Transition-metal-catalyzed reactions of allenes*

Shengming Ma

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China and Laboratory of Molecular Recognition and Synthesis, Department of Chemistry, Zhejiang University, Hangzhou 310027, Zhejiang, China

Abstract: Pathways for carbometallation of simple allenes and allenes bearing a nucleophilic functionality with RMX have been discussed. The bisallene approaches for the efficient synthesis of carbocycles and heterocycles have been developed.

Keywords: allenes; carbopalladation; transition-metal-catalyzed; bisallene; carbometallation.

INTRODUCTION

Although the correct structure of allenes was predicted by van’t Hoff in 1874, this class of compounds was considered as “highly unstable” for a long period of time, which may have induced a negative impact on the development of the chemistry of allenes [1]. However, due to the efforts of many chemists, the reactions of allenes are making an increasingly indispensable contribution to modern synthetic chemistry [2]. In this paper, we will discuss some of the transition-metal-catalyzed reactions of allenes developed in our group.

INTERMOLECULAR CARBOPALLADATION OF ALLENES

In principle, two different metallic species, i.e., π-allyl metallic species 1 and sp² C·M species 2 may be formed via the carbometallation of allenes depending on the regioselectivity of the insertion reaction (Scheme 1) [3].

Scheme 1
The \( \pi \)-allyl metallic species-forming pathway was observed by Schultz in 1964 [4] and van Helden in 1968 [5]. In 1984, Tsuji et al. reported the Pd-catalyzed intermolecular carbometallation of allenes affording 1,3-dienes with low stereoselectivity [6]. In 2000, Cheng et al. developed Pd(dba)\(_2\)/PPh\(_3\)-catalyzed reaction of organic halides with allenes affording 1,3-dienes with a poor stereoselectivity (Scheme 2) [7].

\[
\begin{align*}
\text{Pd(OAc)}_2 & \text{dppe} \quad \text{NMP} \\
\begin{array}{c}
 n\text{-C}_4\text{H}_9 \quad \text{PhI} \\
 \text{Pd}^+ \text{L} \quad \text{L} \\
 \text{Ph} \quad \text{C}_4\text{H}_9 \quad \text{n} \\
 \beta\text{-H elimination}
\end{array} \\
\begin{array}{c}
 \text{Ph} \quad \text{C}_3\text{H}_7 \quad \text{n} \\
 \text{Z/E 1:1}
\end{array}
\end{align*}
\]

Scheme 2

During the course of our study on the chemistry of allenes, we applied Cheng’s conditions to the reaction of 3,4-alkadienoate 3 and \( p \)-ethoxycarbonylphenyl iodide 4 for the synthesis of 4-aryl-2,4-alkadienoate \( E \)-6. However, a 16 % yield of \( E \)-4-(\( p \)-ethoxycarbonylphenyl)-3-butyldiene-4-pentenoate \( E \)-7 was also formed, indicating the low regioselectivity of the \( \beta \)-H elimination of \( \pi \)-allylic intermediate 5 (Scheme 3) [8].

\[
\begin{align*}
\begin{array}{c}
 \text{H} \\
 \text{CHCH}_2\text{CH}_2\text{CH}_3 \\
 \text{H} \\
 \text{COOC}_2\text{H}_5
\end{array} & \begin{array}{c}
 \text{H} \\
 \text{COOC}_2\text{H}_5
\end{array} & \begin{array}{c}
 \text{H} \\
 \text{COOC}_2\text{H}_5
\end{array} & \begin{array}{c}
 \text{H} \\
 \text{COOC}_2\text{H}_5
\end{array} \\
3 & 4 & 5 & 6
\end{align*}
\]

Scheme 3

© 2006 IUPAC, Pure and Applied Chemistry 78, 197–208
After some screening, we observed that the Pd(PPh₃)$_4$ and Ag₂CO₃-cocatalyzed reaction of aryl halides and 3,4-alkadienoates in MeCN using K₂CO₃ as the base afforded 4-aryl-2,4-alkadienates in 44–85 % yields highly regio- and stereoselectively (Scheme 4) [8].

There is one example in the literature reported by Grigg et al. for the formation of 2-type vinylic palladium intermediate [9]. The Pd-catalyzed reaction of N-(2-methylallyl)-N-(4-methoxycarbonyloxy-2-butynyl) benzenesulfonamide 8 in the presence of CO and MeOH afforded 2-bicyclic propenoate 12 via the intermediacy of 2-type vinylic palladium intermediate 11. However, the Heck-type of carbo-palladation-β−H elimination had not been reported (Scheme 5).

Recently, we observed that the Pd-catalyzed Heck-type reaction of 3-methyl-1,2-pentadienyl phenyl sulfone 13 with PhI afforded the phenyl-substituted 1,2-allenyl sulfone 14. The reaction may proceed via the β−H elimination of 2-type vinylic palladium intermediate 15. For 1,3-monosubstituted allenes, 16 bisarylation was observed (Scheme 6) [10].

© 2006 IUPAC, Pure and Applied Chemistry 78, 197–208
INTERMOLECULAR CARBOPALLADATION OF ALLENES WITH A NUCLEOPHILIC FUNCTIONALITY WITH RPDX

For the carbometallation of allenes with a nucleophilic functionality, due to the presence of the nucleophilic center, there are more possibilities. The most notable one would be nucleometallation \[2b,11\]. The Pd(PPh\(_3\))\(_4\)-catalyzed reaction of organic halides and 2-(2',3'-allenyl)malonates afforded vinylic cyclopropanes under conditions A or B and cyclopentenes under conditions C or D highly selectively (Scheme 7) \[12\].

Under conditions C, the reaction of 18a with phenyl iodide afforded cyclopentene derivative 20a in 88 % yield with highly selectivity. However, it is interesting to observe that if the same reaction mixture was treated with 20 mol % of Pd(PPh\(_3\))\(_4\) alone for 6 h first, which was followed by the addition of

© 2006 IUPAC, Pure and Applied Chemistry 78, 197–208
NaH, the reaction afforded vinylic cyclopropane product 19a as the only product! We reasoned that π-allyl metallic intermediate \textit{anti-21a} was formed in the first place. Due to the absence of a nucleophilic center, intramolecular allylation is not possible. Subsequent isomerization of \textit{anti-21a} to \textit{syn-21a}, deprotonation, and cyclic allylation afforded 19a (Scheme 8) [12].

![Scheme 8](image)

Actually, \textit{syn-22a}-type intermediate may further undergo 1,2-addition reaction with an imine to form a new nucleophilic nitrogen atom, which would be followed by intramolecular amination to produce 2,5-\textit{cis} pyrrolidines 23 highly stereoselectively (Scheme 9) [13].

![Scheme 9](image)

A similar reaction pathway has also been observed with Pd(PPh₃)₄-catalyzed coupling cyclization of 2-methyl-3,4-pentadienyl toluenesulfonamide 24 with PhI [14,15]. Azetidine 25 and tetrahydropyridine 26 were formed via the cyclic amination of the π-allyl palladium intermediate 27.
However, when the same reaction conditions were applied to \(N\)-(2-methyl-3-butyl-3,4-pentadienyl)toluenesulfonamide 28, 5-membered 2,3-dihydropyrrole 29 was formed as the only product in 78 \% yield. The coupling-cyclization reaction of 30 (compared with 28, the 2-methyl group is removed) with different ArI afforded a mixture of 2,3-dihydropyrroles 31 and 2-methylenetetrahedro-pyrroles 32 (Scheme 10). The reaction may proceed via the reductive elimination of the \(\pi\)-allyl palladium intermediate 34, which was formed via the nucleometallation of ArPdI with 3,4-alkadienyl toluenesulfonamide 33 (Scheme 10) [14].

![Scheme 10](image)
Similarly, the Pd$_2$(dba)$_3$CHCl$_3$/PPh$_3$-catalyzed reaction of optically active 2-methyl-4-phenyl-2,3-butadienoic acid ($S$-$35$) with PhI afforded optically active butenolide $S$-$(+)$-$36$ in 49 % yield with only 23 % ee, indicating the serious loss of the chirality. However, when $S$-$35$ was converted to its 1:1 salt with (i-Pr)$_2$NEt $S$-$(+)$-$37$ first, the reaction of $S$-$(+)$-$37$ with PhI under the same reaction conditions afforded $S$-$(+)$-$36$ in 62 % yield with 91 % ee (Scheme 11) [16].

The stereochemical information in the starting optically active 2,3-allenic acid may be lost due to the isomerization of $\pi$-allyl palladium intermediate $38$. In the case of the 1:1 optically active salt, the reaction may proceed via the high stereoselective oxypalladation forming 2(5$H$)-furanonyl palladium intermediate $40$ (Scheme 12).
The high efficiency of chirality transfer was also observed in the PdCl₂-catalyzed coupling-cyclization reaction of \( S-41 \) with allyl bromide [17]. Again, oxypalladation of 2,3-alkadienic acid \( S-41 \) forming 2(5\( H \))-furanonyl palladium intermediate 42 may be responsible for the high efficiency of the chirality transfer (Scheme 13).
This type of oxypalladation has also been observed in the Pd(II)-catalyzed coupling cyclization of 2,3-allenoic acids with σ-alkenyl halides. The product 49 was formed via the insertion of the C=C bond of the organic bromide with the C–Pd bond in 45, the subsequent repeated dehydropalladation/hydro-palladation of 46, and dehalopalladation of 48 (Scheme 14) [18].

© 2006 IUPAC, Pure and Applied Chemistry 78, 197–208
TRANSITION-METAL-CATALYZED REACTIONS OF TWO ALLENE MOIETIES

With these results in hand, we started to study the Pd(II)-catalyzed reaction of 2,3-allenoic acid in the presence of an alkyl iodide. To our surprise, the reaction afforded bisbutenolides 50 via double oxy-palladation (Scheme 15) [17]. After further study, it is believed that the I₂ in situ generated by the reaction of I⁻ released by the alkyl iodide with the O₂ in air may act as the oxidant to oxidize the in situ generated Pd(0) to the catalytically active Pd(II) species. Based on these, we also developed the protocols using KI or benzoquinone as the oxidant [19]. In terms of generality, the alkyl iodide-protocol is the best while the benzoquinone protocol provides the bisbutenolides in the highest yields.

We have also developed the double cyclization reaction of 2,3-allenoic acids with 5 equiv of 1,2-allenyl ketones affording β-furanyl butenolides 51 (Scheme 16). By using the optically active starting 2,3-allenoic acids as the probe, X-ray diffraction studies revealed a double oxypalladation mechanism [20].

Recently, we observed the Pd(II)-catalyzed cyclization reaction of 2,3-allenoic acids with 2,3-allenols producing β-(1,3-dien-2-yl)butenolide 54. Obviously, instead of biscyclization, the hydroxyl group in 2,3-allenols was β-eliminated, which may induce the low-efficiency of chirality transfer observed in the reaction of 52 with 54. When the same reaction was conducted in the presence of 0.8 equiv of trifluoroacetic acid (TFA), which was used to neutralize the in situ generated OH⁻, the chirality was transferred highly efficiently (Scheme 17) [21].
When we combined the two allene moieties into one molecule, such as 57, trans-RhCl(CO)(PPh₃)₂ can catalyze its bimolecular cyclization reaction to afford steroid motif 58 in 69% in one step (Scheme 18). Although the mechanism is far away from being clear, two cyclometallation–carbometallation forming a π-allyl metallic species–reductive elimination–intramolecular Diels–Alder reaction of a 1,3-diene moiety with an allene moiety pathways have been proposed [22].

In conclusion, we have observed some interesting reactions of allenes. Due to the relatively unexplored nature of the chemistry of allenes, more reactions of allenes with high synthetic potential will be developed.

ACKNOWLEDGMENTS

Financial support from the National Natural Foundation of China (Grant Nos. 20332060, 20121202, and 20423001), the Major State Basic Research Development Program (Grant No. G2000077500), and the Cheung Kong Scholar Programmes is greatly appreciated. Shengming Ma is jointly appointed by Shanghai Institute of Organic Chemistry and Zhejiang University. I would also like to thank all the coworkers whose names are cited in the references for their hard work.

© 2006 IUPAC, Pure and Applied Chemistry 78, 197–208
REFERENCES


