Palladium-Catalyzed Reactions of Allenes†

Reinhold Zimmer,*,‡ Chimmanamada U. Dinesh,‡ Erathodiyil Nandanan,‡ and Faiz Ahmed Khan§

Institut für Organische Chemie, Technische Universität Dresden, Mommsenstrasse 13, D-01062 Dresden, Germany, and Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

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I. Introduction

Allenes are three-carbon functional groups possessing a 1,2-diene moiety and serve as potential precursors in the synthesis of highly complex and strained target molecules of biological and industrial importance. Their unique reaction behavior where the reactivity is spread over three contiguous carbon atoms has been successfully applied to the field of pharmaceuticals, dyes, polymers, etc.[1] Although the first allene derivative was prepared in 1887 by Burton and Pechmann[2] and the structure confirmed after a long period in 1954,[3] surprisingly van't Hoff, as early as in 1875, was able to recognize and predict that unsymmetrically substituted allenes should be chiral and exist in two enantiomeric forms.[4] Lack of methodologies for their synthesis coupled with the false notion that such a 1,2-diene functional group would be highly unstable severely impeded the initial development of this area. The discovery of 1,2-diene moieties in the naturally occurring molecules by Staudinger and Ruzicka in 1924 triggered the research activities aimed at developing synthetic routes to allenes.[5] At present a variety of preparatively useful methodologies are available to access substituted allenes. Especially in the past three decades the synthesis and applications of allenes have been the subject of extensive studies in both the area of organic and organometallic chemistry.[1,6−10] In particular, palladium-catalyzed reactions of allenes have gained considerable attention in recent years. Over the last few decades, palladium-catalyzed reactions have been most widely investigated and proven extremely useful and advantageous in organic synthesis because they exhibit a high level of chemo-, regio-, and stereoselectivity in numerous transformations.[11,12]

Palladium-catalyzed reactions of allenes with carbon and heteroatom nucleophiles leading to the formation of carbon−carbon and carbon−heteroatom bonds generally proceed with the involvement of a π-allylpalladium intermediate, which plays an ever increasing role in organic synthesis.[13,14] In 1964 Schultz[15] and then Shaw[16] developed methods for the formation of such intermediates from allenes via their insertion into organopalladium compounds with concomitant substitution at the central carbon atom of allenes. Subsequently, allene insertions into Pd−C bonds containing phosphine ligands,[17] bidentate,[18,19] and terdentate[18] nitrogen ligands were efficiently achieved in quantitative yields. The coupling of such intermediates with various nucleophiles was first investigated by Tsuji,[20] and Hegedus demonstrated the synthetic application of these complexes containing two allene units.[21,22]

The feasibility as well as reactivity of these π-allylpalladium species with a wide variety of carbon and heteroatom nucleophiles leading to the new bond-forming processes and the major breakthroughs of successfully applying allenes to synthesize a number of interesting intermediates and natural products are discussed in this review. The scope of this survey also includes carbonylations and carboxylations of allenes, cross-coupling reactions, metala-

† This contribution is dedicated to our mentors Professor Hans-Ulrich Reissig (Berlin, Germany) and Professor Goverdhan Mehta (Bangalore, India).

* To whom correspondence should be addressed. New address: Freie Universität Berlin, Institut für Chemie/Organische Chemie, Takustrasse 3, D-14195 Berlin, Germany. E-mail: rzimmer@chemie.fu-berlin.de.
‡ Technische Universität Dresden.
§ Indian Institute of Technology.

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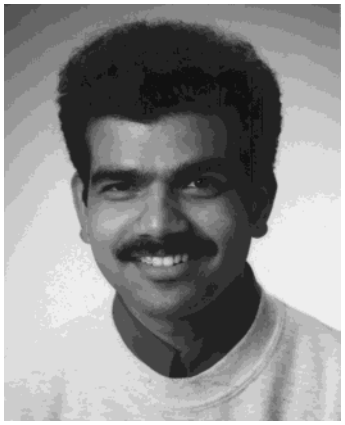
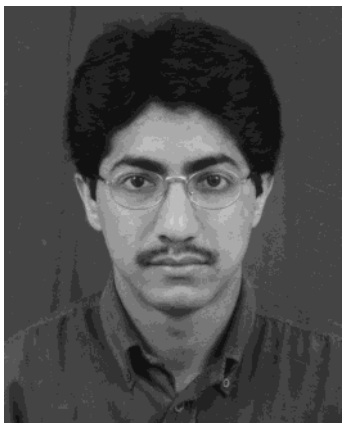
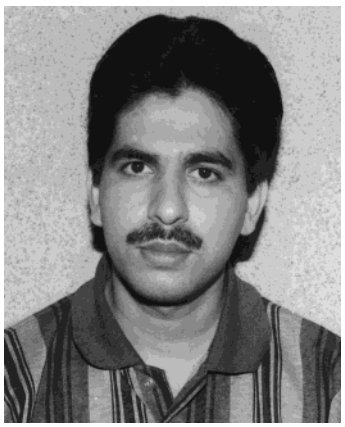
Reinhold Zimmer was born in Wiesbaden, Germany, in 1959. He studied chemistry at the Technical University Darmstadt and graduated in 1988. From 1988 to 1990 he carried out his Ph.D. research under the guidance of Professor Hans-Ulrich Reissig at the same university. From 1992 to 1994 he worked as a Karl-Landsteiner fellow with Dr. Maximilian A. Grassberger at the Sandoz Research Institute in Vienna, Austria, in the modification of FK 506 and ascomycins. From 1994 to 2000 he worked as a research associate with Professor Reissig at the Technical University Dresden, Germany. In 1998 he spent two months as a short-time lecturer (DAAD exchange program) in the Department of Chemistry at the Indian Institute of Technology in Kanpur, India. Recently, he followed Professor Reissig to the Free University of Berlin.



Erathodiyil Nandanan was born in Adakkaputhur (Kerala), India in 1969. After receiving his M.Sc. degree in Chemistry from the University of Calicut, he joined the National Chemical Laboratory, Pune, in 1992 as a CSIR research fellow and received his Ph.D. degree (organic chemistry) in 1997 under the supervision of Dr. T. Ravindranathan. From 1997 to 1998 he worked as a postdoctoral fellow with Dr. Kenneth A. Jacobson in NIDDK, National Institutes of Health, USA, on the chemistry of nucleotide bisphosphates as adenosine $P2Y_1$-receptor antagonists. Since 1999 he has been working as an Alexander von Humboldt fellow with Professor H.-U. Reissig at the Free University Berlin, Germany, and is involved researching the SmI_2-induced radical cyclization reactions toward the synthesis of bioactive molecules.



C. U. Dinesh was born in Karnataka, India, in 1970. After completing his Masters degree in Chemistry, he joined the National Chemical Laboratory, Pune, in 1992 for doctoral work under the supervision of Dr. Bipin Pandey and obtained his Ph.D. degree in 1996. In 1997 he obtained an Alexander von Humboldt fellowship for postdoctoral studies and carried out research in the group of Professor H.-U. Reissig, Technical University Dresden, Germany, until 1998. From 1999 to 2000 he worked as postdoctoral fellow in the group of Professor C. Mioskowski, ULP Strasbourg, France.



Faiz Ahmed Khan was born in Koppal (Karnataka), India in 1965, and he obtained his M.Sc. degree in 1987. Subsequently, he joined the School of Chemistry, University of Hyderabad, for his doctoral work in Professor Goverdhan Mehta's group and was awarded his Doctorate degree in 1994. After postdoctoral research as an Alexander von Humboldt fellow with Professor H.-U. Reissig at the Technical University Dresden, Germany, he accepted a faculty position at the Indian Institute of Technology Kanpur in 1996 and is currently an Assistant Professor in the Department of Chemistry. He is a Young Associate of Indian Academy of Sciences, Bangalore, and Indian National Science Academy's Young Scientist (1997). His research interests are in the application of transition metal-catalyzed reactions in organic synthesis.

tions with Sn, Si etc., and di-, oligo-, and polymerization reactions. We attempt to categorize numerous such reactions, and the mechanistic considerations are highlighted wherever possible. In addition, this review will emphasize the versatility and growing scientific interest of this area, largely dealing with the recent literature.

II. Reactions of Allenes with Carbon Nucleophiles

As mentioned in the Introduction, palladium-catalyzed reactions of allenes have become an important area of study in the present organic chemistry research. Right from the initial work of Coulson[23] to the current research, the work utilizing the formation of a carbon−carbon or carbon−heteroatom bond for the synthesis of compounds such as carbocycles, heterocycles, 1,3-dienes, enynes, etc., has become dramatically significant. By using different nucleophiles it is possible to obtain interesting products from the Pd complex formed between the catalyst and the allene. The use of different Pd catalysts, reaction conditions, and reaction mechanisms and their applications in the synthesis of complex organic molecules are often intriguing.

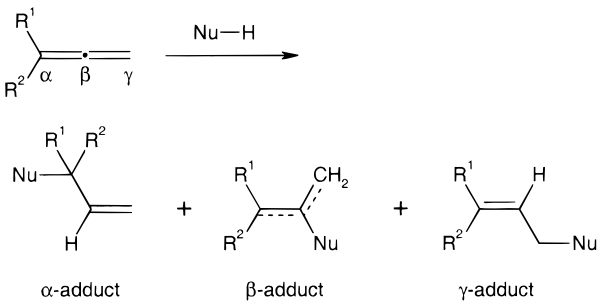
In this section, reactions of allenes with carbon nucleophiles are described. Various nucleophiles such as malonates, organometallics, etc., have been used in the study. Diverse classes of products such as alkenes, 1,3-dienes, carbocycles, and heterocycles with

a wide range of ring sizes were synthesized using carbon nucleophiles in palladium-catalyzed reactions of allenes. Though it is less explored, enantioselective synthesis could also be achieved. The products obtained were further utilized for the synthesis of compounds of biological and academic interest.

A. Palladium-Catalyzed Addition of Pronucleophiles to Allenes

A nucleophilic addition on allene can occur on three carbon atoms depending on the substituents it has at the terminals. All three possible regioisomers can be selectively produced by properly substituting the allene at its terminals (Scheme 1). It was observed

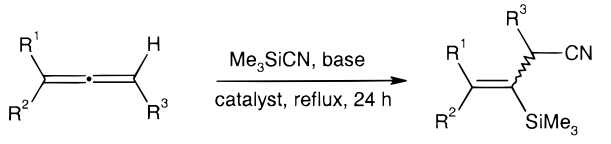
Scheme 1



that alkoxy (aryloxy) allenes afford α-adducts, arylallenes bearing an electron-withdrawing group at the *para*-position afford *β*-adducts, and mono- and dialkyl-substituted allenes afford *γ*-adducts.

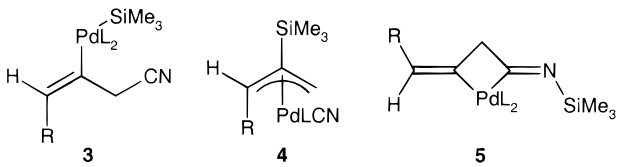
A relatively early report in this area was made by Chatani et al. where trimethylsilylcyanide was added over allenes using Pd and Ni catalysts.[24] In all cases, *γ*-addition was observed with the TMS group generally found at the central carbon of the allene **1**, showing preference for the formation of the (*E*)-isomer of **2** (Scheme 2). Mechanistically, three pathways can

Scheme 2



1 **2**

R^1	R^2	R^3	Catalyst	Base	**2**	*E*/*Z*
n-Hex	H	H	$PdCl_2$	--	70%	89/11
n-Hex	H	H	$PdCl_2$	pyridine	66%	95/5
Ph	H	H	$PdBr_2$	pyridine	75%	89/11
Ph	Me	H	$PdBr_2$	pyridine	60%	67/33
H	-$(CH_2)_6$-		$PdBr_2$	pyridine	59%	--

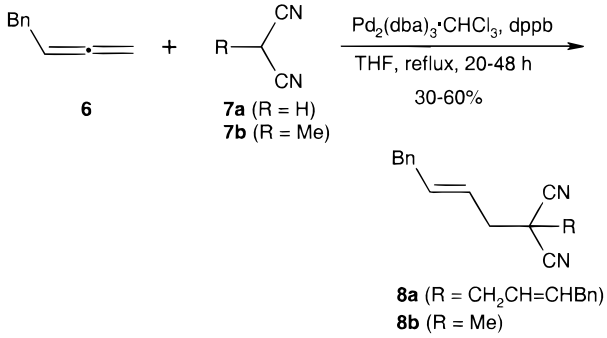


3 **4** **5**

be predicted for this reaction to proceed: (a) addition of Pd—CN to the coordinated allene giving intermediate **3** followed by reductive elimination, (b) involving the *π*-allyl complex **4**, and (c) via complex **5**. Recent studies on similar systems support the involvement of the *π*-allyl complex **4**.[25] However, it must be mentioned here that the more stable η^3-coordination can, due to the orthogonal orbitals of the allene, never be formed directly. The η^1-allyl complex (like **3**) that lacks the conjugation to the remaining double bond is always formed first. Then, after a rotation around the *σ*-C—C bond, η^3-coordination is possible.

Yamamoto and co-workers carried out a series of experiments on allenes bearing various substituents using different pronucleophiles.[14] The palladium-catalyzed addition of activated methylenes and methynes to mono- and disubstituted allenes was found to afford the terminal adducts (*γ*-addition).[26] Representatively, malodinitrile **7a** and methylmalodinitrile **7b** added smoothly over 4-phenyl-1,2-butadiene (**6**) to afford exclusively the *trans*-configurated alkenes **8a** and **8b**, respectively (Scheme 3). Double addition

Scheme 3



6 **7a** (R = H) **7b** (R = Me)

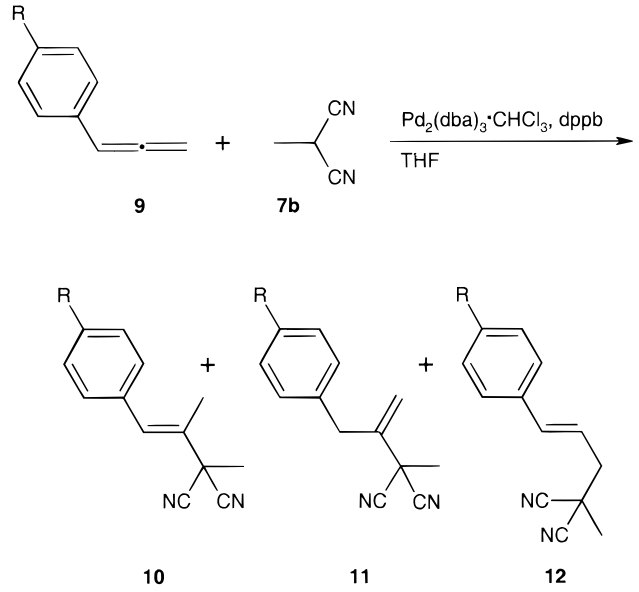
8a (R = CH_2CH=CHBn)
8b (R = Me)

took place in the case of **7a** because of the reactive tertiary C—H bond present in the monoadduct. However, a mixture of stereoisomeric products was observed with other nucleophiles and allenes, though the (*E*)-isomer was predominant.

In another set of experiments, the same authors observed drastic change in the regioselectivity in the reaction of arylallenes having different *para*-substitution.[25,27] It was found that electron-withdrawing groups (e.g., CF_3) at the *para*-position led to carbon—carbon bond formation at the central carbon of the allene (*β*-addition), whereas electron-donating groups (Me or OMe) led to the carbon—carbon bond formation at the unsubstituted terminal position of the allene (*γ*-addition) (Scheme 4). However, a sterically bulky nucleophile afforded the *γ*-addition product regardless of the electronic effect.

From these observations it is possible to explain that an electron-withdrawing group at the *para*-position will ultimately stabilize the positive charge at the *β*-carbon whereas an electron-donating group stabilizes the positive charge at the *γ*-position, thereby making the attack of the nucleophile more feasible at these positions. The observed product formation can be explained either by a carbopalladation (Scheme 5) or hydropalladation (Scheme 6) mechanism. The terminal adducts are produced either via a carbopalladation route involving vinylpalladium intermediates (**13** or **15**) or via a hydropalladation route involving *π*-allylpalladium intermediate **18**. The internal adducts are obtained either via carbopallada-

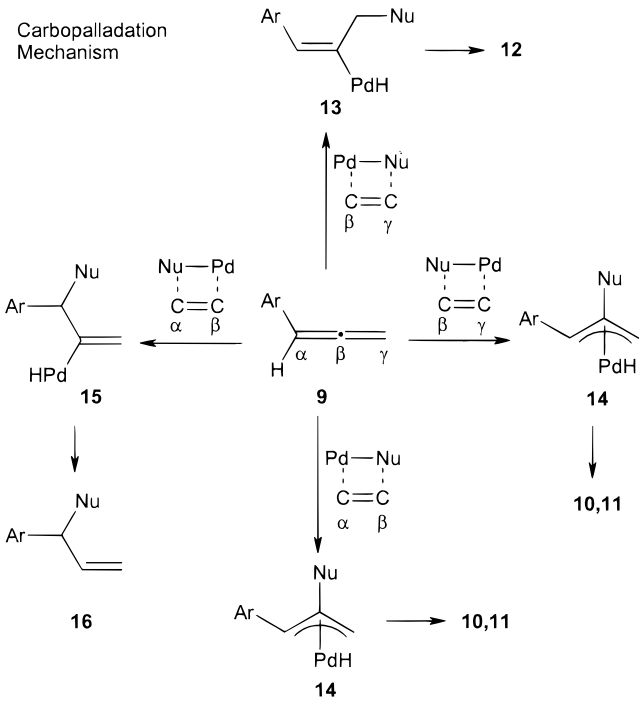
Scheme 4[a]



R	10	11	12
H	19%	6%	33%
F	24%	8%	19%
Br	46%	14%	--
CF_3	47%	20%	--
Me	--	--	51%
OMe	--	--	85%

[a] Adapted with permission from ref 25. Copyright 1995 Elsevier Science.

Scheme 5[a]



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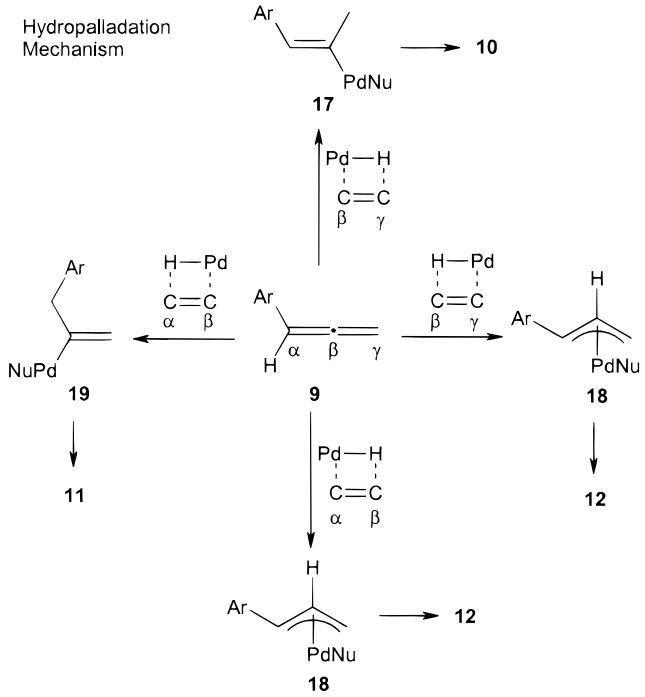
tion involving π-allyl intermediate **14** or via hydropalladation involving vinylpalladium intermediates **17** or **19**.

Scheme 6[a]



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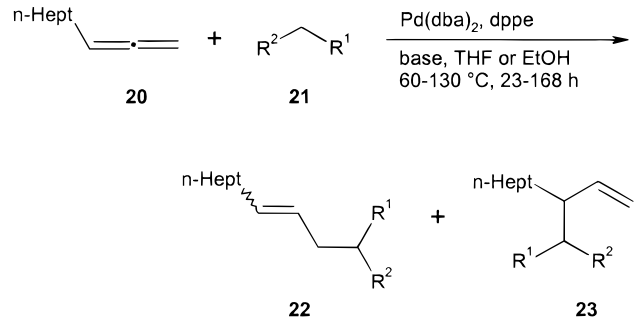
The hydropalladation process was found to operate in the palladium-catalyzed addition of malonates **21** to allenes, e.g., **20**, under basic conditions. In their work, Cazes et al. reported the involvement of a π-allyl intermediate similar to **18** generated through a hydropalladation process which can better account for the obtained results (Scheme 7).[28]

Scheme 7



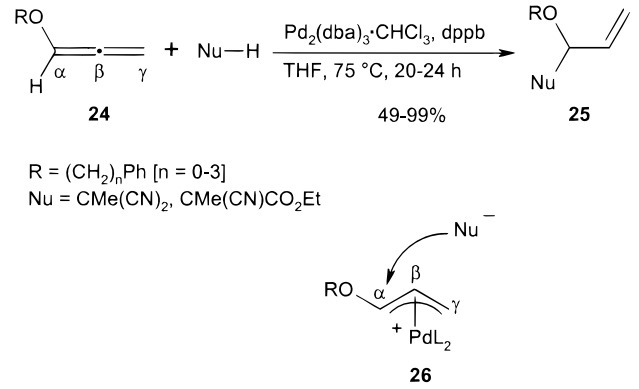
$R^1 = R^2 = CO_2Et$: 30% **22** (*E* only) + 12% **23**

$R^1 = COMe$; $R^2 = CO_2Et$: 50% **22** (*E*/*Z* = 91/9) + 10% **23**

As mentioned earlier, aryloxy- and alkoxy-substituted allenes **24** afford the α-addition products **25** exclusively.[29] Reaction of nucleophiles on a series of alkoxy-substituted allenes using $Pd_2(dba)_3$·$CHCl_3$ has confirmed the logic that an alkoxy group stabilizes a cation present α to it (Scheme 8). It is also implied to note that the reaction proceeds through the formation of π-allylpalladium intermediate **26**.

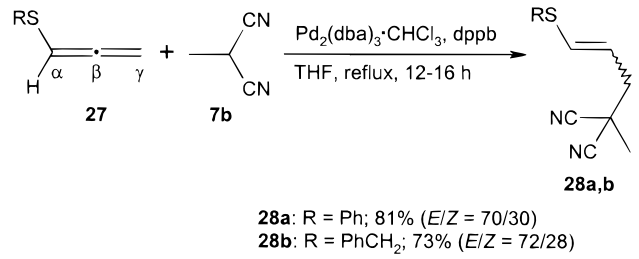
In contrast, allenyl sulfides **27** have shown preference for the γ-addition products **28** (Scheme 9).[30] In all the experiments, $Pd_2(dba)_3$·$CHCl_3$ proved to be the most efficient catalyst in combination with the dppb ligand. An explanation based on the electrophilic nature of γ-carbon can be given for this regioselection,

Scheme 8



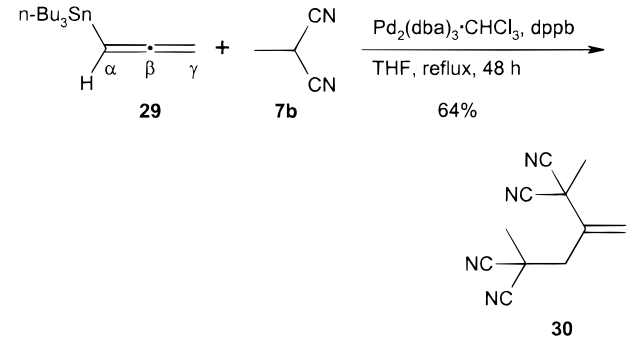
which in turn was verified by ^{13}C NMR studies. The γ-carbon of allenyl sulfides **27** appears at lower field compared to other substituted allenes (alkoxy, alkyl).

Scheme 9



Under similar conditions, allenylstannanes **29** were shown to afford the β-addition product followed by the nucleophilic displacement of the stannyl group (Scheme 10).[31] This double alkylation proceeds through

Scheme 10

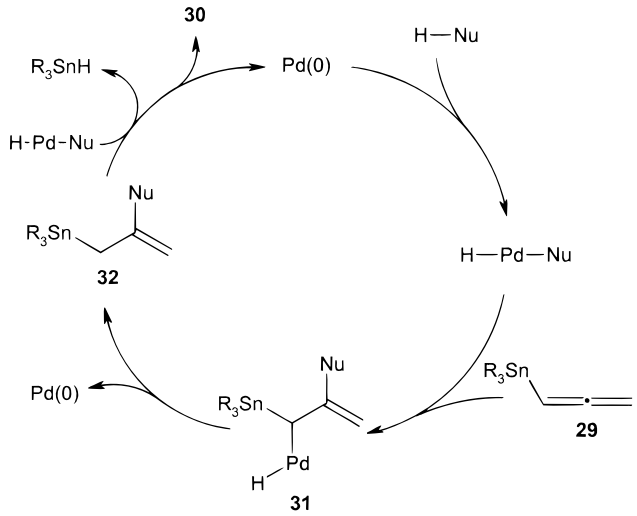


the formation of the allylstannane intermediate **31** at first, followed by reaction with another nucleophile as shown in the carbopalladation−transmetalation cycle as depicted in Scheme 11.

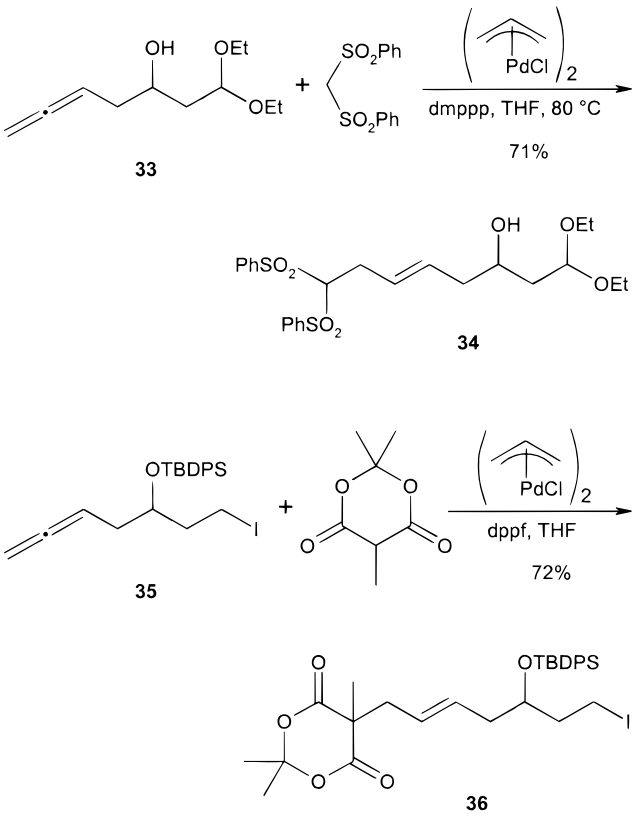
Using $[(\eta^3\text{-}C_3H_5)PdCl]_2$ as the Pd source, allenes **33** and **35** were easily transformed to alkenes **34** and **36** in 71% and 72% yield, respectively (Scheme 12).[32] The authors strongly recommend the hydropalladation pathway in contrast to earlier reports.[33] Carbopalladation of allenes generally favors the carbon−carbon bond formation at the central carbon of the allene, which is not the case here.

In an attempt to induce chirality in the carbopalladation of racemic allenes, Hiroi et al. used chiral phosphine ligands to give high enantioselectivities

Scheme 11

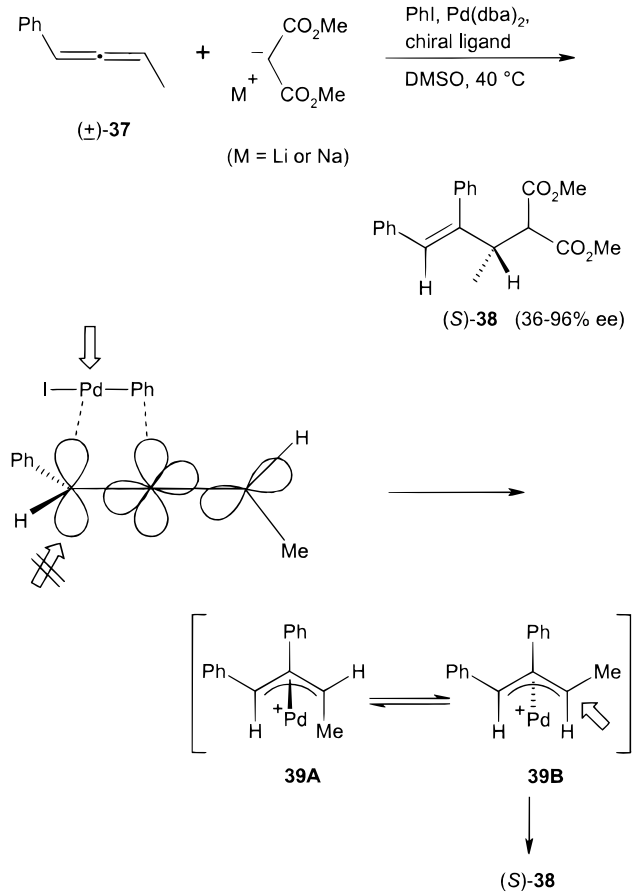


Scheme 12



under mild reaction conditions.[34] Chiral phosphines such as (*S*)-BINAP, (4*R*,5*R*)-DIOP, (4*R*,5*R*)-MOD-DIOP, and different ferrocenyl phosphine ligands were used to afford the corresponding olefins with ee up to 96% (Scheme 13) with the preferential formation of (*S*)-enantiomer. The results indicate that the palladium-catalyzed reactions of (±)-**37** with chiral phosphine ligands would form a sterically preferred π-allyl intermediate via diastereomeric equilibrium. This was illustrated by the reaction of the chiral allene (*R*)-**37** to which two isomeric π-allylpalladium complexes (**39A** and **39B**) could be proposed (Scheme 13). The more stable complex **39B** would then undergo nucleophilic substitution from the backside of the Pd catalyst to afford (*S*)-**38**.

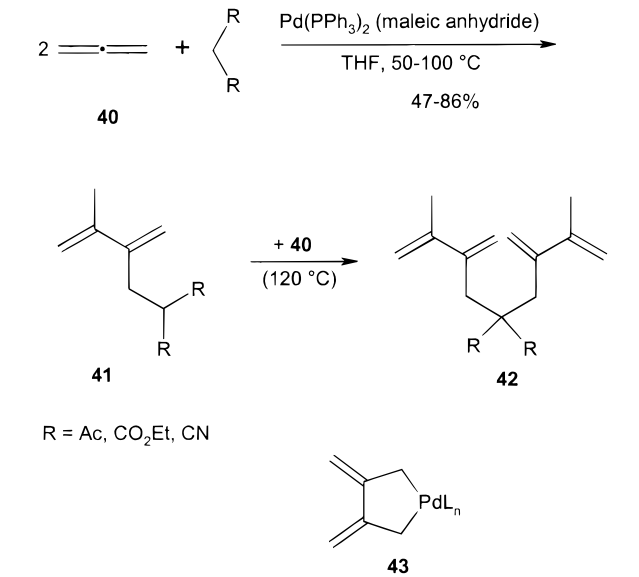
Scheme 13



B. Synthesis of Substituted Alkenes, 1,3-Dienes, and Enynes

In 1973 Coulson first reported the synthesis of 1,3-diene systems by the palladium-catalyzed reactions of 1,2-propadiene (**40**) with nucleophiles[23] using bis-(triphenylphosphine)(maleic anhydride)palladium as the catalyst of choice (Scheme 14). 1,3-Dienes **41** were

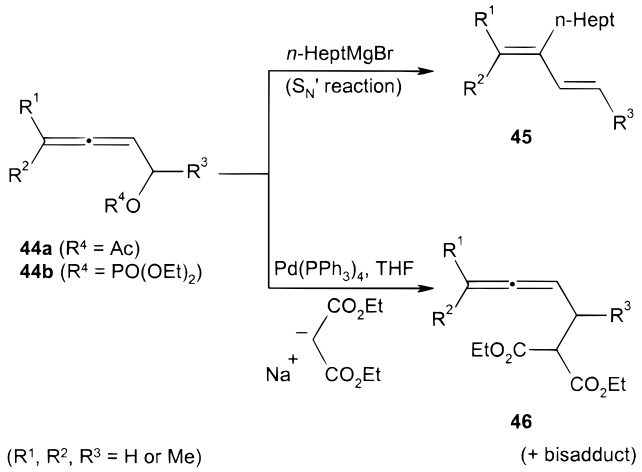
Scheme 14



obtained in moderate to good yields using a catalytic amount of the Pd catalyst. When an excess of 1,2-propadiene (**40**) is employed in the reaction, bisdienes **42** are generally obtained at a reaction temperature of 120 °C. Mechanistically, an intermediate of the type **43** was proposed which was also supported by the studies from other groups.[28,35]

In recent years, Cazes and Goré did an exhaustive work on Pd−allene chemistry.[35] Earlier, an attempt to synthesize 1,3-diene systems from α-allenic acetates and phosphates using a malonate nucleophile and Pd catalyst afforded *β*-allenic malonates **46** (Scheme 15).[36] However, Grignard reagents afforded

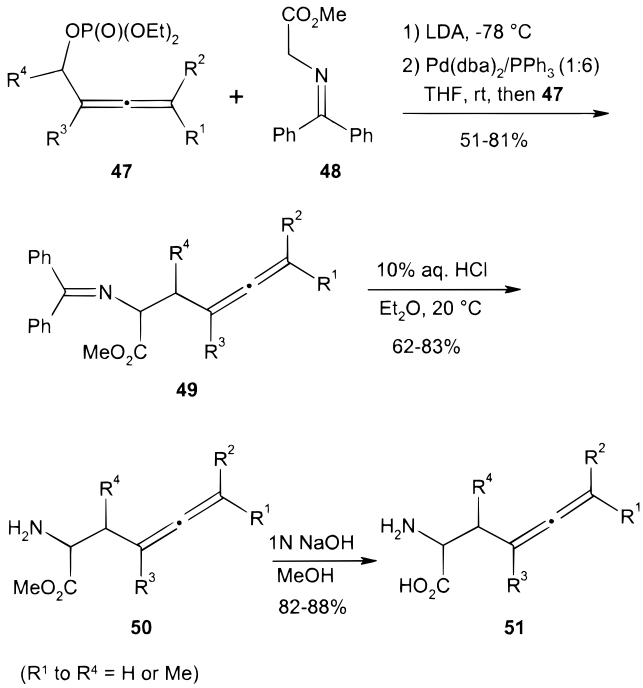
Scheme 15



1,3-dienes **45** in good yields in the absence of Pd(0) catalyst, while in the presence of a catalytic system, only very low yields were obtained.

These findings were successfully applied for the synthesis of *γ*-allenic α-amino acids **51** by a three-step procedure starting from α-allenic phosphates **47**

Scheme 16

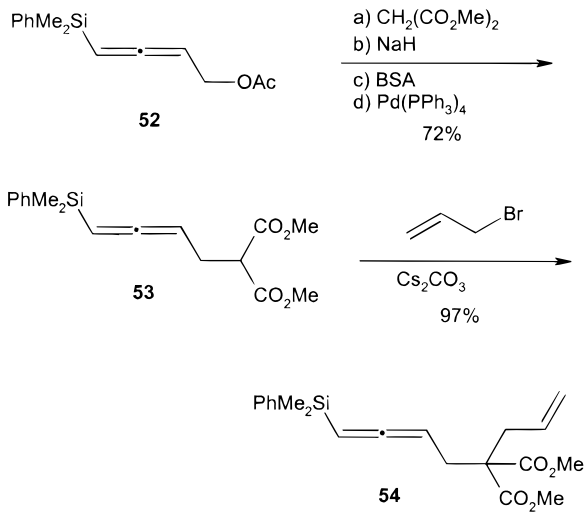


(Scheme 16).[37] Reaction of **47** with the anion of Schiff base methyl *N*-(diphenylmethylene)glycinate (**48**) in

the presence of 4 mol % of catalytic system $Pd(dba)_2$ and PPh_3 (1:6) proceeds efficiently resulting in imino ester **49** in good yields. Amino acids **51** can be obtained by acidic hydrolysis of **49** followed by saponification of the resulting amino esters **50**. The naturally occurring unsubstituted α-amino acid **51** (R^1 to R^4 = H) was easily synthesized by using this protocol.

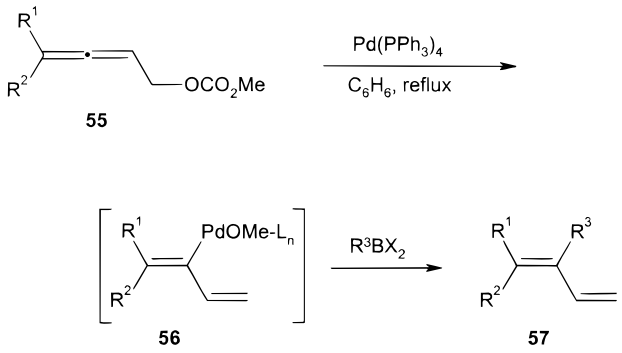
In a similar palladium-catalyzed alkylation, Trost and Tour synthesized eneallenes, e.g. **54**, by the cross-coupling of malonate and allenylsilane **52** (Scheme 17).[38]

Scheme 17



Palladium-catalyzed cross-couplings of 2,3-alkadienyl carbonates **55** with organoboron compounds have been reported to produce 1,3-butadienes **57**.[39]

Scheme 18



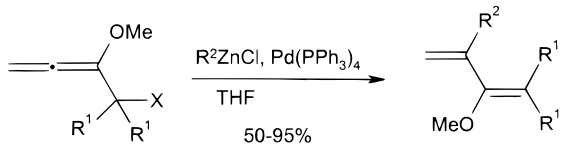
R^1	R^2	R^3BX_2	**57**
H	H	*p*-$MeOC_6H_4B(OH)_2$	88%
Me	Me	*p*-$AcC_6H_4B[-O(CH_2)_2O-]$	91%
Me	Me	1-naphthyl-$B(OH)_2$	92%
$-(CH_2)_5-$		*p*-$MeOC_6H_4B(OH)_2$	97%
Me	Me	*n*-HexCH=CHB[-$O(CH_2)_2O-$]	92%
Me	Me	$THPO(CH_2)_4BBN$	31% (69%)[a]

[a] Addition of 1.2 eq. of K_3PO_4.

The reaction proceeds through the oxidative addition−S_N2'-type displacement in **55** to form **56** followed by reaction with organoboron reagent and reductive elimination of Pd(0) (Scheme 18). Notably, the addition of K_3PO_4 was shown to accelerate the reaction and improve the yield.

Organozinc reagents were used by Vermeer et al. to prepare 3-methoxy-1,3-dienes **59** having aryl, alkenyl, or alkynyl substitution at position 2.[40] Allenes **58** bearing leaving groups such as OAc and OS(O)Me, respectively, underwent smooth coupling with organozinc compounds in the presence of 2 mol % $Pd(PPh_3)_4$ to give dienes **59** in good yields (Scheme 19).

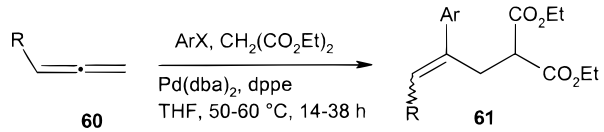
Scheme 19



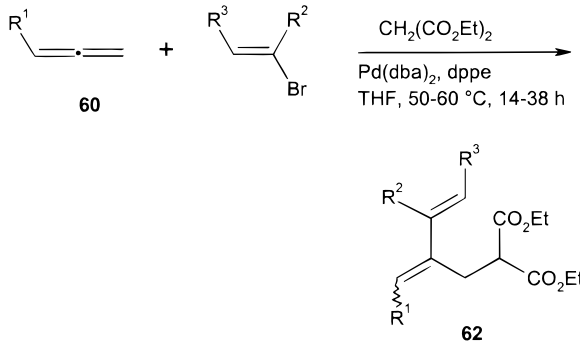
R^1 = H, Me; X = OAc, OSOMe;
R^2 = Ph, vinyl, TMSC≡C

Stereoselective synthesis of styrenes **61** and 1,3-butadienes **62** was achieved by Cazes, Goré, and coworkers with aryl or vinylic halides and malonate nucleophiles (Scheme 20).[41] The reaction generally

Scheme 20



ArX = PhI; R = H: 85%
ArX = PhBr; R = *n*-Hept: 67% (*E*/*Z* = 85/15)

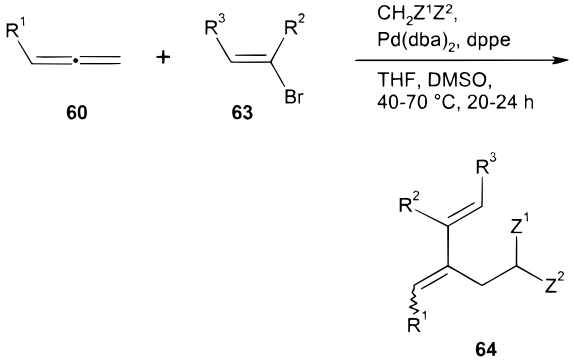


R^1 = R^2 = R^3 = H: 60%
R^1 = *n*-Hept; R^2 = Me; R^3 = H: 85% (only *E*)
R^1 = *n*-Hept; R^2 = H; R^3 = Me: 80% (*E*/*Z* = 56/44)

proceeds through the carbopalladation of allenes by vinylic or arylpalladium species to give π-allylpalladium complexes. This π-allylpalladium complex then undergoes nucleophilic attack to afford the corresponding products.[35]

A number of different allenic systems were used to synthesize different 1,3-dienes having α-amino acids,[42] silanes,[43] vinylcyclopentenes,[44] or cyclopropanes[45] in their structure. Silylated 1,3-dienes (Scheme 21, entries 1−3) were synthesized which can further be used in Diels−Alder reactions. Generally, in all cases, the (*E*)-configurated isomer predominates and

Scheme 21

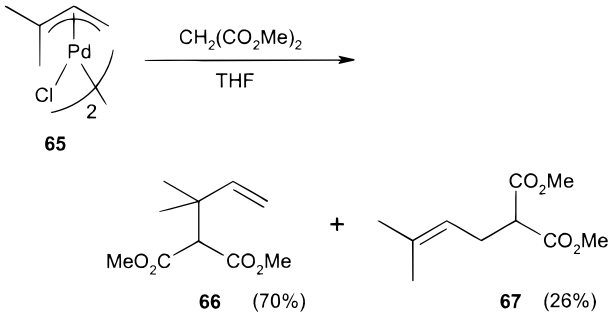


Entry	R^1	R^2	R^3	Z^1	Z^2	**64** (*E*/*Z*)
1	H	H	TMS	CO_2Me	CO_2Me	75%
2	*n*-Hept	CH_2TMS	H	CO_2Me	CO_2Me	66% (95:5)
3	H	TMS	H	CO_2Me	CO_2Me	69%
4	H	H	H	-N=CPh_2	CO_2Me	52%
5	H	Me	H	-N=CPh_2	CO_2Me	56%

there is regioselective preference for the formation of **64**. The Schiff base of methyl glycinate was also used as a nucleophile, affording the products **64** (Z^1 = N=CPh_2), which were later hydrolyzed using methanolic sodium hydroxide to give the corresponding dienic amino acids.

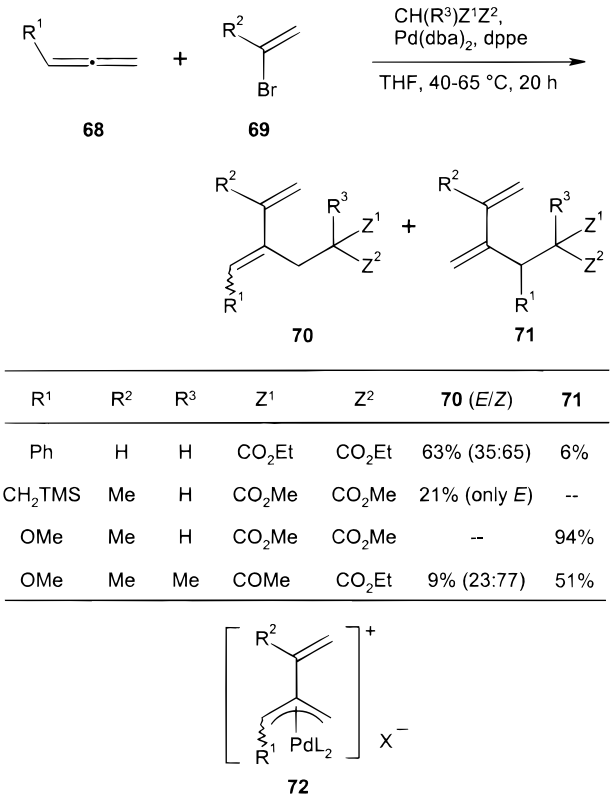
The regioselectivity of these reactions depends on various factors, such as the nature of the ligand (donor or acceptor), the nucleophile, substitution on the allene moiety, the influence of steric and electronic factors, etc. Åkermark et al.[46] showed that 1,1-dialkyl-substituted π-allyl complexes such as **65** react preferentially at the more substituted position (Scheme 22).

Scheme 22



In their work, Cazes, Goré, and co-workers observed that groups such as phenyl directs the nucleophiles toward the terminus. Methoxy-substituted allenes give rise to nucleophilic attack at the secondary terminus (Scheme 23)[47] because of the positive charge stabilization by the methoxy group in intermediate complex **72** on the more substituted terminus. However, in the case of bulky substitution in the allene, nucleophilic attack at the terminus occurs irrespective of the electronic factors.

Scheme 23

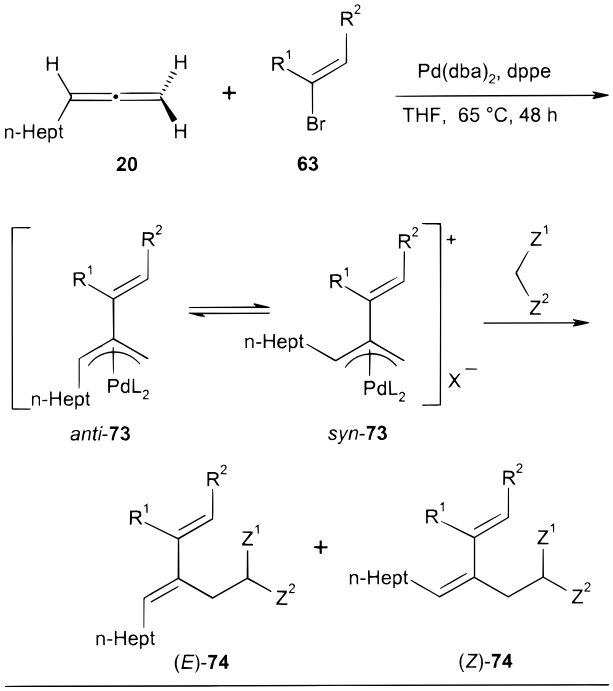


R^1	R^2	R^3	Z^1	Z^2	**70** (*E*/*Z*)	**71**
Ph	H	H	CO_2Et	CO_2Et	63% (35:65)	6%
CH_2TMS	Me	H	CO_2Me	CO_2Me	21% (only *E*)	--
OMe	Me	H	CO_2Me	CO_2Me	--	94%
OMe	Me	Me	COMe	CO_2Et	9% (23:77)	51%

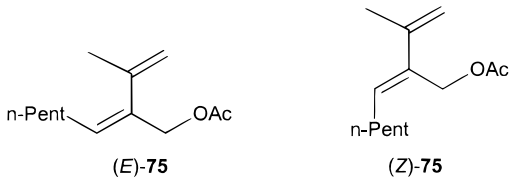
The stereoselectivity of these reactions depends mainly on the steric hindrances of the vinylic component and of the nucleophile.[48] However, a slight influence of the solvents used (mainly THF, DMSO, MeCN, and DMF) and reaction temperature (40−100 °C) was observed.[35] As mentioned earlier, the reaction proceeds through the formation of a π-allylpalladium complex, where the carbon−carbon bond formation occurs preferentially on the less sterically hindered face of the terminal double bond of the allene giving *anti*-π-allylpalladium **73**, which equilibrates with its *syn*-isomer (Scheme 24). In the case of bulky vinyl groups, the *anti*-configuration is preferred for steric reasons, which gives (*E*)-olefins **74** (entries 3 and 4, Scheme 24), whereas in the case of a smaller vinylic component, the steric interaction of it with the *n*-heptyl group of the allene moiety in *syn*-**73** is negligible, which in turn affords a mixture of isomers (entries 1 and 2, Scheme 24). However, combination of a bulky nucleophile and small vinylic component affords preferentially the (*Z*)-isomer (entries 5 and 6, Scheme 24), probably because of a smaller steric interaction between *n*-Hept and R^1 and relatively more interaction between *n*-Hept and the nucleophile. Further evidence about the involvement of the π-allyl intermediate comes from the reactions of the dienic acetates (*E*)-**75** and (*Z*)-**75** which produced results similar to those of the allenes.[48] It could be possible that both reaction pathways involve a similar π-allylpalladium intermediate.

The use of enol triflates has also been shown to be efficient in the carbopalladation of allenes.[49] In this case, the addition of 2.5 equiv of LiCl was found to increase the reactivity of the vinylpalladium species, probably by ligand exchange (Scheme 25). Enol

Scheme 24



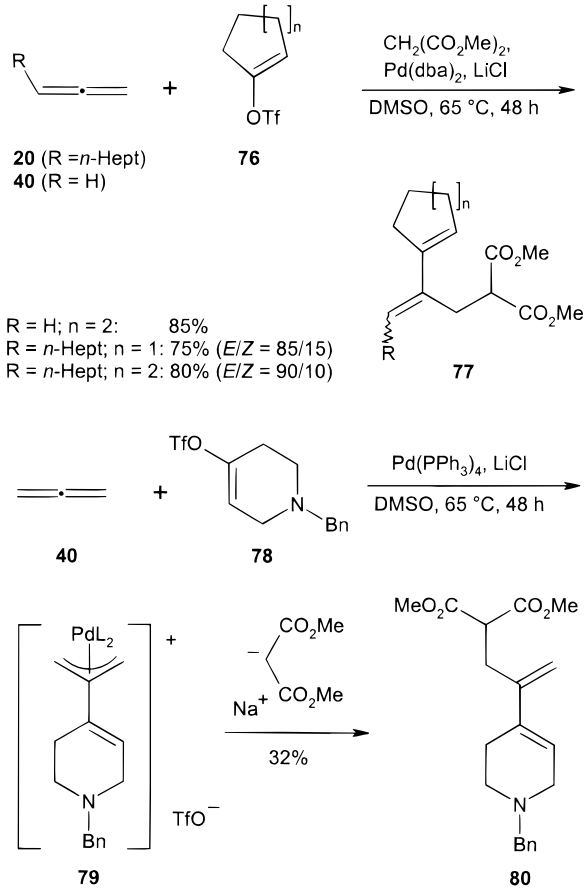
Entry	R^1	R^2	Z^1	Z^2	**74**	*E*/*Z*
1	H	H	CO_2Et	CO_2Et	75%	53/47
2	H	Me	CO_2Et	CO_2Et	80%	56/44
3	Me	H	CO_2Et	CO_2Et	85%	100/0
4	$-(CH_2)_4-$		CO_2Et	CO_2Et	63%	86/14
5	H	H	CO_2Me	SO_2Ph	71%	30/70
6	H	H	$-N=CPh_2$	CO_2Et	43%	15/85



triflates derived from 3- and 4-piperidinone (e.g., **78**) were also subjected to carbopalladation of allenes, which afforded cyclic α- and *β*-aminodienes, the useful precursors for the synthesis of azabicyclic frameworks (Scheme 25).[50]

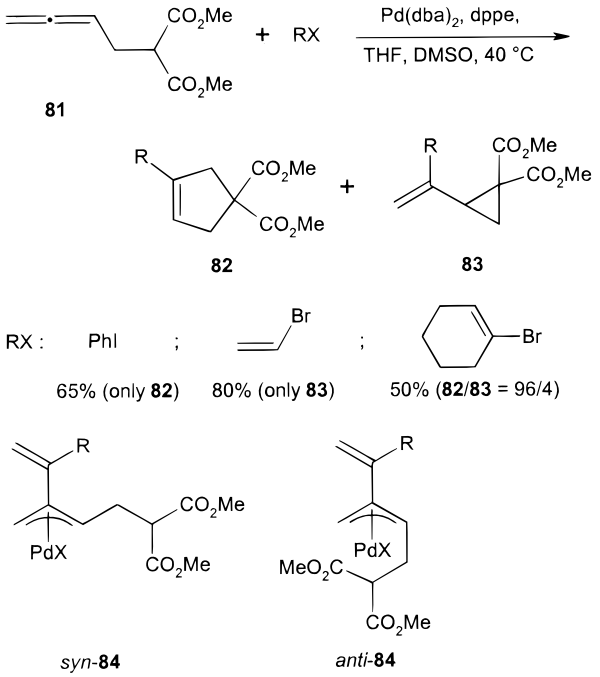
The carbopalladation of allenes carrying a nucleophilic side chain, e.g., *β*-allenylmalonates **81**, leads to the formation of either cyclopropyl or cyclopentene derivatives.[44] The regioselectivity for the formation of these rings depends mainly on the bulkiness of the vinylic or aryl halides used, which allows one to assume that both *π*-allylpalladium intermediates *syn*- and *anti*-**84** are involved in the reaction (Scheme 26). However, 1,1-dimethyl-2,3-butadienylmalonate **85** gave mainly *γ*-lactones under similar reaction conditions.[45] One can then presume that the presence of *gem*-dimethyl groups α to the allene structure makes the formation of both *syn*- and *anti*-*π*-allyl intermediates impossible. The mechanism might involve the oxapalladacycle **88** which gives rise to the lactone **86** by reductive elimination of Pd followed by the addition of water and the loss of ethanol. Decarboxylation

Scheme 25[a]



[a] Adapted with permission from ref 50. Copyright 1995 Elsevier Science.

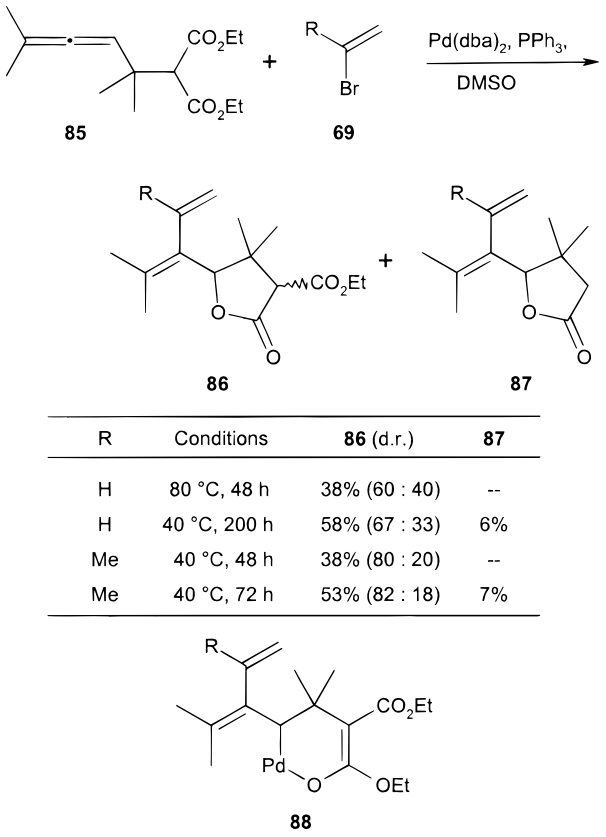
Scheme 26



of **86** should then lead to lactone **87** as a byproduct (Scheme 27).

As mentioned earlier the direct addition of malonate-type nucleophiles to the allenes affords olefins, the regioselectivity of which depends on various

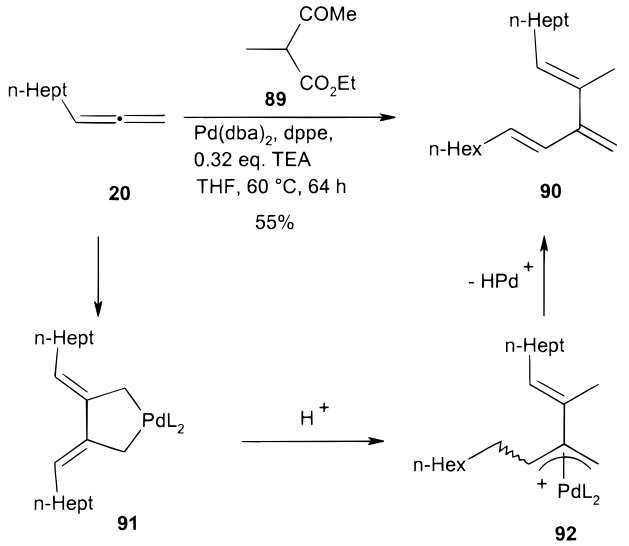
Scheme 27



R	Conditions	**86** (d.r.)	**87**
H	80 °C, 48 h	38% (60 : 40)	--
H	40 °C, 200 h	58% (67 : 33)	6%
Me	40 °C, 48 h	38% (80 : 20)	--
Me	40 °C, 72 h	53% (82 : 18)	7%

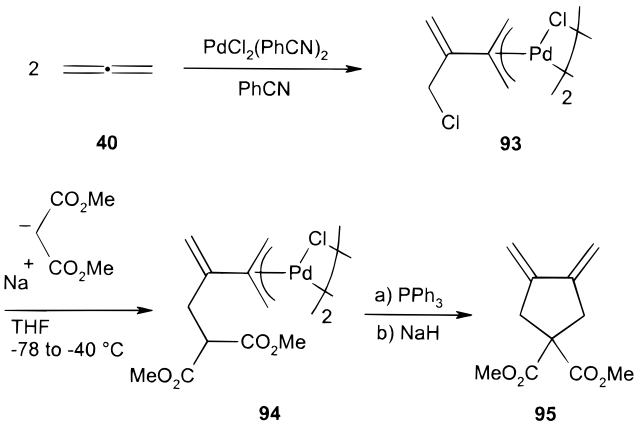
factors. However, it was the case of monosubstituted acetoacetate **89** which gave triene **90** almost exclusively rather than the normal addition product.[28] This might be due to the dimerization of allene **20** in the presence of Pd catalyst. The initially formed palladacycle **91** undergoes protonation to give **92** followed by β-elimination to form the triene **90** (Scheme 28).

Scheme 28



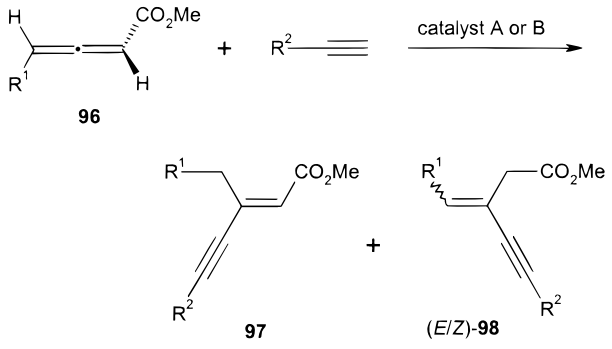
Similar dimerization has been found to give exocyclic dienes, but here it is with the involvement of the nucleophile. Hegedus et al. successfully took advantage of the effect of the phosphine ligand in $PdCl_2(PhCN)_2$-catalyzed reaction for the selective synthesis of exocyclic diene **95**.[21] In the absence of phosphine ligand, the initially formed π-allylpalladium complex **93** undergoes nucleophilic displacement at the allylic chloride to give **94**, while in the following step in the presence of 4 equiv of PPh_3, the intramolecular nucleophilic attack at the π-allyl position leads to ring-closed product **95** (Scheme 29).

Scheme 29



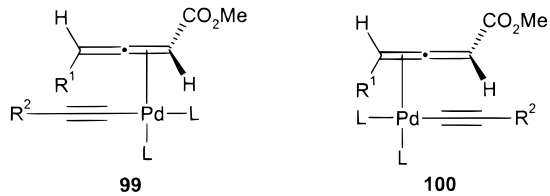
The allene−acetylene cross condensation has also been reported. The direct coupling of acetylenes and 1,3-disubstituted allenes, reported by Trost and Kottirsch, produced enynes in moderate to good yields.[33] The regioselectivity is catalyst dependent, where an electron-rich catalyst gave preferentially the nonconjugated enoate (*E*/*Z*)-**98** (Scheme 30), while an elec-

Scheme 30



				Distribution		Yield
R^1	R^2	Catalyst [a]	**97**	(*E*)-**98**	(*Z*)-**98**	**97**/**98**
Me	*n*-Hex	A	85%	12%	3%	74%
Me	*n*-Hex	B	6%	47%	47%	53%
i-Pr	TMS	A	67%	20%	13%	39%
i-Pr	TMS	B	10%	65%	25%	57%

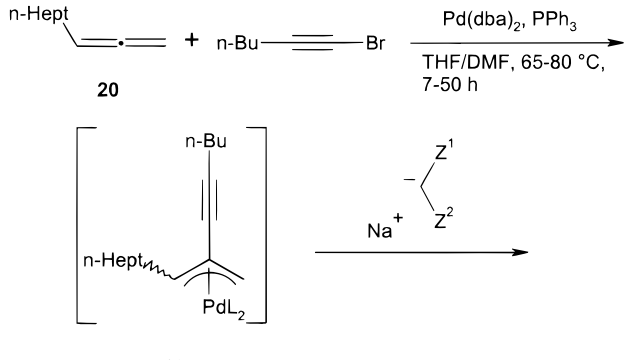
[a] Catalyst A: $Pd(OAc)_2$, TDMPP. Catalyst B: TCPC, TTMPP.



tron-deficient catalyst gave conjugated enoates **97**. The possible reason could be that an electron-rich Pd catalyst coordinates preferentially on the 2,3-double bond (as in **99**) while an electron-deficient Pd catalyst coordinates on the 3,4-double bond (as in **100**), leading to the formation of β,γ- and α,β-unsaturated esters, respectively.

Recently, the use of σ-ethynylpalladium species in carbopalladation of allenes reported by Gorè et al. involves a three-component reaction of allene, alkynyl halide, and nucleophile.[51] The product **102** is formed as its (*Z*)-isomer, which shows the low degree of steric hindrance of the C≡C group leading exclusively to the formation of the *syn*-π-allyl complex **101** (Scheme 31).

Scheme 31

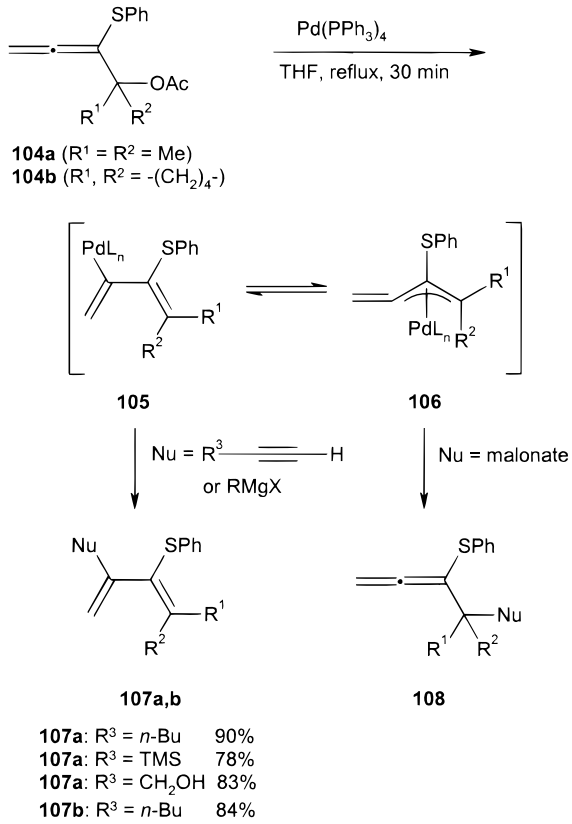


Z^1	Z^2	**102** (*E*/*Z*)	**103**
CO_2Me	CO_2Me	30% (only *Z*)	7%
CO_2Et	SO_2Ph	36% (only *Z*)	--
CO_2Et	COMe	56% (4:96)	8%

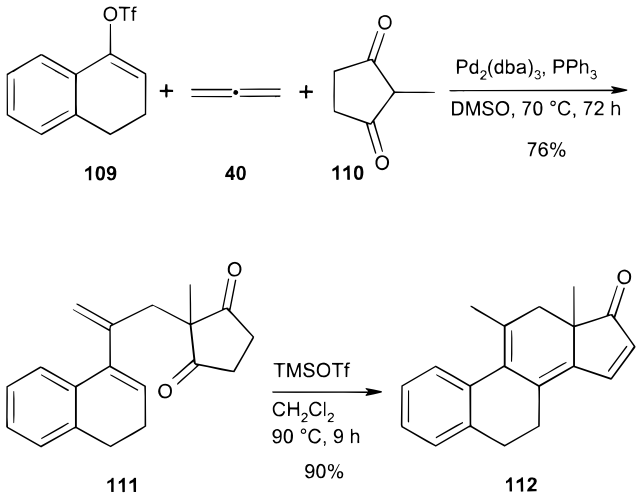
Padwa and Ni selectively synthesized 2-thiophenyl-substituted 1,3-dienes **107** by the reaction of α-allenyl acetates **104**, based on the reactivity difference of hard and soft nucleophiles.[52] In the presence of Pd-$(PPh_3)_4$, soft nucleophiles such as malonate anion gave allenes **108** while hard nucleophiles such as Grignard reagents or terminal alkynes gave rise to 1,3-dienes **107** (Scheme 32).

All of the products which were obtained by the carbopalladation of allenes can further be used for the synthesis of structurally complex molecules. In one attempt, Goré and co-workers successfully synthesized steroid skeleton **112** by the reaction of the 1,3-diene **111** with Lewis acids (Scheme 33).[53]

Scheme 32



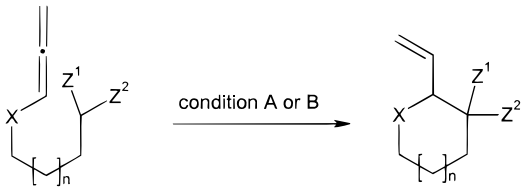
Scheme 33



C. Synthesis of Medium and Large Ring Structures

For allenes carrying nucleophilic centers or in the case of a reaction between an aryl or vinylic halide having a suitable nucleophilic side chain and allenes, the net result is ring closure leading to interesting cyclic compounds. Ring sizes ranging from 3 to 20 can be synthesized by the carbopalladation of allenes. A discussion of the synthesis of the cyclopropanes and cyclopentenes is given in the preceding section, section B. Allenes bearing a nucleophilic center separated by 3−5 atoms afford generally five- to seven-membered rings. Yamamoto and co-workers used allenes of the type **113** for the synthesis of five- to seven-membered rings (Scheme 34).[54,55] It was

Scheme 34



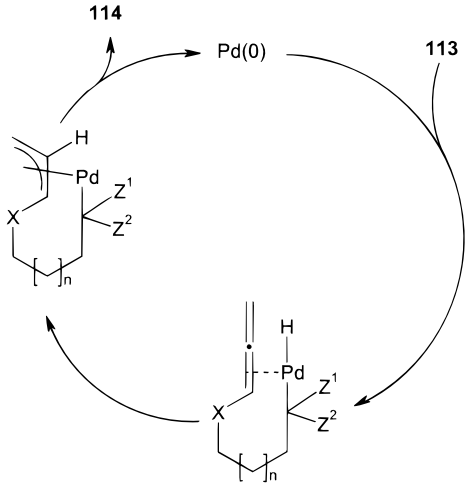
113 **114**

condition A: $[(\eta^3\text{-}C_3H_5)PdCl]_2$, dppf, THF (0.025 M), 70 °C, 1.5-5 h.
condition B: $Pd(OAc)_2$, dppb, CH_2Cl_2 (1.0 M), rt, 0.25-1.5 h.

n	Z^1	Z^2	X	Condition	**114** (d.r.)
0	CN	CN	CH_2	A	88%
0	CN	CN	O	B	79%
0	CN	SO_2Ph	CH_2	A	82% (70:30)
1	CN	CN	CH_2	A	62%
1	CN	CN	O	B	86%
1	SO_2Ph	SO_2Ph	O	B	92%
2	CN	CN	O	B	88%

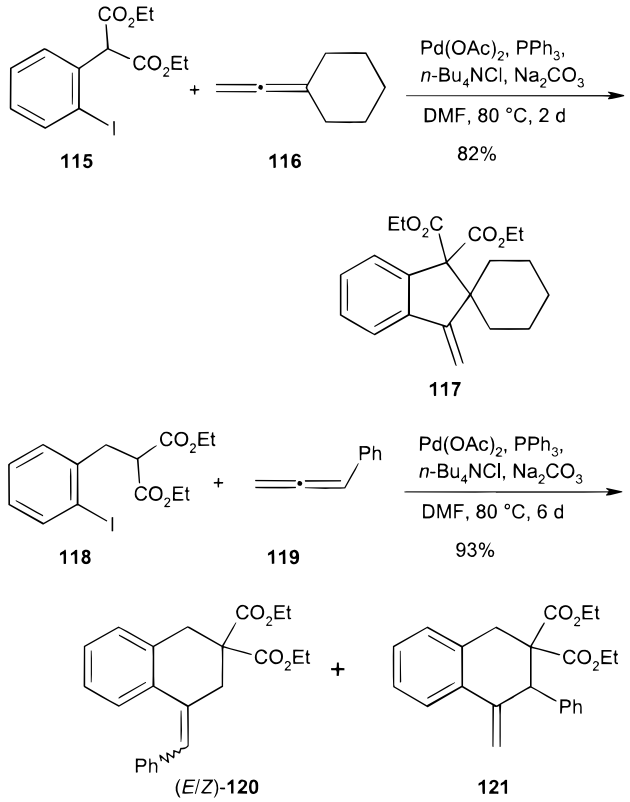
observed that a neutral Pd catalyst system is far superior to the basic one. In the case of condition B, for a few substrates, catalyst amounts as low as 0.1 mol % of $Pd(OAc)_2$ and 0.2 mol % of dppb are enough for good yields. Mechanistically, an intramolecular hydrocarbonation can be presumed for this reaction as depicted in Scheme 35.

Scheme 35



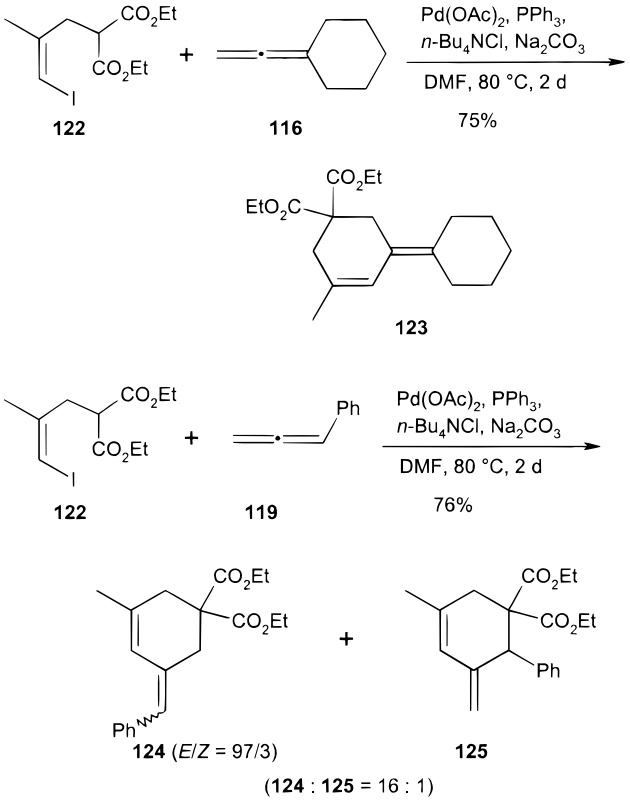
Functionally substituted aryl[56] and vinylic halides[57] were used by Larock et al. for the regioselective palladium-catalyzed carboannulation and heteroannulation of allenes. Aryl halides bearing a nucleophilic center (carbanion or heteroatom) at the *ortho*-position undergo a palladation reaction with allenes in the presence of a carbonate base to give five- or six-membered rings in high yields (Scheme 36). Similar reaction conditions were used for the reaction of vinylic halides bearing a nucleophilic atom (Scheme 37). The use of 1 equiv of *n*-Bu_4NCl has been found to afford better results. The formation of the five-membered ring involves the annulation across the more highly substituted C−C double bond, whereas six-membered ring formation involves ring formation across the less substituted C−C double bond. How-

Scheme 36



(*E*)-**120** : (*Z*)-**120** : **121** = 54 : 35 : 11

Scheme 37

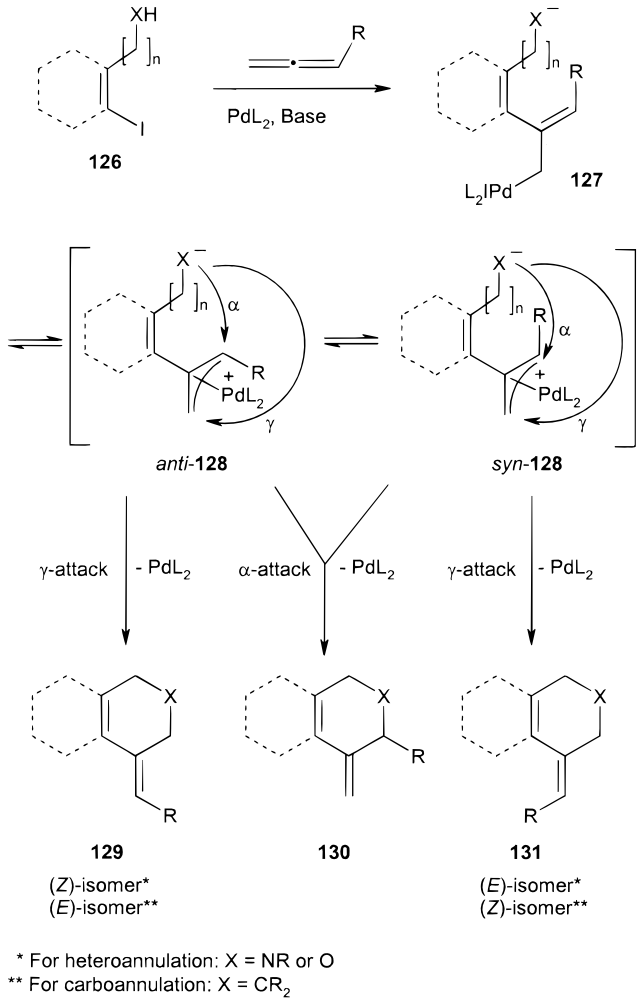


(**124** : **125** = 16 : 1)

ever, in the case of vinylic halides, no five-membered ring formation was observed. It should be mentioned that the same group very recently reported the first palladium-catalyzed asymmetric carboannulation and heteroannulation of allenes using chiral bisoxazoline ligands to afford the corresponding cyclized products with 46−88% ee.[58]

From a mechanistical point of view, the reaction proceeds through the oxidative addition of halide **126** to Pd(0) followed by addition to allene forming σ-allylpalladium species **127**. This immediately equilibrates with its *syn*- and *anti*-π-allylpalladium intermediates **128**, and subsequent intramolecular nucleophilic attack (α or γ) at the π-allyl site provides the corresponding products **129** and **130** with the regeneration of Pd(0) catalyst (Scheme 38).

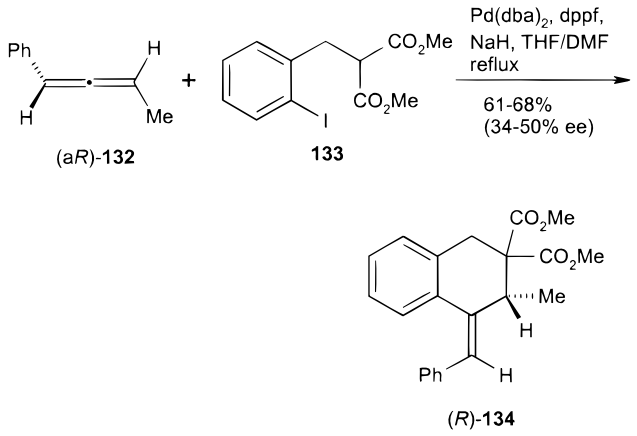
Scheme 38



Very recently, chiral allenes along with 2-halophenyl derivatives bearing nucleophilic centers have been used in the carbopalladation reaction. Starting from the allene (a*R*)-**132** and aryl iodide **133**, the cyclic product (*R*)-**134** was obtained in acceptable yields with moderate enantiomeric excesses under different conditions (Scheme 39).[59]

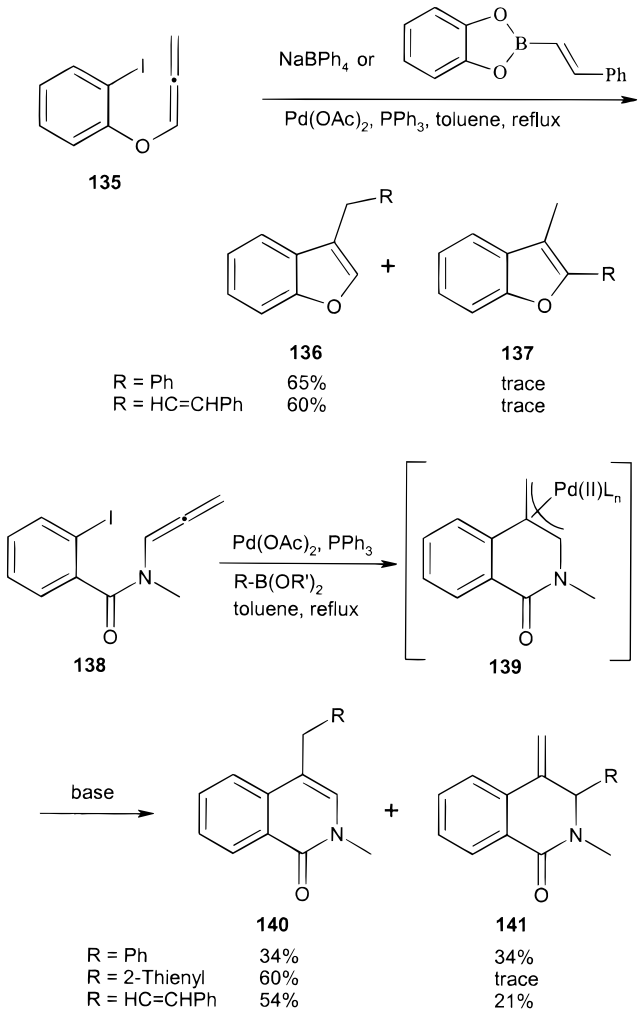
A very attractive palladium-catalyzed tandem cyclization−anion capture process was developed by Grigg and co-workers using allenes as the terminating species.[60,61] The allenes undergo monocyclizations

Scheme 39



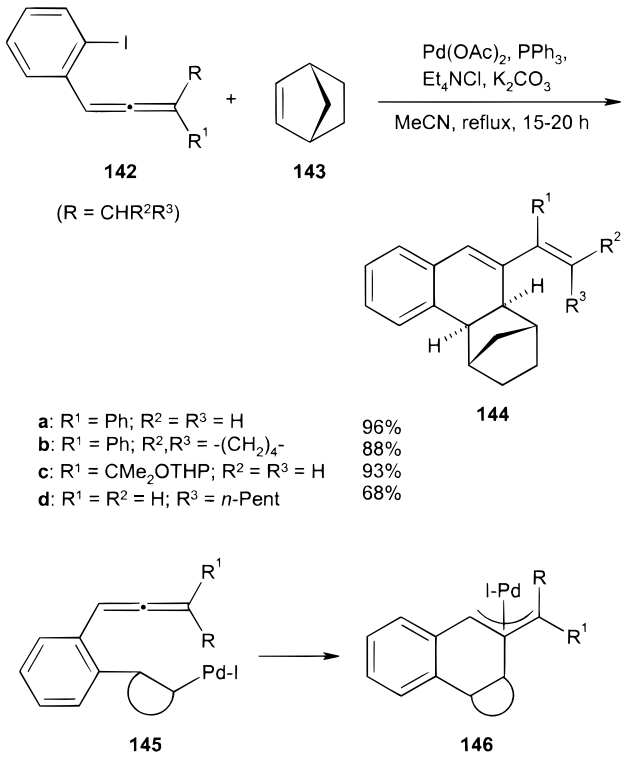
in 5-*exo*-dig or 6-*exo*-dig fashion giving five- and six-membered heterocycles as depicted in Scheme 40.

Scheme 40



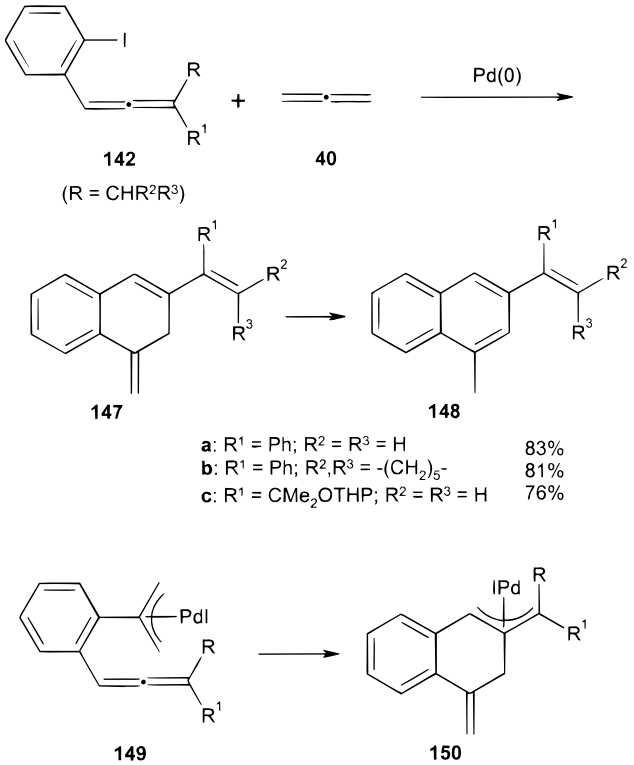
However, in a set of experiments the authors used organoboron anion transfer reagents.[62] The effect of bases such as Na_2CO_3, Ag_2CO_3, or Tl_2CO_3 were studied for boronic acids, and it was found that silver(I) and thallium(I) carbonates promote more selective formation of the product **140**. Similar aryl iodides bearing an allene segment in the *ortho*-position (e.g., **142**) have been used as 4π-components in Diels−

Scheme 41



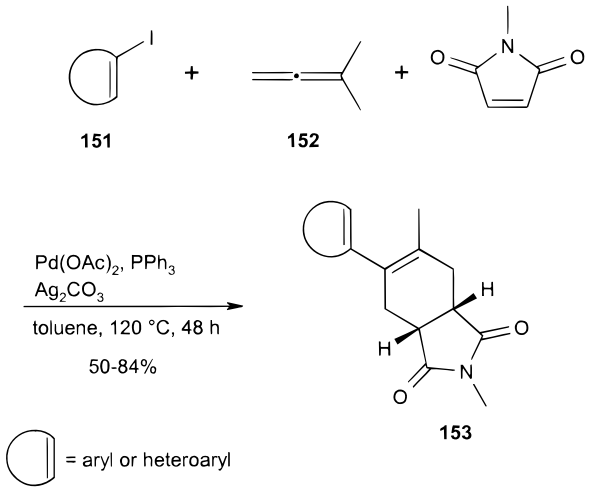
Alder reactions.[63] The reaction proceeds by the attack of the arylpalladium species **145** intramolecularly on the central carbon of the allene moiety to give intermediate **146** followed by β-hydride elimination leading to product **144** (Scheme 41). In another set of experiments, allenes were also used as 2π-components, which involves two different π-allylpalladium species **149** and **150** and an isomerization of the primary products **147**, leading to naphthalenes **148** in good yields (Scheme 42).

Scheme 42



The intermolecular version of Heck−Diels−Alder cascade process has also been reported by Grigg et al. with different aryl and heteroaryl iodides and alkylallenes giving 1,3-dienes in situ, which further underwent Diels−Alder reactions with a suitable dienophile (Scheme 43).[64] The mechanism is very similar to that of the intramolecular reaction.

Scheme 43

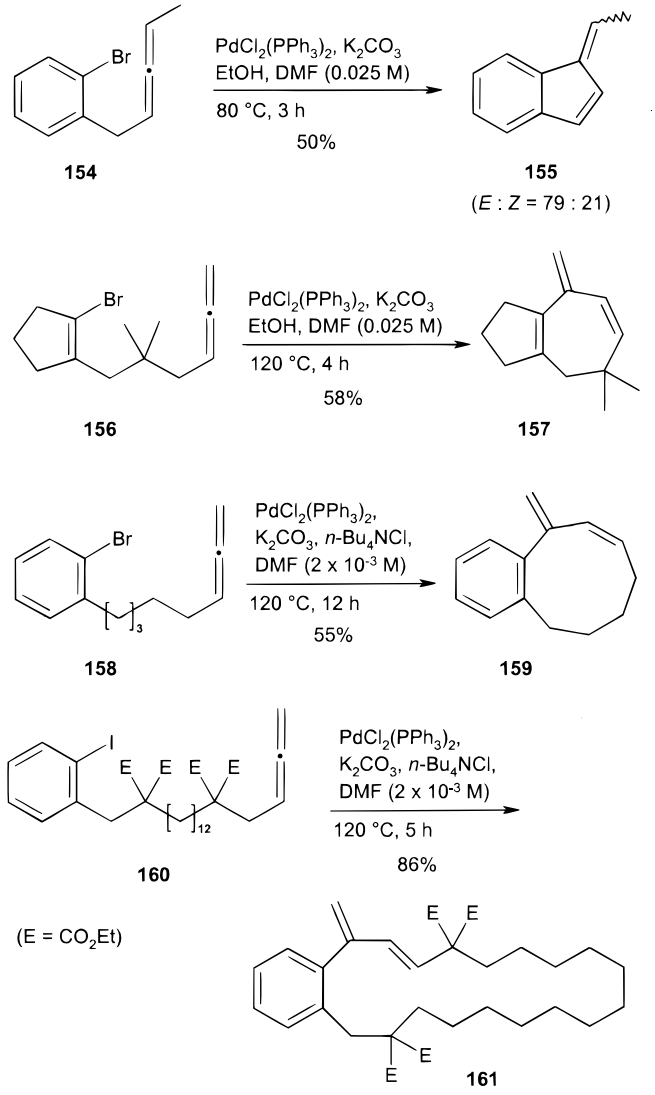


Negishi et al. utilized a similar kind of aryl and alkenyl halides for cyclic carbopalladation reactions in the presence of a catalytic amount of $PdCl_2(PPh_3)_2$ involving a carbon−carbon bond formation at the central carbon of the allenes.[65,66] Five- to twelve-membered and even twenty-membered rings were formed in moderate to good yields. They used the dilute solution technique ($(2-4) \times 10^{-3}$ M) and the addition of 1 equiv of n-Bu_4NCl for an efficient reaction to occur (Scheme 44). To compare the reactivity with alkenes and alkynes, reaction was carried out under similar conditions with substrates having both allene and alkyne or alkene functionalities. However, it was observed that allene reacts much faster than alkenes and alkynes giving the cyclized products.[66]

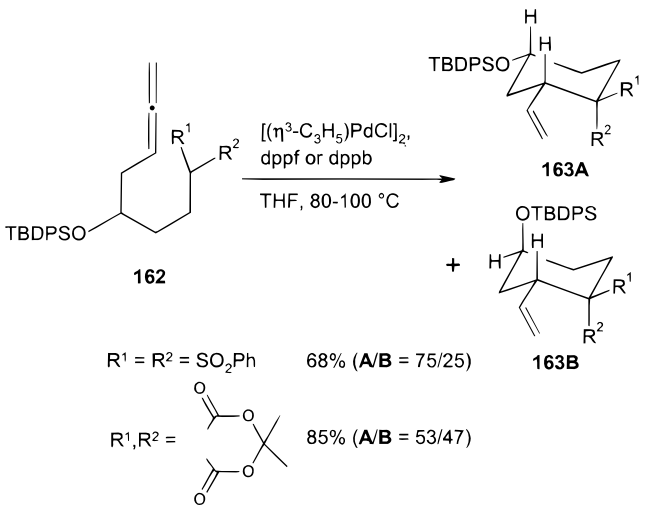
Allenes bearing meldrums acid or bis(benzenesulfonyl)methane groups cyclize in the presence of $[(\eta^3\text{-}C_3H_5)PdCl]_2$ to afford cyclic products. A six-membered ring is easily formed in the case of **162**, where a hydropalladation mechanism is strongly recommended (Scheme 45), since in the carbopalladation process a carbon−carbon bond is generally formed at the central carbon of the allene.[32] Using the same π-allylpalladium chloride dimer, Trost et al. reported the synthesis of 9- to 17-membered carbocycles, lactams, and lactones which are of synthetic interest.[67] In the case of nine-membered rings, the (*Z*)-isomer is exclusively obtained; however, a 10-membered ring is formed as a 1:1 mixture of isomers. On the other hand, in the case of larger rings, the (*E*)-isomer usually predominates, e.g., **165** ($n = 0-2$) (Scheme 46).

One of the most synthetically versatile applications, developed by Nemoto,[68] is the novel intramolecular palladium-catalyzed cascade reaction of alle-

Scheme 44

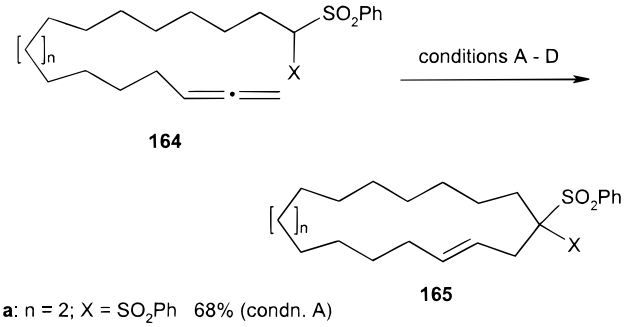


Scheme 45

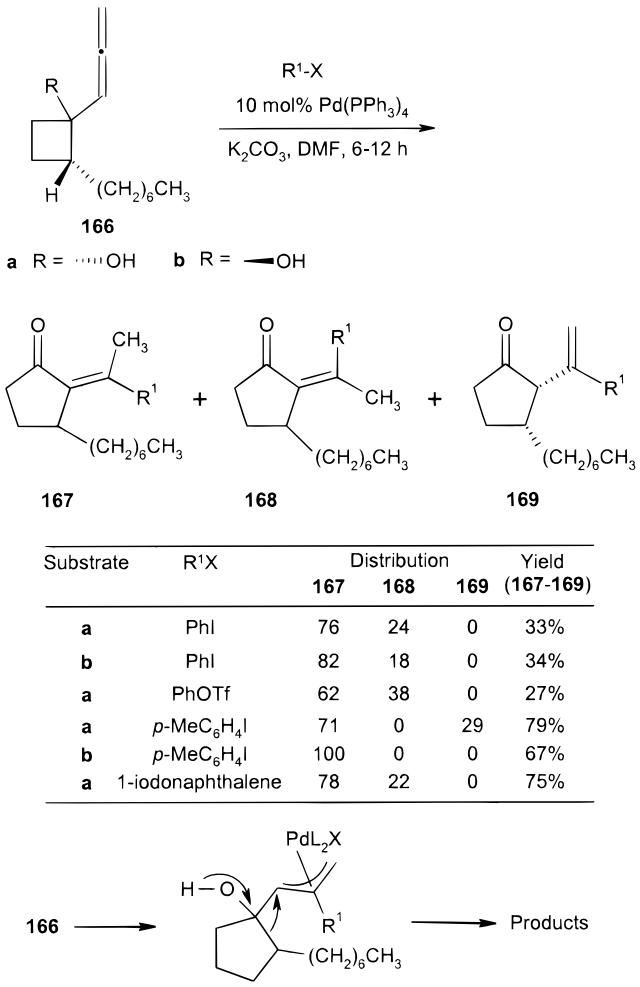


nyl cyclobutanols leading to the 5,7- and 5,8-fused ring systems which are the framework of biologically important natural products. His group first examined the intermolecular cascade reaction of allenyl cyclo-

Scheme 46



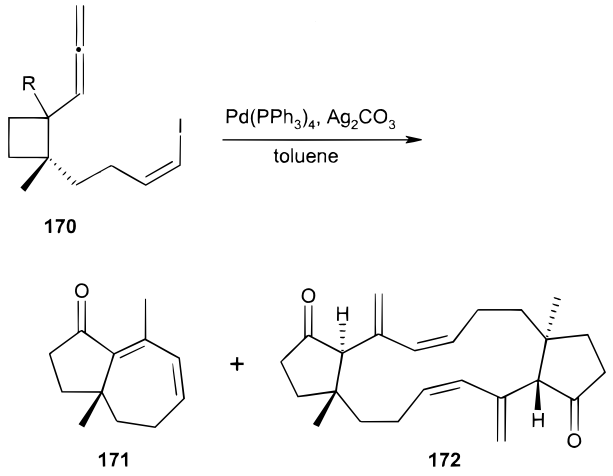
Scheme 47



Substrate	R^1X	Distribution 167	168	169	Yield (167-169)
a	PhI	76	24	0	33%
b	PhI	82	18	0	34%
a	PhOTf	62	38	0	27%
a	*p*-MeC_6H_4I	71	0	29	79%
b	*p*-MeC_6H_4I	100	0	0	67%
a	1-iodonaphthalene	78	22	0	75%

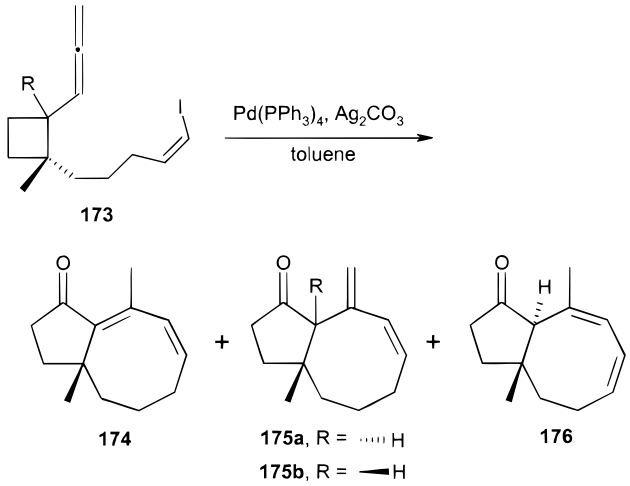
butanols **166** in the presence of $Pd(PPh_3)_4$ giving rise to β-substituted conjugated and unconjugated cyclopentenones **167**, **168**, and **169** (Scheme 47), where the relative stereochemistry of **166** effects the product distribution but not the overall yield of the reaction. Electron-donating groups present in the halide or triflate are found to give better results.

Scheme 48



R	Temp.	171	172	Yield
◄ OH	rt	--	100	80%
····OH	80 °C	100	--	67%
◄ OH	80 °C	100	--	63%

Scheme 49

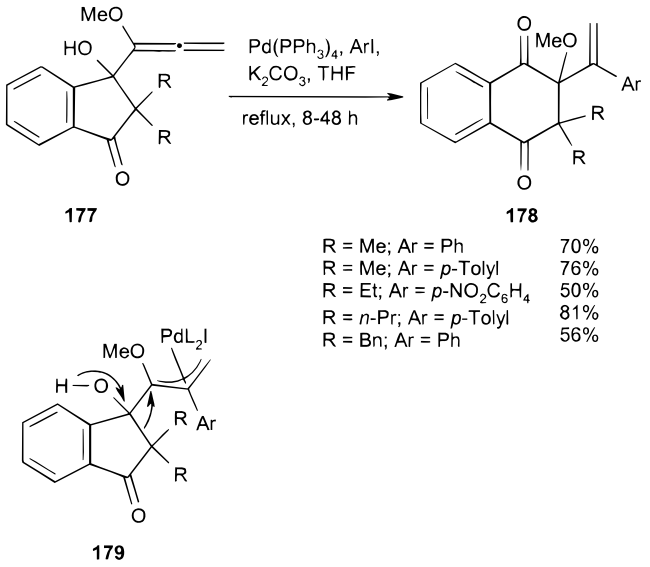


		Distribution				
R	Temp.	174	175a	175b	176	Yield
◄ OH	80 °C	25	63	8	40	60%
····OH	reflux	100	--	--	--	34%
◄ OH	reflux	62	--	--	38	53%
····OH	80 °C	--	100		--	24%

Then the methodology was applied to the ring expansion of cyclobutanols **170** and **173**, where the allene and vinyl iodide moieties are tethered by a four- and five-carbon chain resulting in the [5.3.0] and [6.3.0] ring systems in the presence of the same catalyst (Schemes 48 and 49).

Very recently, in another intramolecular tandem carbopalladation−one-atom ring expansion reaction, 4-oxo-α-tetralones **178** were synthesized from hydroxy-substituted methoxyallenyl indanones **177**.[69] The mechanism involves the formation of π-allylpalladium species **179** and subsequent ring expansion as shown in Scheme 50.

Scheme 50[a]



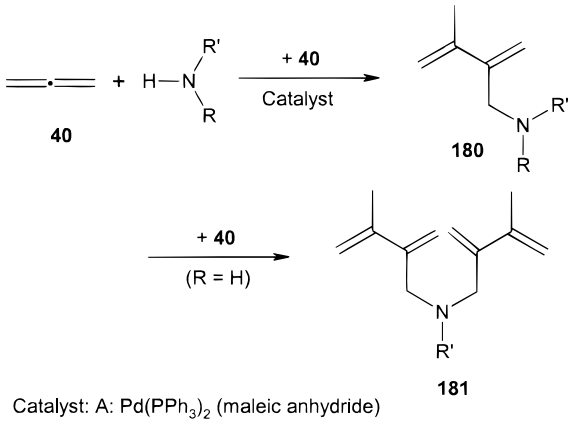
[a] Adapted with permission from ref 69a. Copyright 2000 Thieme.

III. Reactions of Allenes with Heteroatom Nucleophiles

A. Reactions with Nitrogen Nucleophiles

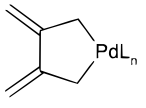
The first palladium-catalyzed intermolecular amination of allenes was reported by Coulson more than

Scheme 51



Catalyst: A: $Pd(PPh_3)_2$ (maleic anhydride)
B: $Pd(dba)_2$, 2 PPh_3

R	R'	Catalyst	180	181	Ref.
c-Hex	Et	A	84%	--	23
Me	Ph	A	62%	--	23
H	Ph	A	12%	--	23
H	H	A	23%	25%	23
H	Me	A	--	58%	23
H	Et	A	--	60%	23
-$(CH_2)_4$-		A	78%	--	23
-$(CH_2)_4$-		B	55%	--	70

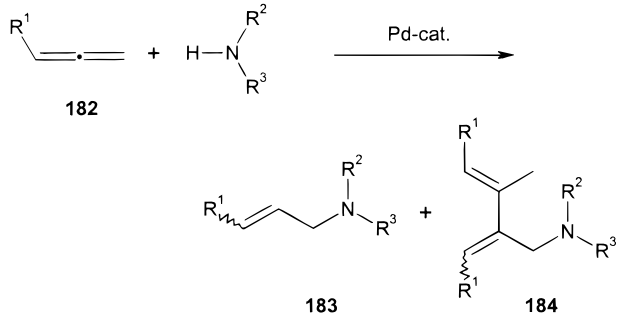


43

a quarter of a century ago.[23] The predominant products in reactions of 1,2-propadiene (**40**) and mono- or disubstituted amines are monodienylamines **180** (Scheme 51). In condensation reactions with ammonia, methylamine, or ethylamine, the formation of the bis(dienyl)amine **181** is also possible. These telomerizations of **40** proceed presumably through the palladacyclopentane species **43**.

Recently, Cazes and Yamamoto independently reported the synthesis of allylamines through palladium-catalyzed intermolecular hydroamination of monosubstituted allenes (Scheme 52). Both demonstrated the beneficial effect of adding the additives triethylammonium iodide[70] and acetic acid[71] forming a hydridopalladium species **185**, which attacks the allene forming a π-allyl species **186** and subsequent nucleophilic attack of the amine leading to the expected allylic product **183** (Scheme 53). An alternative pathway might involve an intermediate **187**, which undergoes nucleophilic addition of the amine followed by reductive elimination of Pd to give the product.[70] The palladium-catalyzed reaction has also been studied with a 1,3-disubstituted allene, but no addition of amine was obtained under the conditions described in Scheme 52.[70]

Scheme 52[a]



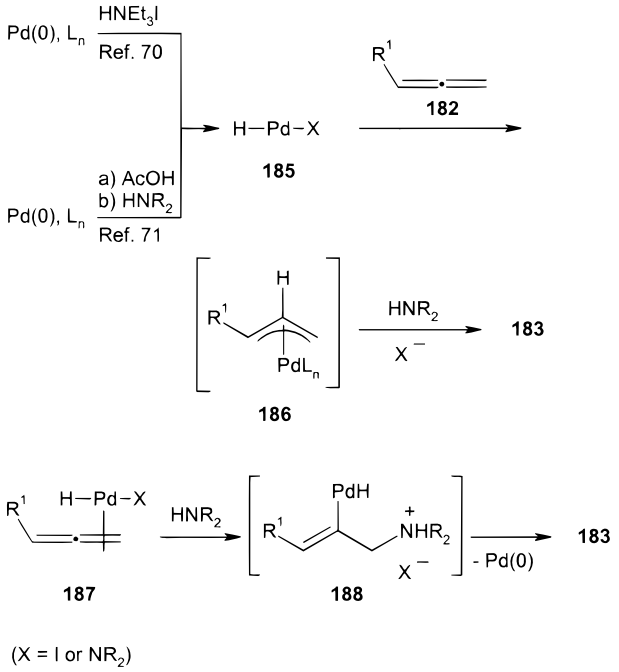
Pd-cat.: A: $Pd(dba)_2$, 2 PPh_3, NEt_3HI, THF
B: $Pd(OAc)_2$, 2 PPh_3, NEt_3HI, DMF
C: $Pd_2(dba)_3 \cdot CHCl_3$, dppf, AcOH, THF

R^1	R^2	R^3	Pd-cat.	**183** (*E*/*Z*)	**184**	Ref.
Ph	-$(CH_2)_4$-		A	89% (98:2)	--	70
n-Hept	Et	Et	A	70% (96:4)	8%	70
n-Hept	Et	Et	B	33% (61:39)	39%	70
Ph	CH_2CO_2Et	CH_2CO_2Et	C	100% (only *E*)	--	71
p-MeC_6H_4	Bn	Bn	C	99% (only *E*)	--	71
p-$F_3COC_6H_4$	Bn	Bn	C	75% (only *E*)	--	71

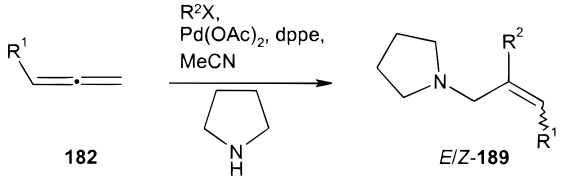
[a] Adapted with permission from ref 70. Copyright 1995 Elsevier Science.

The hydroamination reactions of allenes have been developed in the past few years. The regioselective synthesis of 2,3-disubstituted allylamines **189** by intermolecular palladium-catalyzed aminophenylation and aminoalkenylation was reported earlier by Tsuji (Scheme 54).[20] Moreover, it is worth mentioning that all amination reactions of monosubstituted allenes described above are performed with excellent γ-selectivity.

Scheme 53



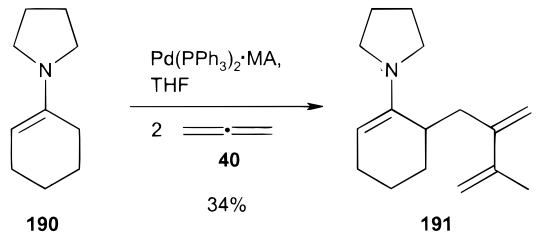
Scheme 54



R^1	R^2X	**189**
i-Bu	PhI	82%
i-Bu	PhCH=CHBr	79%
i-Bu	H_2C=CPhBr	9%
CH(OH)Ph	PhI	85%

Although tertiary amines are unreactive toward allenes, enamines presented an exception. Thus, treatment of 1-(1-cyclohexenyl)pyrrolidine (**190**) with 1,2-propadiene (**40**) in the presence of bis(triphenylphosphine)(maleic anhydride)palladium [$Pd(PPh_3)_2 \cdot$MA] led to the formation of pyrrolidine derivative **191** but in low yield (Scheme 55).[23]

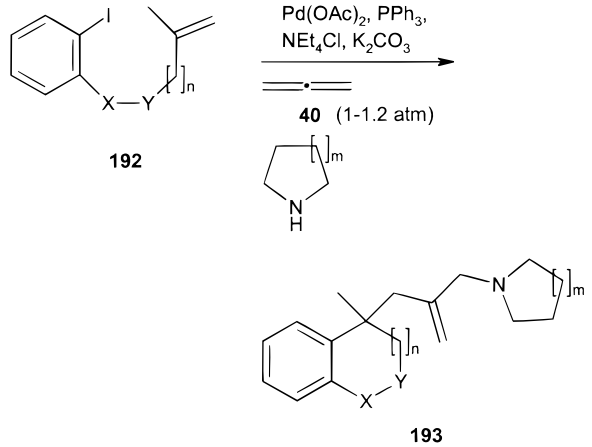
Scheme 55



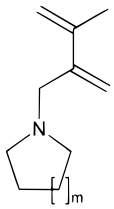
Grigg developed an extremely useful palladium-catalyzed cyclization−anion capture methodology.[60] In the mid-1990s, this powerful strategy was ex-

tended to allenes in intermolecular as well as intramolecular transformations,[72−75] which is an important development basing on Tsuji's primary investigations. The palladium-catalyzed cyclization−anion capture of aryl halides **192** bearing a methallyl moiety in the side chain resulted in the formation of heterocycles **193** as depicted in Scheme 56. When aryl

Scheme 56



X	Y	n	m (amine)	**193**
NMe	CO	0	2	82%
NTs	CH_2	0	1	72%
O	CH_2	0	1	60%
CO	NBn	1	2	50%
CH_2	O	1	2	50%

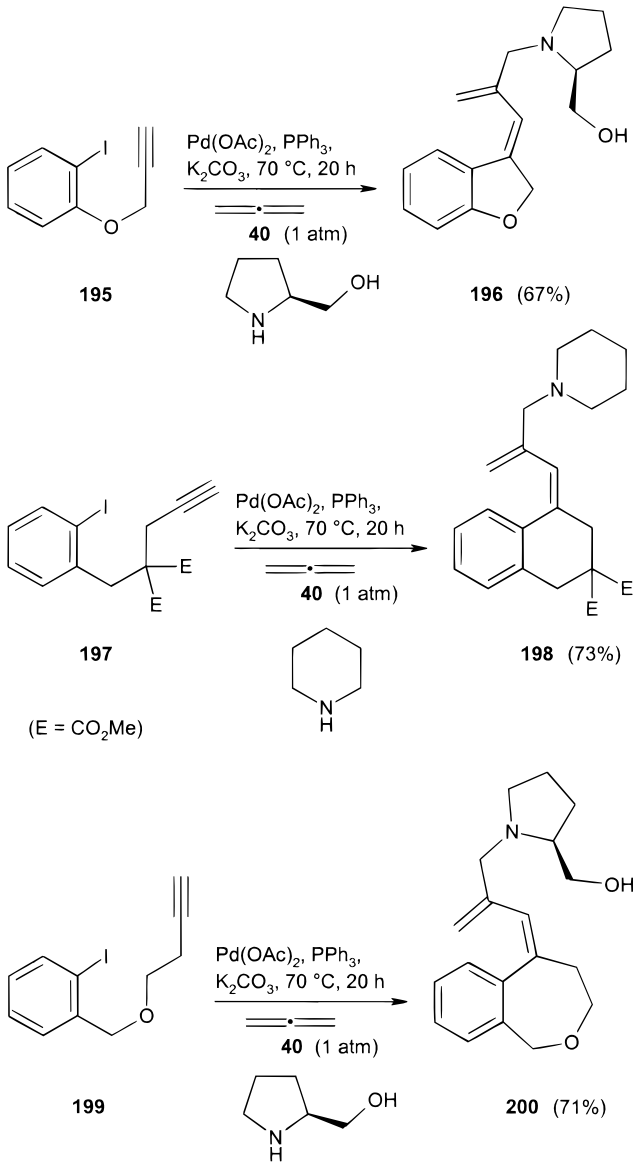


halides having a chain with a terminal C−C triple bond, e.g., **195**, **197**, and **199**, were subjected to similar reaction conditions (Scheme 57), five- to seven-membered ring compounds **196**, **198**, and **200** were isolated in respectable yields.

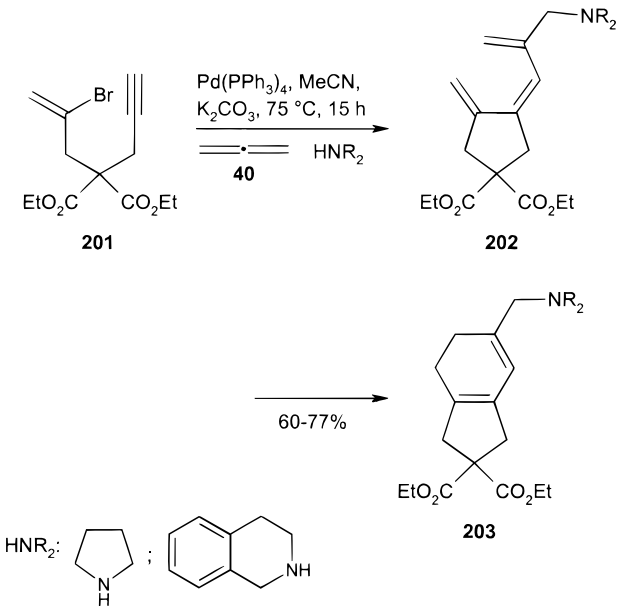
An additional application of this cyclization−anion capture route is described by the reactions of vinylic halide **201**, although the primary products **202** immediately underwent a 6π-electrocyclization reaction leading to compounds **203** (Scheme 58).[73]

In these palladium(0)-catalyzed termolecular queuing processes, the use of **40** as a reaction component showed some side reactions. The excess of secondary amine and **40** in these reactions led to the formation of telomerization products **194** (Scheme 56), which has been observed in varying amounts.[72] On the other hand, the relative rates of 5- to 7-*exo*-dig cyclizations forming five- to seven-membered carbo- and heterocycles under 1 atm pressure of **40** are substantially faster compared with the rate of aryl (or vinylic) insertion of **40** (Scheme 59). Indeed, an exception has been observed only by the formation of the eight-

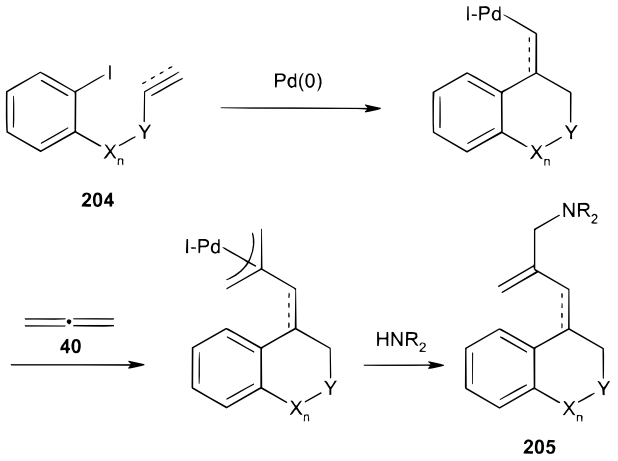
Scheme 57



Scheme 58

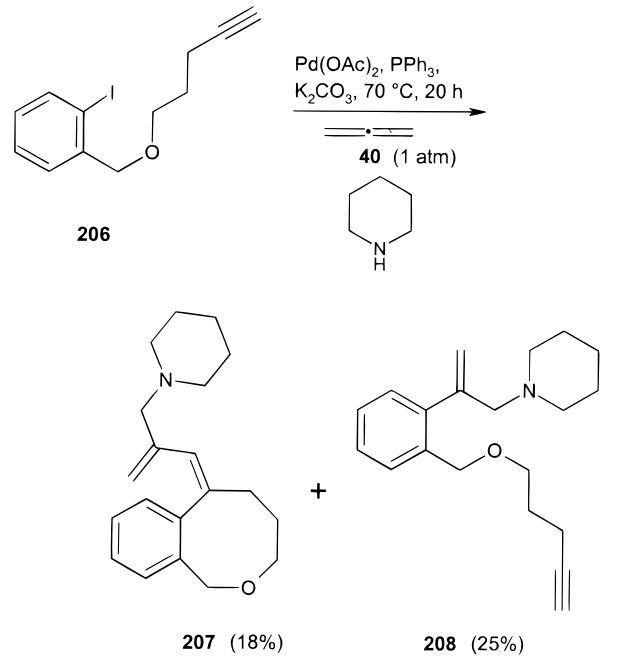


Scheme 59



membered ring **207**, where both reaction rates are comparable. This reaction led to compound **207** together with the direct capture product **208** with less chemoselectivity (Scheme 60).[73] Contrary to the 6-*exo*-

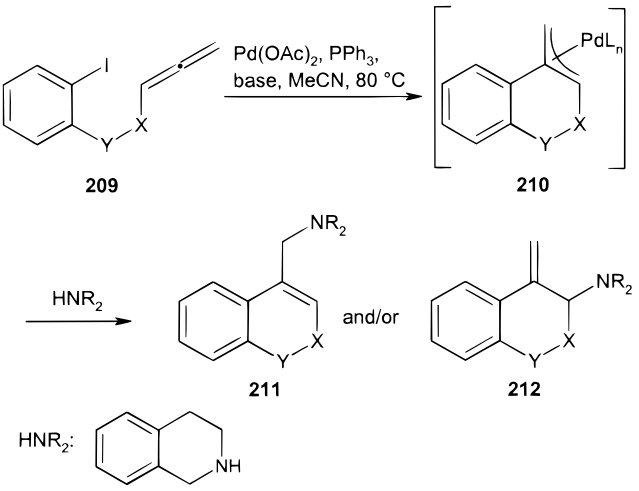
Scheme 60



dig process, the competitive direct allenylation−amine capture was also observed in a similar 6-*exo*-trig cyclization.[72]

The same research group has further reported the efficient intramolecular palladium-catalyzed cyclization of aryl iodides bearing an allene moiety followed by capture of nitrogen nucleophiles. After the palladium-catalyzed cyclization of **209**, the resulting π-allylpalladium species **210** offers two possibilities for the attack of the amine in the subsequent amination reaction leading to the formation of the regioisomers **211** or/and **212** (Scheme 61). The choice of the inorganic base (K_2CO_3 or Ag_2CO_3), steric effects (part Y in **209**), and the nature of the adjacent heteroatom X have a considerable impact on the regioselectivity.[74] In a related investigation, the sequential reaction of aryl halides **213** afforded the

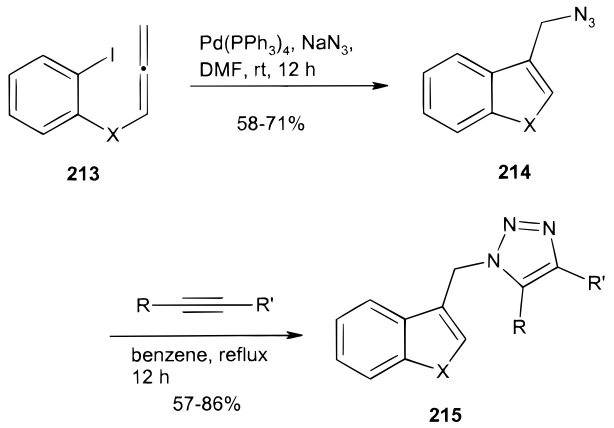
Scheme 61



X	Y	Base	211	212
NTs	CH_2	Ag_2CO_3	47%	12%
NTs	CH_2	K_2CO_3	91%	--
NTs	CHMe	K_2CO_3	96%	--
O	CH_2	K_2CO_3	36%	--
O	CH_2	Ag_2CO_3	--	88%
O	CHMe	Ag_2CO_3	--	78%
O	--	Ag_2CO_3	--	83%
O	--	K_2CO_3	71%	--

azides **214** after the attack of sodium azide (Scheme 62).[75] Notably, upon treatment with electron-deficient

Scheme 62[a]

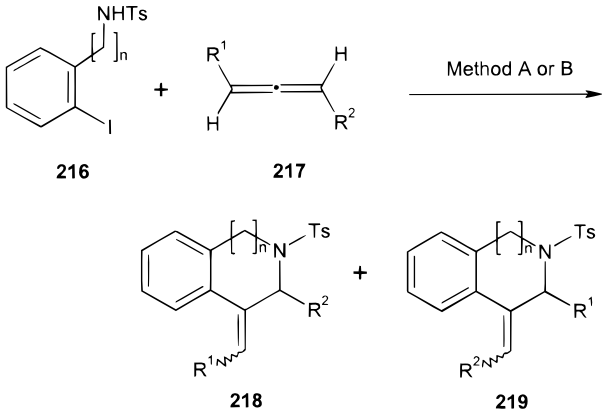


[a] Adapted with permission from ref 75. Copyright 1998 Elsevier Science.

alkynes, the azides **214** can be converted into the corresponding triazole derivatives **215**.

Annulation processes have found numerous applications in organic synthesis;[76] in particular, palladium-catalyzed annulation reactions are effectively employed for the preparation of carbo- and heterocycles.[77] The elegant general method for the regioselective heteroannulation of allenes employing functionally substituted aryl halides and vinylic halides has been subjected to detailed scrutiny by Larock and

Scheme 63



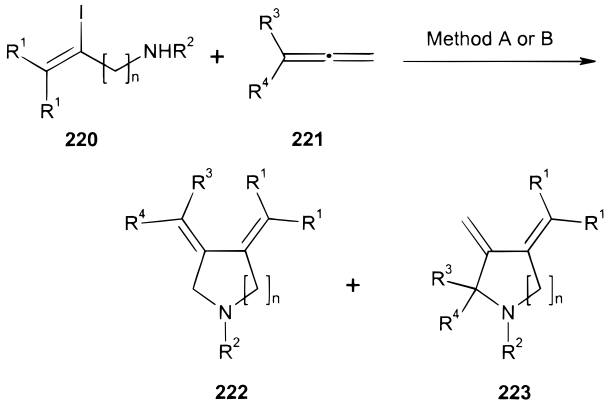
n	R^1	R^2	Method	**218** (*E*/*Z*)	**219**	Ref.
1	*n*-Oct	H	A	49% (36:64)	38%	56
2	Ph	H	B	54% (78:22)	--	78
2	*n*-Pr	*n*-Pr	B	94% (93:7)	--	78
3	Ph	H	B	94% (92:8)	--	78
3	*n*-Oct	H	B	73% (62:38)	--	78
4	Ph	H	B	83% (86:14)	--	78
0	*n*-Oct	H	A	--	85%	56
0	OMe	H	C	--	75%	79
0	$PO(Ot\text{-}Bu)_2$	H	D	80% (70:30)	--	79

Method A: $Pd(OAc)_2$, PPh_3, *n*-Bu_4NCl, Na_2CO_3, DMF
Method B: $Pd(dba)_2$, PPh_3, Na_2CO_3, *n*-Bu_4NCl, DMA
Method C: $Pd(OAc)_2$, PPh_3, $BnEt_3NCl$, Na_2CO_3, DMF
Method D: $PdCl_2(PPh_3)_2$, $BnEt_3NCl$, Na_2CO_3, MeCN

co-workers. Similar to the described carbocyclic compounds prepared by carboannulations of allenes (see section II), a wide variety of five- to eight-membered nitrogen rings have been formed by palladium-catalyzed heteroannulations of various substituted allenes using amide- and amine-containing aryl and vinylic halides (Schemes 63−66).[56,57,78] The reactions in Schemes 64−66 show that the heteroannulation allows the formation of products with an exocyclic or endocyclic C−C double bond depending on the position of the iodo substituent in the vinylic precursors **220**, **224**, and **227**.

The formation of five- to seven-membered rings proceeds quite efficiently, while larger ring closures are more difficult to achieve. For example, starting from aryl iodides, the synthesis of eight-membered rings are also achieved by this palladium-catalyzed annulation process, whereas attempts to generate this ring size by employing vinylic iodides failed. However, only one example using vinylic iodide is known, which gave trace amounts of the expected heterocycle (Scheme 64).[78] More complicated is the synthesis of larger nitrogen heterocycles. Only one example of the formation of a nine-membered arene-containing heterocycle was performed successfully (Scheme 63).[78] So far, the preparation of ring sizes more than nine failed completely. In all palladium-catalyzed heteroannulations of allenes, the best results were obtained by applying the optimized reaction conditions mentioned in Schemes 63−67. It was found that aryl iodides are more efficient than vinylic iodides and tosylamides are better than

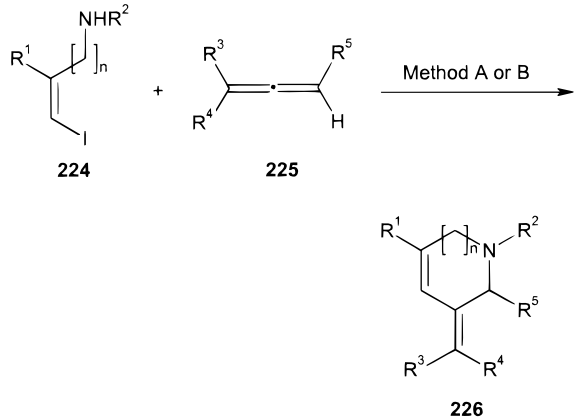
Scheme 64



n	R^1	R^2	R^3	R^4	Method	**222** (*E*/*Z*)	**223**	Ref.
1	Me	Ts	*n*-Oct	H	A	12% (only E)	72%	57
1	H	Ts	*n*-Oct	H	A	4% (only E)	30%	57
3	H	*n*-Bu	Ph	H	B	80% (55:45)	--	78
3	H	*n*-Bu	*n*-Oct	H	B	65% (21:79)	--	78
3	H	Ts	$-(CH_2)_5-$		B	71%	--	78
3	H	Ts	Ph	H	B	91% (67:33)	--	78
3	H	Ts	*n*-Oct	H	B	51% (37:63)	--	78
4	H	Ts	Ph	H	B	trace	--	78
9	H	*n*-Bu	Ph	H	B	--	--	78

Method A: $Pd(OAc)_2$, PPh_3, *n*-Bu_4NCl, Na_2CO_3, DMF
Method B: $Pd(dba)_2$, PPh_3, Na_2CO_3, *n*-Bu_4NCl, DMA

Scheme 65

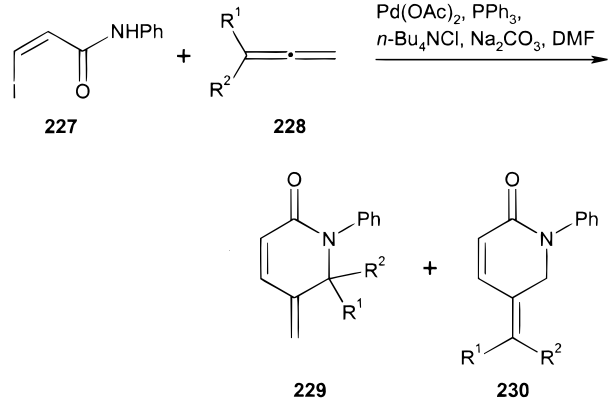


n	R^1	R^2	R^3	R^4	R^5	Method	**226** (*E*/*Z*)	Ref.
1	Me	*n*-Bu	*n*-Pr	H	*n*-Pr	A	65%	57
1	Me	Ph	*n*-Pr	H	*n*-Pr	A	89%	57
1	Me	Ph	$-(CH_2)_5-$		H	A	72%	57
2	H	*n*-Bu	Ph	H	H	B	83% (64:36)	78
2	H	*n*-Bu	*n*-Oct	H	H	B	85% (70:30)	78
2	H	*n*-Bu	$-(CH_2)_5-$		H	B	23%	78

Method A: $Pd(OAc)_2$, PPh_3, *n*-Bu_4NCl, Na_2CO_3, DMF
Method B: $Pd(dba)_2$, PPh_3, Na_2CO_3, *n*-Bu_4NCl, DMA

amines in this reaction. By choosing the right reaction conditions, a wide range of nitrogen heterocycles were synthesized in a regiochemically predictable way. The regioselectivity is highly dependent on the size of the ring being formed and the nature of the functional groups. The annulation afforded predomi-

Scheme 66

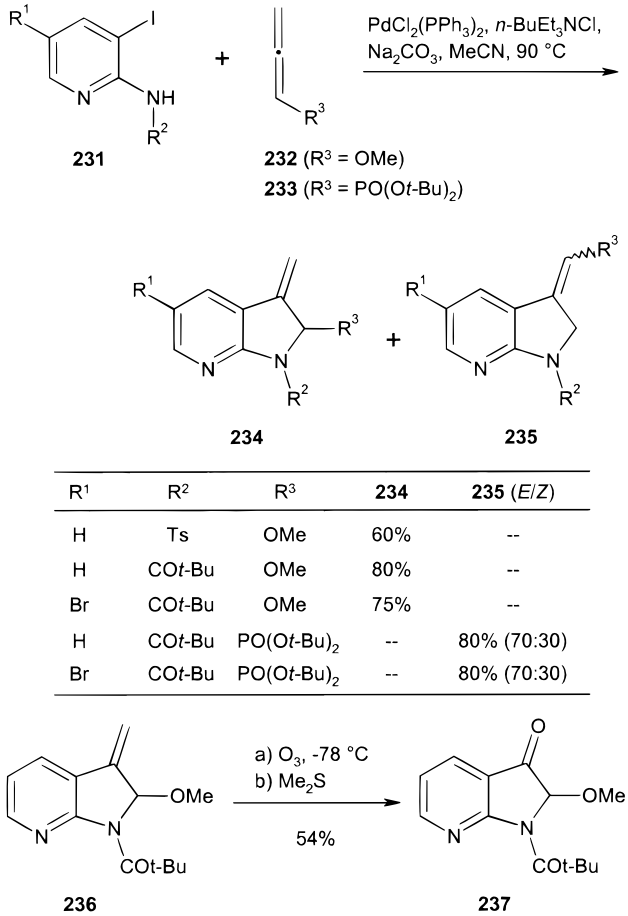


R^1-R^2 = -$(CH_2)_5$- : 93% yield; **229** : **230** = 90 : 10

R^1 = Et; R^2 = H : 77% yield; **229** : **230** = 91 : 9

nantly or exclusively the products by the attack at the more substituted end of the allene when a five-membered ring was formed.[56,57] On the other hand, six-, seven-, and eight-membered nitrogen rings are generally formed by annulation primarily across the less substituted C−C double bond.[57,78] The (*E*/*Z*)-selectivity in the formation of products **218**, **222**, **226**, and **235** is generally moderate with only a few exceptions. Similar to the related carboannulation in section II, the formation of mixtures of (*E*/*Z*)-isomers is presumably due to the generation of *syn*- and *anti*-π-allylpalladium species (Scheme 38, X = NR).

Scheme 67

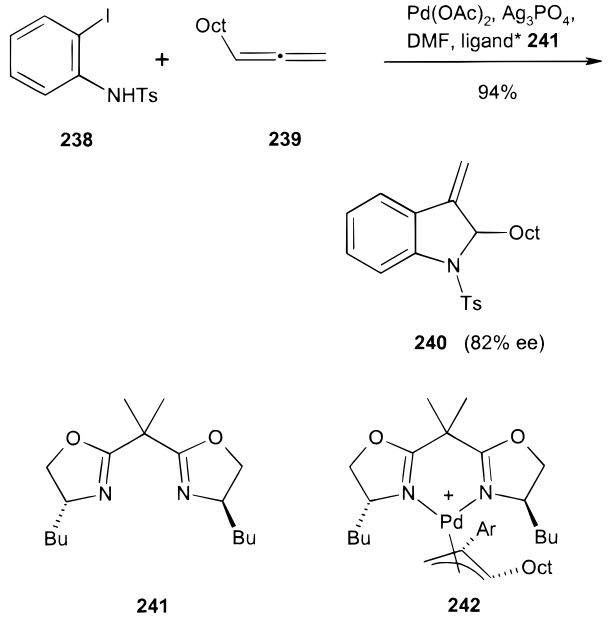


R^1	R^2	R^3	**234**	**235** (*E*/*Z*)
H	Ts	OMe	60%	--
H	COt-Bu	OMe	80%	--
Br	COt-Bu	OMe	75%	--
H	COt-Bu	PO(Ot-Bu)$_2$	--	80% (70:30)
Br	COt-Bu	PO(Ot-Bu)$_2$	--	80% (70:30)

Recently, Mérour and Desarbre described a very useful synthetic application of the palladium-catalyzed annulation process for the preparation of 7-aza-indolinones **234** and **235** (Scheme 67).[79] The subsequent treatment of the primary products, e.g., the methoxyallene derived heterocycle **236**, by ozone and dimethyl sulfide afforded versatile intermediates for the synthesis of azaindolic compounds.

Most of the work in palladium-catalyzed reactions of allenes was focused on the developments of racemic compounds. Very little work has been done on the development of enantioselective palladium-catalyzed reactions of allenes. To date there have been very few contributions in the literature dealing with this subject available. One of them is the enantioselective, palladium-catalyzed annulation of allenes using bis-oxazoline ligand **241**. The reaction of allene **239** and aryl iodide **238**, for example, led to indole derivative **240** in good enantioselectivity (Scheme 68).[58] The

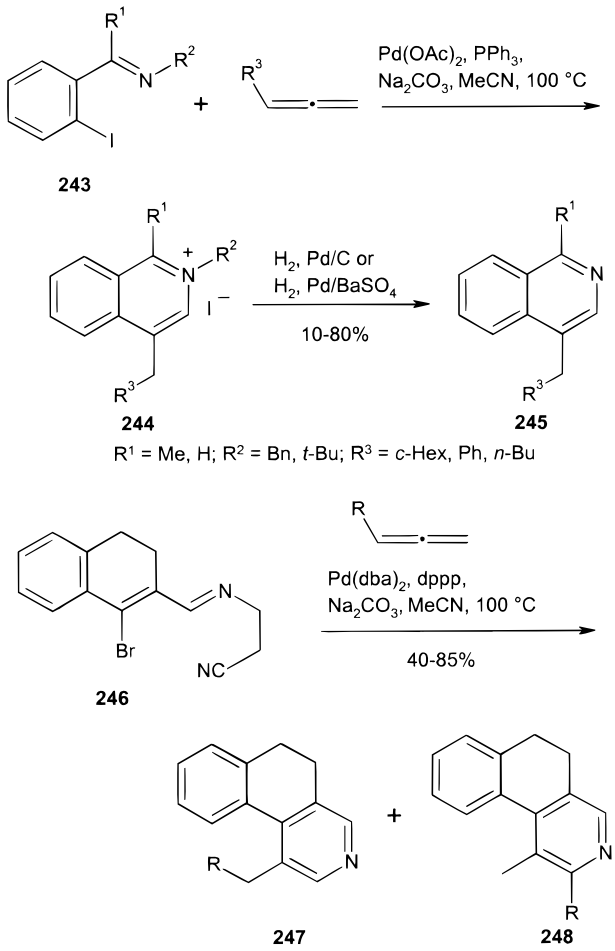
Scheme 68



formation of a 16-electron Pd intermediate is allowed by the presence of silver(I) salt to remove the iodide, which is an important prerequisite for the coordination of the bidentate bisoxazoline ligand **241** and the subsequent generation of the species **242**.

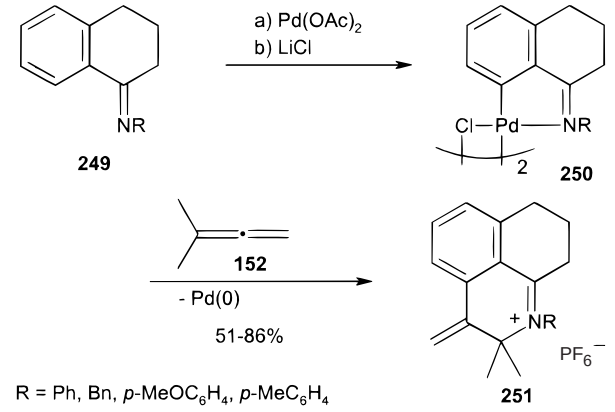
The nitrogen annulation is not confined to amines and amides only; other nitrogen compounds are also useful nucleophiles in the palladium-mediated ring-closure reactions. Recently, Frühauf described the synthesis of nitrogen heterocycles by an intramolecular palladium-catalyzed iminoannulation of aldimines and ketimines with monosubstituted allenes (Scheme 69).[80] The reactions of *N*-*tert*-butyl- and *N*-benzyl-substituted imines **243** gave the iminium salts **244** in excellent yields, but the subsequent removal of the nitrogen protecting group was, in general, less effective. In contrast, it has been observed that when the imines have a more removable nitrogen substituent, e.g., the β-alkylnitrile-substituted imine **246**, the ring closure afforded the desired heterocycles in good to excellent yields. Unfortunately, the latter reactions often gave less or no regioselectivity.

Scheme 69



Stoichiometric amounts of $Pd(OAc)_2$ are necessary to form the cyclopalladated complex **250**[81] starting from the corresponding α-tetralone ketimine **249** (Scheme 70). The insertion of 1,1-dimethylallene

Scheme 70[a]

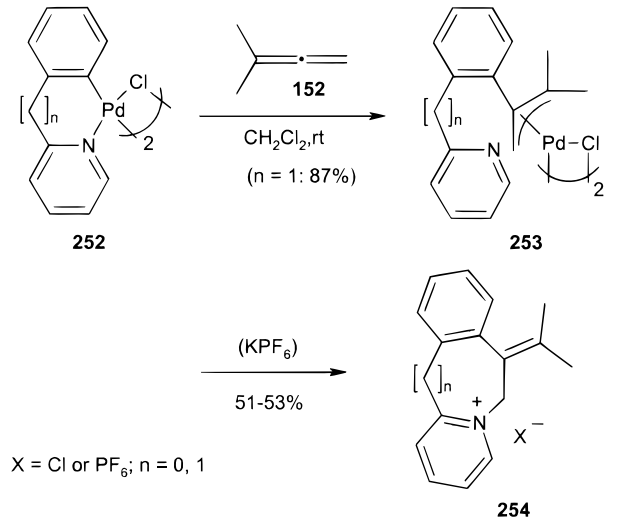


[a] Adapted with permission from ref 82. Copyright 1998 Elsevier Science.

(**152**) into the σ-Pd−C bond of **250**[18] and subsequent intramolecular ring closure led to the formation of iminium salts **251**.[82]

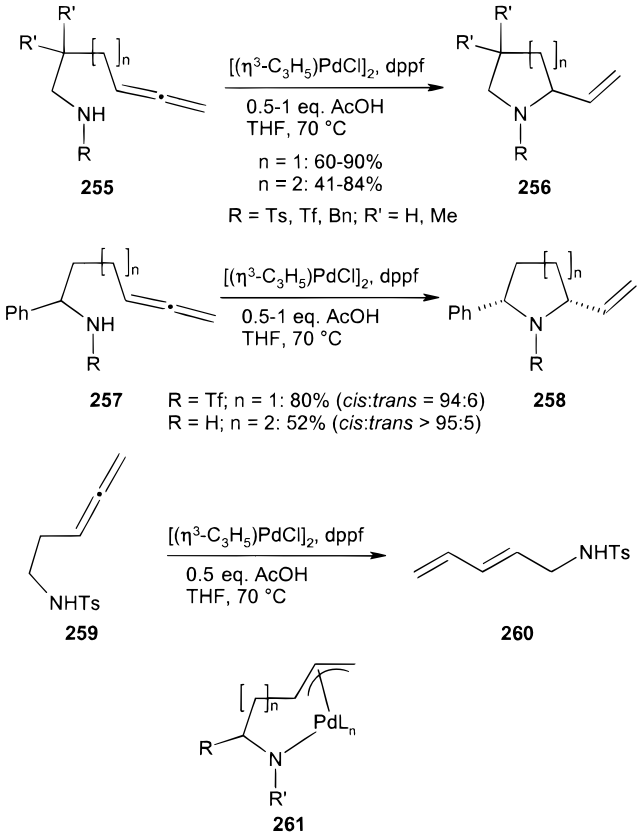
An interesting pyridinoannulation was disclosed by Pfeffer when cyclopalladated precursors **252** were treated with the allene **152**; the desired pyridinium derivatives **254** were formed via η^3-allylpalladium complexes **253** (Scheme 71).[83] Intermediate **252** was formed using stoichiometric amounts of Pd salt.

Scheme 71



Allenes bearing a nitrogen functionality as pronucleophile[14] are extremely useful precursors for intramolecular palladium-catalyzed reactions. The development of these cyclizations by several research groups led to a variety of syntheses of, in part highly

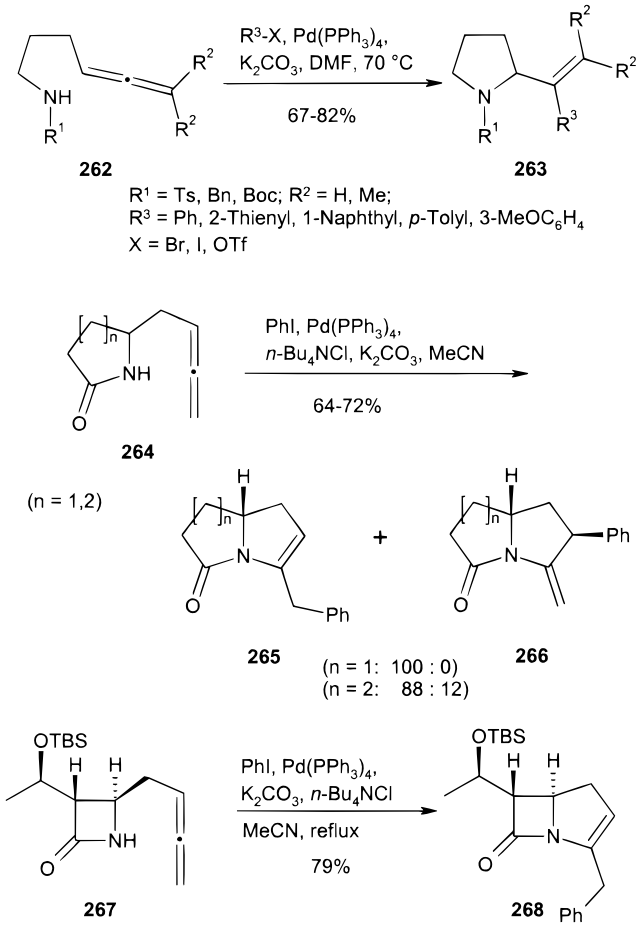
Scheme 72[a]



[a] Adapted with permission from ref 84. Copyright 1998 Elsevier Science.

substituted, 3- to 10-membered nitrogen heterocycles. In a continuation of their work on intermolecular hydroaminations and intramolecular hydrocarbonations (see section II), Yamamoto et al. recently developed a new type of intramolecular hydroamination.[84] As shown in Scheme 72, aminoallenes **255** and **257** react smoothly in a 5-*exo*-trig or 6-*exo*-trig cyclization to afford the corresponding vinyl-substituted heterocycles **256** and **258**, respectively. Similar exposure of **259** to $[(\eta^3\text{-}C_3H_5)PdCl]_2$/dppf and acetic acid did not undergo 6-*endo*-trig cyclization; instead, the unexpected 1,3-diene **260** was formed. It is worth mentioning here that the hydroamination in the absence of acetic acid was very sluggish. The nitrogen-protecting group in the aminoallenes plays an important role. The use of *N*-triflyl-, *N*-tosyl-, or *N*-benzyl-substituted allenylamines appears to be desirable for this type of hydroamination, because the cyclization of aminoallenes with other nitrogen-protecting groups failed. It is presumed that the hydroamination proceeds through the insertion of a Pd−H bond into the allenic double bond, resulting in the formation of intermediate **261** (Scheme 72).

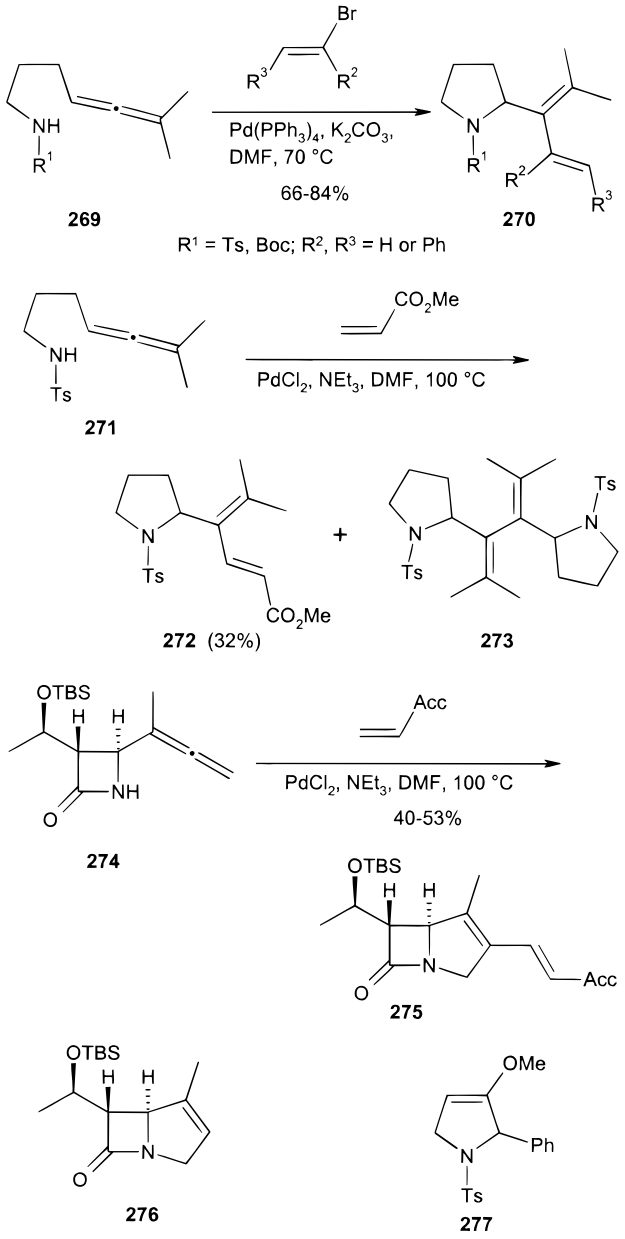
Scheme 73



Contrary to this single contribution concerning intramolecular hydroamination of aminoallenes, more research activities have been executed with palladium-catalyzed carboaminations of tethered aminoallenes. Gallagher et al. showed that the reaction of γ-amino-substituted allenes **262** and aryl halides or triflates in the presence of $Pd(PPh_3)_4$ and base leads to the formation of vinyl-substituted pyrrolidines **263**.[85] Replacing the CH_2NR unit with an amido group, e.g., the lactams **264** and **267**, provided a route to pyrrolidinones **265**/**266** ($n = 1$), indolizidinones **265**/**266** ($n = 2$), and azetidinones **268** (Scheme 73).[86] The latter palladium-catalyzed reactions represent the first examples of a nitrogen attack at the central sp carbon atom of the allene moiety. This reaction type was also extended recently on enantiopure allenic lactams.[87] Unfortunately, the application of this unprecedented type of palladium-catalyzed intermolecular coupling−intramolecular cyclization sequence is limited to aryl iodides; the extension of this methodology to vinylic halides however failed.

Some alkenylation reactions of N-substituted allenes **269** with 1- and 2-bromostyrenes have also been investigated (Scheme 74). Analogous to the arylation,

Scheme 74

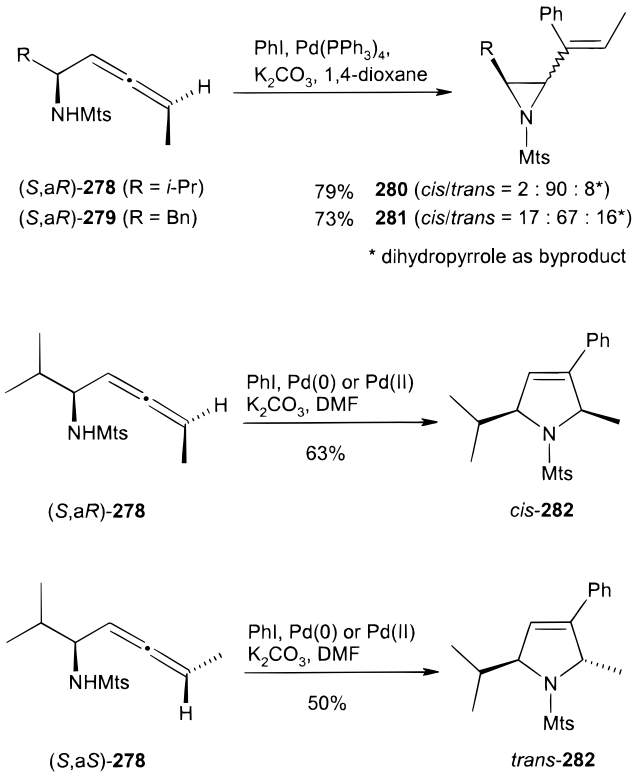


the alkenylation also proceeded smoothly in the presence of $Pd(PPh_3)_4$ and gave the 1,3-diene **270**. However, the tandem palladium(II)-mediated cycliza-

tion−Heck reaction of **271** with methyl acrylate gave the 1,3-diene **272** in low yield accompanied by dimeric product **273** formed in a competing reaction. This competing side reaction cannot be suppressed efficiently.[85] Similar tandem processes of this cyclization type have been applied by Liebeskind and Prasad to synthesize substituted carbapenems **275**.[88] However, in this cyclization, a stoichiometric amount of Pd(II) compound is necessary. Treatment of **274** with Pd(II) reagents in the absence of an alkenyl component gave only traces of the Δ^1-carbapenem **276**. More successful was a similar palladium-catalyzed cyclization of a methoxyallene derivative, which formed the dihydropyrrole **277**.[89]

In a recent report, the first palladium-catalyzed aziridination reaction of aminoallenes was described.[90] Herein the aziridine derivatives were formed in good yields in the presence of $Pd(PPh_3)_4$ or $Pd(OAc)_2/PPh_3$ and 1,4-dioxane as solvent (Scheme 75). On the other

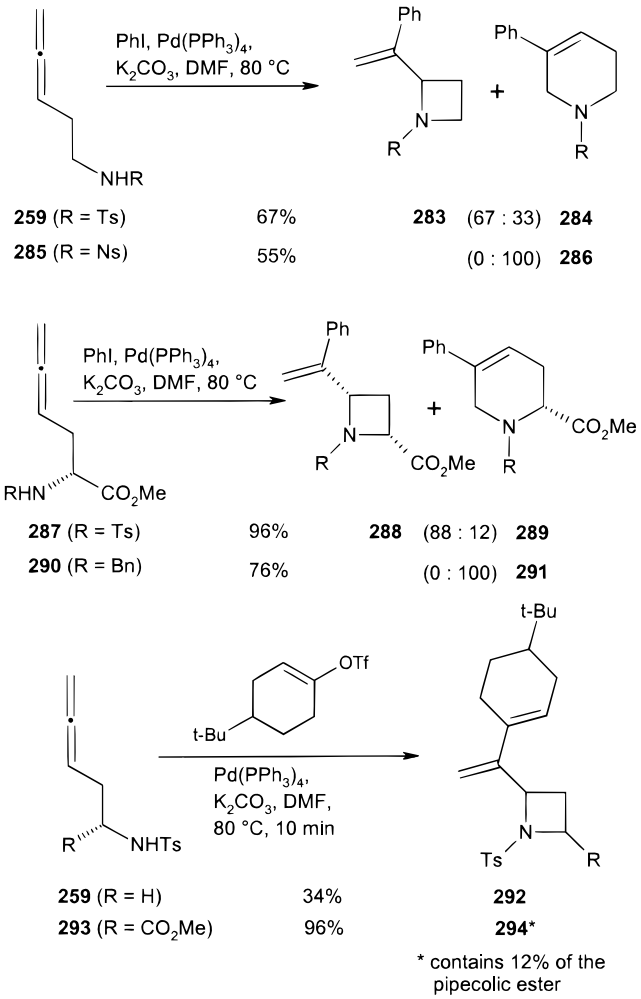
Scheme 75



hand, when the same palladium-catalyzed cyclization was carried out in DMF, the corresponding dihydropyrrole derivative was obtained as the sole product. This investigation demonstrates that the subtle choice of the solvent for the palladium-catalyzed reaction may be crucial.

Very recently, Rutjes, Hiemstra, and co-workers investigated the scope of palladium-catalyzed cyclization of allenyl-substituted amines and α-amino esters leading selectively to azetidines and tetrahydropyridines.[91] In contrast to the attempt to cyclize the unsubstituted β-aminoallene **259** under hydroamination conditions[84] (Scheme 72), palladium-catalyzed cyclization in the presence of benzyliodide was successful and gave a 2:1 mixture of vinyl-substituted azetidine **283** and tetrahydropyridine **284** (Scheme

Scheme 76

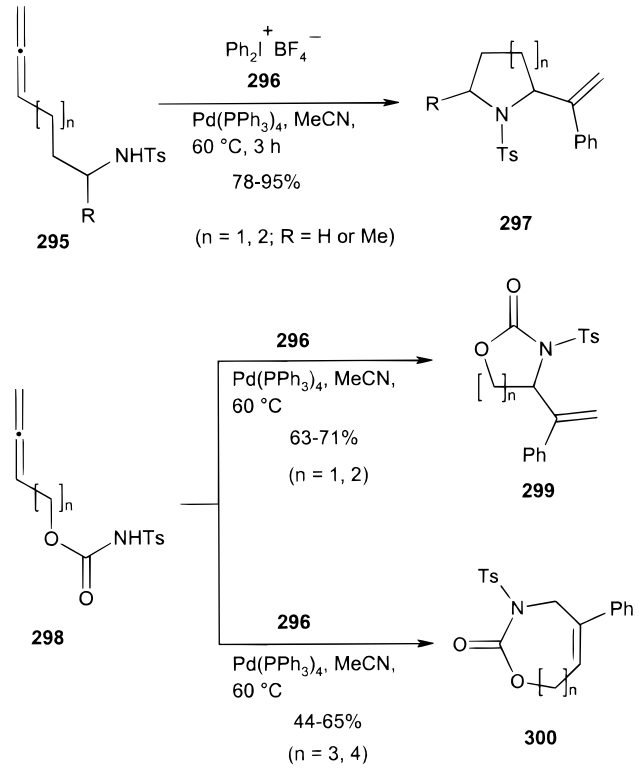


76). Notably, the exchange of the nitrogen-protecting group by *p*-nitrobenzenesulfonyl (Ns) provided exclusively the six-membered heterocycle **286**. Furthermore, when enantiopure allenyl-substituted α-amino esters, e.g., **287** and **290**, were subjected to identical reaction conditions, a similar reaction behavior was observed leading to the formation of azetidine derivative *cis*-**288** and pipecolic esters **289** and **291**, respectively. It was demonstrated that the alkenylation-cyclization sequence employing alkenyltriflates provided the kinetic products (e.g., **292** and **294**, respectively), in a 4-*exo*-trig fashion. The remarkably short reaction time indicates the acceleration of the palladium-catalyzed reaction by triflates. It should be mentioned that a similar palladium-catalyzed procedure using *N*-[2,4,6-trimethylbenzenesulfonyl] (Mts)-substituted β-aminoallenes provided most predominantly the 2,4-*cis*-disubstituted azetidines.[92]

Some other variants of palladium-catalyzed intermolecular coupling−intramolecular cyclization processes have been also developed. One of them is the palladium-catalyzed coupling of allenyl-substituted nitrogen compounds with hypervalent iodonium salts (Schemes 77 and 78).[93,94] Compared to similar palladium-catalyzed coupling-cyclization reactions of allenes, as described above, this procedure used only a slight excess of the aryl component (1.2 equiv) and the reaction works well at lower temperature and shorter reaction times. Although this method shows

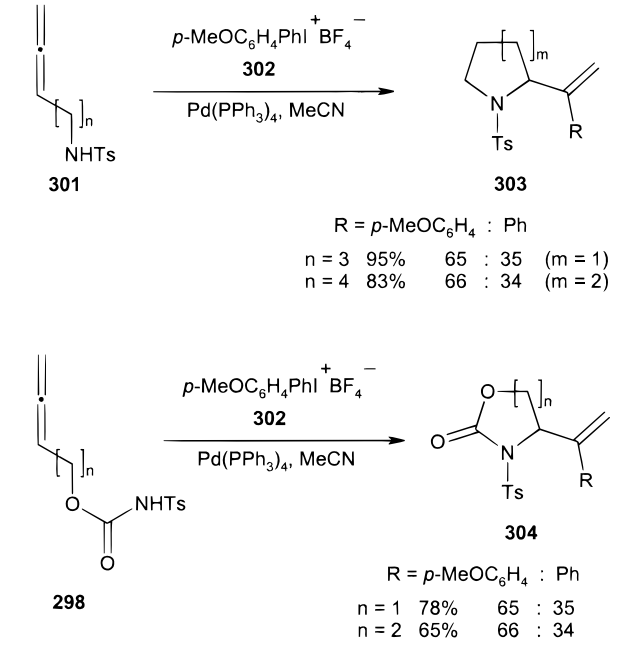
some advantages, the application of hypervalent iodonium salts is restricted to aromatic compounds. Similar application of the reagent **296** on the coupling-cyclization reaction of allenyl *N*-tosylcarbamates, e.g. **298**, afforded oxazolinones **299** ($n = 1$), 1,3-oxazin-2-ones **299** ($n = 2$), and higher membered 1,3-*N*,*O*-heterocycles **300** (Scheme 77).[94] However, the use of

Scheme 77



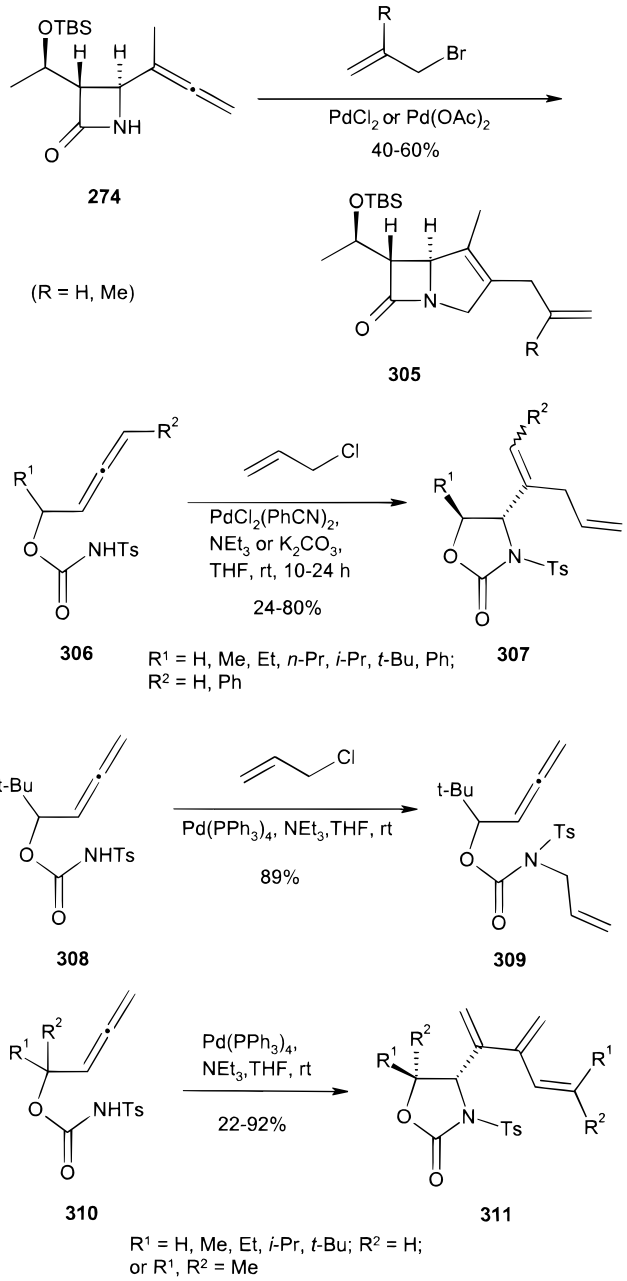
phenyl(*p*-methoxyphenyl)-iodonium tetrafluoroborate (**302**) as the aryl reagent caused a mixture of *p*-methoxyphenyl- and phenyl-substituted products with low chemoselectivity (Scheme 78).[93,94]

Scheme 78



A few examples of palladium-catalyzed cyclization-allylation combination were reported by Liebeskind and Prasad in 1988 preparing allyl-substituted Δ^1-carbapenems **305**.[88] A few years later, Tamaru and co-workers studied the palladium-catalyzed allylaminocyclization of allenyl tosylcarbamates in detail (Schemes 79 and 80).[95,96] The 4,5-disubstituted ox-

Scheme 79

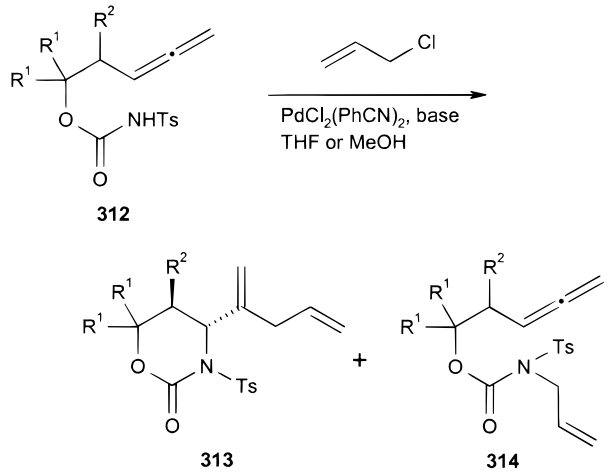


azolidines **307** were obtained in excellent stereoselectivities and generally in good yields by using $PdCl_2(PhCN)_2$, triethylamine, or potassium carbonate and a large excess of allyl chloride (up to 20 equiv). In contrast to the corresponding silver-catalyzed cyclization of *O*-(2,3-butadienyl)-*N*-tosylcarbamates **306**, which provided **307** with moderate trans/cis selectivity,[97] this palladium-catalyzed reaction gave only the trans isomer. However, the palladium-catalyzed allylaminocyclization depends markedly on the use of the Pd species. As mentioned above, $PdCl_2$-

$(PhCN)_2$ is the most effective catalyst in these cyclizations; $Pd_2(dba)_3{\cdot}CHCl_3$ and $PdCl_2$ may be used with similar efficiency. Interestingly, the most common Pd catalyst $Pd(PPh_3)_4$ gave exclusively the *N*-allylation, e.g. **308** → **309** in Scheme 79. When the $Pd(PPh_3)_4$-catalyzed reaction of tosylcarbamates **310** was carried out in the absence of an allylation agent, heterocycle **311**, a formal dimerization product of **310**, was obtained. It should be mentioned here that in spite of the very good stereo- and regioselectivities as well as the high yields achieved under the optimized reaction conditions, all reactions depicted in Scheme 79 are restricted on the application of tosylcarbamates. No other N-substituted carbamate derivatives have undergone this cyclization so far.

Tamaru et al. also reported the synthesis of tetrahydro-1,3-oxazin-2-ones **313** by $PdCl_2(PhCN)_2$-catalyzed reaction of 3,4-pentadienyl tosylcarbamates **312** (Scheme 80).[96] They found that the right choice

Scheme 80



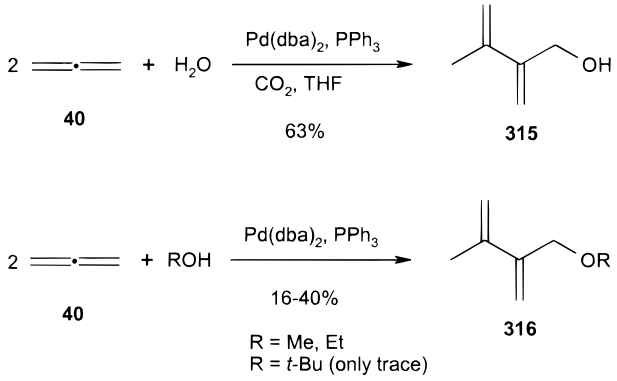
R^1	R^2	Base	313	314
H	H	NEt_3	--	67%
H	Me	NEt_3	--	64%
Me	H	NEt_3	--	78%
Me	H	$ClCH_2CO_2Na$	52%	--
Me	Me	AcONa	44%	25%

of the base for the formation of the six-membered ring is crucial. Employing triethylamine as base, which is usually successfully applied in the allylaminocyclizations of **306**, gave only the *N*-allylated allene **314**, whereas the same reaction performed with sodium acetate or $ClCH_2CO_2Na$ provided the expected product **313** as the major component.

B. Reactions with Oxygen Nucleophiles

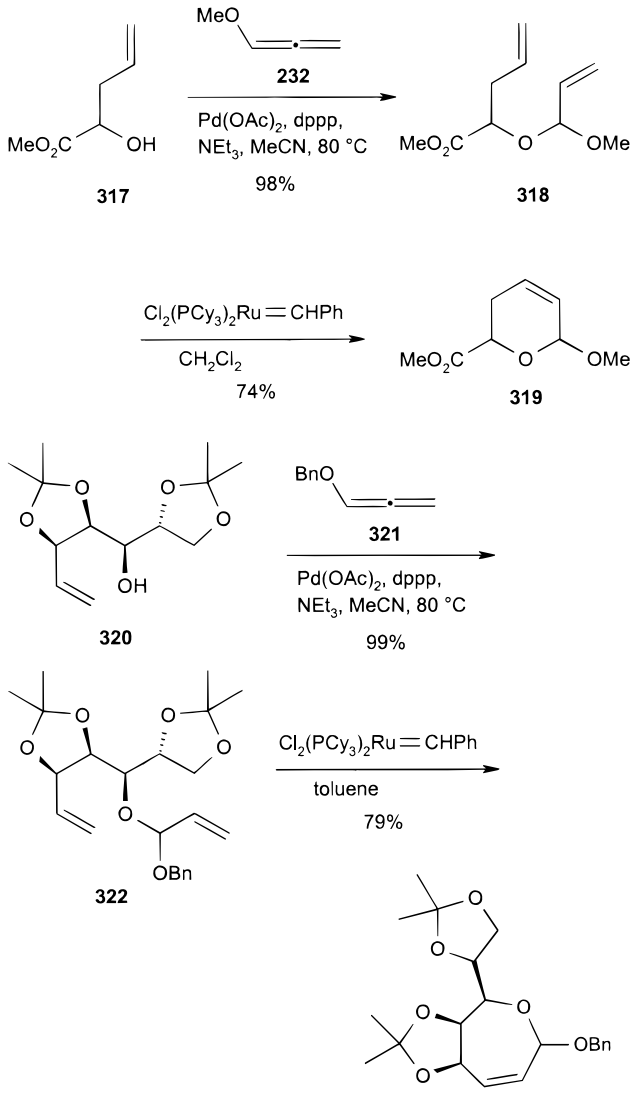
Contrary to the broad application of nitrogen nucleophiles in palladium-catalyzed reactions of allenes, the use of oxygen nucleophiles has remained a less explored area until recently, because nitrogen nucleophiles have proven to be the best among the nucleophiles for π-allylpalladium displacements.[98] The first contributions dealing with intermolecular palladium-catalyzed reactions of allenes with oxygen nucleophiles were reported by Shier[99] and Inoue.[100]

Scheme 81



The reaction involving 1,2-propadiene (**40**) and water took place using $Pd(dba)_2/PPh_3$ catalyst in the presence of carbon dioxide to yield the allylic alcohol **315** (Scheme 81). A related palladium-catalyzed reaction with simple primary alcohols, such as methanol or ethanol, was found to occur without carbon dioxide. Application of the intermolecular reaction of allenes

Scheme 82[a]

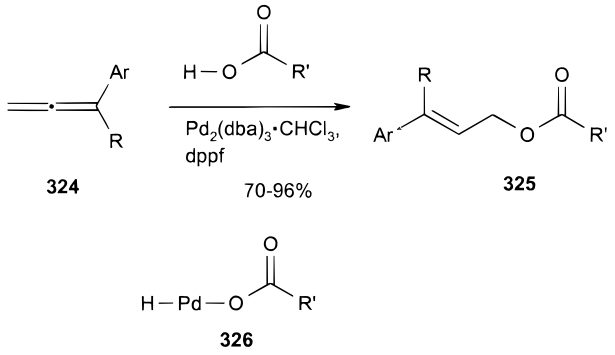


[a] Adapted with permission from refs 101 and 102. Copyright 1998 Thieme and Elsevier Science, respectively.

with oxygen nucleophiles as a key step in the synthesis of the required heterocyclic structures has been published recently. The palladium-catalyzed acetylation reaction of secondary alcohols with alkoxyallenes has been employed to prepare intermediates **318** and **322**, which are useful precursors in the synthesis of highly functionalized chiral dihydropyrans and tetrahydrooxepines (Scheme 82).[101,102]

The intermolecular palladium-catalyzed hydrocarboxylation of aryl-substituted allenes **324** to give allyl esters **325** in high yields and with excellent γ-selectivity was described in 1998 by Yamamoto and Al-Masum (Scheme 83).[103] The plausible mechanism for

Scheme 83

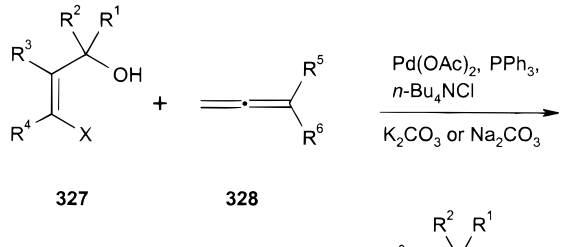


324 **325** **326**

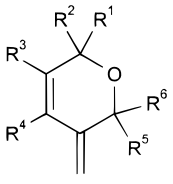
this catalytic reaction includes generation of a hydropalladium species **326** comparable to the mechanism of the hydroamination[14] discussed in Scheme 53.

In context to palladium-catalyzed carbo- and heteroannulations performed by Larock's group, they also investigated a number of oxygen-substituted aryl and vinylic iodides (Schemes 84 and 85).[56−58,104] These heteroannulations employing oxygen-substituted precursors show partly different criteria in terms of ring size and selectivity in comparison with the carboannulations and heteroannulations using the above nitrogen compounds. However, unlike the cyclizations involving amine and malonate functionality, the reactions of hydroxy compounds and acids with allenes proceed by regioselective attack on the π-allylpalladium intermediate at the highly substituted C=C bond (Scheme 84). This is in agreement with the cyclizations of vinylic compounds bearing sulfonamide or amide groups. Similar results in terms of regioselectivity in the palladium(II)-catalyzed reactions of *ortho*-thallated benzoic acid **333** and various allenes **334** were obtained earlier (Scheme 85).[104] It

Scheme 84



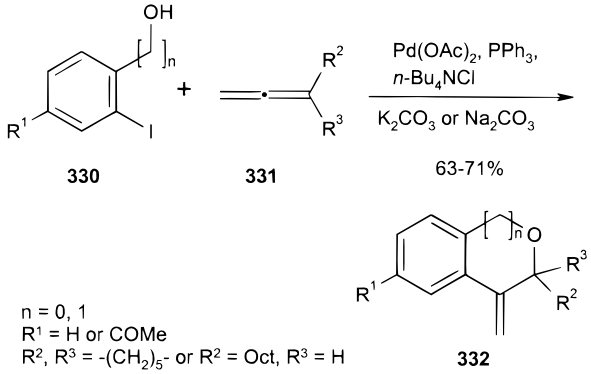
327 **328**



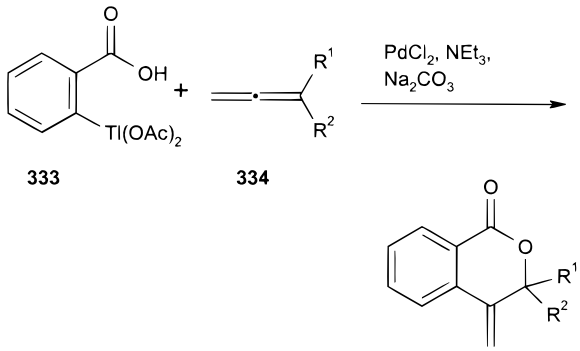
329

R^1	R^2	R^3	R^4	X	R^5	R^6	**329**
Me	H	Me	H	I	*n*-Oct	H	88%
Me	H	H	Ph	I	OMe	H	71%
Me	Me	Ph	Ph	I	*n*-Oct	H	67%
=O		H	H	I	OMe	H	67%
=O		$-(CH_2)_4-$		Br	$-(CH_2)_4-$		53%
=O		$-(CH_2)_4-$		Br	OMe	H	60%

Scheme 85



330 **331** **332**



333 **334** **335**

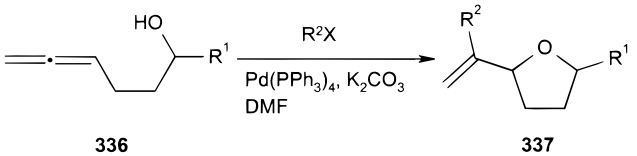
R^1	R^2	**335**
Me	H	39%
Ph	H	54%*
Me	Me	67%
$-(CH_2)_5-$		70%

* Product contains regioisomers as minor components.

should be noted that Larock and Zenner also described the enantioselective heteroannulations using oxygen-functionalized aryl and vinylic iodides, but compared to the nitrogenannulated products, the oxygenannulated compounds showed lower enantioselectivities and yields.[58]

Walkup and co-workers reported the palladium-catalyzed cyclization-coupling reactions of γ-hydroxyallenes, e.g. **336** and **338**, giving alkenyl-substituted tetrahydrofurans **337** and 2-furanones **339**, respectively, in moderate yields and with modest cis/trans selectivity (Schemes 86 and 87).[105] The authors discussed a mechanism that is shown in Scheme 88, which is in contrast with the one proposed by Tsuji[20] and Cazes[35] for their amino- and carboannulations of allenes. Aryl- or alkenylpalladium(II) halides are

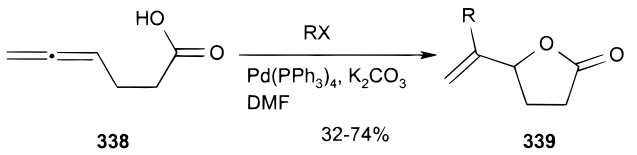
Scheme 86



336 337

R^1	R^2X	337	*cis* : *trans*
Me	PhBr	14%	48 : 52
Me	*p*-$MeOC_6H_4I$	61%	33 : 67
Me	PhHC=CHBr	41%	48 : 52
i-Pr	PhI	69%	36 : 64
t-$BuOCOCH_2$	PhI	68%	41 : 59
Et	*p*-AcC_6H_4Br	48%	46 : 54

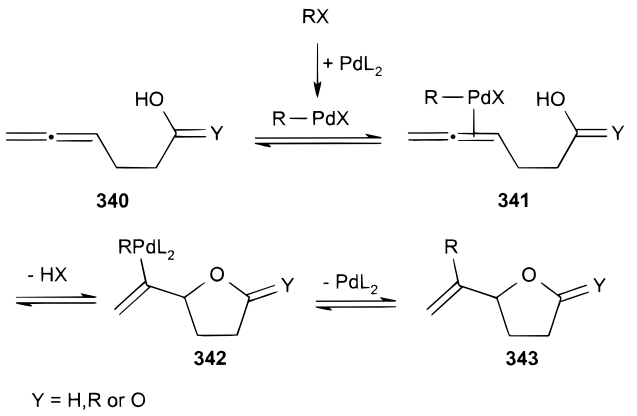
Scheme 87



338 339

R = Ph, *p*-$MeOC_6H_4$, *p*-MeC_6H_4, 1- and 2-Naphthyl, PhHC=CH, *p*-$HalC_6H_4$
X = Br or I

Scheme 88



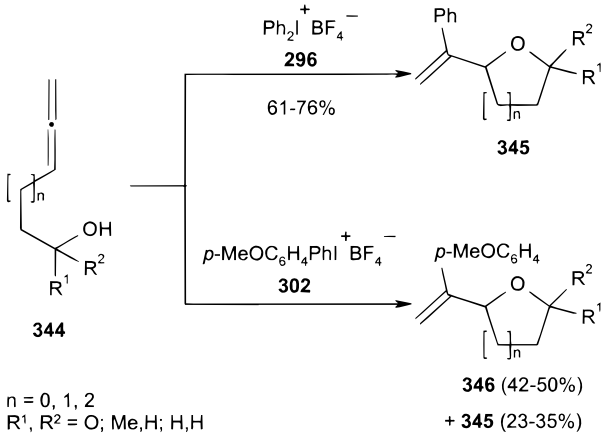
Y = H,R or O

believed to be the key intermediates, which initiate the cyclization by intramolecular oxypalladation.

The palladium-catalyzed coupling reaction employing hypervalent iodonium salts developed by Kang and co-workers was also applied on allenic alcohols and allenic acids to form tetrahydrofurans **345** (n = 1), tetrahydropyrans **345** (n = 2), and γ- and δ-lactones **346** (n = 1 and 2), respectively (Scheme 89).[93] The criteria for the arylation of these oxygen compounds are similar to the nitrogen compounds as discussed in section III.A.

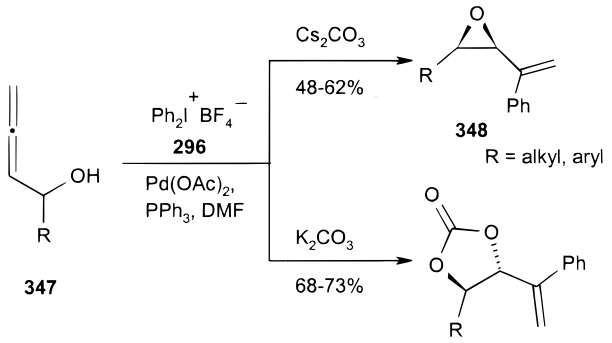
In addition, hypervalent iodonium salts are also used in palladium-catalyzed arylations of α-allenic alcohols **347** to prepare epoxides **348** or cyclic carbonates **349** (Scheme 90).[106] The proposed mechanism is shown in Scheme 91. The authors suggest that interactions between the base and π-allylpalladium species **350** contribute to define the product formation, especially in the case of alkyl-substituted allenes. However, reactions of **296** and α-allenic alcohols **347** in the presence of cesium carbonate gave

Scheme 89



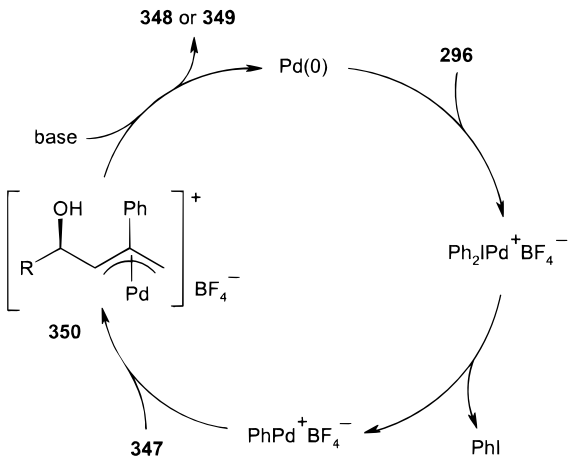
n = 0, 1, 2
R^1, R^2 = O; Me,H; H,H

Scheme 90[a]



[a] Adapted with permission from ref 106. Copyright 1998 Elsevier Science.

Scheme 91[a]

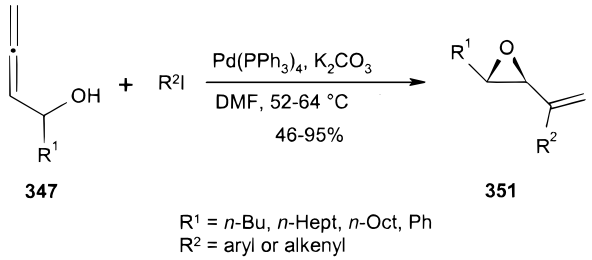


[a] Adapted with permission from ref 106. Copyright 1998 Elsevier Science.

trans-configurated epoxides **348** as the sole product, while using the less basic potassium carbonate the arylation resulted in the formation of cyclic carbonates **349**.

In 1999, Ma and Zhao developed an efficient synthesis of *trans*-2,3-disubstituted vinylic oxiranes **351**.[107] This palladium-catalyzed reaction of α-allenic alcohols **347** with aryl or alkenyl iodides R^2I gave the corresponding epoxides **351** with high diastereoselectivity (dr = 92/8 to 99/1) (Scheme 92). Notably, the

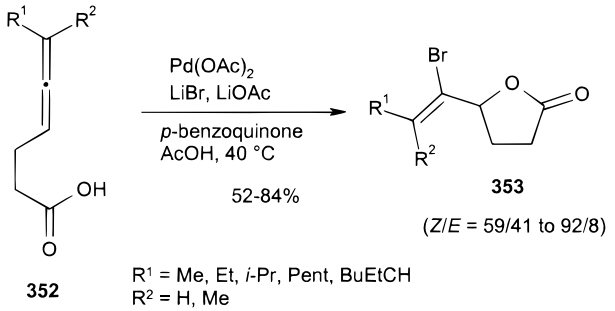
Scheme 92



same cyclization reaction using optically enriched α-allenic alcohols (95−98% ee) has also opened a new way to optically active oxiranes (96−98% ee).

An effective palladium-catalyzed intramolecular 1,2-oxidation of allenic acids **352** in the presence of LiBr and *p*-benzoquinone, giving up to an 84% yield of the bromovinyl-substituted lactones **353** with moderate to good (*Z*/*E*)-selectivity, has been reported (Scheme 93).[108] The intramolecular oxidation can be

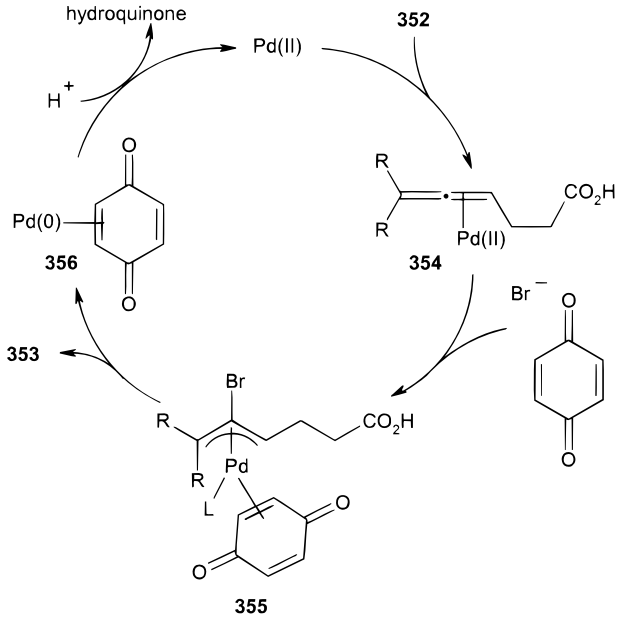
Scheme 93[a]



[a] Adapted with permission from ref 108. Copyright 1998 Elsevier Science.

rationalized by assuming the mechanism shown in Scheme 94. Nucleophilic attack of the bromide ion to the coordinated allene **354** gives π-allylpalladium species **355**. Subsequent intramolecular attack of the

Scheme 94[a]

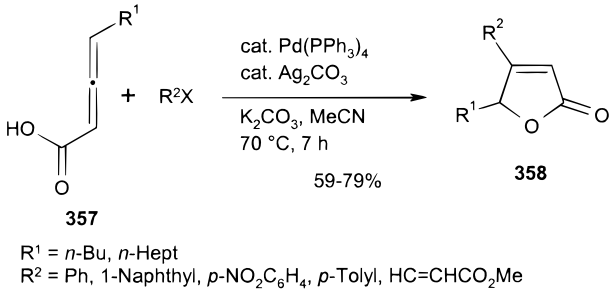


[a] Adapted with permission from ref 108. Copyright 1998 Elsevier Science.

oxygen nucleophile produces the product **353** and a Pd(0)−quinone complex **356**. The latter complex then undergoes an internal redox reaction to give Pd(II) and hydroquinone.

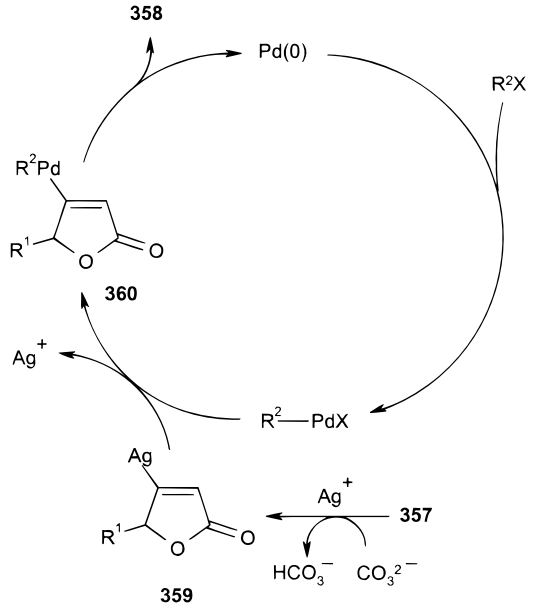
Investigation of the Pd(0)−Ag(I) cocatalyzed cyclization of α-allenic acids **357** with aryl and vinylic halides was done by Ma and Sha in 1998 (Scheme 95).[109] The authors suggest a transmetalation of the

Scheme 95



primary cyclized silver intermediate **359** to the Pd complex **360** (Scheme 96). Low yields of butenolide

Scheme 96

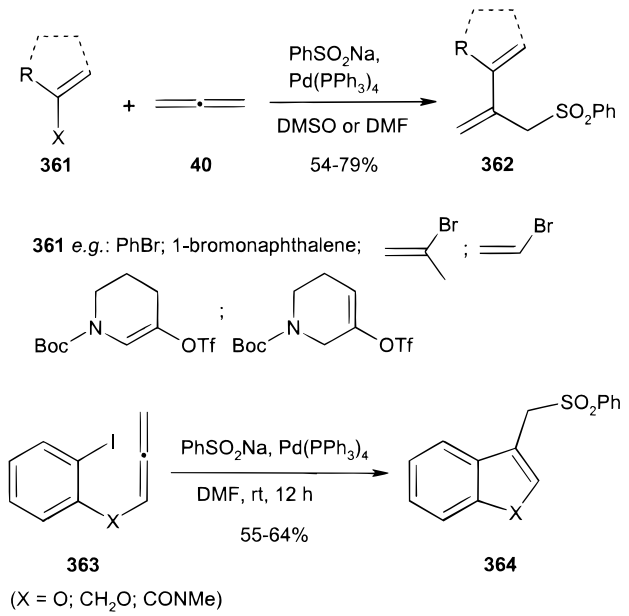


358 were obtained using only Pd in the reaction, implying a direct carbopalladation of the allene is possible. Nevertheless, the higher yields obtained in the presence of silver indicated that transmetalation and ring closure seem to be a more favorable pathway. On the other hand, applying a similar approach on the unsubstituted 2,3-butadienecarboxylic acid in the absence of silver salt to prepare the corresponding butenolide failed.[110]

C. Reactions with Sulfur and Selenium Nucleophiles

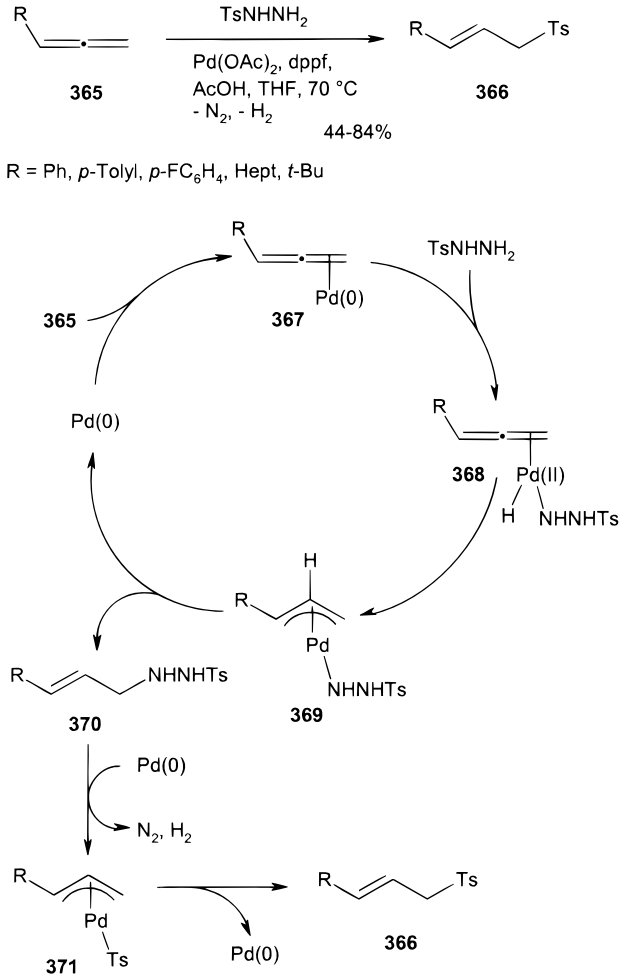
Very few reports have been given for the application of sulfur nucleophiles in palladium-catalyzed reactions of allenes. Highly substituted sulfones such as **362**[111] and **364**[75] could elegantly be constructed by taking advantage of Goré's allene carbopalladation process[35] and Grigg's palladium-catalyzed cyclization−anion capture process,[60] respectively (Scheme 97).

Scheme 97



Recently, Yamamoto and co-workers showed the synthesis of allyl sulfones **366** by the palladium-catalyzed hydrosulfination of allenes **365** with tosylhydrazine in the presence of acetic acid (Scheme 98).[112]

Scheme 98[a]

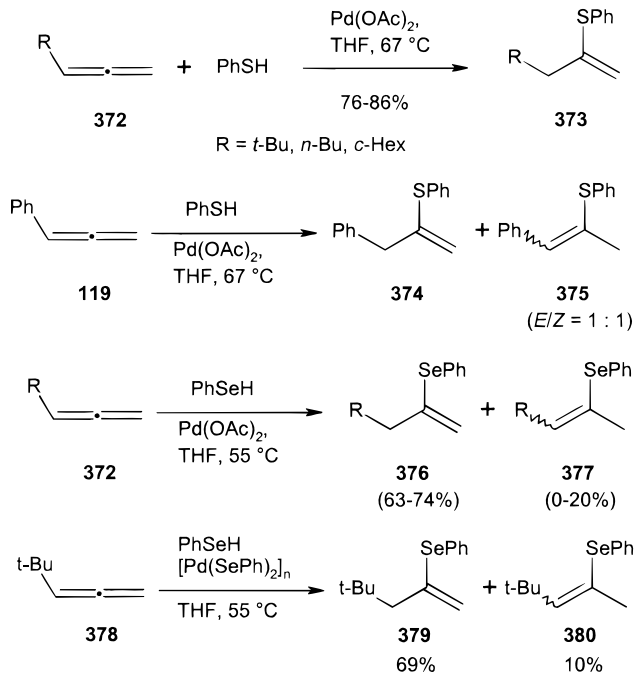


[a] Adapted with permission from ref 112. Copyright 1998 Elsevier Science.

In contrast to the hydrocarbonation of aryl-substituted allenes,[25] the regioselectivity of the product formation was not influenced by the electronic effect of their aromatic moiety. A speculative mechanism for this hydrosulfination described by the authors is depicted in Scheme 98. The hydrosulfination is believed to proceed through reduction of $Pd(OAc)_2$ to Pd(0), coordination of allene **365** to form the complex **367**, which produced **368** by oxidative insertion into the N−H bond of the tosylhydrazine, and followed by hydropalladation to afford **369**. Subsequently, the reduced intermediate **370** would be converted to **371** by releasing nitrogen and hydrogen, and finally, the reductive elimination would give the product **366**. In addition, very few examples of direct palladium-catalyzed reactions of allenes with alkanesulfinic acids are known.[113]

Very limited examples of palladium-catalyzed addition of benzenethiol to allenes are known. Ogawa et al. found that benzenethiol adds regioselectively to alkyl-substituted allenes **372** giving vinylic sulfides **373** in good yields (Scheme 99).[114] On the other hand,

Scheme 99[a]



[a] Adapted with permission from ref 115. Copyright 1998 Elsevier Science.

using the phenyl-substituted allene **119**, a mixture of two isomers was observed. This group also published the first protocol for the preparation of vinylic selenides **376** by palladium-catalyzed hydroselenation of alkyl-substituted allenes **372** and benzeneselenol.[115] The authors believe that $Pd(XPh)_2$ (X = S or Se) is the active catalyst in this reaction, because a single reaction with $[Pd(SePh)_2]_n$ prepared by the treatment of $Pd(OAc)_2$ with benzeneselenol was performed affording the expected product **379** accompanied by the regioisomer **380**.

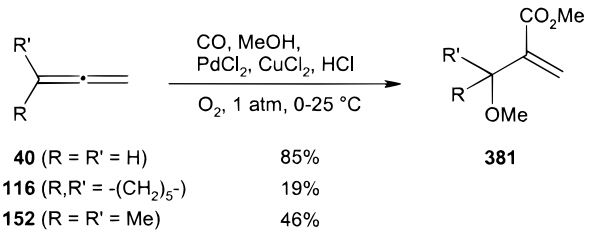
IV. Carbonylations and Carboxylations of Allenes

Carbon monoxide and carbon dioxide are important C1 key building blocks in organic synthesis, and

many transition metal-catalyzed carbonylation (carboxylation) reactions including palladium-catalyzed processes have offered useful methods for the synthesis of various carbonyl and carboxyl compounds in the past decades.[116] Because different products are being formed through different reaction mechanisms, we separate this part of palladium-catalyzed reactions from the preceding chapters.

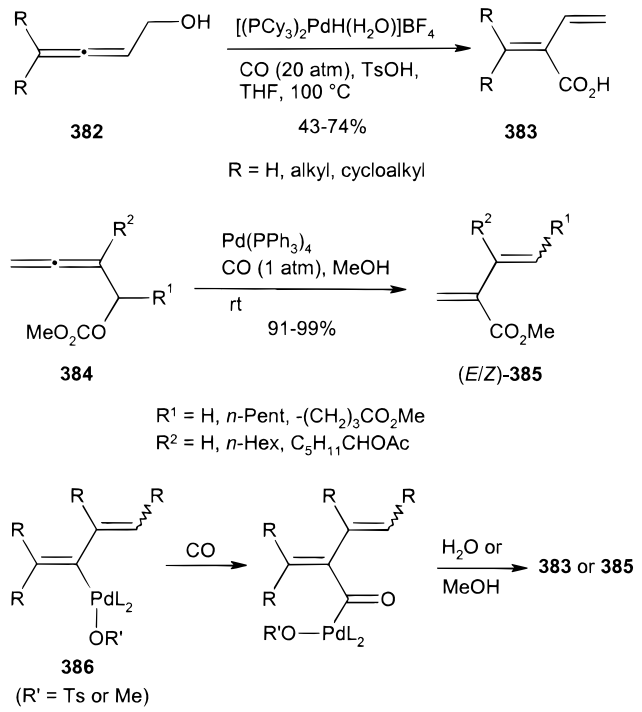
There were few synthetic applications of palladium-catalyzed carbonylation reactions of allenes until the early 1990s; previously, some investigations were done describing mechanistic considerations and kinetics of these reactions or isolations and characterizations of Pd complexes formed by successive insertion reactions of carbon monoxide and allenes.[117,118] One of the first interesting reactions from a synthetic point of view was the alkoxy−alkoxycarbonylation of 1,2-propadiene (**40**) and 1,1-disubstituted allenes **116** and **152** by oxidative carbonylation in the presence of $PdCl_2/CuCl_2$ under acidic conditions; however only reaction of **40** was satisfactory with respect to the yield of **381** (Scheme 100).[119]

Scheme 100



A few years later, Alper et al. observed a regioselective hydrocarbonylation of α-allenic alcohols **382** to α,β-unsaturated acids **383** employing the ionic hydridoaquopalladium complex $[(PCy_3)_2PdH(H_2O)]BF_4$ as a catalyst (Scheme 101).[120] A similar Pd

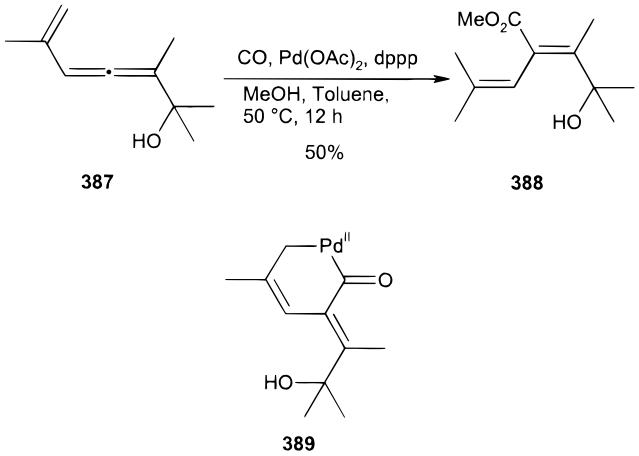
Scheme 101



intermediate **386** for the carbon monoxide insertion and hydrolysis was also suggested by Tsuji in the related carbonylation of methyl carbonates **384** to give α,β-unsaturated esters **385**.[121]

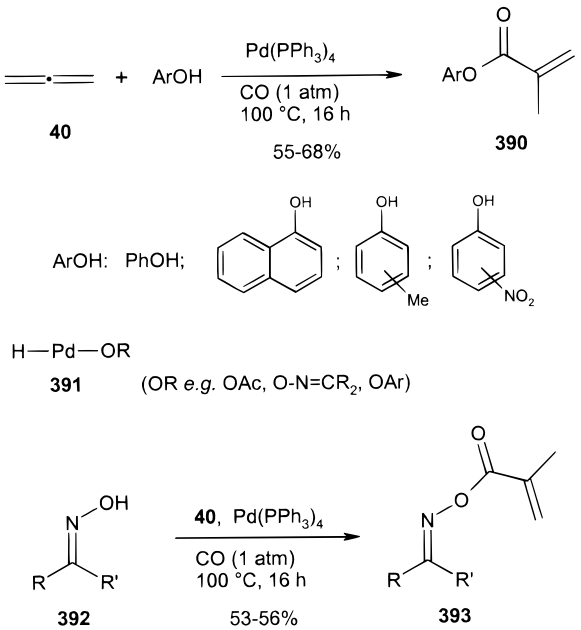
The reaction of ene−allenol **387** under carbon monoxide pressure in the presence of $Pd(OAc)_2$/dppp afforded the hydroxy diene **388** in moderate yield (Scheme 102). The reaction appears to include the palladacycle **389** as a key intermediate.[122]

Scheme 102



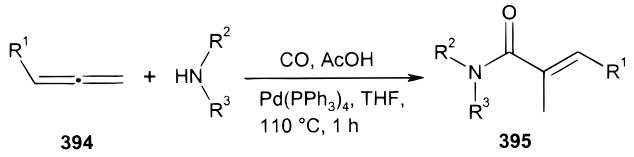
The hydridopalladium(II) species **391** generated in situ by the oxidative addition of Pd(0) to acetic acid or acidic hydroxyl compounds such as phenols or oximes were presumed, by Grigg and co-workers, to be the active species in their palladium-catalyzed reactions of nitrogen or oxygen compounds with allenes and carbon monoxide (Schemes 103 and 104).[123] As depicted in Scheme 103, phenols and

Scheme 103



oximes **392** were converted to their methacrylic esters **390** and **393**, respectively, in reasonable yields. The reaction of primary and secondary aliphatic amines under similar reaction conditions but in the presence

Scheme 104



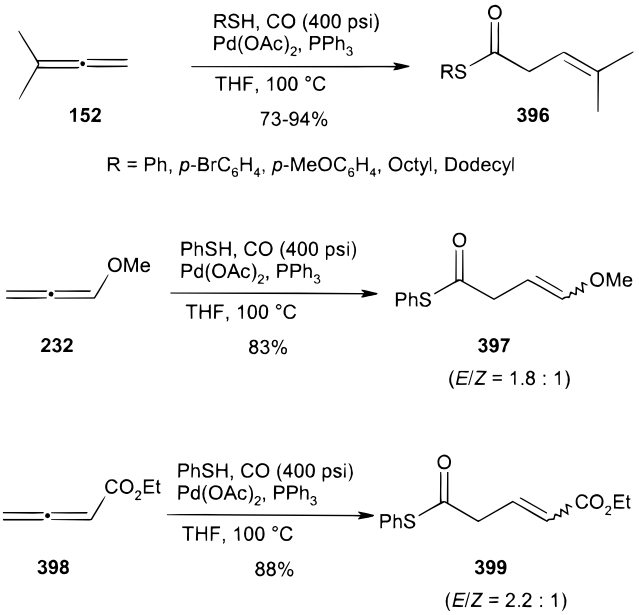
394 395

R^1	R^2	R^3	**395**
2-Pyridyl	-$(CH_2)_4$-		60%
n-Oct	-$(CH_2)_4$-		64%
Ph	-$(CH_2)_4$-		51%
Ph	Allyl	H	67%
H	Me	Me	60%
H	Et	Et	51%
H	Bn	H	80%

of acetic acid gave the corresponding α,β-unsaturated amides **395** in yields up to 80% (Scheme 104). In the case of the amidation of monosubstituted allenes **394**, only the (*E*)-configurated products were obtained. However, the results of the reported amidations of allenes appear to be in contrast to those of Yamamoto's or Cazes' palladium-catalyzed reactions employing amines and allenes in the absence of carbon monoxide.

Recently, Alper's group used thiols instead of alcohols, water, or amines as nucleophiles in the carbonylation reaction with simple allenes.[124] They found that the thiocarbonylation of monosubstituted allenes is unaffected by the substituents as illustrated in Scheme 105. Notably, donor-substituted

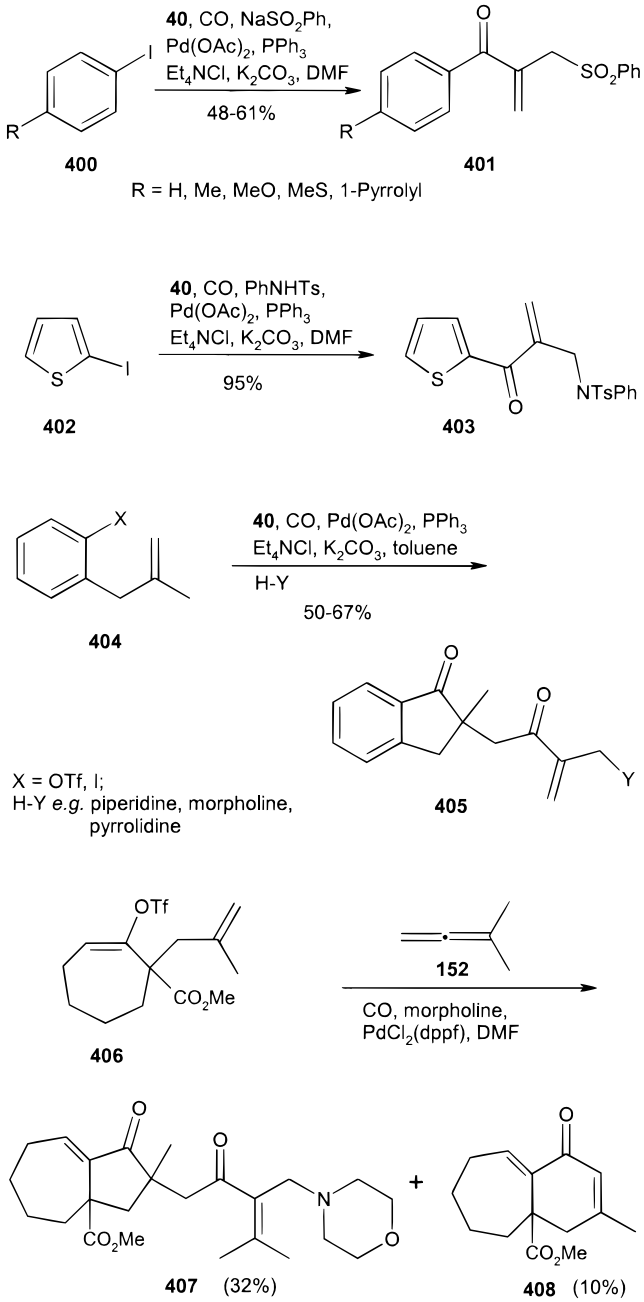
Scheme 105



allenes, e.g., methoxyallene (**232**), as well as acceptor-substituted allenes, e.g., methyl 2,3-butadiene-1-carboxylate (**398**), underwent thiocarbonylation to form the corresponding enol ether **397** or the α,β-unsaturated ester **399** in good yields but with modest (*E*/*Z*)-selectivity. The exclusive γ-regioselectivity observed is consistent with the selectivity obtained in similar reactions with carbo- and heteroatom nucleophiles in the absence of carbon monoxide (see sections II and III). It should be mentioned here that other transition metals which are known to insert into C−S bonds, e.g., Ru, Rh, Ni, and Co, were ineffective catalysts for this thiocarbonylation.

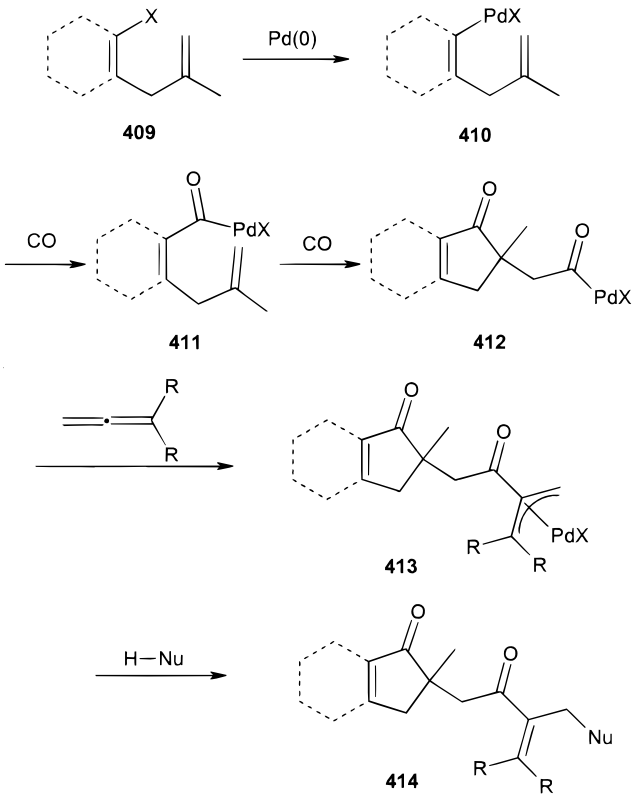
In the past few years, Grigg's group has considerably extended the palladium-catalyzed cyclization−anion capture methodology,[60] especially by the introduction of the relay switch concept.[125] They also investigated the tetra- and pentamolecular queuing cascade processes incorporating allenes and carbon monoxide.[126,127] Some of the most impressive examples of these palladium-catalyzed reactions involving the termolecular assembly of allenes, carbon monoxide, and a range of nucleophiles are represented in Scheme 106. Grigg distinguishes among three dif-

Scheme 106



ferent components in these reaction cascades: (a) vinylic, aryl, and heteroaryl halides or triflates as starter species, (b) allenes and carbon monoxide as species in the relay phase, and finally (c) nitrogen or sulfur nucleophiles as terminating species. The advantage of using both carbon monoxide and allene together in this process is given by the different rate of insertion into an aryl- (alkenyl) or acylpalladium(II) species. The authors showed that carbon monoxide inserts into the aryl (vinylic) species **410** as well as in the acylpalladium(II) complex **411** faster than the allene (Scheme 107). The insertion of the allene

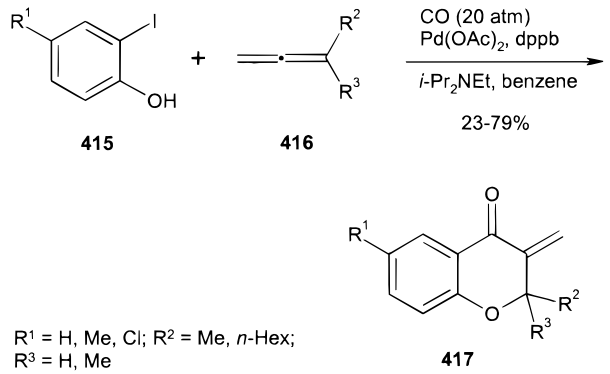
Scheme 107



is squeezed between the insertions of carbon monoxide and the final addition of the nucleophile.

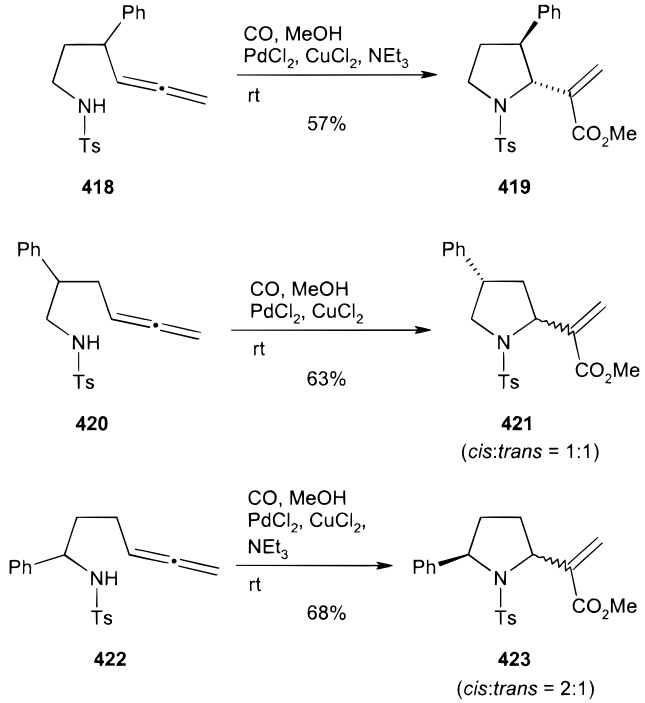
A related three-component process with *ortho*-iodophenols **415**, allenes **416** and carbon monoxide was reported by Alper and Okuro, which resulted in the formation of benzopyran-4-ones **417** (Scheme 108).[128a] Very recently, the same research group described a novel access to thiochroman-4-one derivatives by carbonylative heteroannulation of *o*-iodothiophenols.[128b]

Scheme 108



The intramolecular amino-, amido-, and oxypalladation−methoxycarbonylations of allenes were mainly reported by Gallagher and Walkup. Independently, they developed methodologies for the synthesis of a variety of nitrogen as well as oxygen heterocycles by similar cyclizations of amino- and hydroxyallenes, respectively, using catalytic amounts of Pd(II) salts and stoichiometric amounts of an oxidant such as $CuCl_2$. Studies by Gallagher showed that excellent diastereoselectivity favoring *trans*-configurated 2,3-disubstituted pyrrolidine **419** was obtained by a palladium-mediated amidopalladation−methoxycarbonylation process starting with γ-phenyl-substituted sulfonamide **418** (Scheme 109), while the same cyclization of α- and β-phenyl-substituted precursors **420** and **422** showed a low level of diastereoselectivity, leading to cis/trans mixtures of **421** and **423**, respectively.[129]

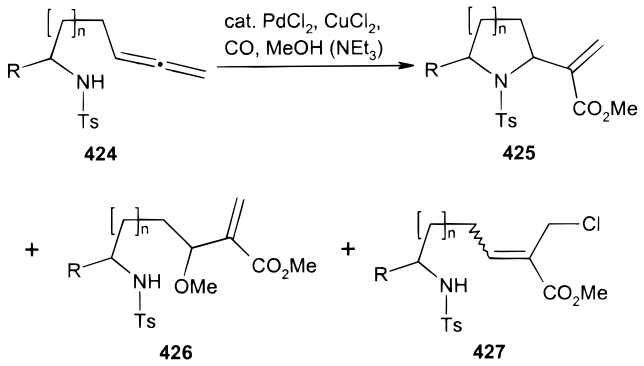
Scheme 109



However, the palladium-mediated cyclization of allenic sulfonamides, e.g., **424**, is plagued by the formation of acyclic byproducts **426** and **427** which may even become the major products depending on the reaction conditions (Scheme 110).[129,130] These side products were formed either by chloropalladation (**427**) or by oxypalladation reactions (**426**). However, the authors suggest that the chloropalladation to form **427** may play a key role in the mechanism of this cyclization sequence. Attempts to generate a seven-membered ring **425** ($n = 3$) were unsuccessful.

In addition to the tosyl group being an amino-protecting group, they also found other relatively basic nitrogen functions, e.g., benzylic groups as shown in Scheme 111, which can be tolerated in the cyclization step. Indeed, Gallagher and Fox used a number of various enantiopure *N*-benzylic-substitut-

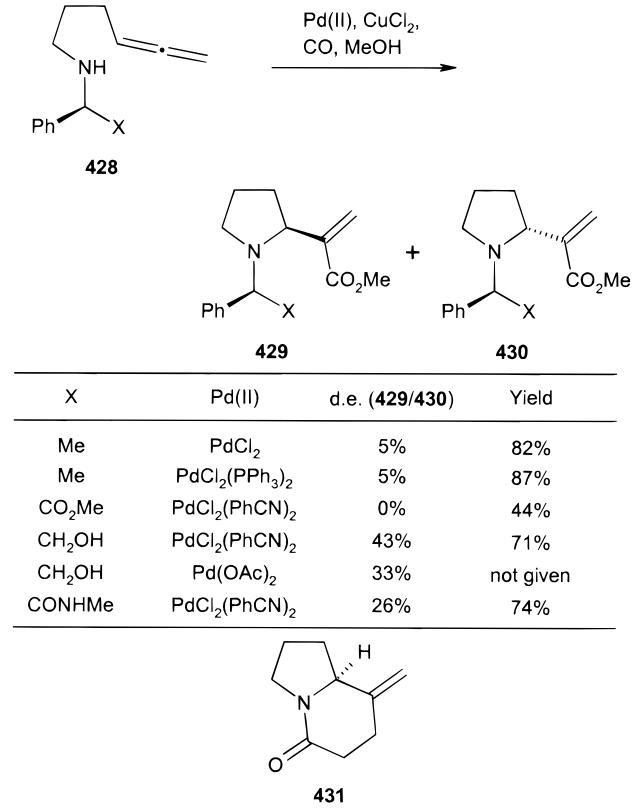
Scheme 110



n	R	Base	425	426	427	Ref.
1	CO_2Et	--	20% [a]	6%	14%	129
1	CO_2Et	NEt_3	68% [b]	--	--	130
2	H	--	--	20%	10%	129
2	H	NEt_3	20%	observed in the crude product		129
3 [c]	H	--	--	13%	--	129

[a] *cis* : *trans* = 1 : 3.- [b] *cis* : *trans* = 1 : 1.- [c] without $CuCl_2$.

Scheme 111

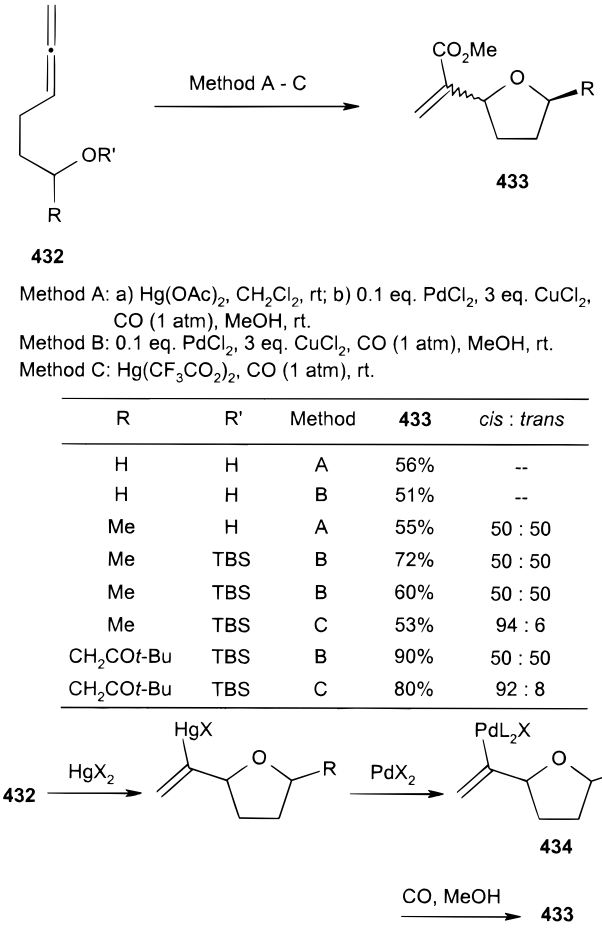


X	Pd(II)	d.e. (**429**/**430**)	Yield
Me	$PdCl_2$	5%	82%
Me	$PdCl_2(PPh_3)_2$	5%	87%
CO_2Me	$PdCl_2(PhCN)_2$	0%	44%
CH_2OH	$PdCl_2(PhCN)_2$	43%	71%
CH_2OH	$Pd(OAc)_2$	33%	not given
CONHMe	$PdCl_2(PhCN)_2$	26%	74%

ed γ-aminoallenes **428** as precursors to synthesize the pyrrolidines **429** and **430**.[131] The best result in terms of diastereoselectivity was obtained with the allene derivative **428** (X = CH_2OH) and $PdCl_2(PhCN)_2$ as catalyst. It should be noted that, in general, the level of the diastereoselectivity of this palladium-mediated cyclization−methoxycarbonylation sequence is significantly lower than the corresponding silver-mediated cyclization−methoxycarbonylation processes. Nevertheless, the functionality that the allene moiety imparts to **428** (*X* = Me) allowed the rapid transformation to the enantiomerically pure indolizidinone derivative **431** as a key compound in Gallagher's synthesis of pumiliotoxin 251D.[132]

In the mid-1980s, Walkup and Park found that γ-allenic alcohols and their *O*-silylated derivatives **432** were cyclized by oxymercuration−transpalladation (method A) or direct oxypalladation (method B) to form the vinylpalladium species **434** which undergoes methoxycarbonylation giving the 2,5-disubstituted tetrahydrofurans **433** in good yield but without any diastereoselectivity.[133] Only method C (oxymercuration) preferentially gave *cis*-configurated product. Scheme 112 shows different examples and

Scheme 112



Method A: a) $Hg(OAc)_2$, CH_2Cl_2, rt; b) 0.1 eq. $PdCl_2$, 3 eq. $CuCl_2$, CO (1 atm), MeOH, rt.
Method B: 0.1 eq. $PdCl_2$, 3 eq. $CuCl_2$, CO (1 atm), MeOH, rt.
Method C: $Hg(CF_3CO_2)_2$, CO (1 atm), rt.

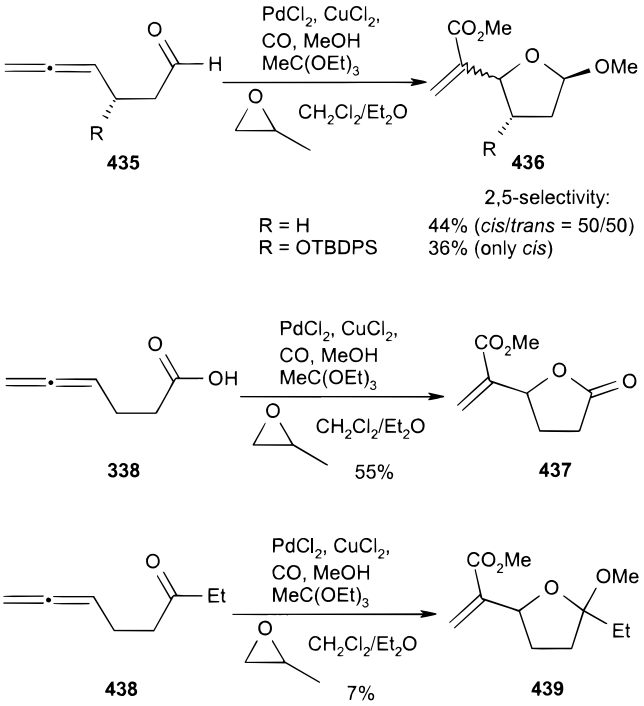
R	R'	Method	433	*cis* : *trans*
H	H	A	56%	--
H	H	B	51%	--
Me	H	A	55%	50 : 50
Me	TBS	B	72%	50 : 50
Me	TBS	B	60%	50 : 50
Me	TBS	C	53%	94 : 6
CH_2COt-Bu	TBS	B	90%	50 : 50
CH_2COt-Bu	TBS	C	80%	92 : 8

the proposed mechanism. The one-pot oxymercuration−transpalladation−methoxycarbonylation procedure became an attractive key step in the stereoselective synthesis of a number of nactin antibiotic subunits, e.g., nonactic acid and homononactic acid.[134]

A few years later, the same group extended the intramolecular direct oxypalladation−methoxycarbonylation on γ-oxoallenes, e.g., 4,5-hexadienal **435** and 4,5-hexadienoic acid **338**, as an effective method for preparing furanosides **436** and furanone **437** (Scheme 113).[135] The palladium-mediated cyclization of **435** (R = OTBDPS) to form the corresponding 2,5-*cis*-**436** exclusively was employed as a key step in the synthesis of a nucleoside analogue.[136] Nevertheless, Walkup encountered limitations while applying this attractive acetalization−cyclization−methoxycarbonylation procedure to β-allenyl ketones. When **438**

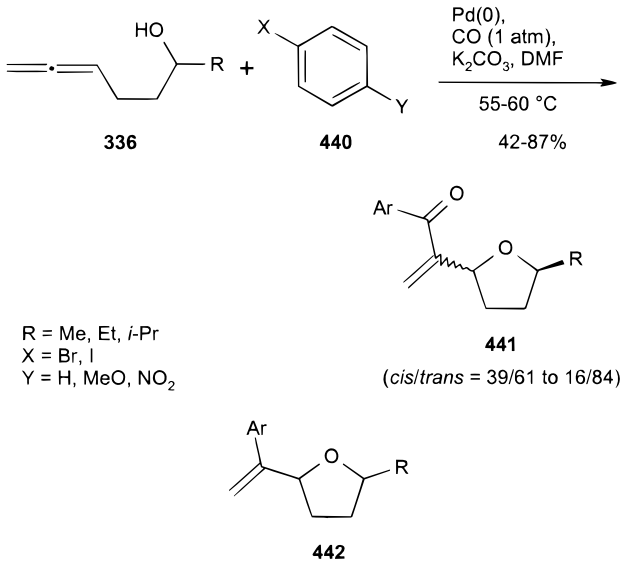
was subjected to these conditions, only 7% yield of the expected **439** was obtained.

Scheme 113



Subsequently, Walkup and co-workers studied the palladium-catalyzed cyclization−coupling reaction of γ-hydroxyallenes and aryl halides in the presence of carbon monoxide.[137] The reaction showed a strong dependence on the reaction temperature. However, treatment of the γ-allenic alcohol **336** with aryl halide **440** at 55−60 °C gave the carbonylated product **441** (Scheme 114). On the other hand, performing the same reaction at 80 °C, the formation of the noncarbonylated heterocycle **442** was predominant.

Scheme 114[a]

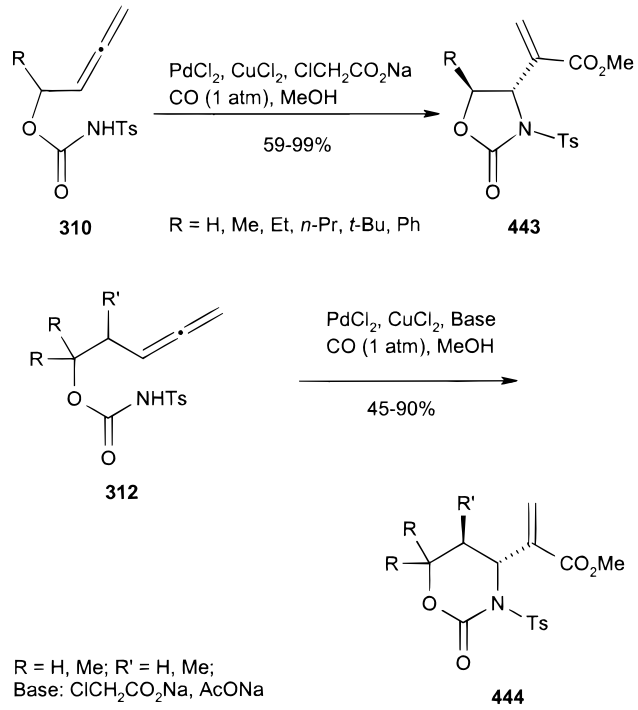


[a] Adapted with permission from ref 137. Copyright 1995 Elsevier Science.

It should be mentioned here that Gallagher's observation of competing oxypalladation and chloropalladation side reactions as described above was not observed in Walkup's oxygen systems.

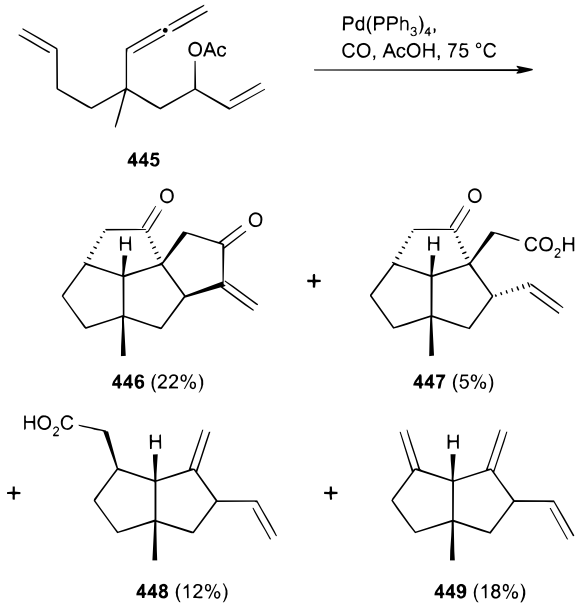
The tosylcarbamates **310** and **312**, which were mentioned in section III, undergo stereospecific cyclization followed by methoxycarbonylation to give oxazolidines **443** and 1,3-oxazines **444**, respectively, in the presence of $PdCl_2/CuCl_2$ and a base, e.g., $ClCH_2CO_2Na$ or AcONa (Scheme 115).[138]

Scheme 115

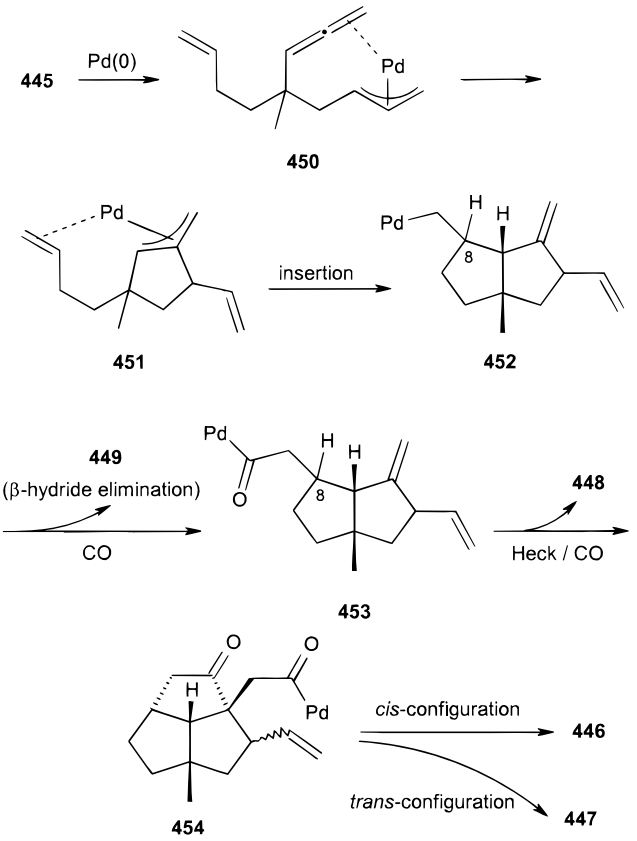


The outstanding synthetic utility of palladium-catalyzed cyclizations including carbonylation has stimulated attempts to develop reaction processes especially with good atom economy, a concept which has attracted much interest in organic syntheses in the past decade.[139] A particularly interesting example involving a domino cyclization−carbonylation process of alkenyl−allenyl−allylic acetate was provided by Yamamoto, Takahashi, and co-workers.[140,141] For example, the $Pd(PPh_3)_4$-catalyzed reaction cascade of **445** produced a mixture of tetracyclic diketone **446**, tricyclic keto acid **447**, and bicyclic compounds **448** and **449** (Scheme 116). The proposed mechanism for this one-pot procedure (Scheme 117) includes (a) generation of π-allylpalladium complex **451** from the intermediate **450** initially formed, (b) insertion intramolecularly leading to σ-Pd species **452** followed by the first carbon monoxide insertion to form **453**, (c) the complex **453** α-configurated at C-8 undergoes the next insertion intramolecularly with the exomethylene unit followed by a second carbonyl insertion to **454**, and finally (d) the *trans*-configurated acylpalladium complex **454** undergoes a further insertion followed by β-hydride elimination to produce the main component **446** of this reaction cascade. However, application of this domino reaction to compounds such as **445** did not give satisfactory results due to the formation of undesirable premature products. To overcome this problem, the use of 5,8-

Scheme 116



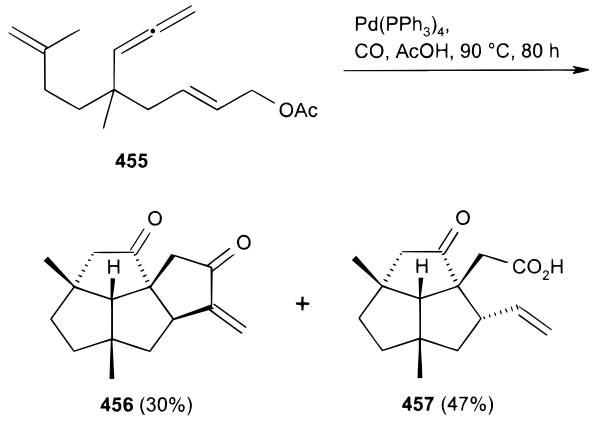
Scheme 117



dimethyl-5-(1,2-propadienyl)-2,8-nonadienyl acetate (**455**) as a substrate has been introduced. The reaction under the optimized conditions, as given in Scheme 118, produced only the tetracyclic and tricyclic products **456** and **457** in acceptable yields.[141]

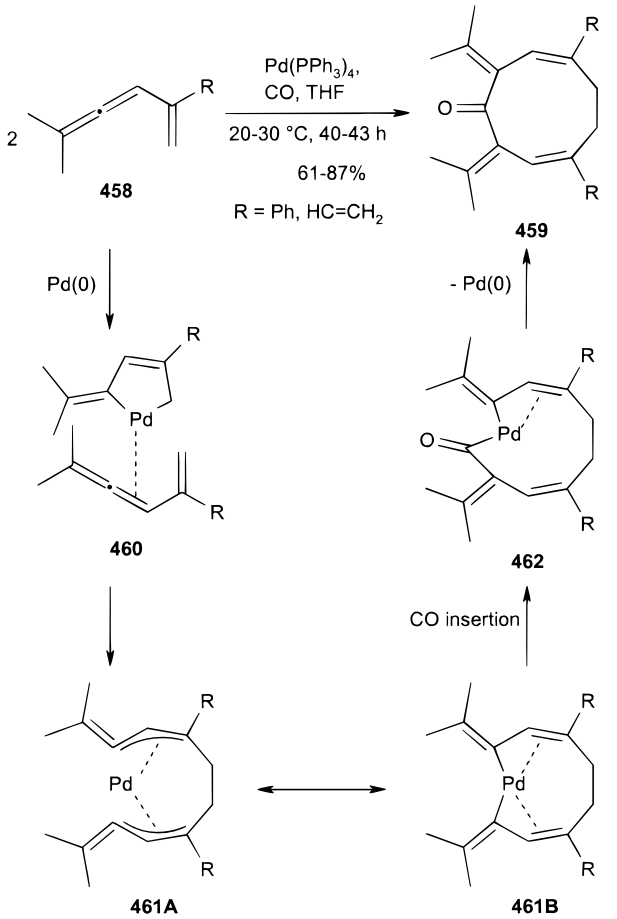
Other efforts for the synthetic utility of palladium-catalyzed reactions have been focused on a conceptually new [4+4+1] cycloaddition which was recently developed by Murakami, Ito, and Itami.[142] Palladium-

Scheme 118



catalyzed cyclization of vinylallene **458** in the presence of carbon monoxide provided a highly functionalized cyclononadienone **459**. It has been shown that terminal dimethylated allenes are better starting materials which exert the stereo- and regiochemistry in the products formed. The plausible mechanism of the [4+4+1] cycloaddition is via a σ-bis(alkenyl)-palladium intermediate **461A**/**B** which undergoes carbon monoxide insertion and subsequent reductive elimination to **459** as shown in Scheme 119.

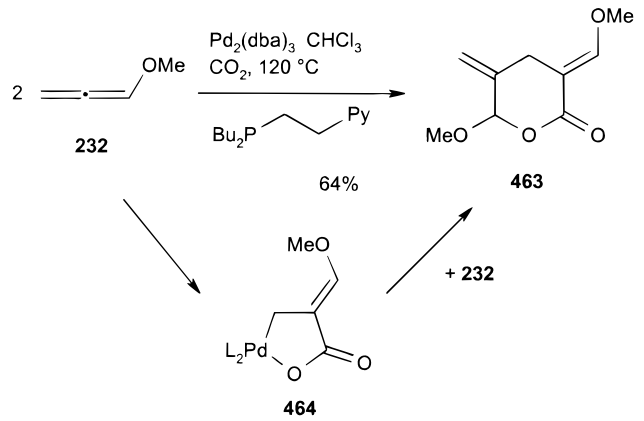
Scheme 119



Contrary to the numerous applications of palladium-catalyzed reactions including a carbonylation step, very little attention has been given to the use

of carbon dioxide as a component for similar palladium-catalyzed reactions.[143,144] The reaction of methoxyallene (**232**) and carbon dioxide with 5 mol % of $Pd_2(dba)_3 \cdot CHCl_3$ and 1 equiv of 1-(2-pyridyl)-2-(di-*n*-butylphosphino)ethane resulted in the regioselective formation of the pentanolide **463** (Scheme 120).[143] It

Scheme 120



is postulated that the reaction proceeds via the palladacycle intermediate **464**. The present reaction is characterized by the crucial role of a methoxy substituent in the allene. In agreement with these findings, 1,2-pentadiene did not react under the same reaction conditions.

V. Stannylation, Silylation, and Germanylation of Allenes

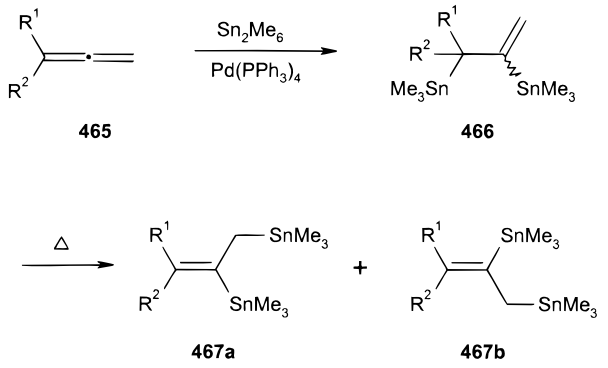
Organosilanes and stannanes, especially allyl- and vinylstannanes, are increasing in importance as powerful agents in the arsenal of the synthetic organic chemist, particularly for C−C bond formation by a large variety of chemical reactions.[145] The diversely functionalized allylstannanes have already found interesting applications in the stereodirected synthesis of natural products. In light of this versatility, the development of methods for the selective generation of these classes of compounds is of great synthetic value. Transformation of allenes into various such organic reagents catalyzed by Pd complexes has continued to attract tremendous attention.

Mitchell and Killing first reported that hexamethylditin adds readily to several allenes in the presence of $Pd(PPh_3)_4$.[146] Three products, **466**, **467a**, and **467b**, can, in principle, be formed when an unsymmetrically substituted allene **465** reacts with Me_6Sn_2 (Scheme 121). Under kinetically controlled conditions, the products **466** are formed, while at higher temperatures, the formation of the thermodynamically more stable products **467a**/**b** are observed. The same authors later described a series of reactions using these bifunctional organotin synthons.[147]

Notably, (1-hydroxy-1-cyclohexyl)allene **468** gave the monostannyl-substituted 1,3-butadiene **469**, possibly due to the elimination of trimethyltin hydroxide (Scheme 122). Mechanistically, it has been proposed that a π-allylpalladium intermediate such as **470** or **471** is involved in the reaction.

The reaction between ditin and allenes was found to be apparently reversible. For instance, ^{119}Sn NMR

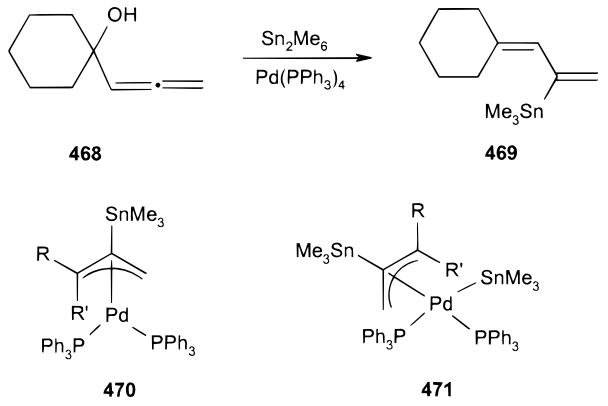
Scheme 121



R^1	R^2	Reaction Conditions	Yield 466+467	Distribution 466	467a	467b
H	H	65 °C / 2h	89%	100%	--	--
H	H	150 °C / 3d	90%	67% [a]	--	--
Ph	H	25 °C / 2d	40%	100%	--	--
Ph	H	85 °C / 12d	73%	--	100%	
OMe	H	35 °C / 14d	81%	62%	17%	22%
OMe	H	95 °C / 6d	79%	--	58%	42%
Me_3Sn	H	85 °C / 15h	62%	77%	23%	--
Me	Me	85 °C / 15h	63%	59%	41%	
Ph	Me	80 °C / 2h	39%	79%	4%	17%

[a] 33% of $[H_2C{=}C(SnMe_3)CH_2]_2$ formed.

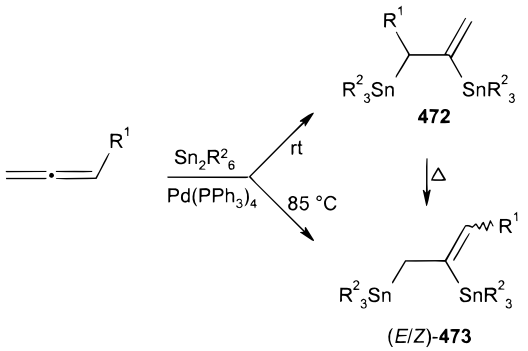
Scheme 122



of the products in the reaction of Et_6Sn_2 or *n*-Bu_6Sn_2 with $Me_3SnCH{=}C{=}CH_2$ showed a very large number of products. According to Mitchell and Schneider, not only hexamethyl- but hexaethyl- and hexa-*n*-butylditin also add readily to a variety of allenes in the presence of $Pd(PPh_3)_4$ and both kinetic and thermodynamic control of the reaction can be achieved (Scheme 123).[148,149] In general, the yield does not decrease on going from Me_6Sn_2 to *n*-Bu_6Sn_2, though the latter may require a longer reaction time. However, *tert*-butylallene is an exception, the yield falling very significantly due to steric effects in the catalytic cycle.

The same group converted cyclic 1,2-dienes (C_9−C_{13}) into synthetically promising 2,3-bis(trimethylstannyl)cycloalk-1-enes by palladium(0)-catalyzed addition of hexaalkyldistannanes.[150] For example, the reaction of 1,2-cyclononadiene (**474**), the smallest cyclic allene, with Sn_2Me_6 and $Pd(PPh_3)_4$ provided the distannane *trans*- and *cis*-**475** in excellent yield, the

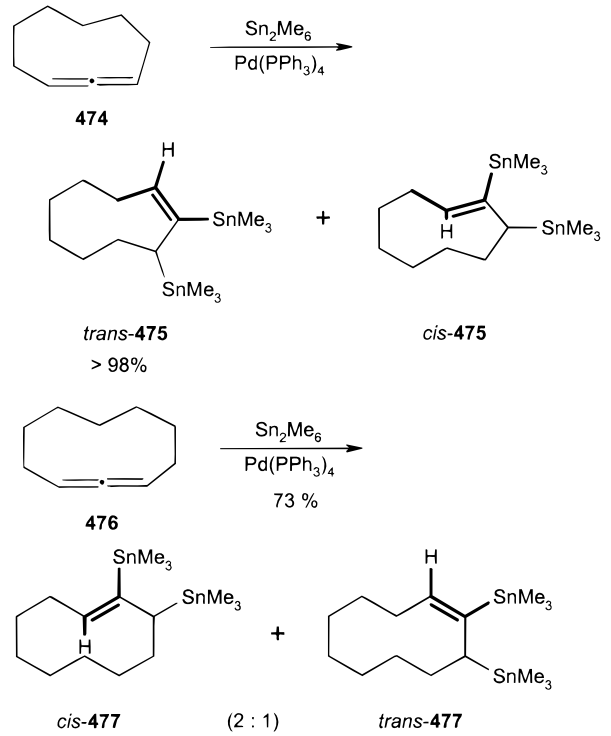
Scheme 123



R¹	R²	Reaction Conditions	Yield 472+473	Distribution 472	E-473	Z-473
Me	Me	85 °C / 48 h	39%	12%	59%	29%
Bu	Me	75 °C / 24 h	92%	3%	82%	15%
Bu	Bu	85 °C / 66 h	90%	--	66%	34%
c-Hex	Et	90 °C / 40 h	74%	6%	75%	19%
t-Bu	Me	85 °C / 48 h	51%	93%	6%	1%
t-Bu	Et	95 °C / 192 h	14%	9%	85%	6%
t-Bu	Bu	85 °C / 144 h	5%	--	100%	--
Ph	Et	85 °C / 19 h	51%	--	90%	10%
OMe	Et	85 °C / 20 h	80%	--	48%	52%
OMe	Bu	75 °C / 96 h	89%	3%	65%	32%
EtO_2CCH_2	Me	80 °C / 20 h	72%	7%	69%	24%
EtO_2CCH_2	Bu	80 °C / 20 h	85%	15%	74%	11%

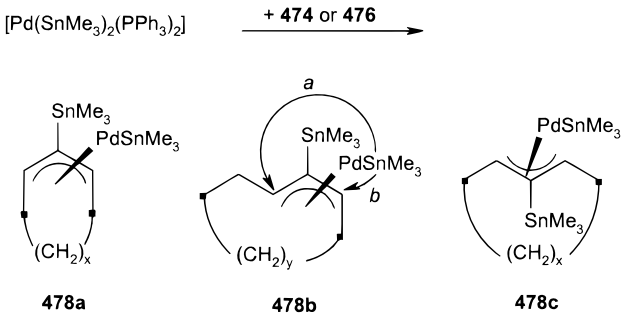
stereochemistry of which was confirmed by extensive NMR studies (Scheme 124). The 1,2-distannylation

Scheme 124



of 1,2-cyclodecadiene (**476**) is particularly instructive as both *trans*-**477** and *cis*-**477** (2:1) are present after purification. This palladium-promoted addition probably proceeds by the oxidative addition of Me_6Sn_2, followed by the formation of an η^3-allylpalladium complex **478** within which the second $SnMe_3$ group is delivered from the palladium-bearing face providing compound *cis*-**477**. However, three η^3-allylpalladium isomers are possible, but **478a** and **478b** (path a) can provide *trans*-**475** whereas **478b** and **478c** (path b) should lead to the formation of *cis*-**475**, which is not observed (Scheme 125).

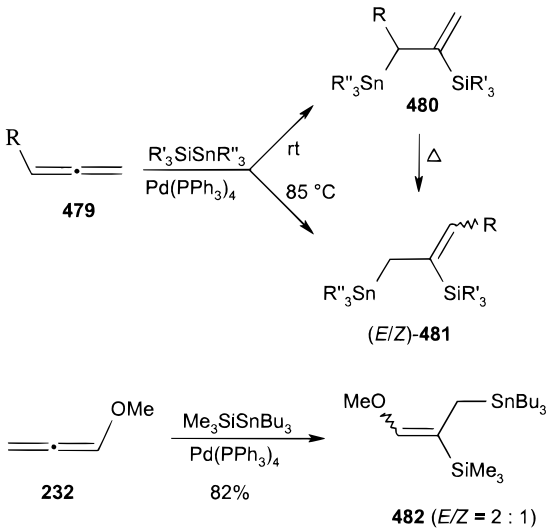
Scheme 125



For **474**: x = 4, y = 3
For **476**: x = 5, y = 4

Mitchell and Schneider also showed that silylstannanes $R'_3SiSnR''_3$ undergo addition reaction with allenes regiospecifically, the silyl residue always being attached to the central carbon atom of the allene moiety.[148,149] The kinetic product **480** is isomerized to (*E*/*Z*)-**481** upon heating by a 1,3-allyl shift of the stannyl moiety (Scheme 126). To extend the scope

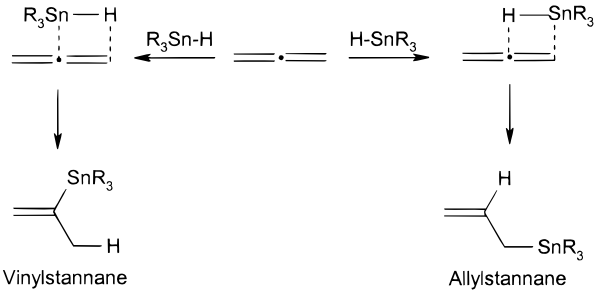
Scheme 126



of palladium-catalyzed metalation of allenic ethers, Goré et al. studied silylstannation of methoxyallene (**232**) using $Me_3SiSnBu_3$ as reagent, and this reaction provided exclusively two geometrical isomers (*E*)- and (*Z*)-**482** in good yield.[151]

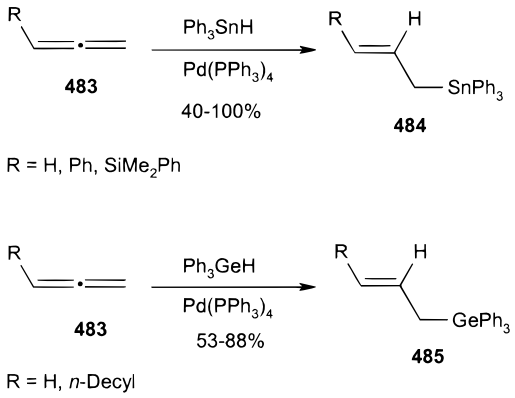
One of the most useful syntheses of functionalized vinyl- and allylstannanes is given by the palladium-catalyzed hydrostannation of allenes. The two modes by which the Sn−H bond can add across an allene are the addition of tin to the central carbon atom of the 1,2-diene to give vinylstannane and to the terminal carbon atom to give allylstannane, respectively (Scheme 127). Oshima et al. demonstrated that

Scheme 127



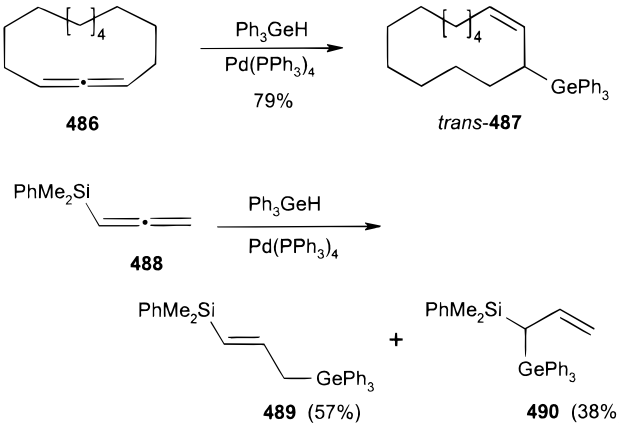
treatment of allenic compounds **483** with triphenylstannane or triphenylgermane in the presence of a catalytic amount of $Pd(PPh_3)_4$ resulted in the exclusive formation of allylic triphenylstannanes **484** or allylic triphenylgermanes **485** in moderate to good yields (Scheme 128).[152]

Scheme 128



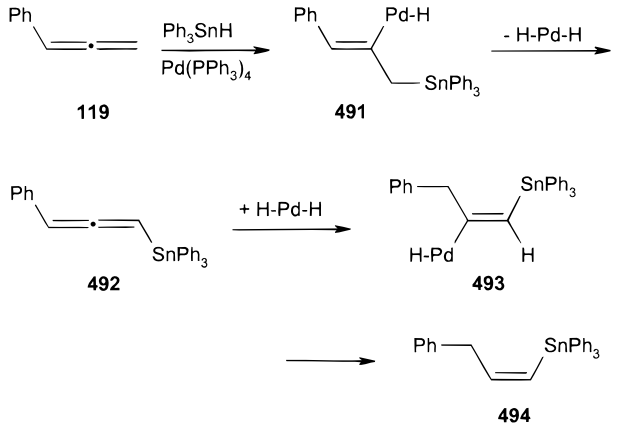
The distribution of two regioisomeric products depends on the nature of the substitution pattern of the starting allenic compounds. For instance, hydrogermylation of 1,2-tridecadiene (**486**) afforded 3-triphenylgermyl-1-tridecene (**487**) selectively, while 1-(dimethylphenylsilyl)-1,2-propadiene (**488**) gave a mixture of 1-dimethylphenylsilyl-3-triphenylgermyl-1-propene (**489**) and 3-dimethylphenylsilyl-3-triphenylgermyl-1-propene (**490**) upon treatment with $Ph_3GeH-Pd(0)$ (Scheme 129).[152]

Scheme 129



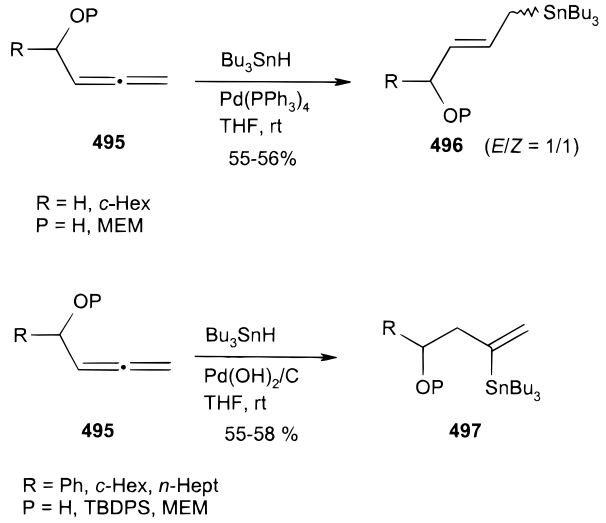
The exclusive formation of (*Z*)-3-phenyl-1-triphenylstannyl-1-propene (**494**) from 1-phenyl-1,2-propadiene (**119**) is explained by the following reaction path. Oxidative addition of Ph_3SnH to Pd(0) followed by stannylpalladation to give vinylpalladium species **491**, elimination of palladium hydride from **491**, subsequent readdition from the opposite and less hindered end of the 1,2-diene **492**, and finally reductive elimination give **494** (Scheme 130).[152]

Scheme 130



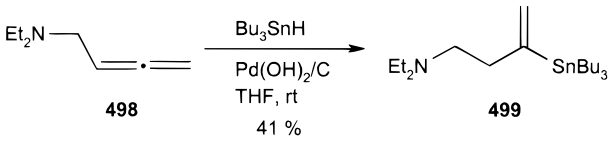
Lautens and co-workers carried out a regioselective hydrostannation using $Pd(OH)_2/C$ as catalyst to form vinylstannanes, complementary to the results obtained using $Pd(PPh_3)_4$.[153] Thus, a slow addition of Bu_3SnH to allenes **495** in the presence of 5 mol % of $Pd(PPh_3)_4$ gave the allylstannanes **496** in moderate yields and with no stereoselectivity (Scheme 131). On

Scheme 131



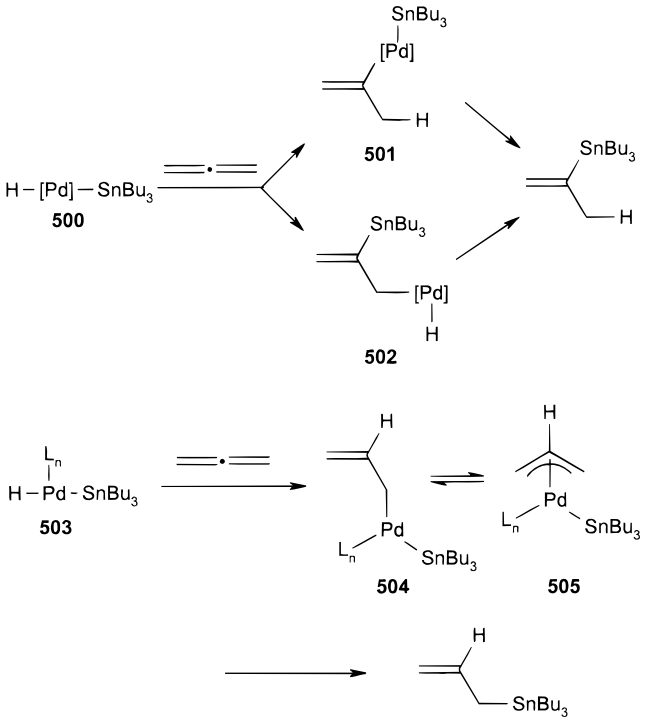
the other hand, when using 5 mol % of the ligand-free heterogeneous catalyst, $Pd(OH)_2/C$, allenes **495** were transformed to 2-tributylstannyl-1-alkenes **497** in reasonable yields. Substrates **495** with a bulky group (e.g., P = TBDPS) in the proximity of the reaction center or with a chelating group (such as P = MEM) as well as the parent unprotected allenic alcohol reacted, indicating that the steric environment α to the allene does not affect hydrostannation to any appreciable extent. The nature of group R in the allenic alcohols plays no significant role. Allenylamine **498** was also reacted with Bu_3SnH in the presence of $Pd(OH)_2/C$, and the stannylamine **499** was isolated in 41% yield (Scheme 132).

Scheme 132



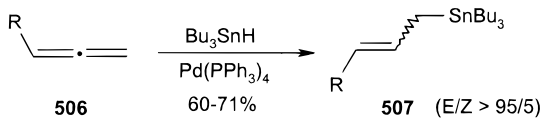
Mechanistically, it was presumed that Pd(II)−hydroxide is reduced by tin hydride to a Pd(0) species, which is the active catalyst. Subsequent oxidative insertion into the Sn−H bond would generate **500**, which can hydropalladate or stannylpalladate the allenes to give **501** or **502**, respectively. Reductive elimination would give the observed vinylstannane. The hydrostannation pathway using $Pd(PPh_3)_4$ proceeded through the allylpalladium species **504** via the preformed species **503**, which may be in equilibrium with the π-allyl complex **505**, followed by reductive elimination, giving the allylstannane (Scheme 133).

Scheme 133



It deserves a special note that hydrostannation of aromatic allenes **506** proceeded regio- and stereoselectively, producing (*E*)-allylstannanes **507** exclusively (Scheme 134).[154] This reaction is kinetically con-

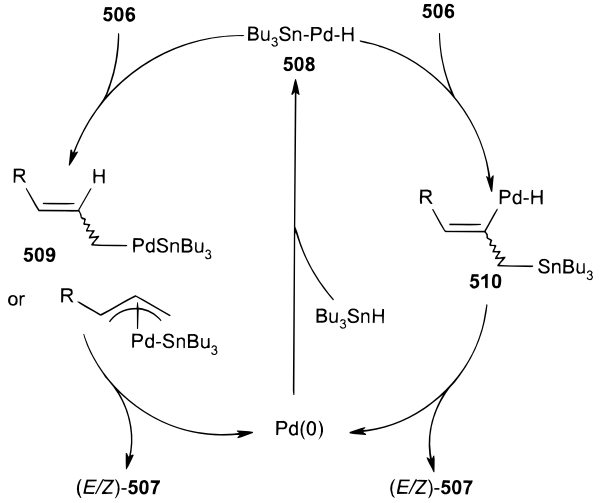
Scheme 134



R = Ph, *p*-MeC_6H_4, *p*-FC_6H_4, R = *p*-$MeOC_6H_4$

trolled since the ratios of (*E*/*Z*)-isomers in all cases did not depend on temperatures. A proposed mechanism for the regiospecific palladium-catalyzed hydrostannation of allenes **506** with Bu_3SnH is shown in Scheme 135. Pd(0) would insert oxidatively into the

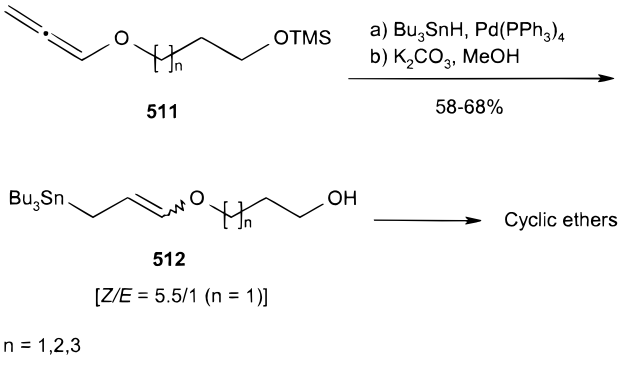
Scheme 135



Sn−H bond of hydrostannane, forming the reactive species **508**, which either via the hydropalladation pathway or via the palladastannation pathway would add across the terminal double bond of allene **506** producing the allylpalladium intermediate **509** or vinylpalladium species **510**, respectively. Either **509** or **510** would undergo reductive elimination of Pd to give the products (*E*/*Z*)-**507** along with the Pd catalyst. The same authors further studied hydrostannation of allenes with $Ph_3SnH/Pd(PPh_3)_4$, and contrary to Oshima's observation, who reported exclusive formation of (*Z*)-vinylstannanes,[152] formation of (*E*)-allylstannanes as a single product was obtained.

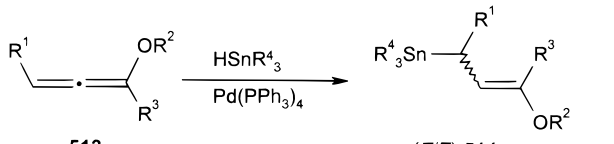
To extend the application of hydrostannation toward synthesis of polyether natural products, Yamamoto et al. carried out addition of Bu_3SnH in the presence of $Pd(PPh_3)_4$ to the allenic ethers **511** forming a mixture of (*Z*)- and (*E*)-allylstannanes **512**, which were subsequently converted to various cyclic ethers (Scheme 136).[155]

Scheme 136



Goré et al. showed that the reaction of allenic ethers **513** with Bu_3SnH or Ph_3SnH in the presence of 2−4 mol % $Pd(PPh_3)_4$ lead to the regiospecific formation of allylstannanes **514** in acceptable yields with a moderate to excellent (*E*/*Z*) ratio.[151] The stereoselectivity of the addition in the case of nonsubstituted alkoxyallenes depends both on the bulkiness of the alkoxy group and the substituents on the tin atom. The bulkier groups favor the preferential formation of (*Z*)-isomer (Scheme 137). However,

Scheme 137



513 (*E*/*Z*)-**514**

R¹	R²	R³	R⁴	**514**	*E* : *Z*
H	Me	H	Bu	72%	25 : 75
H	Me	H	Ph	72%	9 : 91
H	TBDMS	H	Bu	70%	13 : 87
H	Me	Bu	Bu	45%	55 : 45*
H	Me	SMe	Bu	52%	53 : 47*
H	Me	TMS	Bu	82%	0 : 100
Bu	Et	H	Bu	41%	45 : 55

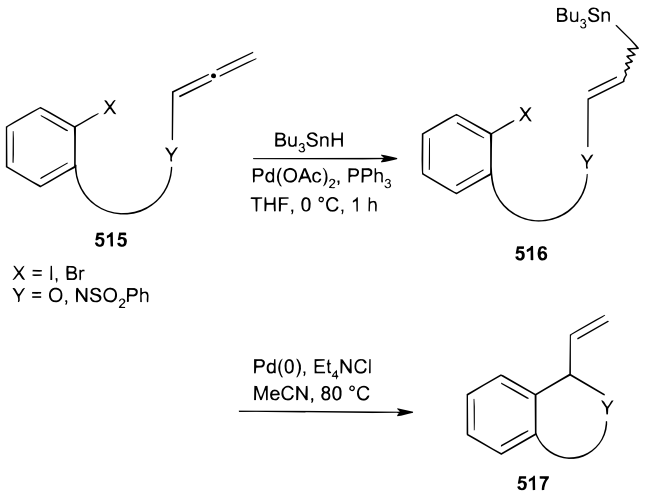
*The geometry of the double bond of each isomer was not determined

according to these findings, the regioselectivity of the hydrostannation of allenic ethers is in contrast with the results obtained by Mitchell et al.[148,149] on the silyl- and stannylstannation of mono- and 1,1-disubstituted allenes.

A comparative study of the free-radical and palladium-catalyzed hydrostannation of allenes has also been carried out; the latter reaction occurs via a regioselective attack of the organotin moiety at the less highly substituted terminal carbon atom of the allene framework.[156]

Grigg and Sansano found that a series of δ- and ω-aryl-substituted allenes **515** underwent regiospecific and stereoselective hydrostannation on treatment with Bu_3SnH in THF at 0 °C in the presence of 10 mol % $Pd(OAc)_2$ and 20 mol % PPh_3 to form allylstannanes **516**.[157] These allylstannanes were successfully cyclized to small, large, and spirocyclic rings **517**, where cyclization occurs at the proximal carbon atom of the original allene (Scheme 138). Several

Scheme 138

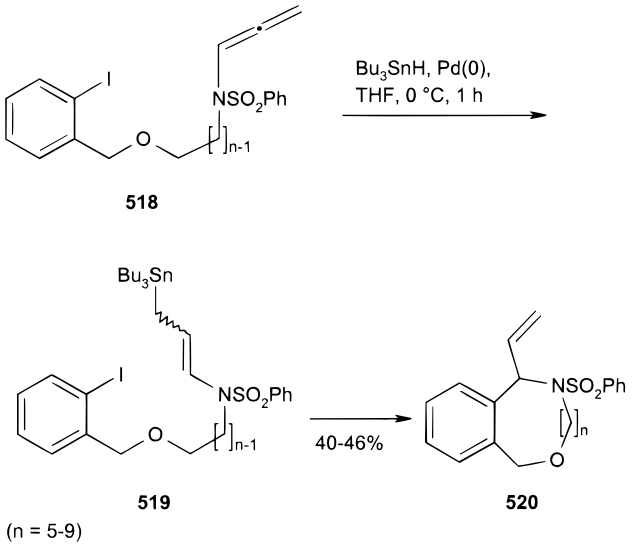


515 516 517

X = I, Br
Y = O, NSO_2Ph

attempts to cyclize to the corresponding eight-membered ring were unsuccessful. However, sequential palladium-catalyzed hydrostannation of **518** to **519** followed by sp^3-sp^2-Stille macrocyclization under high dilution afforded a series of 11- to 15-membered N,O-macrocycles **520** in moderate yields (Scheme

Scheme 139

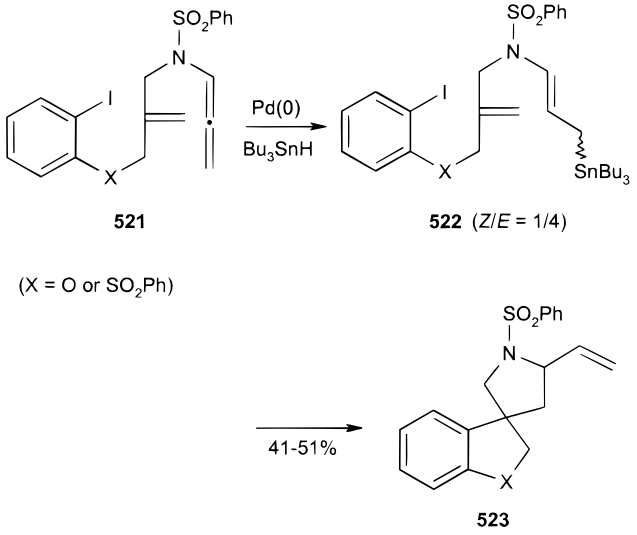


519 520

(n = 5-9)

139).[157] The scope of palladium-catalyzed cyclization–anion capture methodology was explored by these authors by several hydrostannation–biscyclization processes. Thus, the substrates **521** were hydrostannylated to give allylstannanes **522** as a 1:4 mixture of (*Z*/*E*)-isomers, which were further cyclized to afford the spiro compounds **523** (Scheme 140).[157]

Scheme 140



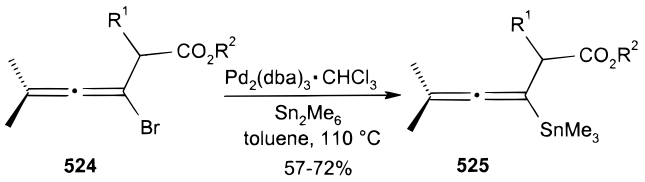
521 522 (*Z*/*E* = 1/4)

(X = O or SO_2Ph)

523

Very recently, Saalfrank and co-workers described an umpolung reaction for the preparation of stannylallenes **525** from the corresponding bromoallenes **524** and hexamethyldistannane with $Pd_2(dba)_3 \cdot CHCl_3$ catalyst in toluene at 110 °C in reasonable yields (Scheme 141).[158]

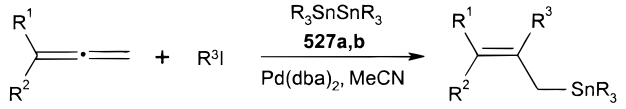
Scheme 141



524 525

R¹ = H, Me, Et, *i*-Pr; R² = Me, Et

Scheme 142



526

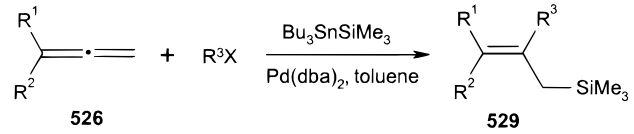
528a (R = Me)
528b (R = *n*-Bu)

a: $R^1 = R^2$ = Me
b: R^1 = H, R^2 = *c*-Hex
c: $R^1 = R^2$ = *n*-Bu

527a (R = Me)
527b (R = *n*-Bu)

Entry	R^3I	526	527	Yield (*Z*/*E*)
1	IC_6H_4COMe	**a**	**a**	76%
2	IC_6H_4COMe	**a**	**b**	77%
3	*o*-$MeOC_6H_4I$	**a**	**b**	26%
4	*p*-$MeOC_6H_4I$	**a**	**a**	35%
5	*p*-$MeOC_6H_4I$	**a**	**b**	40%
6	*m*-$MeOC_6H_4I$	**a**	**b**	55%
7	*p*-$NO_2C_6H_4I$	**a**	**a**	75%
8	*p*-$EtO_2CC_6H_4I$	**a**	**a**	69%
9	*p*-$EtO_2CC_6H_4I$	**a**	**b**	80%
10	$ICH{=}CHCO_2Et$	**a**	**a**	40%
11	$ICH{=}CHCO_2Et$	**a**	**b**	81%
12	*p*-$NO_2C_6H_4I$	**b**	**a**	73% (75/25)
13	$ICH{=}CHCO_2Et$	**c**	**b**	98% (68/32)
14	1-I-C_4H_3S	**a**	**a**	72%

Scheme 143



526 529

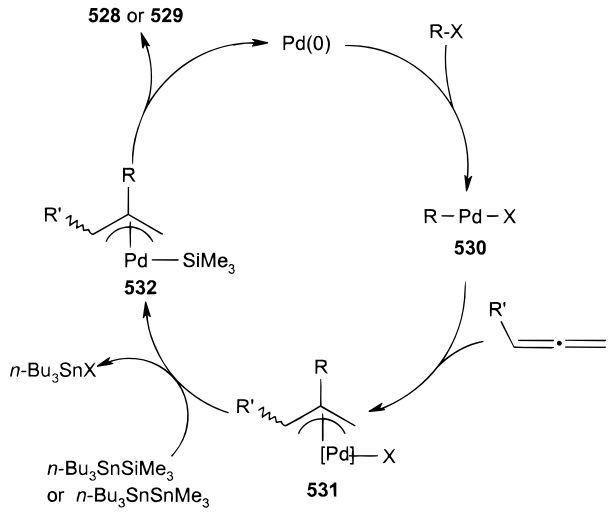
a: $R^1 = R^2$ = Me
b: R^1 = H, R^2 = *c*-Hex
c: $R^1 = R^2$ = *n*-Bu

Entry	R^3X	526	529 Yield (*Z*/*E*)
1	C_5H_5I	**a**	85%
2	*p*-$CH_3COC_6H_4I$	**a**	92%
3	*p*-$NO_2C_6H_4I$	**a**	88%
4	*p*-$MeOC_6H_4I$	**a**	86%
5	*p*-$MeOC_6H_4I$	**a**	83%
6	*m*-$EtOC_6H_4I$	**a**	82%
7	1-I-C_4H_3S	**a**	85%
8	(*z*)-$EtO_2CCH{=}CHI$	**a**	78%
9	$C_6H_4(Br)C{=}CH_2$	**a**	83%
10	C_6H_5I	**b**	85% (92/8)
11	*p*-$MeCOC_6H_4I$	**b**	80% (92/8)
12	C_6H_5I	**c**	82% (80/20)

In 1999, Cheng et al. reported a three-component coupling in which an aryl or alkenyl iodide react with allenes **526** and hexaalkyldistannanes **527** (R = Me or *n*-Bu) or $Bu_3SnSiMe_3$ in the presence of $Pd(dba)_2$ to give substituted allylstannanes **528** or allylsilanes **529**, respectively (Schemes 142 and 143).[159,160] These reactions are regioselective, with the aryl (alkenyl) group adding to the central carbon atom and the stannyl or silyl group to the nonsubstituted terminal carbon atom of the allene. Aryl iodides with an electron-withdrawing substituent such as an acetyl, an ester, or a nitro group (entries 1, 2, 7, and 8, Scheme 142) at the *para* position give higher yields of allylstannanes than those with an electron-donating substituent such as a methoxy group (entries 4 and 5, Scheme 142). *Ortho*-substituted aryl iodides (entry 3, Scheme 142) generally give lower yields than those with the substituent at the *para* position. However, aryl halides with an electron-donating or -withdrawing group at the *ortho*, *meta*, or *para* position did not effect the carbosilylation reaction (see Scheme 143). Bromobenzene and chlorobenzene were unreactive under carbostannylation conditions, whereas bromobenzene was reactive under carbosilylation conditions. Heteroaromatic and alkenyl iodides also reacted to afford the corresponding allylstannanes and allylsilanes, respectively (entries 10, 11, 13, and 14, Scheme 142; entries 7−9, Scheme 143). The cis stereochemistry of the acrylate group was faithfully retained in the products. Monosubstituted allenes such as cyclohexylallene and *n*-butylallene also undergo carbostannylation and carbosilylation with aryl iodides, producing the corresponding allylstannanes and allylsilanes regioselectively in 73−98% yield (entries 12 and 13, Scheme 142; entries 10−12, Scheme 143). Bulkier organic halides and allenes give products with higher (*Z*/*E*) ratios. The authors found that $Pd(dba)_2$ in the absence of a phosphorus ligand is the most active and stereoselective.

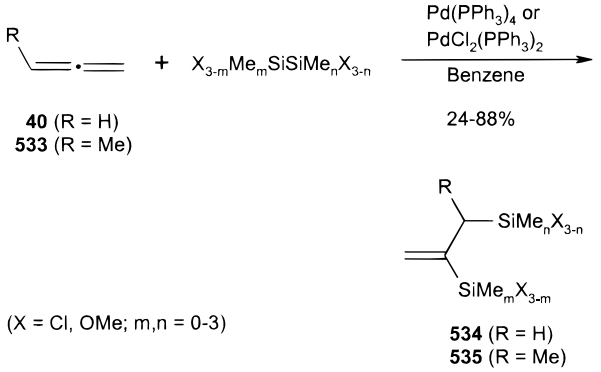
The possible mechanism involves oxidative addition of the organic halide to the Pd(0) complex to give a Pd(II) intermediate **530**, subsequent coordination of allene, followed by migratory insertion of allene into the Pd−C bond to give a π-allylpalladium(II) species **531**. Transmetalation between ditin or organosilylstannane and π-allylpalladium complex to **532** followed by reductive elimination affords the final product **528** (or **529**) (Scheme 144).

Scheme 144



The first example of the addition of disilanes to allenic compounds was reported by Watanabe and coworkers,[161] in which addition of chloromethyl and methoxymethyldisilanes, $X_{3-m}Me_mSiSiMe_nX_{3-n}$ (X = Cl, OMe; *m*, *n* = 0−3) as well as hexamethyldisilane to 1,2-propadiene (**40**) and 1,2-butadiene (**533**) in the

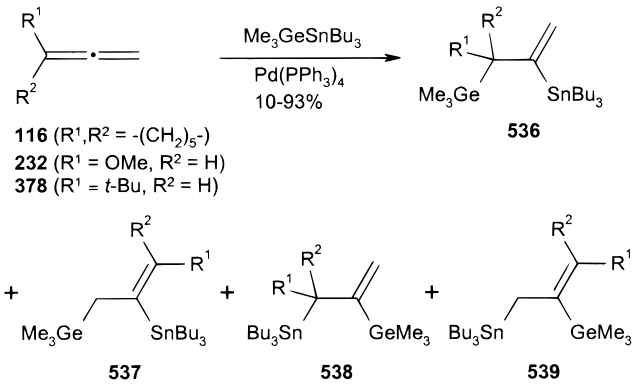
Scheme 145



presence of $Pd(PPh_3)_4$ or $PdCl_2(PPh_3)_2$ gave regioselectively new functionalized organosilicon compounds 2,3-bis(organosilyl)-1-propenes **534** and 2,3-bis(organosilyl)-1-butenes **535**, respectively (Scheme 145).[161,162] It should be emphasized that the reaction of 1,2-butadiene (**533**) gave 2,3-adducts only; no attack at the terminal C−C double bond to obtain 1,2-products was observed. Furthermore, the orientation of the double silylation with unsymmetrical disilanes gave in each case only one disilyl-1-butene regioisomer, exclusively the α-isomer as depicted in the Scheme 145.

Mitchell et al. reported a palladium-catalyzed addition of the Sn−Ge bond to allenes with reversal of regioselectivity; the direction of its addition to allenes is dependent on the structure of the allene (Scheme 146).[149,163] In the case of methoxyallene (**232**), only

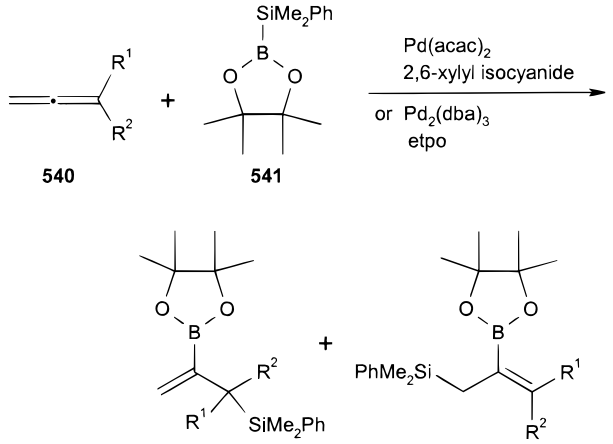
Scheme 146



regioisomeric vinylstannanes **536** and **537** are formed, while with increasing size of R, regioselectivity of the reaction decreases; for allenes **116** and **378**, only allylstannanes **538** and **539** are formed (Scheme 146).

Very recently, Ito et al. showed a new and regioselective silaboration of 1,2-dienes **540** with (dimethylphenylsilyl)pinacolborane **541**, which was efficiently catalyzed by 2 mol % of $Pd(acac)_2$ in the presence of 8 mol % 2,6-xylyl isocyanide resulting in the formation of the corresponding 2-boryl-3-silyl-1-alkenes **542** (Scheme 147).[164] The silaboration of **540** was also promoted by Pd/1,1,3,3-tetramethylbutyl isocyanide complex, providing **542** in high yield, however, accompanied by its regioisomer **543**. Noteworthy, in the case of 3-perfluoro-hexyl-1,2-propadiene (**544**), a remarkable reverse of regioselectivity was observed, suggesting a significant electronic effect in the regiochemical control of this reaction (Scheme 148).

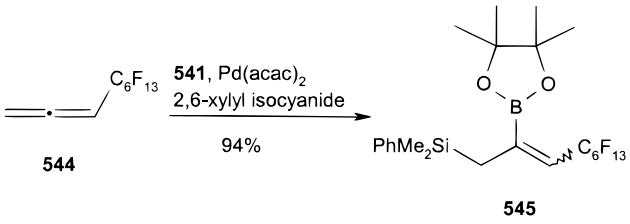
Scheme 147



Entry	R^1	R^2	542/543	Distribution 542 : 543	Ref.
1	Me	H	88%	100 : 0	165
2	MeO	H	86%	100 : 0	165
3	H	H	91%	--	165
4	Ph	Ph	94%	0 : 100	165
5	Me	Me	84%	52 : 48	165
6	$(CH_2)_2Ph$	H	99%	>99 : 1	164
7	*c*-Hex	H	91%	>99 : 1	164
8	*t*-Bu	H	88%	94 : 6	164
9	Ph	H	95%	86 : 14	164

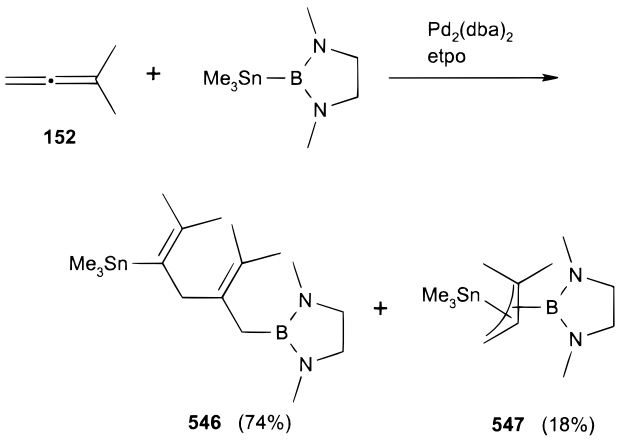
For entries 1-5: $Pd_2(dba)_3$-etpo was used as catalyst
For entries 6-9: $Pd(acac)_2$-2,6-xylyl isocyanide was used as catalyst

Scheme 148



Contemporarily, Tanaka et al. reported borylsilylation and borylstannylative dimerization of 1,2-dienes using a mixture of $Pd_2(dba)_3$/etpo as the catalyst to afford high yields of alkenylboranes **542** (Scheme 147) having allylsilane moieties and telomer **546** (Scheme

Scheme 149



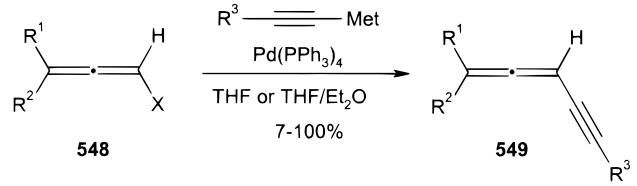
149), respectively.[165] The regioselectivity of Pd/etpo-catalyzed borylsilylation of allenes is strongly influenced by the nature of the substituents on allenes and the structure of the boryl group.

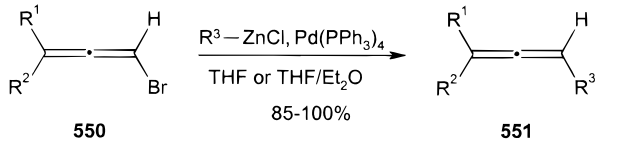
VI. Cross-Coupling Reactions

Transition metal-catalyzed cross-coupling reactions of olefins and alkynes, respectively, are among the multitude of important synthetic transformations which proceed quite conveniently and thus increasing the applicability and feasibility of these reactions for the preparation of numerous target molecules.[166] Taking into account the easy access of halogenated[1,6] and metalated[7,8,89] allenes, the cross-coupling reactions of these substrates are an attractive method for C−C bond formation leading to useful precursors for organic synthesis, e.g., allenes with alkynyl groups as in the case of Myers−Saito−enyne−allene cycloaromatization reactions[167] or aryl- and heteroaryl-functionalized allenes in the synthesis of preparatively very useful α,β-unsaturated carbonyl compounds.[168] From this angle, substitution on allenes by cross-coupling reactions seems to be a very useful task.

Vermeer and co-workers in 1981 reported the synthesis of aryl-, vinyl-, 1-alkynylallenes and diallenes by the $Pd(PPh_3)_4$-catalyzed reaction of allenic halides.[169] When bromo- or iodoallenes were treated with phenyl zinc chloride in the presence of 0.5−2.0 mol % $Pd(PPh_3)_4$, substituted allenes were formed in excellent yields and with high regioselectivity. Allenynes were also synthesized by the reaction of allenic bromides and 1-alkynyl zinc chlorides (Scheme 150).

Scheme 150

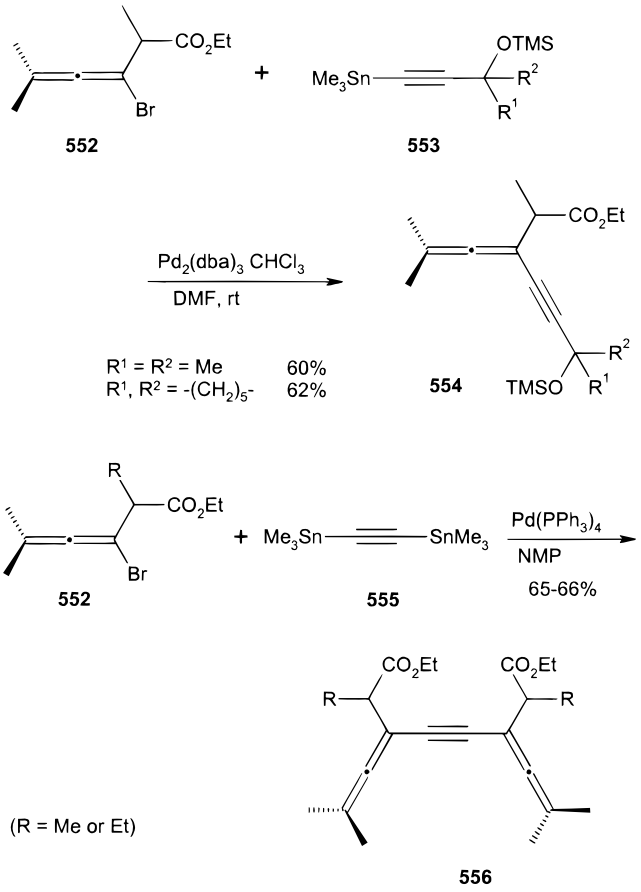




In a continuation of their work, the same authors reported the use of other organometallic reagents for the cross-coupling reactions, even though RZnCl, RMgCl, and cuprate reagents were found to be very suitable for the coupling.[170] A very similar kind of cross-coupling reaction was reported by Linstrumelle and Jeffery-Luong where allenic or propargylic halides were reacted with Grignard reagents by having catalytic amounts of $PdCl_2/PPh_3$/DIBAL-H.[171]

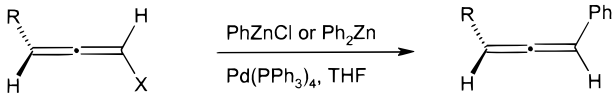
Saalfrank and co-workers reported the synthesis of yne−allenes by a Stille cross-coupling of bromoallenes **552** with stannylalkynes in the presence of $Pd_2(dba)_3 \cdot CHCl_3$.[158] A double-Stille cross-coupling was observed in the case of distannylalkyne **555** (Scheme 151).

Scheme 151



Reactions of organozinc reagents with chiral haloallenes have shown interesting results.[172,173] The $Pd(PPh_3)_4$-catalyzed reactions of allenic chlorides (*R*)-**557a**/**559a** and allenic bromides (*R*)-**557b**/**559b** with phenyl zinc chloride or diphenyl zinc have afforded the substituted allenes (*S*)-**558** and (*S*)-**560**, respectively, with the inversion of configuration (entries 1−3 and 5; Scheme 152). However, allenic iodides (*R*)-

Scheme 152



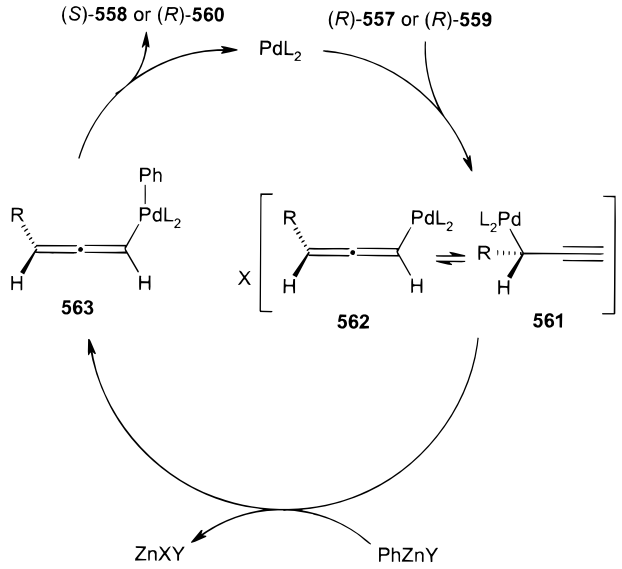
a: X = Cl; **b**: X = Br; **c**: X = I

Entry	Substrate	Reagent	Product	ee
1	(*R*)-**557a**	PhZnCl	(*S*)-**558**	62%
2	(*R*)-**557a**	Ph_2Zn	(*S*)-**558**	36%
3	(*R*)-**557b**	PhZnCl	(*S*)-**558**	80%
4	(*R*)-**557c**	PhZnCl	(*R*)-**558**	12%
5	(*R*)-**559b**	Ph_2Zn	(*S*)-**560**	73%
6	(*R*)-**559c**	PhZnCl	(*R*)-**560**	73%
7	(*R*)-**559c**	Ph_2Zn	(*R*)-**560**	68%

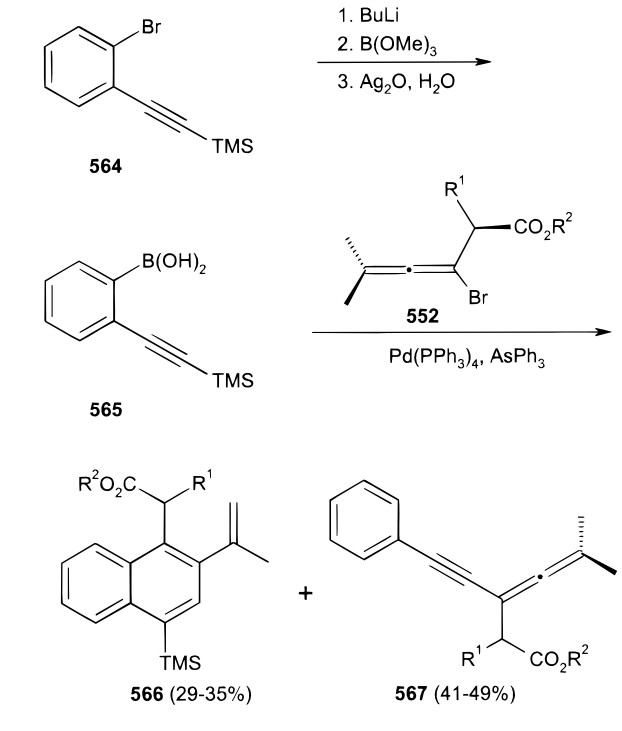
557c and (*R*)-**559c** gave products (*R*)-**558** and (*R*)-**560** with the retention of configuration (entries 4 and 6−7; Scheme 152). The rationalization of the stereochemical outcome was done as follows: In the first step, the active Pd species [$Pd(PPh_3)_2$] adds over the allene in an *anti*-S_N2' way, giving 2-propynylic Pd(II) intermediate **561** which undergoes a suprafacial [1,3]-shift to form **562**. Further reaction of **562** with phenyl zinc chloride or diphenyl zinc affords the diorganopalladium(II) species **563** with the retention of configuration. Finally, the reductive elimination of the product regenerates the catalytically active species, thereby completing the cycle, also with retention of the configuration (Scheme 153). However, the retention of configuration in the case of iodoallenes can be explained by the simple logic that a C−I bond adds oxidatively more easily to transition metals such as Pd. Therefore, a direct oxidative addition at position 1 of 1-iodoallene affords the phenyl-substituted allene with retention of configuration.

Very recently, Saalfrank and co-workers described the Suzuki coupling of bromoallene **552** with the in situ generated boronic acid **565** from (2-bromophenylethynyl)trimethylsilane (**564**) leading to the formation of the naphthalene derivatives **566** and the yne−allenes **567** (Scheme 154).[174] The suggested pathway involves the proton (or metal)-catalyzed rearrangement of intermediate **568**, resulting in the vinyl cation via transition state **569**, which after simultaneous 1,2-TMS shift and C_2-C_7 cycloaromatization forms cation **570**. Transfer of a methyl proton from **570** to palladium (M = Pd) gives **566** (Scheme 155).

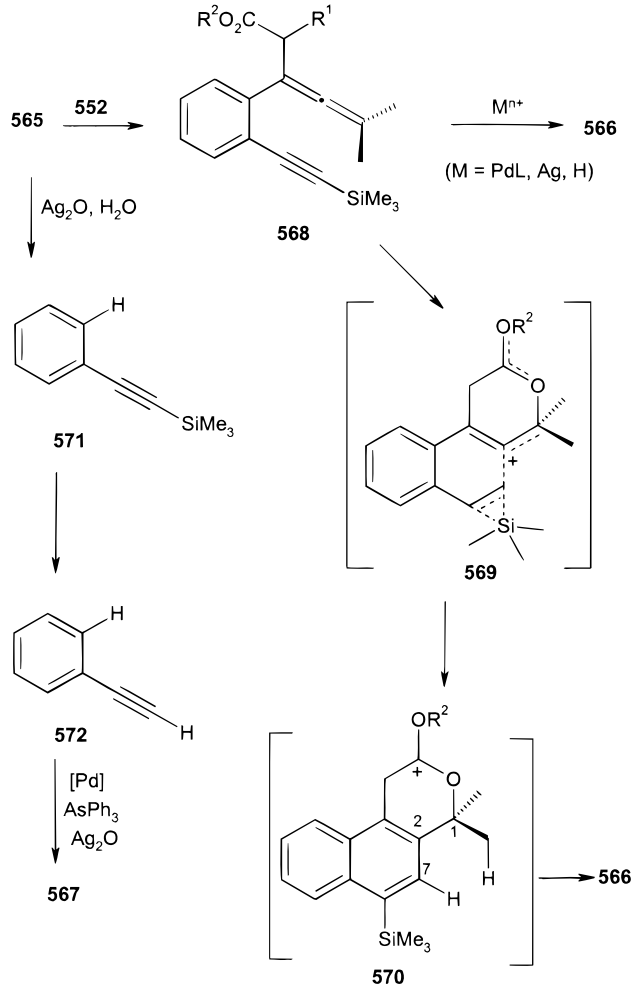
Scheme 153



Scheme 154



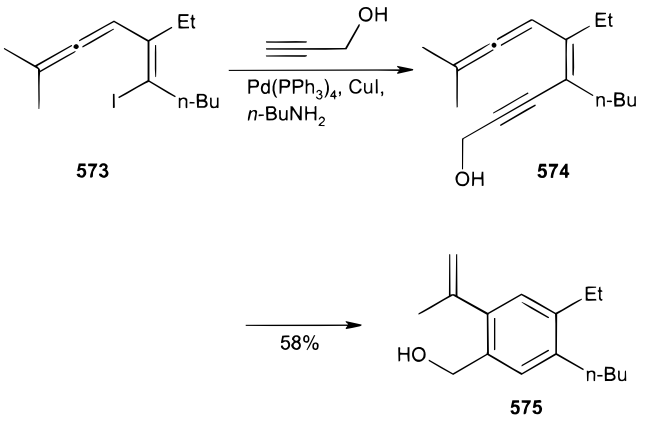
Scheme 155



The formation of **567** was proposed to proceed through the [Pd(0)/Ag(I)]-catalyzed reaction of **552** with the phenylacetylene (**572**), which results from the hydrolysis of **565** followed by spontaneous desilylation of the intermediate **571** as depicted in Scheme 155. This was also independently confirmed by the [Pd(0)/Ag(I)]-catalyzed reaction of phenylacetylene with **552**.

Enyne−allenes are important precursors for cycloaromatization reactions, e.g., the Myers−Saito reaction. The enyne−allene **574** having a tetrasubstituted central C−C double bond was synthesized by Wang et al. by coupling of propargylic alcohol with

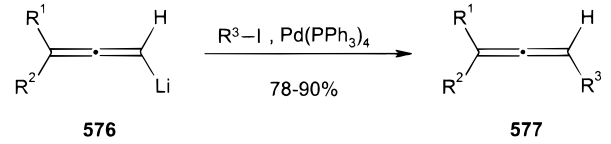
Scheme 156



allene **573**, which further undergoes cycloaromatization under the reaction conditions to give **575** (Scheme 156).[175]

Cross-coupling reactions between the allenyllithium compounds **576** and aryl or vinylic halides can also be carried out. In this way, arylallenes and 1,2,4-trienes **577** were synthesized by the use of $Pd(PPh_3)_4$ (Scheme 157).[176] The coupling reactions can also be

Scheme 157

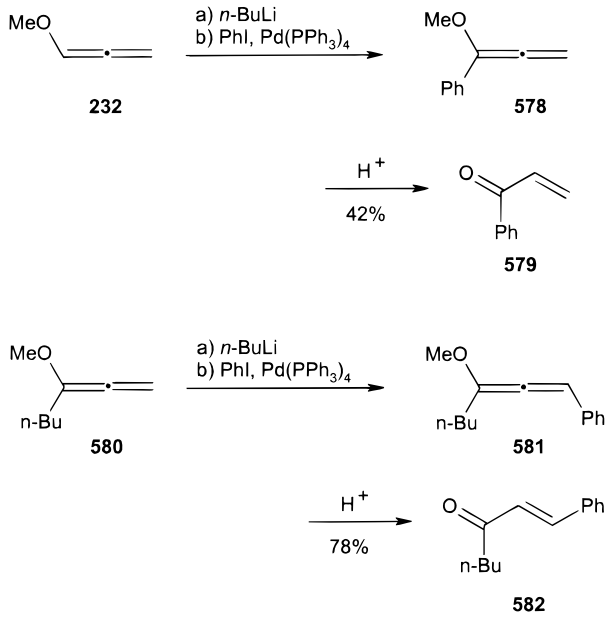


R^1 = Me, *n*-Bu; R^2 = H, Me; R^3 = Ph, *n*-HexCH=CH (*E* or *Z*)

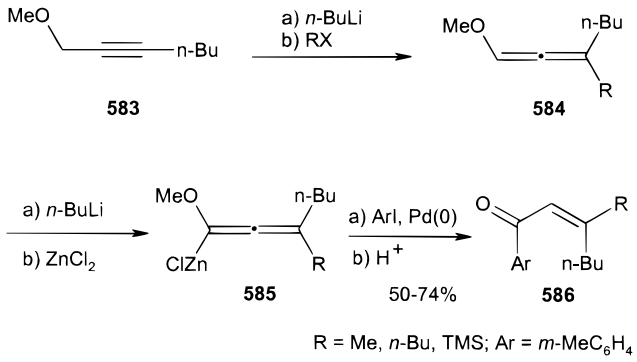
carried out by having another organometallic moiety on the allene such as Mg, Cu, Ag, and Zn.[177]

Methoxyallenes are promising precursors of 1-alkenyl ketones because one of the key features of alkoxyallenes is the smooth deprotonation of the hydrogen atom at C-1.[7,8,89] However, a similar lithiation−arylation sequence described above can give rise to substituted vinyl ketones (Scheme 158).[176] Depending on the nature of the substitution on the starting allene, different substituted alkenyl ketones can be obtained. A similar synthesis of 1-alkenyl ketones was reported by Hegedus et al. using zinc salts of allenic ethers. Even β,β-disubstituted α,β-unsaturated aryl ketones were synthesized by this route (Scheme 159).[178] On the other hand, in the case

Scheme 158



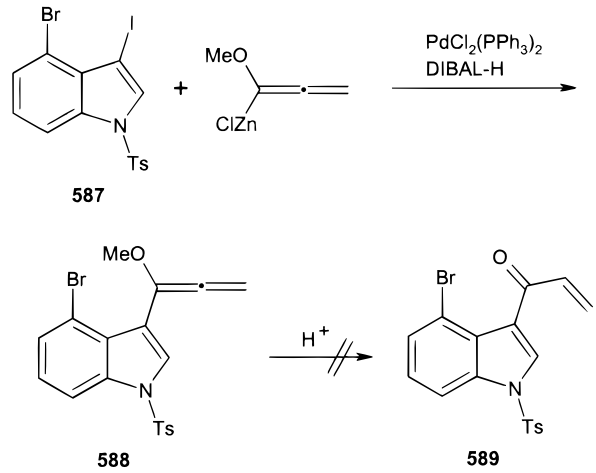
Scheme 159



R = Me, *n*-Bu, TMS; Ar = *m*-MeC_6H_4

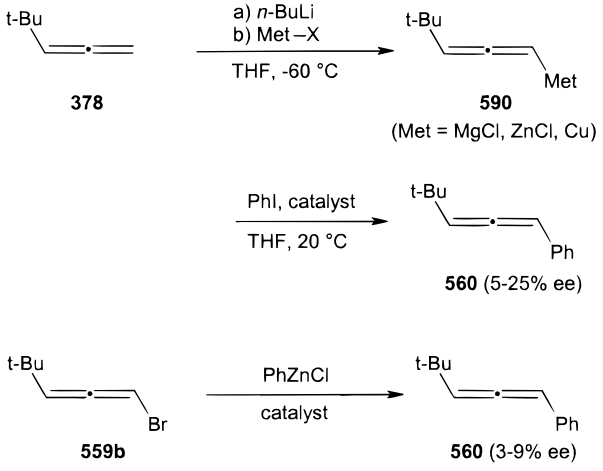
of the iodoindole **587**, the cross condensation did occur to give **588** but the desired hydrolyzed product **589** was not obtained (Scheme 160).[179]

Scheme 160



Chiral induction in the synthesis of 1-phenyl-3-*tert*-butylallene (**560**) was also described by Elsevier et

Scheme 161

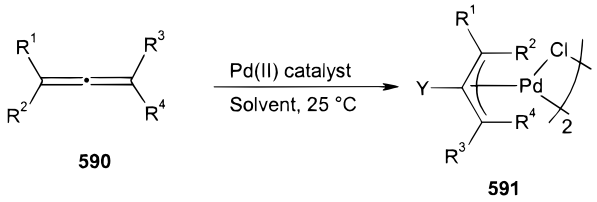


al.[180] The synthesis involves two different cross-coupling reactions, i.e., either between (a) in situ prepared 4,4-dimethylpenta-1,2-dienyl zinc chloride and iodobenzene or (b) 1-bromo-4,4-dimethylpenta-1,2-diene and phenyl zinc chloride (Scheme 161). Out of the several palladium phosphines tried, the highest ee (25%) was obtained via path a from the catalyst combination of $PdCl_2$ and (*R*,*R*)-diop.

VII. Di-, Oligo-, and Polymerization Reactions of Allenes

This section presents an overview of useful palladium-catalyzed di-, oligo-, and polymerization reactions of allenes, which are of course not as explored as the alkenes and alkynes. In 1964, Schultz[15] and then Shaw[16,181] working independently demonstrated the formation of π-allylpalladium complexes **591a** (Y = $ClCH_2C{=}CH_2$) and **591b** (Y = Cl), important intermediates in organic synthesis, in satisfactory yields from the reaction of allenes **590** with Pd(II) catalysts depending upon the catalyst used and the solvent polarity. The bridged chloro complex **591a** containing two allene units can be explained by successive coordination of two allene molecules to Pd followed by dimerization with migration of chlorine from Pd to carbon.[16] The use of polar solvents such as benzonitrile, dichloromethane, or methanol resulted in the formation of complex **591a**, whereas complex **591b** was exclusively formed with nonpolar solvents such as benzene. This is probably because chlorine migration takes place at a rate much faster than the insertion of the second molecule of allene. However, the substituted allenes **590** are reported to only produce complex **591b**, derived from undimerized allenes (Scheme 162).

Scheme 162

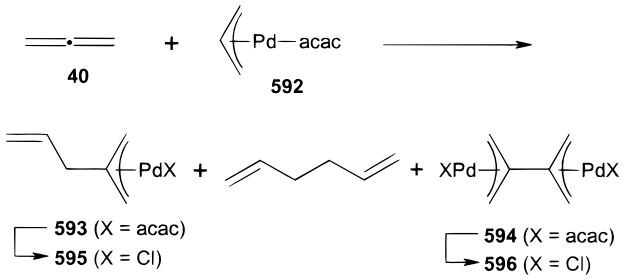


Catalyst A: $PdCl_2(PhCN)_2$
Catalyst B: Na_2PdCl_4

R^1	R^2	R^3	R^4	Solvent	Catalyst	Y	**591**	Ref.
H	H	H	H	PhCN	A	$ClCH_2C{=}CH_2$	79%	15
H	H	H	H	CH_2Cl_2	A	$ClCH_2C{=}CH_2$	42%	16
H	H	H	H	C_6H_6	A	Cl	81%	15
H	H	H	H	MeOH	B	$ClCH_2C{=}CH_2$	88%	16
H	H	H	Me	C_6H_6	A	Cl	50%	16
H	H	Me	Me	C_6H_6	A	Cl	29%	16
Me	Me	Me	Me	C_6H_6	A	Cl	79%	15

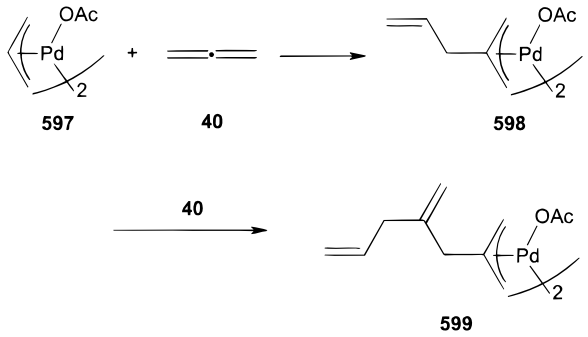
In a related study, Hughes and Powell explored the insertion of 1,2-propadiene (**40**) with acetyl acetonato-π-allylpalladium complex **592**.[182] Surprisingly, the unexpected 2,2′-bisallylpalladium(II) complex **594** was formed as a significant side reaction product along with the allyl−allyl coupling product, 1,5-hexadiene, and the usual insertion product **593** (Scheme 163). Complexes **593** and **594** can be converted to the corresponding dimeric (and polymeric) bridged chloro complexes **595** and **596**, respectively. Complex **594** arising from the coupling of two allene molecules can be synthesized up to a maximum of 40% yield and is important in the synthesis of oligomers of allenes with unusual structure.

Scheme 163



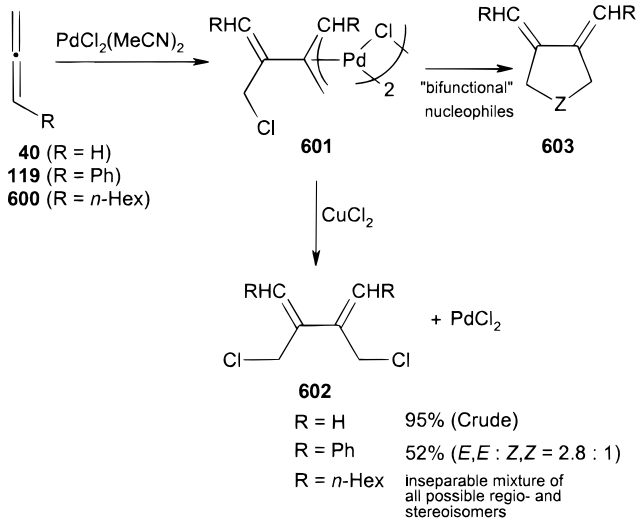
In a detailed account dealing with the mechanistic aspects of oligomerization of dienes, Medema and van Helden studied the reaction of 1,2-propadiene (**40**) with π-allylpalladium acetate **597** as the catalyst in benzene leading to a mixture of products.[183] The mixture of products results due to the successive insertion of **40** since the product **598** formed after addition of one molecule reacts further with allenes (Scheme 164).

Scheme 164



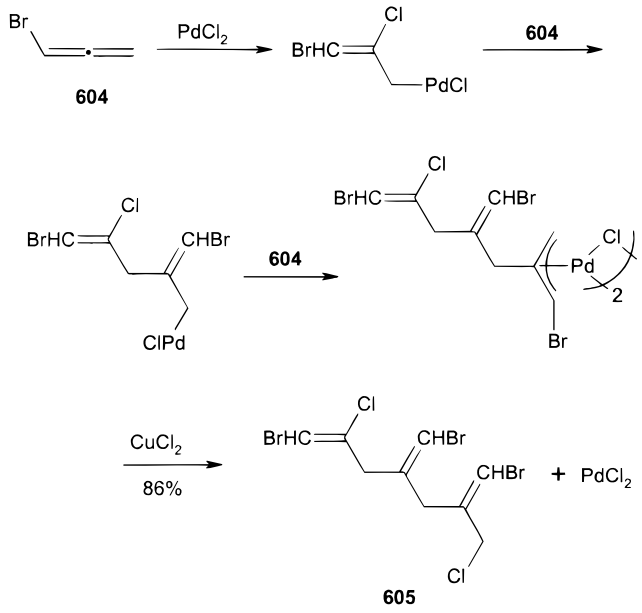
Hegedus utilized the π-allylpalladium complex containing dimerized allene[15,181] initially by using a stoichiometric amount of Pd to synthesize conjugated exocyclic dienes **603** by reaction with certain "bifunctional" nucleophiles.[21] Subsequently, his group reported a modified procedure employing the reaction of allenes **40**, **119**, and **600** with $PdCl_2(MeCN)_2$ (0.5−1 mol %) and $CuCl_2$ (2 equiv).[22] Under these conditions, π-allylpalladium complex **601** is oxidatively cleaved to allylic chlorides by $CuCl_2$ with simultaneous release of $PdCl_2$, which continues the catalytic cycle (Scheme 165). Using this method, multigrams of pure and synthetically useful 2,3-bis-(chloromethyl)-1,3-butadiene **602** (R = H) can be prepared in less than 24 h. Interestingly, using $CuBr_2$ in place of $CuCl_2$, the corresponding bis(bromomethyl) compound can be prepared, of course in diminished yield (32%). Complicated mixtures of regio- and geometric isomers were obtained in the case of 1-substituted allenes **119** and **600**. Ethoxyallene and 1,1-dimethylallene were found to give polymeric products. However, treatment of 1-bromoallene **604** with the same catalytic system leads to the corre-

Scheme 165



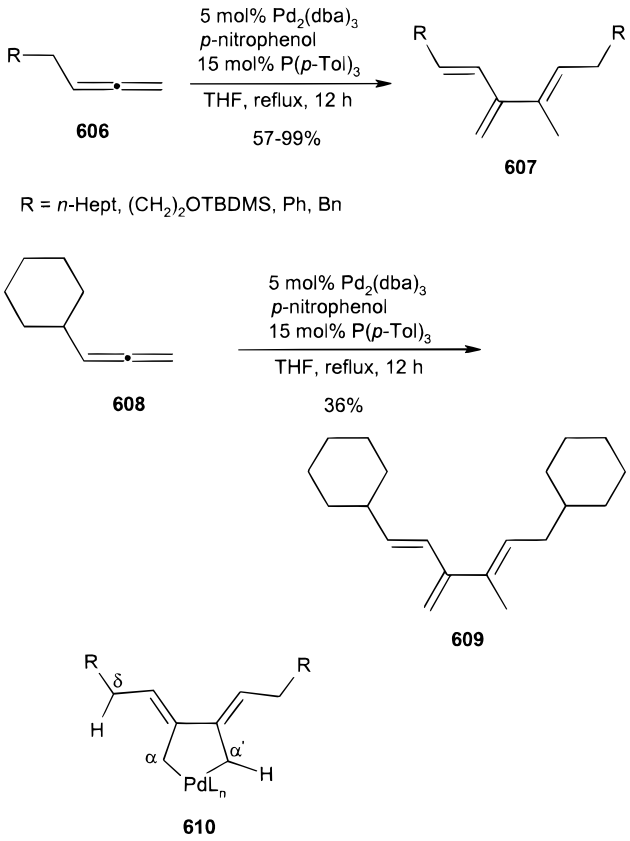
sponding trimerization product **605** in excellent yield, apparently via the initial chloropalladation occurring with opposite regiochemistry as that of allene itself (Scheme 166).

Scheme 166



In an interesting application of the palladium-catalyzed dimerization of allenes, Yamaguchi recently described an efficient synthesis of the cross-conjugated trienes **607** by the reaction of allenes **606** with a novel catalyst combination of $Pd_2(dba)_3$, *p*-nitrophenol, and P(*p*-Tol)$_3$ (Scheme 167).[184] Use of phenols as a promoter and P(*p*-Tol)$_3$ were essential for the success of the reaction. Apparently *p*-nitrophenol, which acts as a Brønsted acid, was found to give better results than phenol or substituted phenols having electron-donating groups. While the methylene-substituted allenes converted in almost quantitative yields of the corresponding (*E*,*E*)-trienes, the methine-substituted allene such as 1-cyclohexyl-1,2-propadiene (**608**) showed diminished reactivity. A plausible mechanism which involves the initial formation of a five-membered palladacycle **610** followed

Scheme 167



by the reductive elimination with simultaneous phenol-catalyzed proton transfer from δ- to the α'-position gives the desired product.

The cycloisomerization−dimerization of allenyl ketones **611** using palladium catalysts A, B, and C under mild conditions leading to the expected monomeric product **612** along with the dimeric product **613** was most extensively investigated by Hashmi and co-workers in a series of publications (Scheme 168).[185−188] The reaction was successfully carried out

Scheme 168

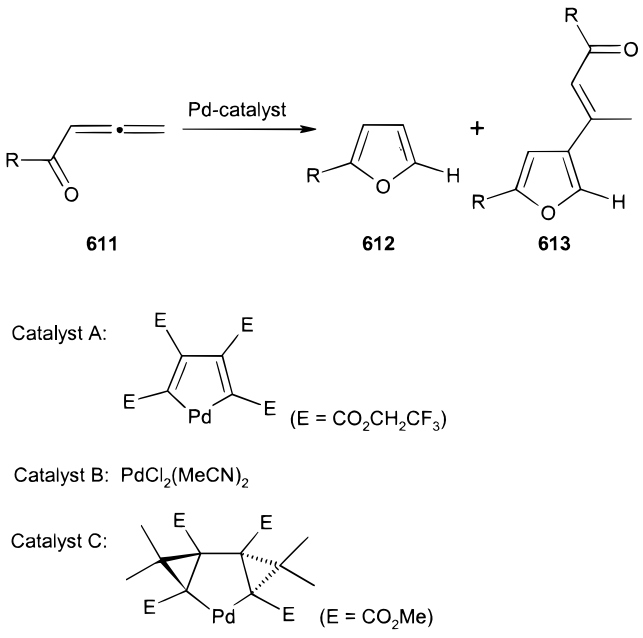
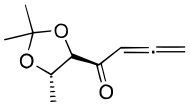


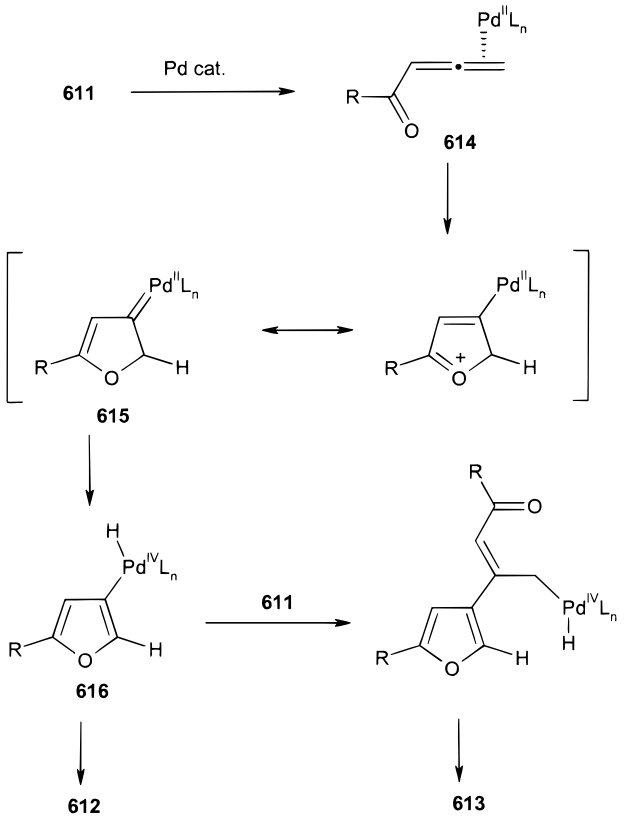
Table 1. Pd-Catalyzed Cycloisomerization/Dimerization of Allenyl Ketones 611

			ratio	isolated yield %		
611	R	cond.	**612**:**613**	**612**[d]	**613**	ref
a	CH_3	A	1:8.8		86	186
		B	1:30		89	186
		C[a]	1:2.1		70	187
b	$CH(CH_2)_4$	A	1:3		67	186
		B	1:3.8		82	186
c	$C(CH_3)_3$	A	1:1		33	185
		B	1:2.9	11	54	186
d	CH_2Cl	A	1:2.2		60	186
		C[b]	3.6:1		29	187
e	$(CH_2)_3OH$	B	1:1.4	8	79	186
f	$CH(OMOM)CH_3$	A	1:2.8		42	186
g	$CH(OTBDMS)CH_3$	A	1:3.6	8	84	186
h		B	1:17		83	186
i	$C(CH_2)_3CCH_2CH{=}CH_2$	B	1:2		60	186
j	$3\text{-}(CH(OH)CH{=}C{=}CH_2)C_6H_4$	B	1:0.5	38	43	186
k	$CH(OCH_2C{\equiv}CH)CH_3$	B	1.9:1	44	46	187
		C[c]	20:1	80	8	187
l	$C(CO_2CH_3)(CH_2C{\equiv}CH)_2$	B	1:14		61	186
m	$C(CH_2C{\equiv}CH)(OCH_2C{\equiv}CH)CH_3$	B	1.3:1	32	49	187
		C	20:1	*e*	*e*	187
n	$CH_2C_6H_5$	A	1:6	4	76	186
o	C_6H_5	A	1:6.1	5	81	186
p	$2,5\text{-}(OMe)_2C_6H_3$	A	1:7.2	5	75	186
		B	1:32		81	186
q	$2\text{-}XC_6H_4$ (X = F, Cl, Br, I)	A	1:8.2− 1:16	3−5	76−90	186
r	$C{\equiv}CC_6H_5$	A	*e*	6	18	186
s	3-furyl	A	1:5.5		69	186
t	2-thienyl	A	1:9.4		75	186
u	$2\text{-}(NO_2)C_6H_4$	B	*e*	3	90	188
v	$4\text{-}(CN)C_6H_4$	B	*e*		77	188
w	$4\text{-}(AcNH)C_6H_4$	B	*e*	3	87	188
x	CH_2CH_2SMe	B				188
y	$4\text{-}(MeS)C_6H_4$	B				188

[a] In CD_3CN. [b] In CD_2Cl_2. [c] In C_6D_6. [d] Too volatile to be isolated. [e] Not reported.

with a wide variety of substrates, a partial listing of which is shown in Table 1. The terminal allenic ketones produce **612** or **613** depending upon the choice of the catalyst and solvent, but **612** is the sole product from nonterminal ketonic allenes. With Trost's catalyst $TCPC^{TFE}$ (catalyst A) in acetone, the 2,4-disubstituted furans **613** are predominant over **612,**[185,186] but better selectivity in product distribution leading to the formation of **613** was observed using readily available $PdCl_2(MeCN)_2$ in acetonitrile (catalyst B).[185,187,188] Under similar conditions, using his newly developed PTH catalytic system (catalyst C)[187] in benzene, dichloromethane, or acetonitrile, the 2-substituted furans **612** resulted almost exclusively, acting as a powerful alternative to Marshall's pioneering Ag(I) and Rh(I) catalysts.[189] It was found that the yield of **613** is suppressed over **612** with increasing steric bulk of the R group in allenic ketones (Table 1, **611a**−**c**,**i**). A variety of functional groups such as α-halo ketones **611d**, aryl halides **611q**, alkenes **611i**, alkynes **611k**−**m**, oxygen-containing functional groups such as free hydroxy functionalities **611e**,**j**, α-alkoxy **611f**, α-siloxy **611g**, acetalic, ketalic **611h**, carboxylic ester **611l,** and nitrogen functionalities **611u**−**w** remain inert under the present reaction conditions, thus increasing the applicability and importance of the methodology. The allenic ketones having a chiral α-carbon, for example as for **611h,** converted to a single isomer without any racemization. Moreover, α-halo ketones and alkynes which cannot be utilized by Marshall's catalytic systems can be directly reacted using Pd catalysts. An excellent chemoselectivity is observed for substrates containing aryl bromides, terminal alkynes, 1,6-enyne **611l,** and α-allenic alcohol **611j** moieties which are highly prone in palladium-catalyzed reactions. Furthermore, unique reaction behavior was observed with the substrate **611j** containing two terminal allene units where the other allene unit is an α-allenic alcohol. However, conjugated alkyne **611r** shows diminished reactivity, and the reaction fails with sulfur-containing substrates, for example as for thioethers **611x**,**y** and γ-halogen allenyl ketones (halogen on the other terminal). The possible pathway leading to the formation of **612** and **613** can be explained by the heterocyclic vinyl carbene intermediate **615** obtained via the intramolecular carbopalladation of Pd-coordinated allene complex **614**. The furyl hydridopalladium(IV) species **616** formed after β-hydrogen elimination of **615**, undergoes reductive elimination resulting in **612**, and **613** is formed by the addition of another molecule of **611** to **616** followed by reductive elimination as depicted in Scheme 169. The observed (*E*)-selectivity of the trisubstituted double bond in **613** is due to carbopalladation on the side of the double bond away from

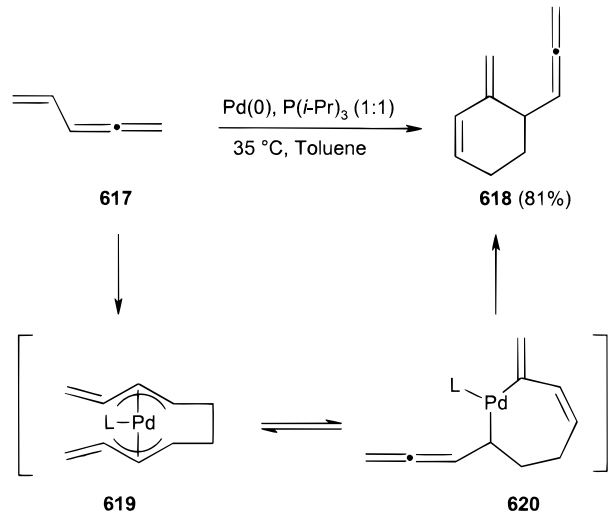
Scheme 169



the carbonyl group. The switching of selectivity leading to the exclusive formation of **612** in the case of PTH is because of steric crowding, showing a strong deviation from an ideal square-planar complex where the approach of the second allenyl ketone becomes difficult. Solvents which are good donor ligands, for example acetonitrile, acetone, EtOH, MeOH, nitrogen, and oxygen, stabilize **616**, eventually leading to **613**, and weaker donor ligands, such as $CDCl_3$, ethers, and benzene, favor reductive elimination of **616** giving **612**.

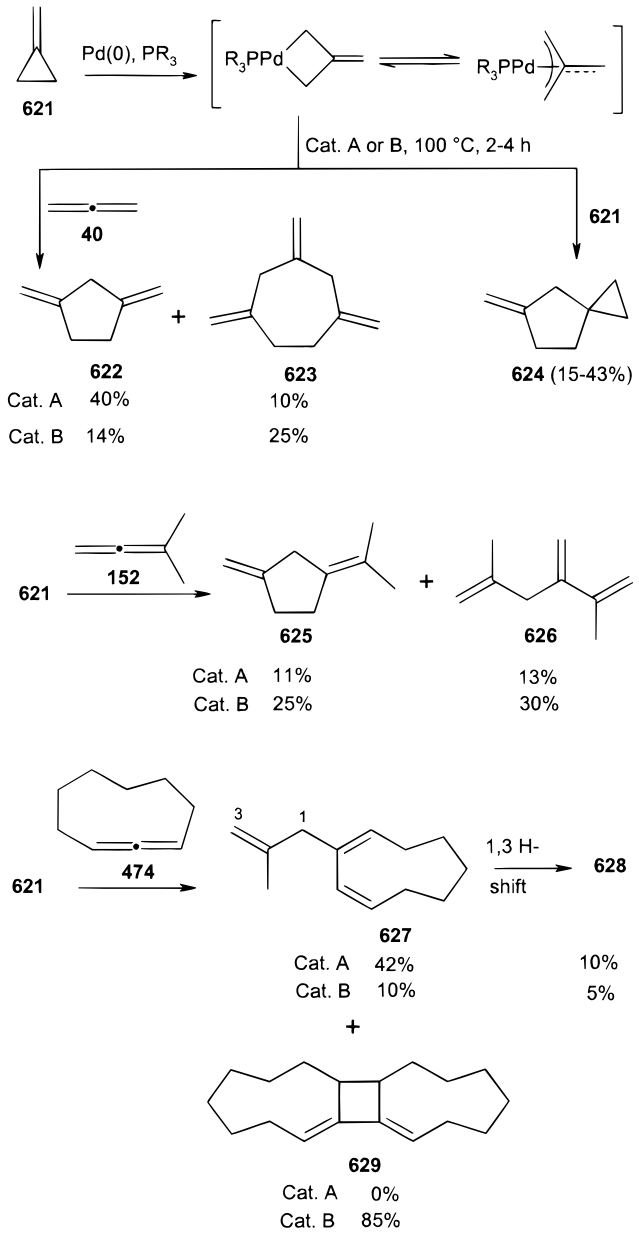
The palladium-catalyzed cyclodimerization of vinylallene **617**, the smallest molecule possessing a conjugated diene and a cumulative diene, was also reported.[190] Under mild conditions, a mixture of six-membered ring dimers is formed out of which the predominant formation of **618** can be explained by oxidative addition of Pd(0) to the butadiene part followed by tail-to-tail coupling involving intermediates **619** and **620** (Scheme 170).

Scheme 170



The co-oligomerization of methylene cyclopropane **621** with 1,2-propadiene (**40**), 1,1-dimethylallene (**152**), and 1,2-cyclononadiene (**474**) using Pd(0) catalyst precursors A and B was described by Binger and Schuchardt (Scheme 171).[191] Reaction of 1 mol of **621** with 2 mol of 1,2-propadiene (**40**) furnished the cyclodimerization product **622** and the cyclotrimerization product **623**. The allene **152** affords the cyclic codimer **625** along with the open-chain dimeric product **626**, and the cyclic allene **474** yields the corresponding products depending upon the catalyst used. In the presence of catalyst A, **474** is converted

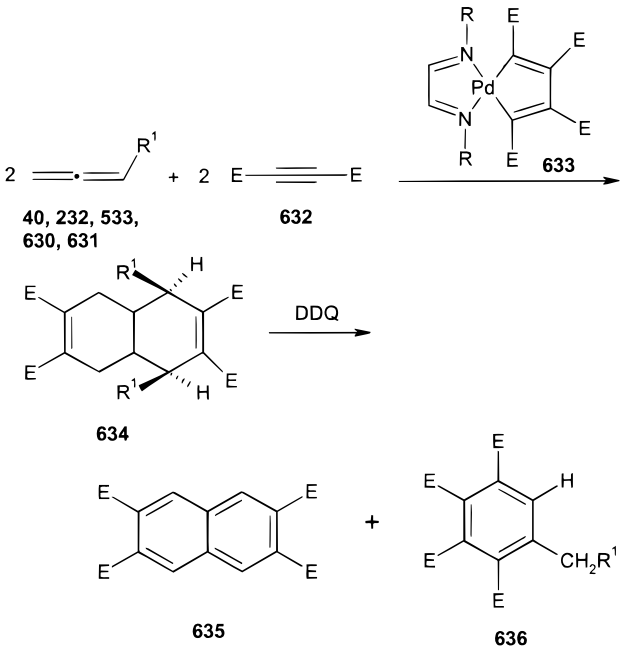
Scheme 171



to **627** and **628** wherein **628** is the result of 1,3-H shift of **627** while **629**; the thermal cyclodimer of **474**, was the major product with catalyst B. In all cases, the spiro derivative **624**, the cyclodimer of **621**, was found as one of the side products.

tom Dieck's group reported the synthesis of tetrasubstituted naphthalene ester **635**, an important class of organic compounds for the preparation of polyimides from the reaction of 2 mol of allenes with 2 mol of acetylene dicarboxylate **632** in the presence of diazadiene-stabilized palladacyclopentadiene **633** as the catalyst (Scheme 172). Compound **635** can be

Scheme 172



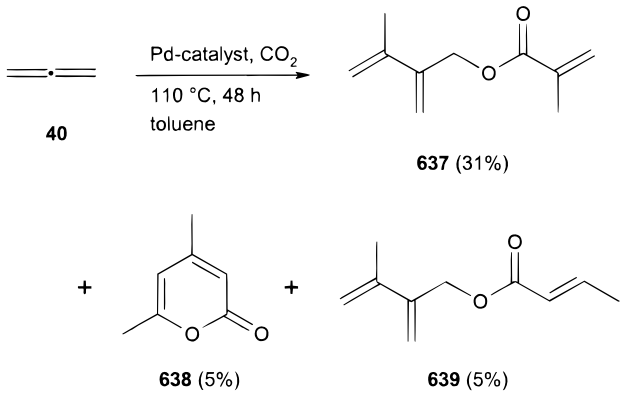
Allene	R^1	E	634	635	636
40	H	CO_2Me	82%	quant.	--
40	H	CO_2Et	70%	quant.	--
40	H	COMe	20%	quant.	--
232	OMe	CO_2Me	28%	33% [a]	--
630	OCHMeOEt	CO_2Me	--	8% [b]	--
631	OPh	CO_2Me	--	--	22%
533	Me	CO_2Me	--	--	80%

[a] At 40 °C (one step) **635** was obtained.
[b] At 0 °C by one step from **630**.

obtained from the reaction of 1,2-propadiene (**40**) in high yield by a two-step procedure and by a novel one-step procedure from allenic ethers **232** and **630**, of course in diminished yields, both via **634**.[192,193] Interestingly, in the case of phenoxyallene (**631**) and methylallene **533**, no **635** but cotrimerization product **636** was formed, possibly due to steric reasons.

Döhring and Jolly studied the palladium-catalyzed co-oligomerization of 1,2-propadiene (**40**) and carbon dioxide leading to a mixture of esters **637** and **639**, δ-lactone **638**, hydrocarbon oligomers, and polymer (Scheme 173).[144] Among the various metal−ligand combinations probed, the Pd catalyst prepared by treating $(\eta^3\text{-}C_3H_5)_2Pd$ with bis-di(cyclohexyl)phosphinoethane (1:1) at 110 °C in toluene was found to be the most effective and furnished the highest yields

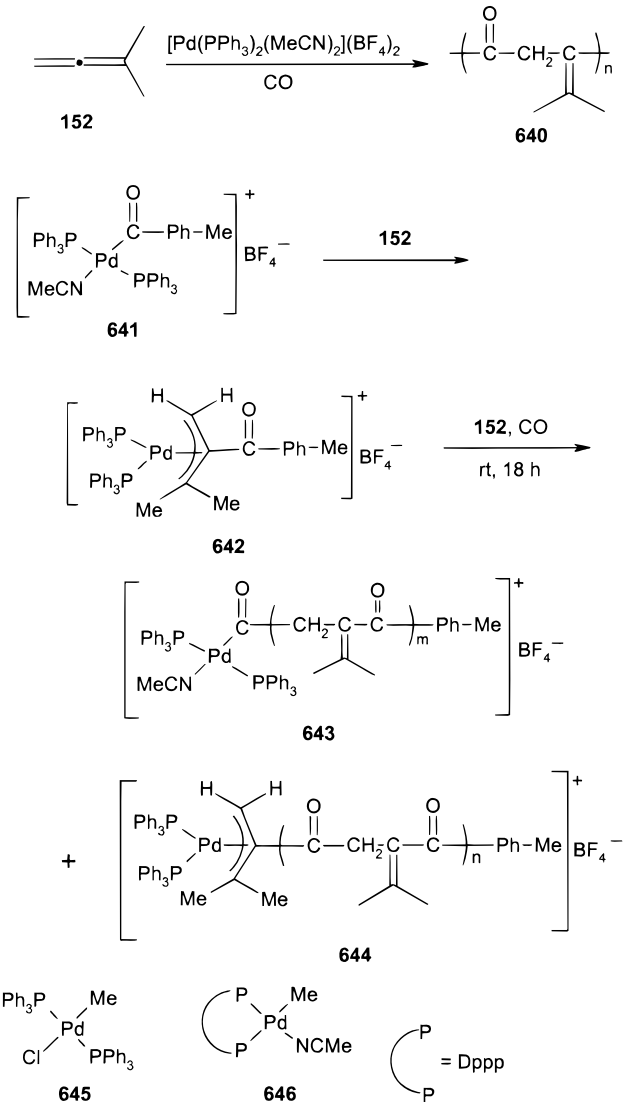
Scheme 173



(ca. 41% at 48% of conversion). The process was significantly less efficient with other catalyst precursors such as $Pd(dba)_2$ or ligands, e.g., dppe, PPh_3, $P(i\text{-}Pr)_3$. Also, lower reactivity was observed with other solvents such as DMF or in the presence of H_2O.

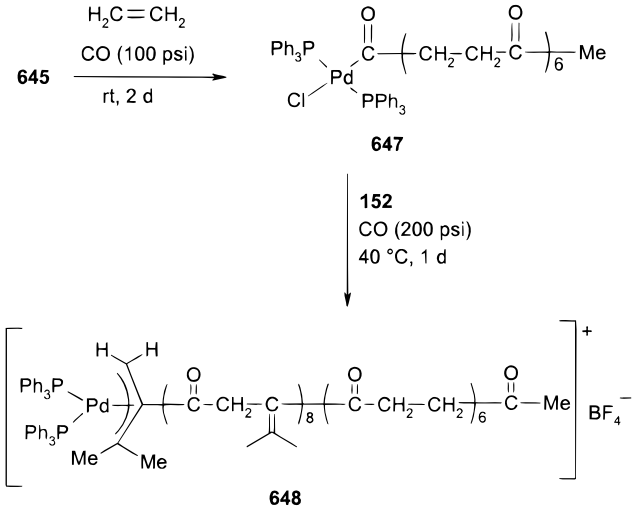
The palladium(II)-catalyzed alternating copolymerization of 1,1-dimethylallene (DMA, **152**) with carbon monoxide using $[Pd(PPh_3)_2(MeCN)_2](BF_4)_2$ as catalyst in a 2:1 (v/v) solvent mixture of nitromethane

Scheme 174



and MeOH was recently developed by Sen (Scheme 174).[194] The alternate DMA−CO copolymer of possible structure **640** was predominantly formed, and a considerable decrease in reactivity was observed with the bidentate ligands such as dppp and (*R*,*R*)-Me-duphos. The stepwise successive insertion of **152** and carbon monoxide into Pd−C bonds was performed using complexes **641**, **645**, and **646**. Catalyst **641** with a noncoordinating anion was found to be significantly more reactive than **645** and gave two different types of oligomers of **152** and carbon monoxide, **643** and **644** by alternate insertion of **152** and carbon monoxide via intermediate **642** (Scheme 174). Similar types of DMA−CO copolymers were also observed in the case of **645**, except that the anion was chloride. Complex **646** with a bidentate, chelating ligand gave an η^3-allyl complex similar to **642** but failed to undergo insertion of a carbon monoxide molecule even at 200 psi. The insertion of the substituted end of the allene is not smooth as demonstrated by a similar experiment with tetrasubstituted 1,1,3,3-tetramethylallene. This technology was successfully applied to prepare a terpolymer with alt−ethene−carbon monoxide and alt−allene−carbon monoxide blocks incorporating three different classes of monomers, viz. alkene, allene, and carbon monoxide (Scheme 175). In the first step, ethylene

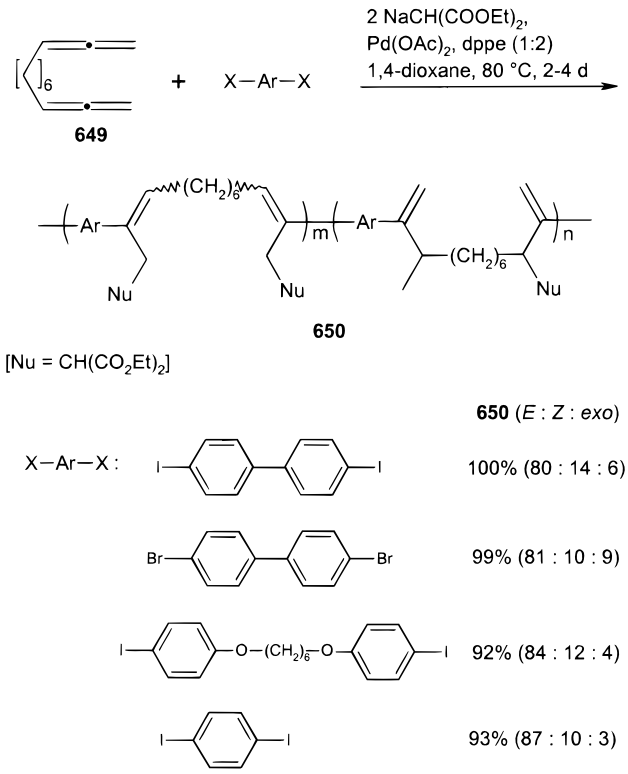
Scheme 175



and carbon monoxide at 100 psi each in the presence of complex **645** introduce a living copolymer **647**, which then reacted with **152** and 200 psi carbon monoxide to give **648**, a living terpolymer.

A novel polycondensation between bifunctional allene **649**, a variety of aryl dihalides, and sodium diethyl malonate as nucleophile, developed by Endo and co-workers, proceeds extremely efficiently using $Pd(OAc)_2$ and dppe as the catalytic system in 1,4-dioxane leading to the formation of polymer **650** with three building blocks (Scheme 176).[195] The molecular weight of the resulting polymers varied over a range of $M_n = 8300-13700$. Using a stoichiometric amount of **649** and X−Ar−X, the highest molecular weight was achieved and quite surprisingly the molecular weight of the polymer decreased drastically with increasing concentration of the catalyst. In all cases, the polymer

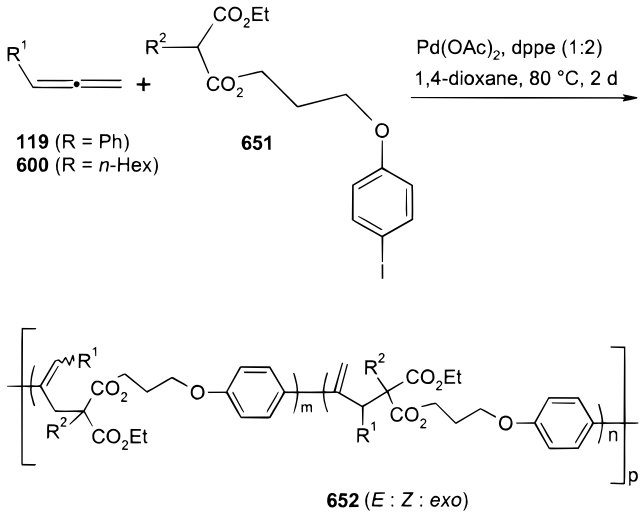
Scheme 176



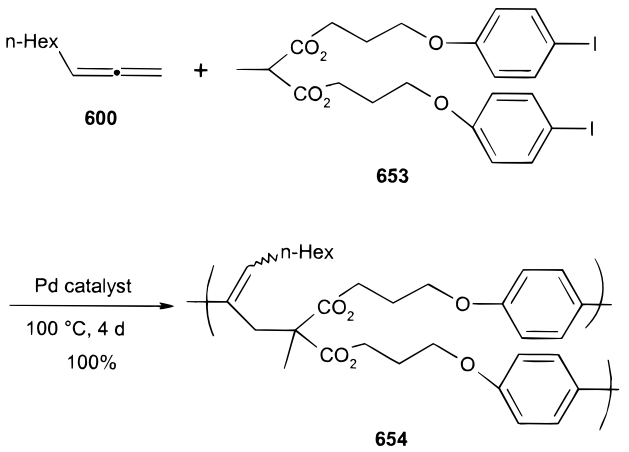
backbone was composed with double bonds with predominant (*E*)-isomer and exomethylene units.

The same group also developed the polymerization of monofunctional allenes **119** and **600** with nucleophiles containing aryl halide moieties **651** in the presence of 1.5 mol % of $Pd(OAc)_2$ and dppe (1:2) (Scheme 177).[196] Excellent yields of the corresponding polymers **652** resulted consisting of three components−allene−nucleophile−aryl−in the chain with molecular weights varying in the range of $M_n = 4600-5900$. The polymer obtained from *n*-hexylallene (**600**) was composed of both internal and exomethylene double bonds, whereas only internal (*E*)- and

Scheme 177



Scheme 178

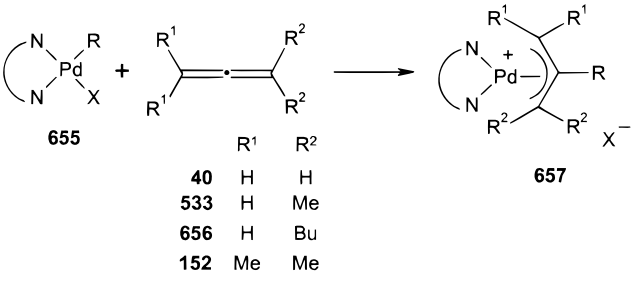


(*Z*)-double bonds were found in the polymer backbone of phenylallene (**119**). The polymerization of *n*-hexylallene (**600**) with nucleophiles containing two aryl halide units **653** gave a high yield of a multibranched polymer **654** (Scheme 178).

VIII. Miscellaneous Reactions

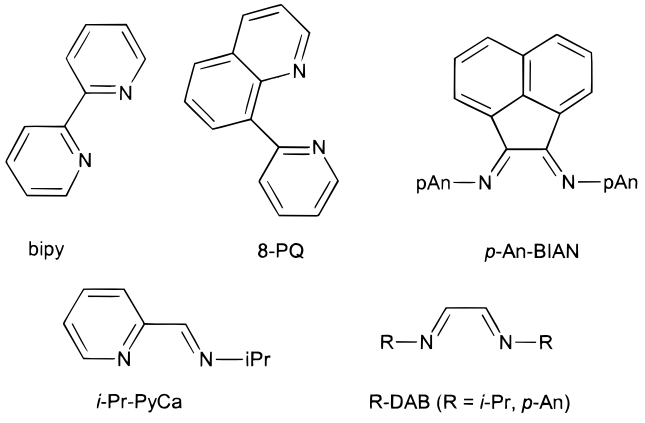
Vrieze, for the first time, investigated the insertion of allenes into Pd−C bonds of complexes containing

Scheme 179



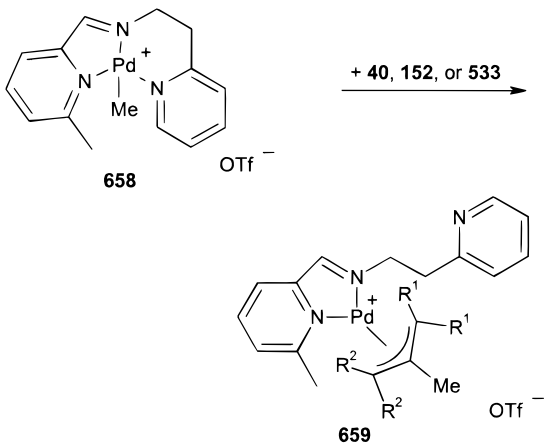
	R^1	R^2
40	H	H
533	H	Me
656	H	Bu
152	Me	Me

655 N⌒N	R	X
a, bipy	Me, C(O)Me, Bn, C(O)Ph, $CH_2C(O)OMe$	Cl, OTf, BF_4
b, 8-PQ	Me, C(O)Me	Cl, Br
c, 8-PQ	C(O)Ph, C(O)*i*-Pr	Cl
d, *p*-An-BIAN	C(O)Me, C(O)Ph	Cl
e, *i*-Pr-DAB	C(O)Me	Cl
f, *i*-Pr-PyCa	C(O)Me	Cl



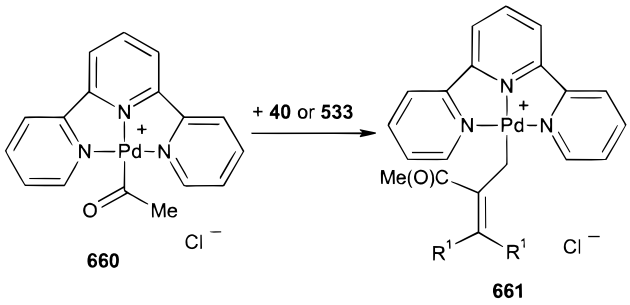
bidentate[15,19] and terdentate[15] N ligands. A variety of substituted highly fluxional and stable η^3-allylpalladium complexes **657** were prepared in quantitative yields from the insertion of allenes to Pd complexes containing bidentate ligands **655a**−**f** (Scheme 179).[15,19] In the case of Pd complexes containing terdentate ligands such as flexible mmap in complex **658**, allenes form η^3-allyl products **659** by changing the terdentate coordination to bidentate (Scheme 180).[15] Whereas

Scheme 180



the strong tendency of terpy ligand **660** to maintain its terdentate coordination resulted in the unexpected η^1-allyl product **661** (Scheme 181).[15] The insertion of

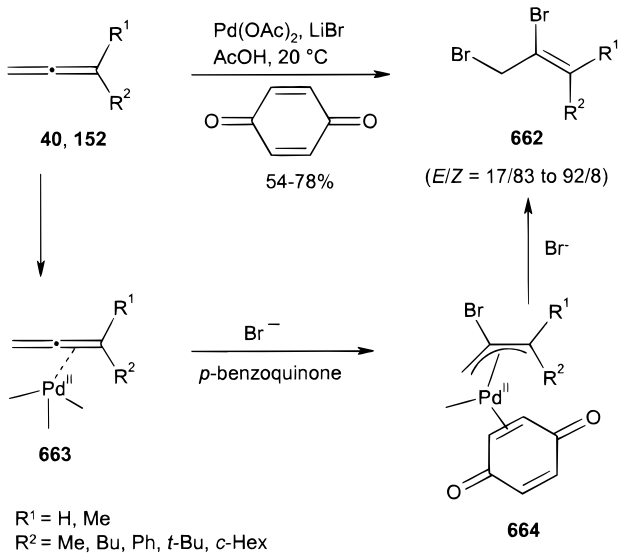
Scheme 181



1,2-propadiene (**40**) and *n*-butylallene (**656**) to bidentate N ligands was demonstrated in a detailed manner dealing with the structural and mechanistic studies.[19] Both **40** and **656** insert in complexes **655b,** while complexes **655c** react only with **40**. Complexes **655d**−**f** react with **656** to give the corresponding η^3-allyl products **657**. Quite surprisingly, X-ray crystallographic determination established the monodentate coordination of N ligand 8-PQ in complex **655a** (when R = C(O)Me). Further NMR NOE data indicated that the ligand 8-PQ coordinates as a monodentate ligand in nonpolar solvents, whereas bidentate coordination was observed in polar solvents. The allene insertions are of first order in concentration of metal complex **655** and proceed via an allene-independent and -dependent pathway as revealed from the kinetic studies.[19] As per the proposed mechanistic pathway, the rate-determining step involves the migration of R group to the electrophilic central carbon atom of the allenes.

1,2-Bromination of allenes **40** and **152** was achieved by Bäckvall in a highly regioselective manner using

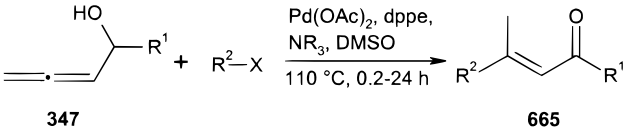
Scheme 182



$Pd(OAc)_2$ as the catalyst and *p*-benzoquinone as the oxidant in the presence of LiBr in acetic acid (Scheme 182).[197] Using a mixture of LiCl and LiBr in a competitive experiment, the palladium-catalyzed oxidation of dimethylallene **152** ($R^1 = R^2 = Me$) gave a mixture of the corresponding 1,2-dibromide **662** and 1-chloro-2-bromo product, implying that the halide in the 2-position is always bromide. The reaction profile involves Pd complex **663** as well as Pd−quinone complexes **664**.

Another important demonstration by Tsuji is the synthesis of conjugated and polyconjugated enones **665** by palladium-catalyzed reaction of α-allenols **347** with aryl or alkenyl halides in the presence of tertiary amines (Scheme 183).[198] The method provides *β*-aryl- or *β*-alkenyl-*β*-methyl-α,*β*-unsaturated carbonyl compounds, which are difficult to prepare even by the most fundamental aldol condensation, for example, the preparation of keto aldehyde **665** with $R^1 = i$-Bu and $R^2 = C_6H_4CHO$. In this method, $Pd(OAc)_2$ is used as the catalyst in the presence of NMP or NEt_3 as base and dppe and DMSO as the preferred ligand and solvent, respectively.

Scheme 183

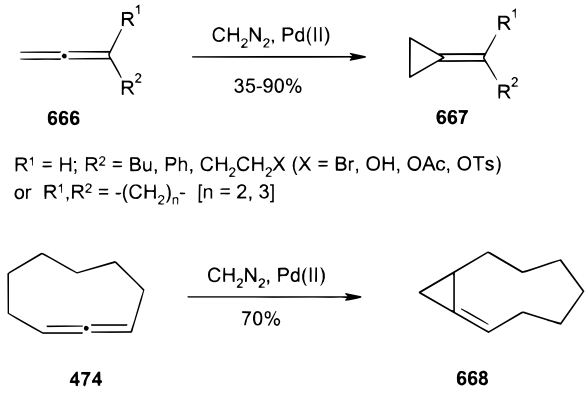


R^1	R^2—X	NR_3	**665** (*E* : *Z*)
H	PhI	NMP	88% (7 : 3)
H	PhI	NMP [a]	84% (5 : 3)
H	PhI	NMP [b]	67% (5 : 3)
H	PhI	NEt_3 [b]	69% (3 : 2)
H	PhI	NEt_3	57% (7 : 3)
H	PhCH=CHBr	NMP	69%
Ph	PhI	NMP	65%
Ph	PhCH=CHBr	NMP	94% (2 : 1)
i-Bu	PhCH=CHBr	NMP	77% (2 : 1)
i-Bu	*p*-BrC_6H_4CHO	NMP	61% (8 : 1)

[a] PPh_3 as ligand.- [b] MeCN as solvent.

Cyclopropanation of allenes can be efficiently achieved by using diazomethane in the presence of Pd(II) catalysts (Scheme 184).[199−201] The reaction

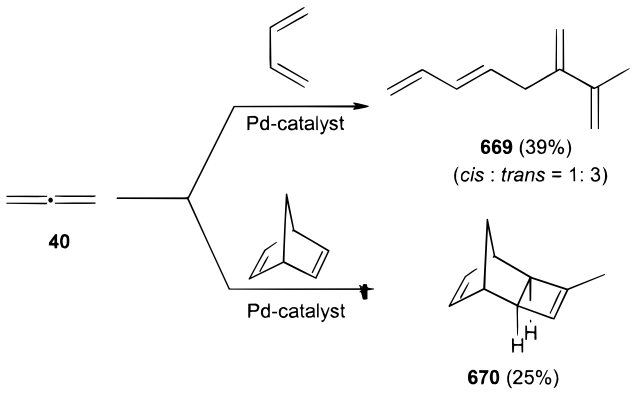
Scheme 184



procedure is superior over others in terms of high regioselectivity in the sense that the addition occurs at the less substituted terminus with the exclusion of double addition products giving rise to the alkylidine cyclopropanes **667** in good yield. 1,2-Cyclononadiene (**474**) produces the corresponding monomethylenation product **668**,[199] and in the case of vinylidine cyclopropane **667** [$R^1,R^2 = -(CH_2)_2-$], bicyclopropylidine was postulated to be an intermediate, which rearranges to form ring-opening products.[200]

By using a catalytic amount of bis(triphenylphosphine)(maleic anhydride)palladium, the reaction of 1,2-propadiene (**40**) with diolefins, butadiene, and bicyclo[2.2.1]hepta-2,5-diene resulted in a 3:1 mixture of *trans*- and *cis*-2-methyl-3-methylene-1,5,7-octatriene (**669**) and *exo*-3-methyltricyclo[4.2.1.0]nona-3,7-diene (**670**), respectively (Scheme 185).[202]

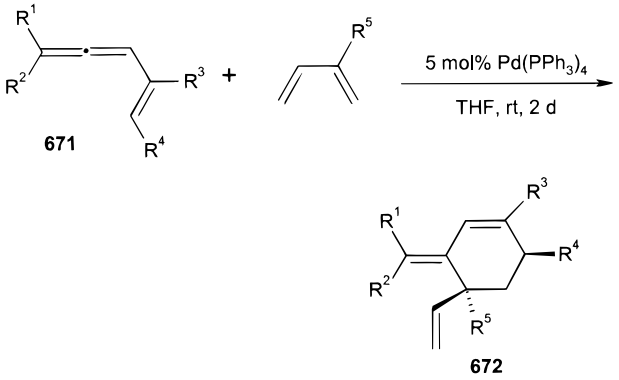
Scheme 185



Murakami and Ito developed an extremely useful and straightforward procedure for a highly regio- and stereoselective intermolecular-directed [4+2] cycloaddition reaction between vinylallenes **671** and 1,3-dienes lacking the electron demands.[203] The reaction proceeds highly efficiently with a variety of substrates including heteroatom functionalities under very mild conditions using 5 mol % of $Pd(PPh_3)_4$ in THF at room temperature (Scheme 186). In the case of vinylallenes **671c**−**f**, (R^4 cis to R^3), the cycloadducts formed have cis stereochemistry, whereas the geometric isomer of **671c** (R^4 trans to R^3) gave the trans

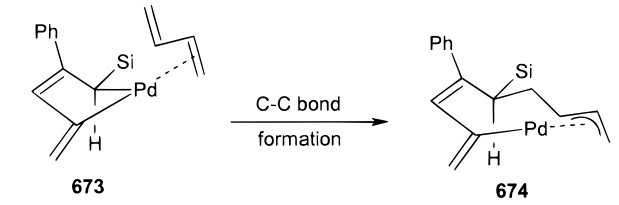
isomer. A plausible pathway to account for the observed regio- and stereochemistry involves the selective formation of complex **674** via a five-membered bent palladacycle **673**, which was formed by η^4-coordination of Pd(0) to the allene, followed by coordination of 1,3-diene in an s-trans form to Pd as shown in Scheme 186. Subsequent reductive elimination affords the [4+2] cycloadduct **672**. The excellent stereoselectivity is mainly governed by the stereoelectronic factors. Only one isomer is obtained from unsymmetrical allene **671f** due to the face-selective binding of Pd to the less hindered side. In the case of the 2-phenyl-substituted 1,3-diene, the exclusive product formed is the one where the more substituted C−C bond acts as the dienophile part.

Scheme 186



671 672

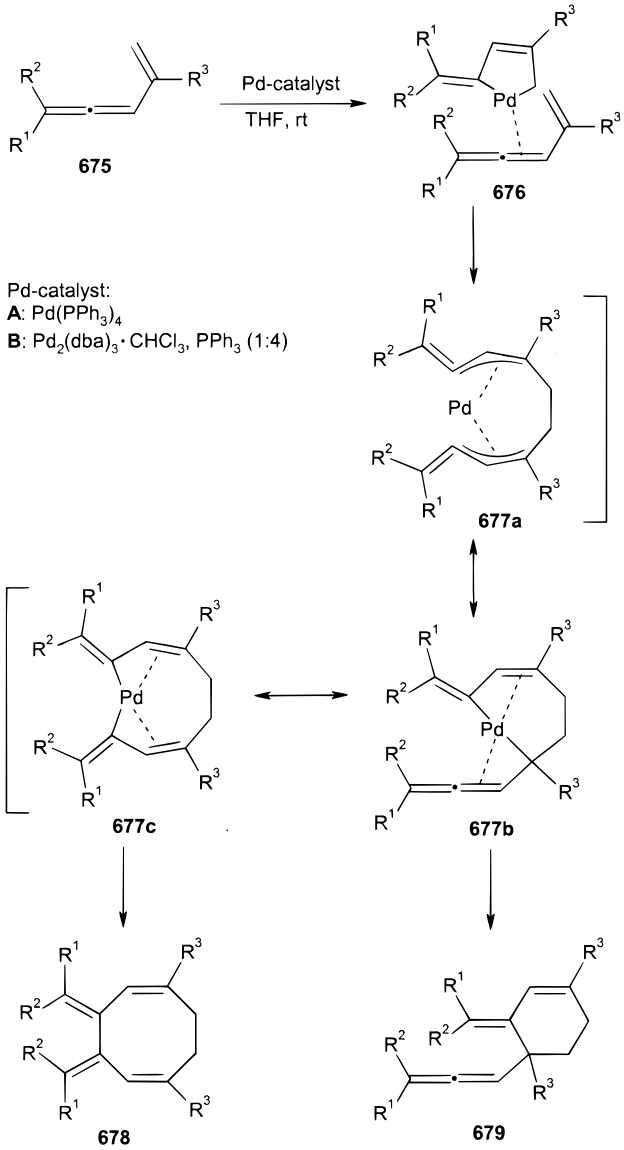
671/672	R^1	R^2	R^3	R^4	R^5	672
a	H	H	Ph	H	H	93%
b	Me	Me	TMS	H	H	98%
c	H	H	Ph	TMS	H	96%
d	Me	Me	Ph	Ph	H	92%
e	Me	Me	*n*-Pr	*n*-Pr	H	92%
f	Me	H	CO_2Et	Ph	H	87%
g	Me	Me	Ph	H	Ph	85%



673 674

The same authors also established the palladium-catalyzed head-to-head [4+4] cycloaddition of vinyl allenes **675** with a pendant phenyl or vinyl substituent giving rise to the formation of symmetrical eight-membered carbocycles.[204] The probable mechanism involves a five-membered palladacycle by reaction of **675** with Pd(0) followed by coordination of another molecule of allene to Pd as shown in **676**, forming bis(π−allyl)palladium intermediate **677a** in the carbon−carbon bond-forming step. Subsequent reductive elimination from the resonance-stabilized σ-di(alkenyl)palladium **677c** leading to the formation of cyclooctanoid derivative **678** and the resonance form **677b** was proposed to give the [4+2] cycloadduct **679** (Scheme 187). Since only **679** was formed from the silyl-substituted vinylallene, it implies the requirement of pendant unsaturated substituents to stabilize intermediate **677c** by extended conjugation for [4+4] cycloaddition to occur.

Scheme 187

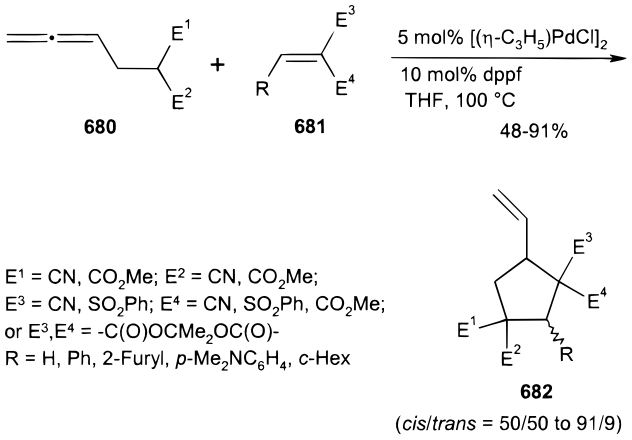


675 676 677a 677c 677b 678 679

R^1	R^2	R^3	Catalyst	678	679
H	H	Ph	A	84%	--
Me	Me	Ph	A	48%	32%
Me	Me	Vinyl	B	71%	24%
Me	Me	TMS	B	--	92%

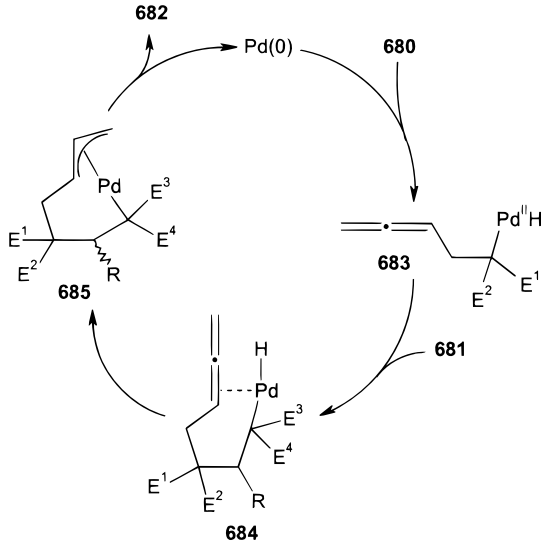
Another nice illustration recently demonstrated by Yamamoto is the novel [3+2] cycloaddition of both electron-deficient allenes **680** and alkenes **681** giving the corresponding vinyl-substituted cyclopentane derivatives **682** using catalytic system [(η^3-C_3H_5)-PdCl]$_2$/dppf in moderate to good yields (Scheme 188).[205] The reaction fails with allene **680** when both groups at the carbon terminus are CO_2Me. This implies the necessary requirement of at least one nitrile functional group. The stereochemistry of the major isomer is mostly cis. The authors proposed that the reductive elimination of π-allylpalladium complex **685**, formed via the hydropalladium intermediate

Scheme 188



684, gives the desired product. Complex **684** is formed by the oxidative addition of Pd(0), generated in situ, into the C−H bond of **680** followed by insertion of alkene **681** as depicted in Scheme 189.

Scheme 189



IX. Concluding Remarks

In this review we have presented numerous applications of palladium-mediated reactions of allenes. The reactions discussed herein demonstrate the high synthetic potential of 1,2-dienes as useful precursors in organic synthesis. It should be mentioned here that most of the reactions work with 10 mol % (or less) of the Pd catalyst. However, the palladium-catalyzed reactions of allenes will surely have a magnificent future, which is understood from the recent rapid progress as evidenced by the increasing number of publications in the past 3−4 years. We have no doubt that many further applications will appear in the future.

X. Abbreviations

acac	acetylacetonate
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
dba	dibenzylideneacetone
diop	2,3-*O*-isopropylidine-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane
dmppp	1,3-bis[di-(2-methoxyphenyl)phosphino]propane
dppb	1,4-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1′-bis(diphenylphosphino)ferrocene
dppp	1,3-bis(diphenylphosphino)propane
duphos	1,2-bis(diphenylphosphino)benzene
etpo	4-ethyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane
mmap	2-[2-((6-methyl-2-pyridyl)methylene)aminoethyl]pyridine
TCPC	tetrakis(carbomethoxy)palladacyclopentadiene
TDMPP	tris(2,6-dimethoxyphenyl)phosphine
TTMPP	tris(2,4,6-trimethoxyphenyl)phosphine

XI. Acknowledgment

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XII. References

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