl	85	0	:	100

Scheme 17

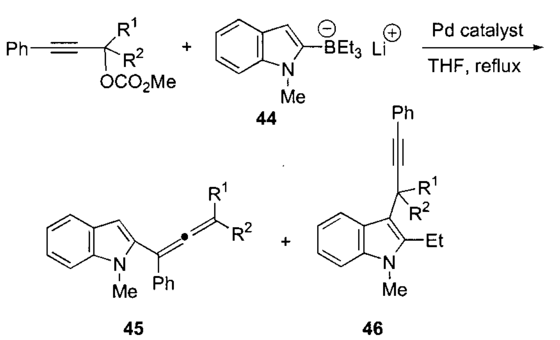
Coupling Reaction of Propargylic Carbonates with Organoboron Reagents

Under the catalysis of Pd^0, 1-alkenyl-, 1-alkynyl- or arylboronic acids, or their esters, and 9-alkyl-9-BBN **42** couple with propargylic carbonates **41** to afford 1,2-allenes **43** (Scheme 18).[24]



Scheme 18

Interestingly, Ishikura and Agata have reported the coupling reaction of propargylic carbonates with triethyl (1-methylindol-2-yl)borates **44** affording allenyl indoles **45** and propargylindoles **46** (Scheme 19).[25]



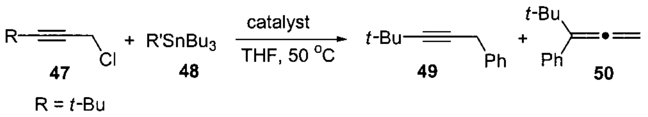
R^1	R^2	Catalyst	**45** (%)	**46** (%)
H	C_5H_{11}	$Pd_2(dba)_3{\cdot}CHCl_3$	47	0
		$PdCl_2(PPh_3)_2$	16	31
		$Pd_2(dba)_3{\cdot}CHCl_3$ + 8 PPh_3	0	63
		$Pd(PPh_3)_4$	0	60
$(CH_2)_5$		$Pd_2(dba)_3{\cdot}CHCl_3$	65	0
		$PdCl_2(PPh_3)_2$	63	0
		$Pd_2(dba)_3{\cdot}CHCl_3$ + 8 PPh_3	63	0
		$Pd(PPh_3)_4$	64	0

Scheme 19

From Scheme 19, it is interesting to note that: (1) with a different catalyst, the ratio of allene **45** to alkyne **46** may be different, indicating the ligand-dependent nature of this coupling reaction, and (2) with more bulky R^1 and R^2 groups the reaction tends to favor the formation of allene products **45**.

Coupling of Propargylic Chlorides with Organotin Reagents and Organic Halides with 1,2-Allenylic Tin Reagents

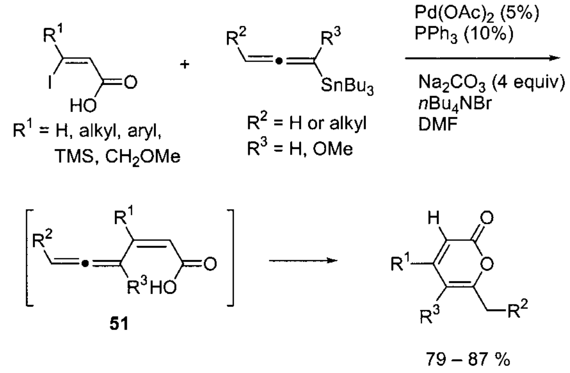
In 1999, Kurosawa et al.[26] reported the Pd-catalyzed coupling reaction of propargylic chloride with aryl- or 1-alkynyltributyltin, affording alkynes or allenes depending on the nature of the R and R′ groups as well as the catalyst (Scheme 20). In this reaction an η^3-allenyl/propargylpalladium intermediate was proposed to explain the issue of regioselectivity. It is obvious that the steric hindrance is controlling the regioselectivity.



R'	catalyst	yield (%)	**49 / 50**
Ph	$Pd(PPh_3)_4$	26	99 : 1
Ph	1/2 $Pd_2(dba)_3$, PPh_3	95	96 : 4
Ph—≡	$Pd(PPh_3)_4$	100	3 : 97
Ph—≡	1/2 $Pd_2(dba)_3$, PPh_3	73	4 : 96

Scheme 20

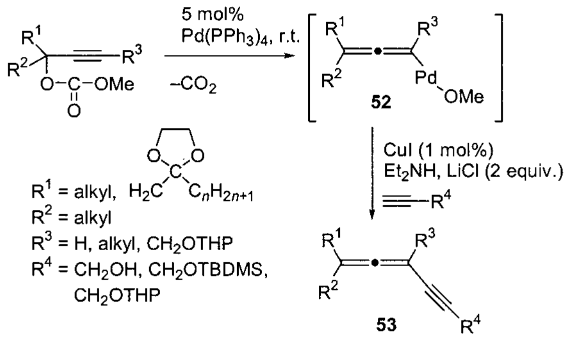
In 2000, Duchêue and Parrain et al. reported the Pd-catalyzed coupling reaction of allenyltin with 3-iodo-2-alkenoic acids, affording 2-pyrone derivatives (Scheme 21).[27] In this coupling reaction allene-type products, i.e. 2,4,5-alkanetrienoic acids **51**, were formed as the intermediates.



Scheme 21

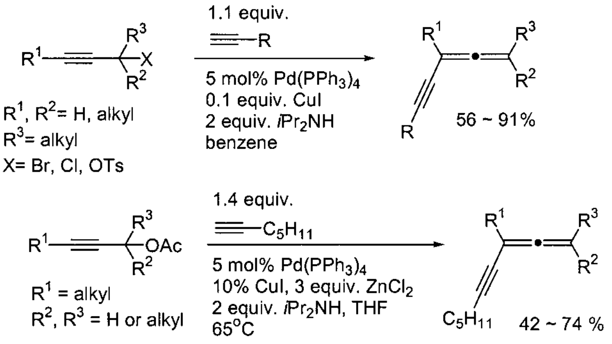
Coupling of Propargylic Carbonates Halides, Acetates, Tosylates with Terminal Alkynes

In 1990, Tsuji et al. reported that the η^1-allenylic palladium species formed from the oxidative addition of Pd^0 with propargylic carbonate can couple with a terminal alkyne in the presence of CuI to afford allenylic products, i.e., alka-1,2-dien-4-ynes **53** (Scheme 22).[28–29]



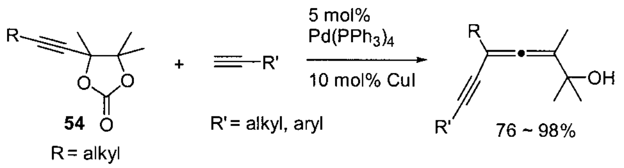
Scheme 22

In 1993 and 2000, Linstrumelle et al. also reported a similar reaction with propargylic halides (X = Cl, Br), tosylates or acetate (Scheme 23).[30,31]



Scheme 23

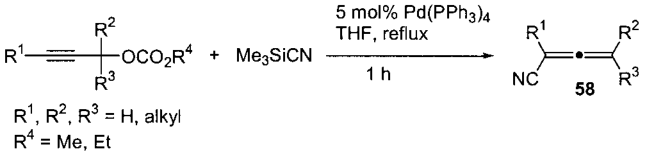
A similar reaction was observed with the Pd-catalyzed coupling reaction of cyclic alkynyl carbonates **54** and terminal alkynes by Dixneuf in 1994 (Scheme 24).[32]



Scheme 24

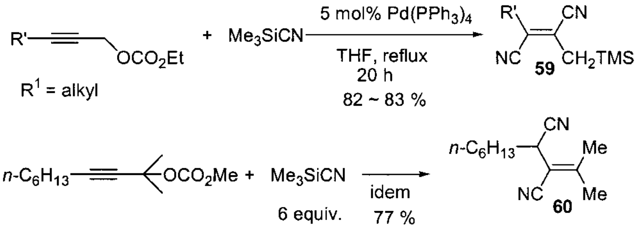
The η¹-allenylic palladium species formed by the oxidative addition of propargylic acetate, ether or carbonates with Pd⁰ can also induce the cyclization reaction of 4-alkynoic acids **55** or *o*-(1-alkynyl)phenols **57**, leading to the exclusive formation of allenylic γ-lactone derivatives and benzo[*b*]furans, respectively (Scheme 25).[33]

The Pd⁰-catalyzed coupling reaction of propargylic carbonates with Me_3SiCN in THF produces cyanoallenes **58** (Scheme 26).[34]



Scheme 26

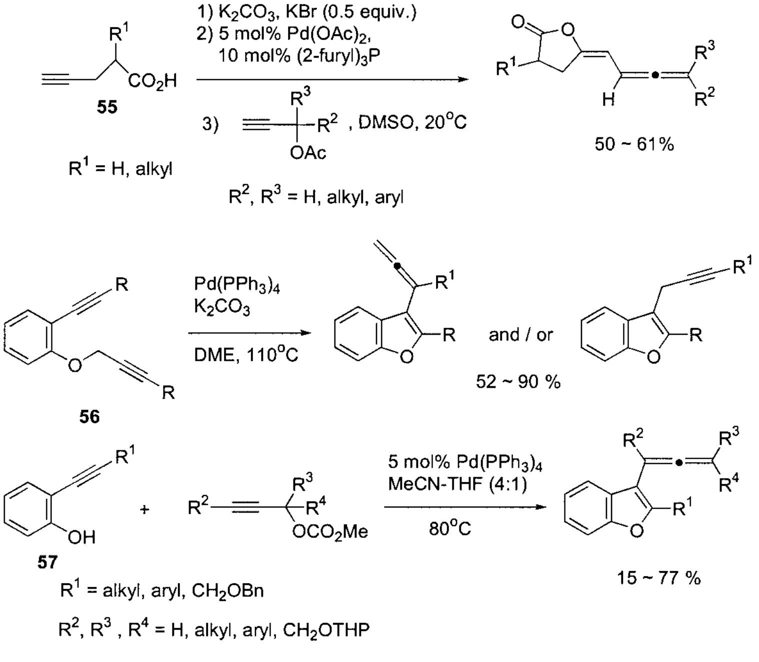
With an excess of Me_3SiCN, dicyanated products **59** or **60** were formed depending on the structures of the propargylic carbonates (Scheme 27).[34]



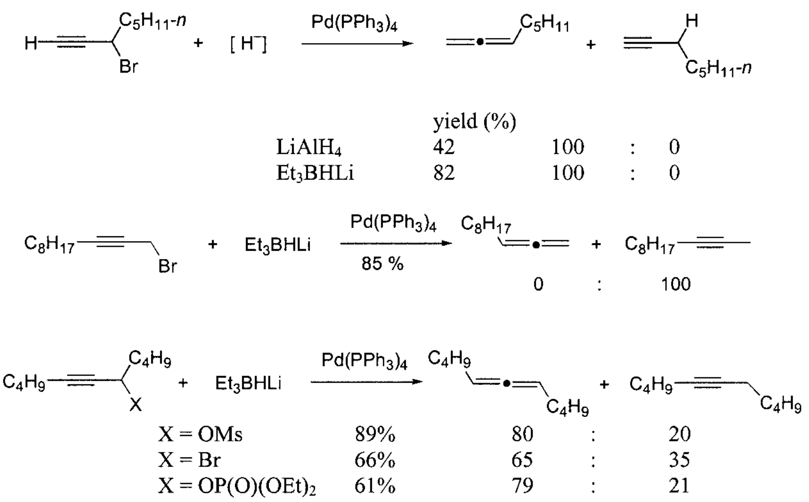
Scheme 27

Coupling of Propargylic Carbonates, Formates, and 1-Alkynyl Epoxides with Hydride

The Pd-catalyzed reduction of propargylic bromides, tosylates, phosphonates with $LiAlH_4$ or Et_3BHLi affords all-



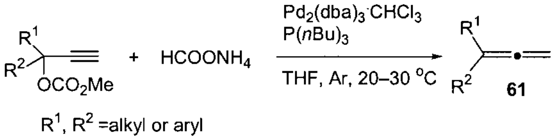
Scheme 25



Scheme 28

enes and/or alkynes. The ratios of the products depend on the structures of the propargylic derivatives (Scheme 28).[35]

In 1986 Tsuji et al. reported the Pd-catalyzed synthesis of 1,1-disubstituted allenes **61** via the selective hydrogenolysis of alk-2-ynyl carbonates using ammonium formate as the hydride source (Scheme 29).[36]



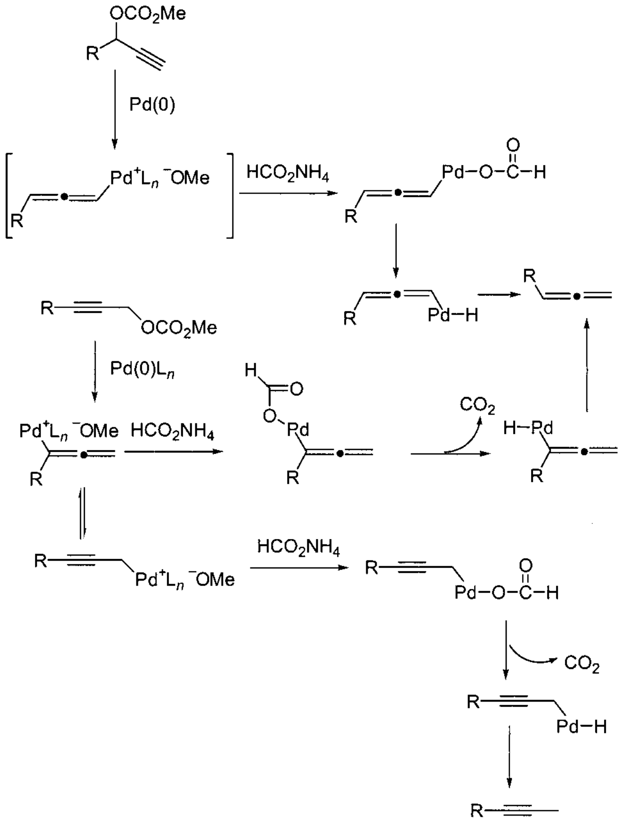
Scheme 29

With undeca-2-ynyl carbonate, a 5:1 mixture of undeca-1,2-diene and undeca-2-yne was obtained in a combined yield of 81%.[36] With 1-alkynyl epoxide, a mixture of 2,3-dienols **62/64** or 3-alkyn-1-ols **63/65** was obtained, with the latter being the major product (Scheme 30).[36]

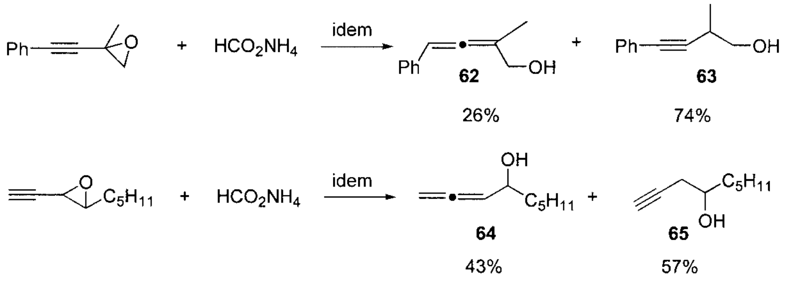
In these reactions an η^1-allenylic or η^1-proparylic palladium species was proposed as the key intermediate (Scheme 31).[37]

In 1993, Tsuji et al. demonstrated the Pd^0-catalyzed decarboxylative reduction of propargylic formates.[38,39] In this reaction the leaving group OCHO served as the [H$^-$] source and the major product is allene (Scheme 32).

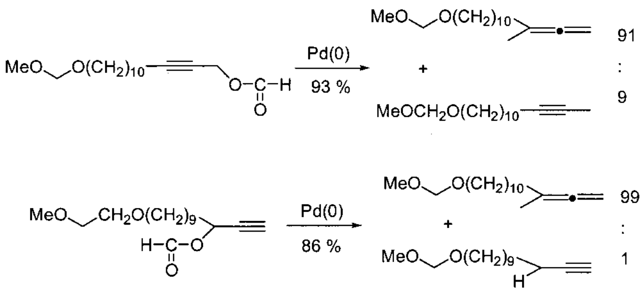
It is interesting to note that with an internal carbon−carbon triple bond, the Pd(acac)$_2$/nBu$_3$P-catalyzed



Scheme 31

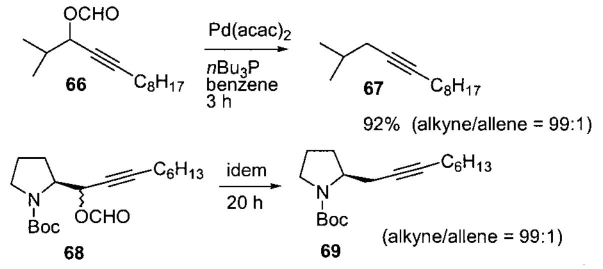


Scheme 30



Scheme 32

reaction in THF or benzene affords the decarboxylative reduction alkynylic products **67** or **69** (Scheme 33).[39]

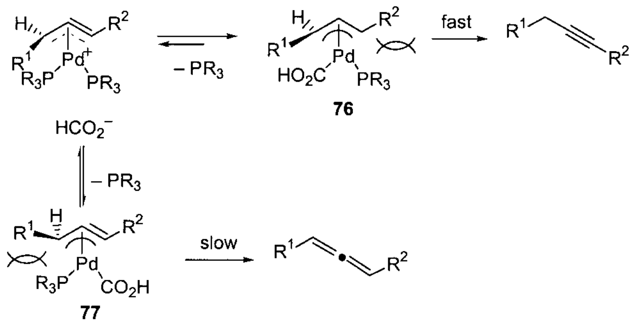


Scheme 33

In 1994, Dixneuf et al.[40] observed a ligand effect in the corresponding reaction of cyclic alkynyl carbonates (Scheme 34).

In 1999, Radinov[41] also reported a ligand effect in the decarboxylative reduction of propargylic formates **73** or carbonates (Scheme 35).

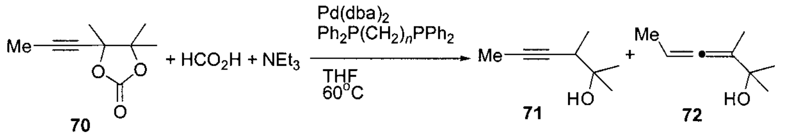
The steric effect of the ligands may be playing a key role in intermediates **73** or **74** in determining the reactivity and regioselectivity. With a relatively larger R^2 group, no reaction was observed in the presence of a sterically bulky ligand, i.e., $P(iBu)_3$, while with less sterically hindered phosphanes, the coupling reaction could proceed via the less sterically demanding intermediate **76** leading to the highly selective formation of alkyne **74** (Scheme 36).



Scheme 36

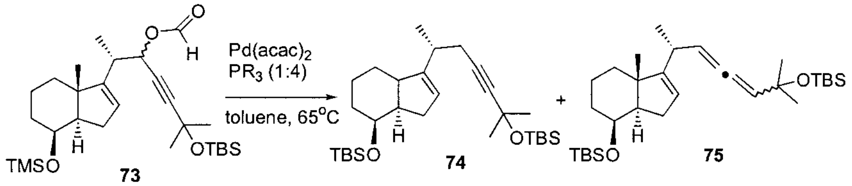
Homocoupling of Propargylic Carbonates

In 1995 Ogoshi and Kurosawa et al. reported the $Pd(PPh_3)_4$-catalyzed reductive homocoupling of propargylic carbonates. The ratio of 1,2-alkadien-5-ynes **78** and



	yield of **71** and **72**	**71** / **72**
$n = 1$	56%	72 : 28
$n = 3$	74 ~ 76%	0 : 100
$n = 4$	61%	18 : 82
$n = 6$	62%	83 : 17

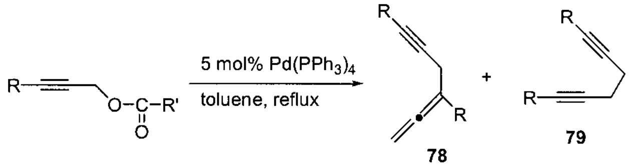
Scheme 34



PR_3			
*i*Bu	No reaction		
*n*Bu	87	:	13
Et	91	:	9
Me	95	:	5

Scheme 35

1,5-alkadiynes **79** depends also on the steric hindrance of the R group (Scheme 37).[42]



R	yield	ratio of **77** : **78**
$SiMe_3$	48%	79 : 21
$Si(iBu)_3$	73%	93 : 7
$Si(iPr)_3$	85%	95 : 5
*t*Bu	7%	71 : 29

Scheme 37

Concluding Remarks

Pd-catalyzed coupling reactions involving propargylic/allenylic species demonstrate that both allenes and alkynes can be formed depending on the steric and electronic effects of the substrates. A ligand effect on the control of regioselectivity of this coupling reaction has also been observed. It is obvious that more attention must be paid to the control of the regioselectivity by using different ligands, which may provide chances for the enantioselective formation of optically active allenes or alkynes.

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