778 Bull. Chem. Soc. Jpn. Vol. 82, No. 7, 778–792 (2009)

Award Accounts
The Chemical Society of Japan Award for Young Chemists for 2008

Metal-Mediated Retro-Allylation of Homoallyl Alcohols for Highly Selective Organic Synthesis

Hideki Yorimitsu* and Koichiro Oshima*

Department of Material Chemistry, Graduate School of Engineering, Kyoto University,
Kyoto-daigaku Katsura, Nishikyo-ku, Kyoto 615-8510

Received February 23, 2009; E-mail: yori@orgrxn.mbox.media.kyoto-u.ac.jp, oshima@orgrxn.mbox.media.kyoto-u.ac.jp

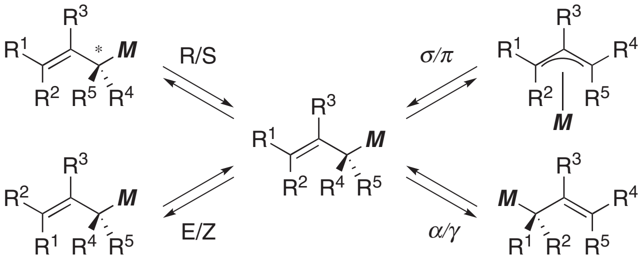
Metal-mediated or -catalyzed retro-allylation of homoallyl alcohol that proceeds via a six-membered transition state has appeared as a new useful method to prepare allylmetals. A crotylzirconium reagent undergoes stereoselective allylation of aromatic aldehyde at −78 and 25 °C to provide *threo*- and *erythro*-homoallyl alcohols, respectively. Although the threo isomer is formed as usual via a six-membered chair transition state under kinetic control, the erythro selectivity is rationalized by considering isomerization of the threo adduct through a retro-allylation process. The retro-allylation of a bulky gallium homoallyloxide occurs to generate (*Z*)- and (*E*)-crotylgallium reagents stereospecifically, starting from *erythro*- and *threo*-homoallyl alcohols, respectively. The (*Z*)- and (*E*)-crotylgallium reagents react with aromatic aldehydes in situ to afford the corresponding *erythro*- and *threo*-homoallyl alcohols, respectively. Treatment of rationally designed tertiary homoallyl alcohols with aryl halides under palladium catalysis yielded the corresponding allylarenes stereo- and regioselectively, by replacing the conventional transmetalation step in the cross-coupling reaction with alkoxide–halide exchange followed by a retro-allylation reaction. The retro-allylation reaction is also applicable to nickel and rhodium at this stage, and may to any other metals in principle. Reversible additions of pentamethylcyclopentadienyl anion to carbonyl compounds are also described.

1. Introduction

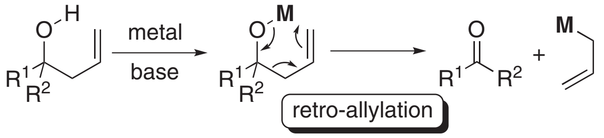
Allylation reactions with σ-allylmetal reagents are among the most fundamental and important reactions in organic chemistry and have often been employed in organic synthesis.[1] Organic molecules required nowadays have become much more complex than ever before, and modern organic synthesis thus necessitates a wider variety of σ-allylmetal reagents.

In general, σ-allylmetal reagents are difficult to manage despite their usefulness. They can react rapidly with water and oxygen in air to decompose. The scope of functional group compatibility is not wide due to the inherent high reactivities of σ-allylmetals. Except for allylmetals of group 14 metals and allylborons, σ-allylmetals are usually configurationally fluxional at ambient temperature (Scheme 1).[1a,2] Isomerizations between σ-allylmetals and their π-isomers are quite common, especially for transition-metal complexes. 1,3-Metallotropic rearrangement is also facile, resulting in α/γ isomerism. These two isomerization processes render the geometry of the double bond and the absolute configuration of the metalated stereogenic center fluxional. Hence, it is not trivial to prepare desired σ-allylmetal reagents in a universal, precise, and concise manner.

During the course of our studies on zirconium-mediated reactions,[3] we were excited to serendipitously find a carbon–carbon bond cleavage reaction, i.e., zirconium-mediated retro-allylation of homoallyl alcohols (Scheme 2). Although the reversibility of the reactions of carbonyl compounds with allylmetals has been known for 40 years,[4–7] synthetic organic chemists had paid little attention to this peculiar and seemingly useless phenomenon.[5,7] Since our finding, we have investigated retro-allylation by using various metals as mediators. In this



Scheme 1. Fluxional configuration of allylmetal.



Scheme 2. Retro-allylation.

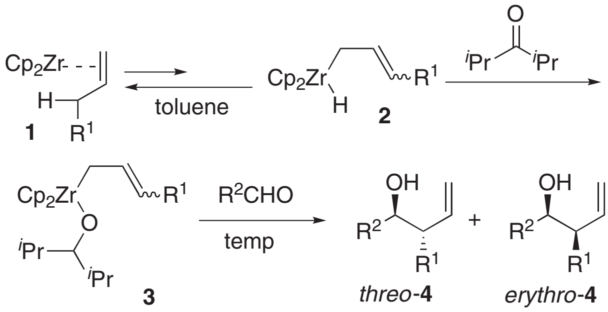
Account, we describe how we came across the chemistry of retro-allylation and how we established retro-allylation of homoallyl alcohols as a useful method for selectively preparing σ-allylmetal species in situ.[8]

2. Zirconium-Mediated Retro-Allylation

In 2001, we reported that preparation of zirconocene(1-alkene) **1** in toluene results in the allylic C–H bond activation of the 1-alkene to afford zirconocene(allyl)hydride **2** in equilibrium with **1**.[9] We then envisaged that trapping **2** with bulky ketone would yield **3**, which would be a new method for generating allylzirconium species.

This was indeed the case.[10] The reaction of benzaldehyde with **3** ($\mathrm{R^1} = \mathrm{Me}$) at room temperature yielded desired homoallyl alcohol **4a** quantitatively (Table 1). Interestingly, the reaction proceeded with slight erythro[11] selectivity (threo/erythro = 35:65), whereas the reactions of aldehydes with crotylzirconium[12] reagents usually proceed with threo selectivity.[13] To improve the erythro selectivity, the crotylation reaction was performed at −78 °C. Contrary to our expectations, the reaction at low temperature showed a reversed threo/erythro selectivity of 68:32. The degree of the reversal was significant when R^1 of **3** and R^2 of aldehydes were large. For instance, the reaction of cyclohexanecarbaldehyde with the 2-hexenylzirconium reagent at 25 °C afforded **4b** with a threo/erythro selectivity of 17:83, whereas the same reaction at −78 °C showed high threo selectivity. The bulky alkoxy group of **3** was essential for the reversal, and such reversal was not observed when **3** was replaced with a crotylzirconium reagent simply prepared from zirconocene dichloride and crotylmagnesium bromide.

Table 1. Stereoselectivity in Allylation Reaction of Aldehyde with **3**



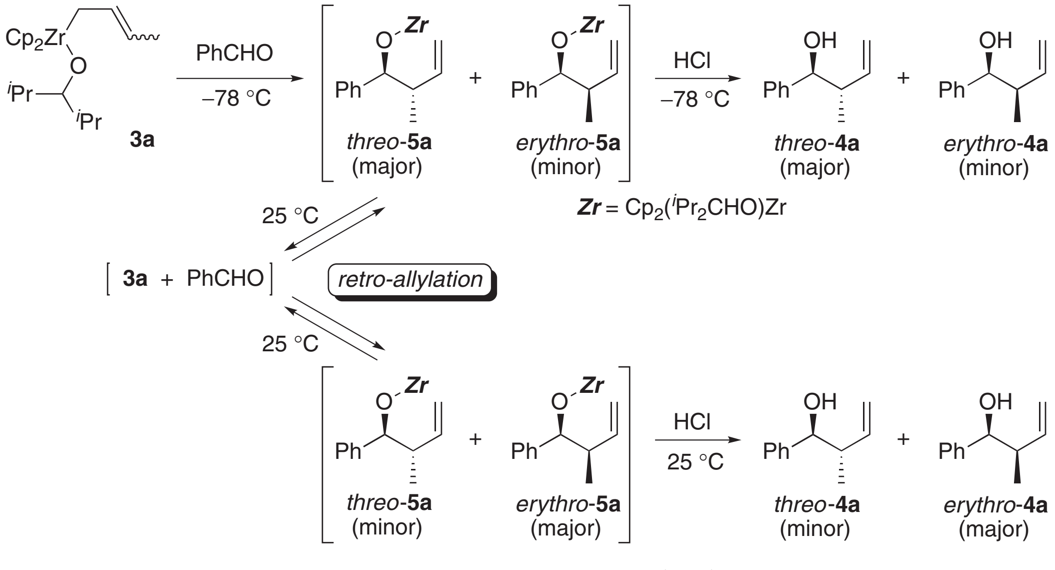
R^1	R^2	Temp/°C	**4**	Yield/%	threo/erythro
Me	Ph	25	**4a**	99	35:65
Me	Ph	−78	**4a**	98	68:32
$^n\mathrm{C_3H_7}$	$^c\mathrm{C_6H_{11}}$	25	**4b**	95	17:83
$^n\mathrm{C_3H_7}$	$^c\mathrm{C_6H_{11}}$	−78	**4b**	99	94:6

After several mechanistic studies, we concluded that the retro-allylation of zirconium alkoxide **5a** can rationalize these results (Scheme 3). The formation of *threo*-**5a** would predominate kinetically at −78 °C. The retro-allylation of **5a** would take place at ambient temperature, forming trace amounts of **3a** and benzaldehyde. Since *erythro*-**5a** would be thermodynamically more stable than *threo*-**5a**, the equilibrium between *erythro*-**5a**, *threo*-**5a**, and **3a** would shift to *erythro*-**5a** at 25 °C. The bulky alkoxy group, $^i\mathrm{Pr_2CHO}$, on the zirconium center is indispensable to destabilize **5a**, hence facilitating the retro-allylation.

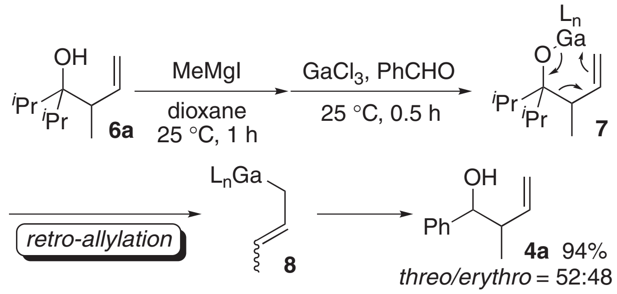
It is accepted wisdom that allylation reactions of carbonyl compounds proceed under kinetic control. Taking advantage of retro-allylation, one can control the allylation both kinetically and thermodynamically by simply changing reaction temperatures.

3. Gallium-Mediated Retro-Allylation

We were sure that other metal salts would mediate retro-allylation. After screening a variety of metal salts, we found that gallium trichloride can promote retro-allylation.[14] Homoallyl alcohol **6a** bearing two isopropyl groups at the oxygenated carbon was deprotonated with a Grignard reagent in dioxane (Scheme 4). Gallium trichloride and benzaldehyde were sequentially added at 25 °C. After the mixture was stirred for 0.5 h, homoallyl alcohol **4a** was obtained in excellent yield. Formation of crotylgallium species **8** by retro-allylation from **7** followed by the reaction of benzaldehyde with **8** is most

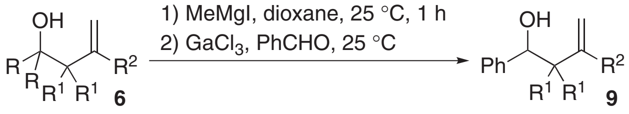


Scheme 3. Rationale for selectivity in zirconium-mediated crotylation reaction.



Scheme 4. Gallium-mediated allylation of benzaldehyde following retro-allylation.

Table 2. Gallium-Mediated Allyl, Methallyl, and Prenyl Transfer

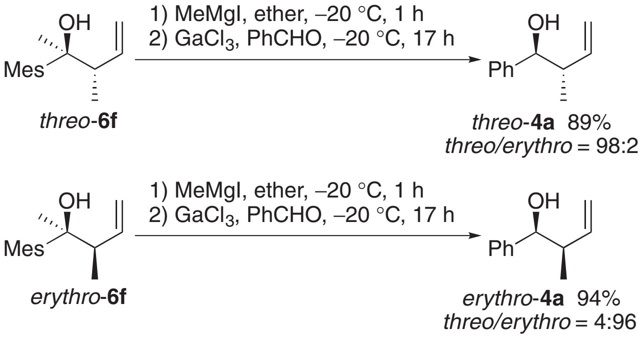


6	R	R^1	R^2	Time/h	9	Yield/%
6b	^{i}Pr	H	H	13	**9a**	68
6c	^{i}Pr	H	Me	0.5	**9b**	94
6d	^{i}Pr	Me	H	11	**9c**	32
6e	Me	Me	H	1	**9c**	78

probable. The crotyl-transfer reaction was applicable to various carbonyl compounds including aliphatic aldehydes, α,β-unsaturated aldehyde, and ketones. Disappointingly, no erythro/threo selectivity was observed in each case.

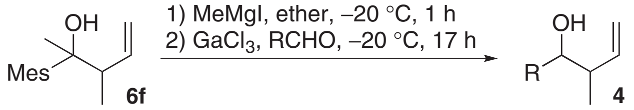
Allyl-, methallyl-, and prenylgallium reagents were available (Table 2). The generation of allylgallium was less efficient, and the allyl transfer from **6b** to benzaldehyde required prolonged reaction time. Methallyl transfer from **6c** took place as smoothly as that from **6a**. Interestingly, **6e** bearing two methyl groups at the oxygenated carbon underwent more efficient prenyl transfer than diisopropyl-substituted **6d**. Alcohol **6d** would be so crowded that the gallium alkoxide of **6d** could not adopt a proper transition state for retro-allylation. The influence of the substituents at the hydroxylated carbon proved to be quite important.

Having noticed the delicate influence of the substituents, we further investigated the crotylation reaction by employing other homoallyl alcohols. We found that homoallyl alcohol **6f**, which has a bulky mesityl (2,4,6-$Me_3C_6H_2$, abbreviated as Mes) group and a small methyl group at the oxygenated carbon, effected crotyl-transfer reaction in ether even at −20 °C (Scheme 5). Gratifyingly, the reaction with **6f** proceeded stereospecifically when diastereomerically pure **6f** was used; the reactions of benzaldehyde with *threo*- and *erythro*-**6f** afforded *threo*- and *erythro*-**4a**, respectively. Both isomers of **6f** were prepared by treatment of mesityl methyl ketone with crotyl Grignard reagent and readily separated from each other by conventional column purification on silica gel. Other aromatic aldehydes underwent the stereospecific crotylation reaction to yield **4c**–**4e** (Table 3). The reactions of α,β-unsaturated and aliphatic aldehydes yielded **4f** and **4g**, respectively, with lower stereoselectivities.



Scheme 5. Stereospecific crotyl-transfer reactions.

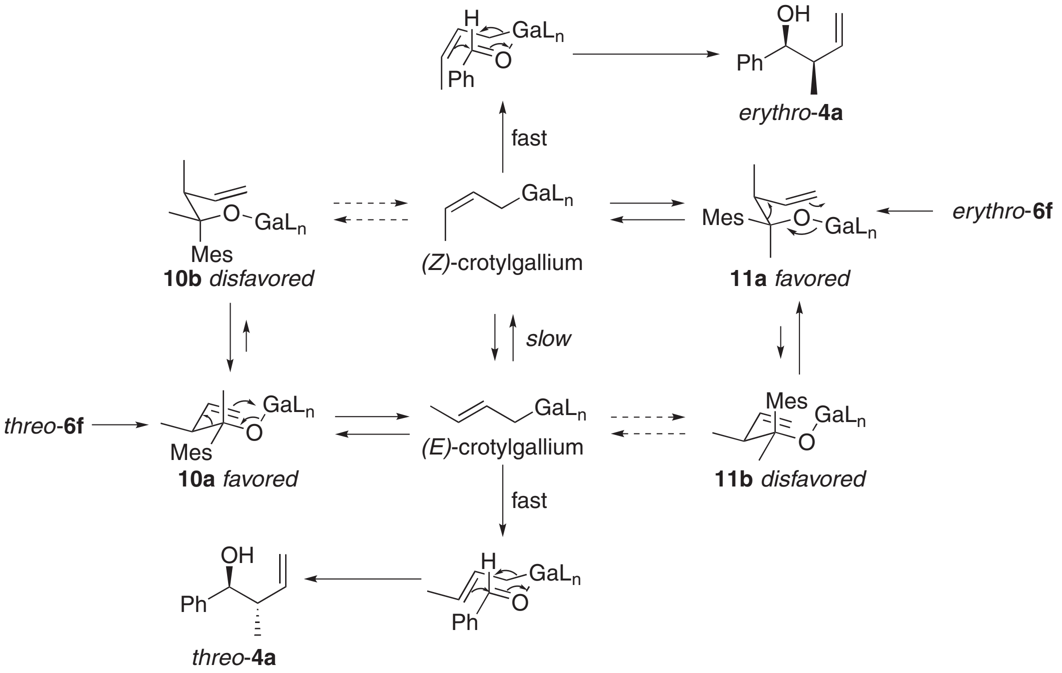
Table 3. Stereospecific Crotyl Transfer from **6f** to Various Aldehydes



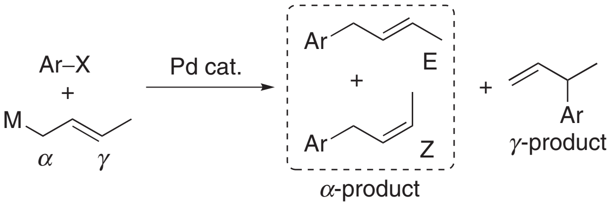
6f	R	4	Yield/%	threo/erythro
threo	p-$CF_3C_6H_4$	**4c**	92	98:2
erythro	p-$CF_3C_6H_4$	**4c**	84	4:96
threo	o-ClC_6H_4	**4d**	83	97:3
erythro	o-ClC_6H_4	**4d**	87	1:99
threo	p-MeC_6H_4	**4e**	64	98:2
erythro	p-MeC_6H_4	**4e**	95	2:98
threo	PhCH=CH	**4f**	66	79:21
erythro	PhCH=CH	**4f**	86	9:91
threo	$PhCH_2CH_2$	**4g**	62	58:42
erythro	$PhCH_2CH_2$	**4g**	87	31:69

Scheme 6 outlines a plausible reaction mechanism that rationalizes the stereospecificity. The retro-allylation reaction of *threo*-**6f** would predominantly proceed via chair-like transition state **10a** bearing the bulky mesityl group at the equatorial position since **10a** would be most stable among other transition states including another chair-like transition state **10b**. The retro-allylation via **10a** should yield (*E*)-crotylgallium. The (*E*)-crotylgallium reagent would react with benzaldehyde stereoselectively according to the conventional rule of carbonyl allylations to afford *threo*-**4a** selectively. The retro-allylation reaction of *erythro*-**6f** would follow a similar pathway via **11a** bearing the equatorial mesityl group. The (*Z*)-crotylgallium thus generated would react with benzaldehyde to yield *erythro*-**4a**. The low stereospecificity in the reactions of the less reactive α,β-unsaturated and aliphatic aldehydes would result from the occurrence of the E/Z interconversion of the crotylgallium species prior to the crotylations of these aldehydes.

The conventional methods for the preparation of allylmetals such as transmetalation and Barbier/Grignard methods have not realized stereoselective preparations of both (*E*)- and (*Z*)-crotylgallium reagents. Only the retro-allylation strategy can provide such a stereoselective access. Through the studies on the gallium-mediated reactions, we became more interested in the retro-allylation as a useful method for preparing σ-allylmetals that are otherwise difficult to prepare.



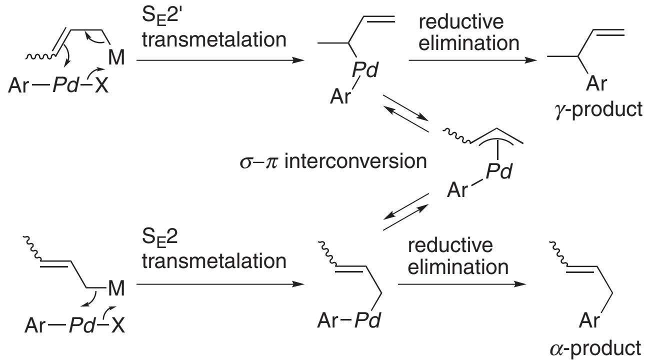
Scheme 6. Rational explanation for stereospecific crotylation.



Scheme 7. Conventional cross-coupling reaction of aryl halide with crotylmetal.

4. Palladium-Catalyzed Retro-Allylation

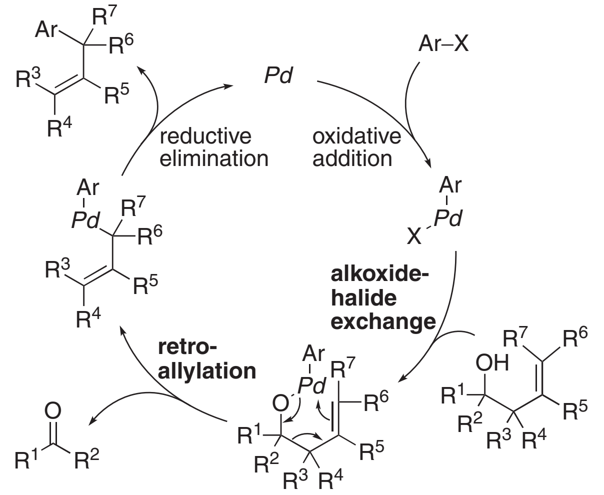
4.1 Problems in Palladium-Catalyzed Allylation of Aryl Halides and the Solution. Despite their seeming simplicity and obvious usefulness, palladium-catalyzed cross-coupling reactions of aryl halides with allylmetals have rarely been reported and are known to be difficult transformations. The most critical problem is the regio- and stereochemical control when substituted allylmetals are employed. For instance, a cross-coupling reaction with a crotylmetal reagent can occur competitively at the α- and γ-positions of the crotyl group (Scheme 7). In addition, the product coupled at the α-position can be a mixture of E and Z isomers. Without regio- and stereochemical control, cross-coupling allylation would remain useless for modern organic synthesis. Although there are several reports of regioselective allylations,[15] the generality and practicability of the allylation are far from satisfactory. As illustrated in Scheme 8, the lack of regio- and stereoselectivities stems from (1) the difficulty in correctly preparing allylmetals having an arbitrary substitution pattern, (2) mixing of two possible modes of transmetalation, S_E2' and S_E2, and (3) slow reductive elimination from σ-allyl(aryl)palladium intermediates that results in σ–π interconversion with loss of the initial regio- and stereochemical information of σ-allylmetals.



Scheme 8. Complexity of palladium-catalyzed reaction of aryl halide with crotylmetal.

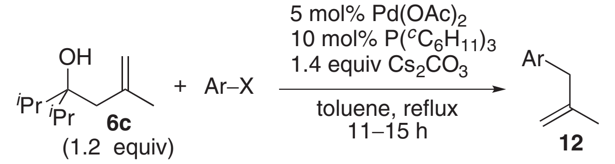
We came up with the idea of applying the concept of selective preparation of σ-allylmetals from homoallyl alcohols via retro-allylation to palladium-catalyzed cross-coupling allylation reactions (Scheme 9). We envisaged that the conventional transmetalation could be replaced with alkoxide–halide exchange followed by a retro-allylation reaction. The hydroxy group of the homoallyl alcohol would serve as a directing group, and the subsequent retro-allylation via a six-membered cyclic transition state would generate the desired σ-allyl(aryl)palladium exclusively. With a proper phosphine ligand that renders the subsequent reductive elimination sufficiently fast, we would be able to establish the stereo- and regiospecific allylation of aryl halides. More advantageously, homoallyl alcohols are superior to allylmetals in terms of configurational stability, inertness under air, and practical availability.

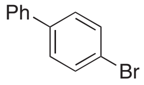
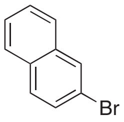
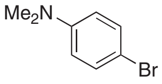
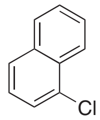
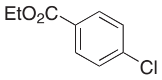
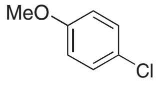
Several precedents that utilize tertiary alcohols as organometallic equivalents motivated us to perform our initial experiments.[16] However, the mode of the carbon–carbon bond cleavage is likely to be β-carbon elimination via a four-



Scheme 9. Mechanistic design of palladium-catalyzed allylation of aryl halide with homoallyl alcohol.

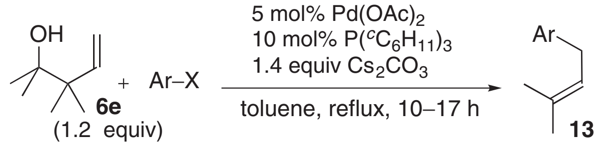
Table 4. Palladium-Catalyzed Methallylation of Aryl Halides with **6c**

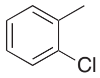
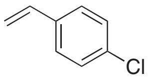
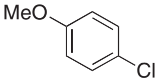
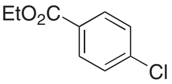
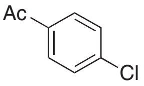
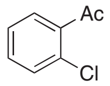
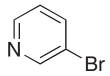


Entry	Ar–X	**12**	Yield/%
1		**12a**	83
2		**12b**	86
3		**12c**	80
4		**12d**	79
5		**12e**	79
6		**12e**	78[a),b)]
7		**12f**	70
8		**12f**	98[a),c)]

a) Performed at 250 °C under microwave irradiation for 15 min. b) 0.05 mol % $Pd(OAc)_2$ and 0.30 mol % $P(^cC_6H_{11})_3$. c) 30 mol % $P(^cC_6H_{11})_3$.

Table 5. Palladium-Catalyzed Prenylation of Aryl Halides with Homoallyl Alcohol **6e**



Ar–X	**13**	Yield/%
	**13a**	100
	**13b**	84[a)]
	**13c**	95[a)]
	**13d**	100
	**13e**	80
	**13f**	67
	**13g**	62[a)]

a) Under microwave irradiation at 250 °C for 15 min.

membered cyclic transition state from the corresponding palladium alkoxides, which is different from our retro-allylation mechanism.

4.2 Regio- and Stereospecific Allylation of Aryl Halides. Fortunately, the palladium-catalyzed retro-allylation indeed proceeded. A variety of aryl bromides underwent methallyl-transfer reactions with **6c** in the presence of cesium carbonate and catalytic amounts of $Pd(OAc)_2$ and $P(^cC_6H_{11})_3$ in refluxing toluene (Table 4).[17] The reactions under microwave irradiation at 250 °C enabled us to complete the reaction within 15 min (Entries 6 and 8).[18] In the reaction of ethyl 4-chlorobenzoate, we could reduce the amount of the palladium catalyst in addition to reaction time (Entry 6).

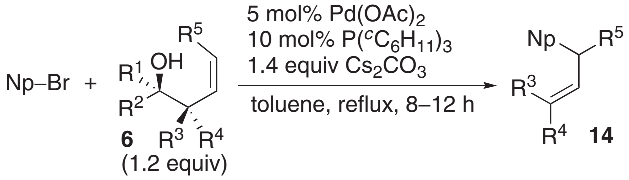
Our initial idea illustrated in Scheme 9 practically operated to realize regiospecific prenyl transfer utilizing 2,3,3-trimethyl-4-penten-2-ol (**6e**) (Table 5).[19] Conventional cross-coupling reactions with prenylmetals always provide regioisomeric mixtures. Thus, the reactions with **6e** provide a useful access to biologically intriguing prenylarenes.

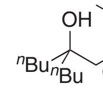
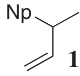
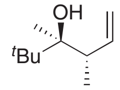
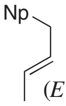
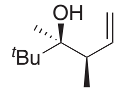
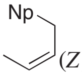
The reaction of 1-bromonaphthalene (hereafter Np = 1-naphthyl) with homoallyl alcohol **6g** afforded branched product **14a** exclusively without contamination by its regioisomer **14b** (Table 6).[17] According to the success in the gallium-mediated stereoselective retro-allylation, we rationally designed **6h** to establish the stereoselective synthesis of both (*E*)- and (*Z*)-1-(2-butenyl)naphthalene (**14b**). As expected, treatment of 1-bromonaphthalene with *threo*-**6h** and with *erythro*-**6h** under the standard conditions afforded (*E*)- and (*Z*)-**14b**, respectively, with high stereoselectivity. Conventional cross-coupling allylation cannot control such regio- and stereoselectivity universally.

The stereospecificity of the reactions with **6h** is rationalized in a fashion similar to Scheme 6 (Scheme 10). On the basis of conventional conformational analysis of the transition states of retro-allylation, chair-like transition state **15a** possessing the *tert*-butyl group at the equatorial position would predominate over **15b** in the reaction with *threo*-**6h**. Preferable **15a** leads to the selective formation of (*E*)-**17**. Intermediate (*E*)-**17** would undergo sufficiently rapid reductive elimination thanks to the bulky $P({}^{c}C_6H_{11})_3$ ligand, which would promote smooth reductive elimination to avoid undesirable σ–π interconversion. In the reaction with *erythro*-**6h**, **16a** would be favorable to yield (*Z*)-**17** and finally (*Z*)-**14b**.

The regio- and stereospecific transformation was applicable to a variety of homoallyl alcohols (Table 7).[17,18] Phenoxy-substituted *erythro*- and *threo*-alcohols **6i** were suitable for the stereoselective synthesis of vinyl ethers **18**. The arylative ring-opening reactions of unstrained cyclic medium-sized homoallyl alcohols **19** and **20** provided ketones having a branched or linear allylarene moiety at the remote terminus.

Table 6. Selective Synthesis of Three Butenyl Isomers



Alcohol **6**	Product **14**	Yield/%
 **6g**	 **14a**	48
 *threo*-**6h**	 (*E*)-**14b**	95 (E/Z = 97:3)
 *erythro*-**6h**	 (*Z*)-**14b**	70 (E/Z < 1:99)

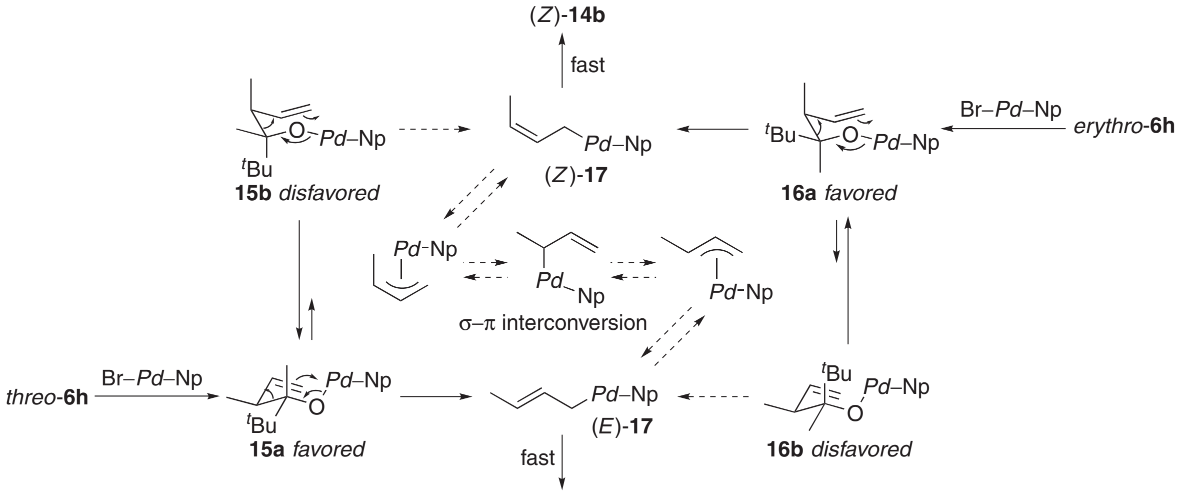
The palladium-catalyzed allyl transfer from homoallyl alcohols to aryl halides has realized regio- and stereospecific synthesis of a wide variety of allylarenes. Homoallyl alcohols will replace allylmetals in the palladium-catalyzed cross-coupling allylation.

4.3 Synthesis of Vinyl- and Allylsilanes by Palladium-Catalyzed Regiospecific and Stereoselective Allyl Transfer. The palladium-catalyzed allyl transfer was applied to the selective synthesis of (*E*)-3-aryl-1-propenylsilanes.[20] The palladium-catalyzed reactions of aryl halides with **6j** bearing a ${}^{t}BuMe_2Si$ group at the allylic position provided vinylsilanes **23** with excellent E selectivity (Table 8). Transition state **24** with the ${}^{t}BuMe_2Si$ group at the equatorial position would explain the E selectivity (Figure 1).

Starting from **6k** having a (*Z*)-1-alkenylsilane moiety, the palladium-catalyzed reaction of aryl bromides afforded allylsilanes **25** (Table 9, Entries 1 and 2). Interestingly, alcohols **6l**–**6o** with one alkyl group at the allylic position were converted to (*E*)-1-aryl-2-alkenylsilanes stereoselectively (Entries 3–8). The E selectivity would stem from the predominant formation of **26a** that is free from the 1,3-allylic repulsion between the methyl and silyl groups (Figure 2).

We were delighted to observe excellent chirality transfer in the reaction with optically active (*S*)-**6n** (Scheme 11). Transition state **28** would be the most preferable since the methyl group at the allylic position of **28** occupies the equatorial position to minimize steric repulsion. The palladium center would approach the Re face of the silylated olefinic carbon, which leads to the formation of **29** having E,R configuration. Reductive elimination from **29** prior to the loss of chirality provides (*E,S*)-**27**.

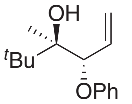
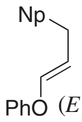
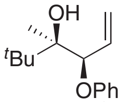
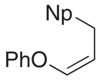
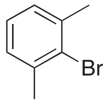
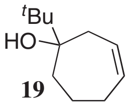
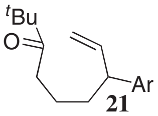
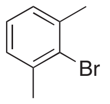
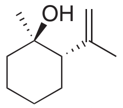
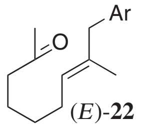
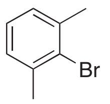
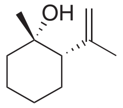
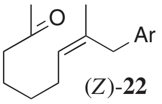
4.4 Retro-Propargylation for Synthesis of Multisubstituted Allenes. We expected the regio- and stereoselective retro-allylation would be extended to retro-propargylation of homopropargyl alcohols, which would represent a powerful method to prepare arylallenes. Due to the rigid and linear structure of the triple bond, the retro-propargylation occurred sluggishly at the initial stage. After extensive screening of reaction conditions, a combination of $[Pd_2(dba)_3]/P(C_8H_{17})_3$



Scheme 10. Mechanism for palladium-catalyzed stereospecific allylation.

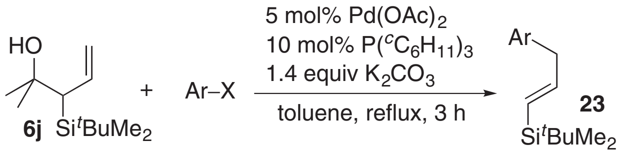
Table 7. Other Regio- and Stereospecific Transformation

$$\text{Ar–Br} + \text{homoallyl alcohol} \xrightarrow[\text{toluene}]{\substack{\text{5 mol\% Pd(OAc)}_2 \\ \text{x mol\% P(}^c\text{C}_6\text{H}_{11})_3 \\ \text{Cs}_2\text{CO}_3}} \text{product}$$

Entry	Ar–Br	Homoallyl alcohol	x /mol %	Heating	Product	Yield/%
1	Np–Br	 *erythro*-**6i**	10	reflux, 12 h	 (*E*)-**18**	88 (E/Z > 99:1)
2			10	MW, 250 °C, 15 min		93 (E/Z = 95:5)
3	Np–Br	 *threo*-**6i**	10	reflux, 12 h	 (*Z*)-**18**	67 (E/Z < 1:99)
4			10	MW, 250 °C, 15 min		92 (E/Z < 1:99)
5		 **19**	15	reflux,[a] 12 h	 **21**	80
6			20	MW, 200 °C, 15 min		88
7		 *threo*-**20**	15	reflux, 6 h	 (*E*)-**22**	86 (E/Z > 99:1)
8		 *erythro*-**20**	15	reflux, 6 h	 (*Z*)-**22**	76 (E/Z < 1:99)

a) Xylene was used instead of toluene.

Table 8. Synthesis of (*E*)-3-Aryl-1-propenylsilanes **23**



Ar–X	**23**	Yield/%	E/Z
Np–Br	**23a**	93	95:5
4-$CF_3C_6H_4Br$	**23b**	75	96:4
4-$CH_3COC_6H_4Br$	**23c**	89	95:5
4-$HCOC_6H_4Br$	**23d**	87	94:6
4-$EtO_2CC_6H_4Cl$	**23e**	89	97:3
4-$CH_3OC_6H_4Cl$	**23f**	92	95:5

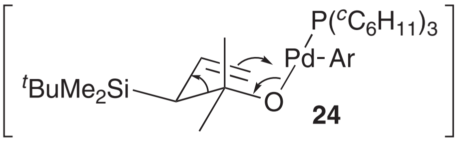
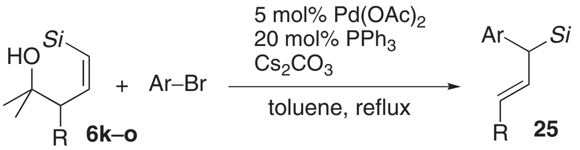


Figure 1. A favorable transition state in the retro-allylation of **6j**.

Table 9. Synthesis of Allylsilanes



Entry	Ar–Br	Si	R	**6**	**25**	Yield/%
1	Np–Br	^{t}BuMe$_2$Si	H	**6k**	**25a**	88
2[a]	4-$EtO_2CC_6H_4Br$	^{t}BuMe$_2$Si	H	**6k**	**25b**	88
3	Np–Br	^{t}BuMe$_2$Si	Me	**6l**	**25c**	92 (E/Z > 99:1)
4	Np–Br	Me_3Si	Me	**6m**	**25d**	92 (E/Z > 99:1)
5	4-$EtO_2CC_6H_4Br$	Me_3Si	Me	**6m**	**25e**	91 (E/Z = 96:4)
6	Np–Br	Me_2PhSi	Me	**6n**	**25f**	93 (E/Z > 99:1)
7	4-$EtO_2CC_6H_4Br$	Me_2PhSi	Me	**6n**	**25g**	84 (E/Z = 94:6)
8[b]	4-$EtO_2CC_6H_4Br$	Me_3Si	^{n}Bu	**6o**	**25h**	92 (E/Z > 99:1)

a) 2.5 mol % $Pd(OAc)_2$ and 10 mol % P(4-tolyl)$_3$. b) 2.5 mol % $Pd(OAc)_2$ and 10 mol % PPh_3.

(dba = dibenzylideneacetone) catalyst, KOH, and *N*,*N*-dimethylacetamide (DMA) proved to effect the allenylation of aryl bromides without contamination by propargylated products (Table 10).[21] DMA was essential to improve the conversion. Various aryl bromides including electron-deficient, electron-rich, and sterically demanding ones could react smoothly with homopropargyl alcohols **30**. The scope of homopropargyl alcohols was moderate. Homopropargyl alcohols **30d** and **30e** bearing one or two methyl groups at the propargylic position were converted to tri- or tetrasubstituted arylallenes, respectively, although a higher temperature was required.

The reactions of diastereomerically pure homopropargyl alcohols *threo*- and *erythro*-**33** with **32** provided tetrasubstituted allenes **34a** and **34b**, respectively, in good yields (Scheme 12). The synthesis of arylallenes by retro-propargylation is thus useful for the selective synthesis of multisubstituted allenes.

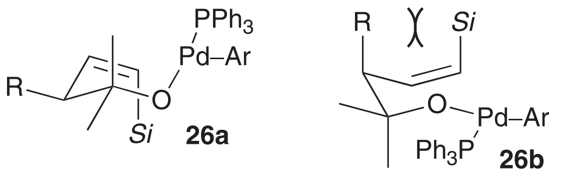
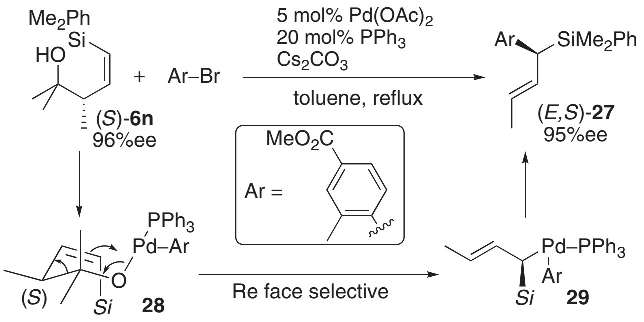


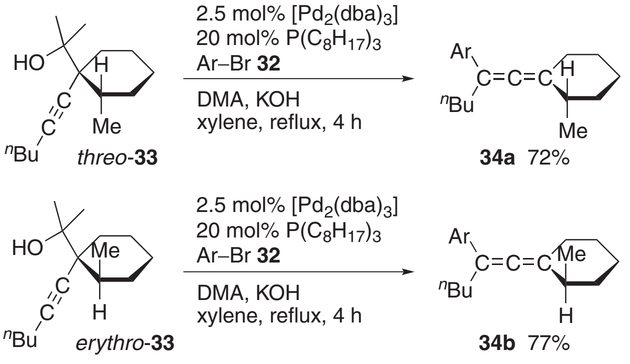
Figure 2. Favorable (**26a**) and unfavorable (**26b**) chair-like transition states for palladium-mediated retro-allylation of **6l**–**6o**.



Scheme 11. Chirality transfer from homoallyl alcohol.

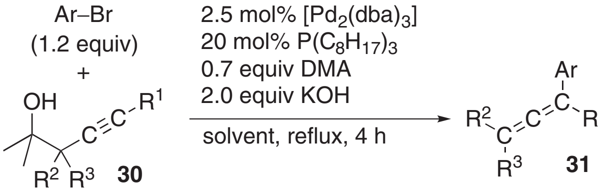
4.5 Synthesis of 2-Aryl-1,3-butadienes by Palladium-Catalyzed Reactions with 3,4-Alkadien-1-ols. The palladium-mediated retro-allylation allowed 3,4-alkadien-1-ols to act as 1-methylene-2-propenyl metals.[22,23] Allenyl alcohol **35a** reacted with aryl bromides to provide the corresponding arylated 1,3-butadienes (Table 11). A combination of potassium carbonate as a base and bis(diphenylphosphino)methane (DPPM) as a ligand proved to be most efficient. In the event Diels–Alder dimerization of the products **36** was problematic, *N*-methylpyrrole should be added to avoid the side reaction (Entries 4–8). We assume that *N*-methylpyrrole would coordinate to palladium, diminishing the catalytic performance of palladium for the Diels–Alder reaction.[24]

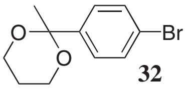
Alcohol **35b** reacted with aryl bromides with the aid of a combination of palladium acetate, tris(4-fluorophenyl)phosphine, and cesium carbonate to afford highly substituted diene **37** (Scheme 13). Allenyl alcohol **35c** bearing a branched methyl group reacted with a variety of aryl bromides to yield



Scheme 12. Stereoselective synthesis of tetrasubstituted arylallenes.

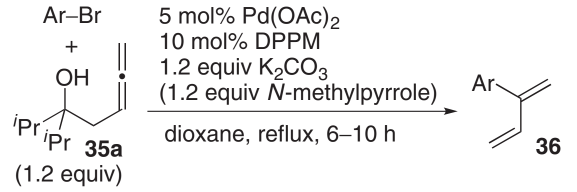
Table 10. Palladium-Catalyzed Allenylation of Aryl Bromides with Homopropargyl Alcohols



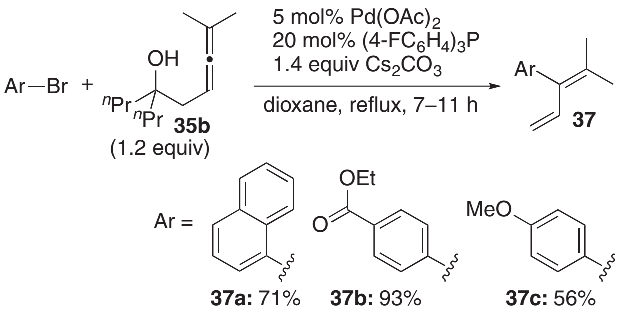
R^1	R^2	R^3	**30**	Ar–Br	Solvent	**31**	Yield/%
^{n}Bu	H	H	**30a**	$4\text{-}CF_3C_6H_4Br$	Toluene	**31a**	63
^{n}Bu	H	H	**30a**	$4\text{-}MeOC_6H_4Br$	Toluene	**31b**	63[a)]
^{n}Bu	H	H	**30a**	$2\text{-}MeC_6H_4Br$	Toluene	**31c**	65
^{n}Bu	H	H	**30a**	$4\text{-}^tBuCOC_6H_4Br$	Toluene	**31d**	85
^{n}Bu	H	H	**30a**	 **32**	Toluene	**31e**	82
^{i}Pr	H	H	**30b**	**32**	Toluene	**31f**	62
^{t}Bu	H	H	**30c**	**32**	Toluene	**31g**	0
^{n}Bu	Me	H	**30d**	**32**	Xylene	**31h**	71
^{n}Bu	Me	Me	**30e**	**32**	Xylene	**31i**	79

a) 1.0 equiv $4\text{-}MeOC_6H_4Br$ and 2.0 equiv **30a**.

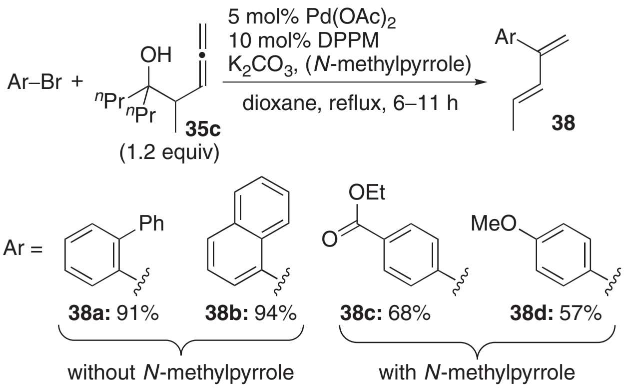
Table 11. Synthesis of 2-Aryl-1,3-butadienes from Allenyl Alcohol **35a**



Entry	Ar	*N*-Methylpyrrole	36	Yield/%
1	1-Naphthyl	without	**36a**	79
2	2-PhC$_6$H$_4$	without	**36b**	71
3	4-MeOC$_6$H$_4$	without	**36c**	64
4	4-EtO$_2$CC$_6$H$_4$	without	**36d**	12
5		with	**36d**	71
6	4-MeCOC$_6$H$_4$	with	**36e**	66
7	4-PhC$_6$H$_4$	without	**36f**	4
8		with	**36f**	75



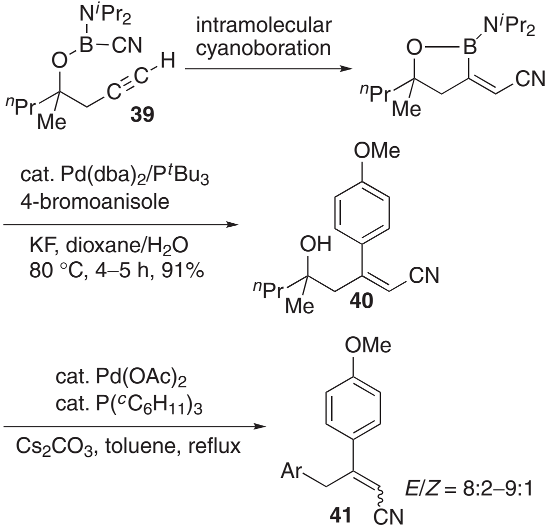
Scheme 13. Reactions with allenyl alcohol **35b**.



Scheme 14. Reactions with **35c** for stereoselective synthesis of (*E*)-2-aryl-1,3-pentadienes.

(*E*)-2-aryl-1,3-pentadienes **38** with exclusive stereoselectivity (Scheme 14). The E selectivity can be rationalized in a fashion similar to Figures 1 and 2.

4.6 Summary for the Palladium-Catalyzed Regio- and Stereoselective Allylation. The palladium-catalyzed reactions of aryl halides with homoallyl and related unsaturated alcohols represent highly regio- and stereoselective allylation, taking advantage of the configurational stability, inertness under air, and practical availability of the alcohols. One can predict the regio- and stereoselectivities by configurational analysis of the six-membered transition states of the retro-allylation. We believe that homoallyl alcohols will substitute allylmetals for palladium-catalyzed cross-coupling reactions with allylmetals.



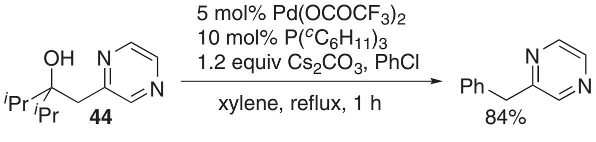
Scheme 15. Retro-allylation as a method for removal of tethering group.

4.7 An Application of Palladium-Catalyzed Retro-Allylation. The palladium-catalyzed retro-allylation will find many applications as a useful bond cleaving strategy.

Although intramolecular cyanoboration reaction was developed by Suginome et al.,[25] intermolecular variants are difficult processes. They utilized retro-allylation as a method for removing a tethering group (Scheme 15).[26] Intramolecular cyanoboration of homopropargyl alcohol derivative **39** followed by Suzuki–Miyaura cross-coupling afforded homoallyl alcohol **40**. The subsequent reaction of aryl bromide with **40** yielded 3,4-diaryl-2-butenenitrile **41**. The overall transformation is formally equivalent to intermolecular regio- and stereoselective addition across propargylarene.

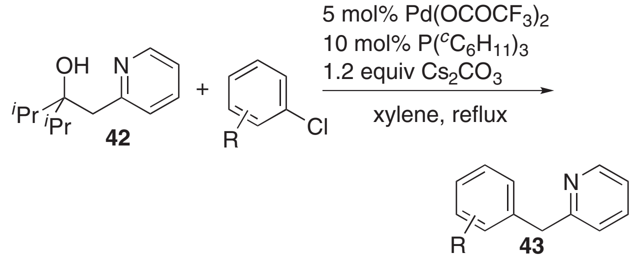
5. Palladium-Catalyzed 2-Pyridylmethyl Transfer Reactions from 2-(2-Pyridyl)ethanol Derivatives to Aryl Chloride

When aryl chlorides reacted with pyridylethanol **42** in the presence of a Pd(OCOCF$_3$)$_2$/P(^{c}C$_6$H$_{11}$)$_3$ catalyst and cesium carbonate in refluxing xylene, pyridylmethyl group transfer took place (Table 12).[27] Pyrazinyl alcohol **44** also underwent a similar reaction (eq 1). However, a 4-pyridylmethyl group as well as a benzyl group was not transferred from the corresponding alcohols under conditions we extensively tested. The assist of the nitrogen atom at the 2 position proved to be important. A plausible reaction mechanism is outlined in Scheme 16. The key would be the coordination of the nitrogen atom in intermediate **45**, which would assist the following carbon–carbon bond cleavage. After initially formed palladium amide **46** would isomerize to benzylic palladium **47**, reductive elimination would take place to yield **43**.

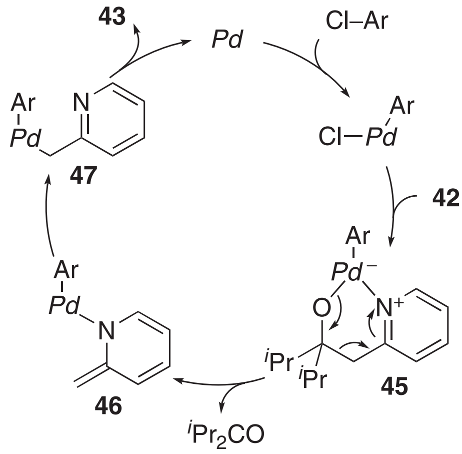


(1)

Table 12. Palladium-Catalyzed 2-Pyridylmethyl Transfer to Aryl Chloride from Alcohol **42**



R	**43**	Yield/%
H	**43a**	88
4-CF_3	**43b**	89
4-CO_2Et	**43c**	80
4-CN	**43d**	70
4-OMe	**43e**	90
2-Me	**43f**	79
4-CH_2=CH	**43g**	81



Scheme 16. A Plausible mechanism for pyridylmethyl transfer.

6. Nickel-Catalyzed Retro-Allylation for the Synthesis of 1,5-Hexadienes

Although palladium-catalyzed cross-coupling reactions of allyl electrophiles with allylmetals are seemingly useful for the synthesis of 1,5-hexadienes, the reactions often suffer from low efficiency due to slow reductive elimination, the formation of undesired homo-coupling products, and the use of toxic allylstannanes. Taking advantage of the retro-allylation strategy, we performed palladium-catalyzed reaction of cinnamyl acetate with homoallyl alcohol **6a** (eq 2). However, the reaction underscored the difficulty in achieving efficient synthesis of 1,5-hexadienes: branched-coupling product **48a** was obtained in only 25% yield, and β-methylstyrene was mainly formed.

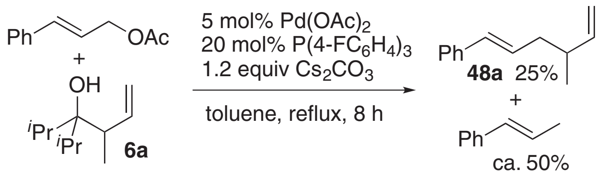
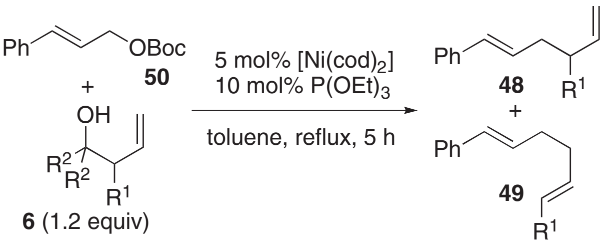
 (2)

Table 13. Nickel-Catalyzed Allylation of Boc-Protected Cinnamyl Alcohol **50** with Homoallyl Alcohols **6**



R^1	R^2	**6**	Yield/%	**48/49**
Me	^{i}Pr	**6a**	91	**48a/49a** = 37:67
$^n C_7H_{15}$	Me	**6p**	60	**48b/49b** = 26:74
$^c C_6H_{11}$	Me	**6q**	77	**48c/49c** = 9:91
^{t}Bu	Me	**6r**	79	**48d/49d** = 3:97

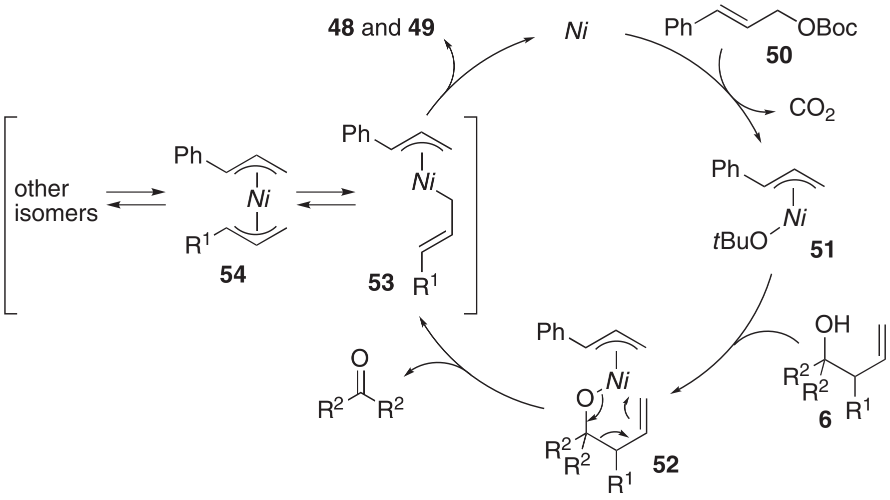
We then turned our attention to nickel catalysis.[28] After extensive screening of reaction conditions, a combination of 5 mol % of [Ni(cod)$_2$] (cod = 1,5-cyclooctadiene) and 10 mol % of triethyl phosphite proved to catalyze the allylation reaction of Boc-protected cinnamyl alcohol **50** (Boc = *t*-butoxycarbonyl) with **6a** (Table 13). The reaction afforded a 37:63 mixture of the corresponding coupling products **48a** and **49a** in high yield. The highest linear selectivity was observed in the reaction of **50** with bulky *t*-butyl-substituted homoallyl alcohol **6r**.

After several mechanistic experiments, we are tempted to propose the reaction mechanism as shown in Scheme 17. Oxidative addition of **50** followed by decarboxylation would afford alkoxy(π-allyl)nickel intermediate **51**. Alkoxide exchange between **51** and **6** would yield **52**. Retro-allylation would then occur to yield **53**. Unfortunately, the configuration of the diallylnickel complex would be fluxional to yield a mixture of several diallylnickel species such as **54**. Reductive elimination prior to β-hydride elimination would afford **48** and **49**.

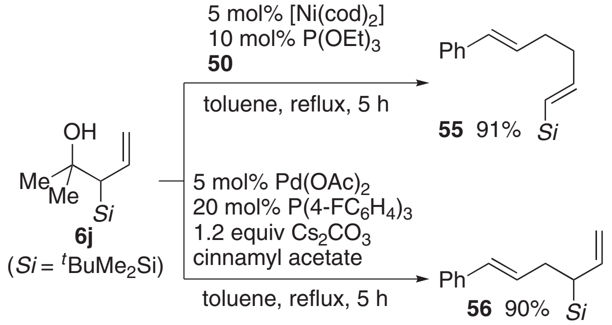
The nickel-catalyzed reactions of **50** with silyl-substituted homoallyl alcohols **6j** yielded the corresponding linear cross-coupling products **55** in high yields (Scheme 18). Intriguingly, the sense of regioselectivity was opposite when a palladium catalyst was used in the reaction of cinnamyl acetate. The mode of reductive elimination from diallylnickel species would be different from that from diallylpalladium.

7. Rhodium-Catalyzed Retro-Allylation Forming Nucleophilic Allylrhodiums

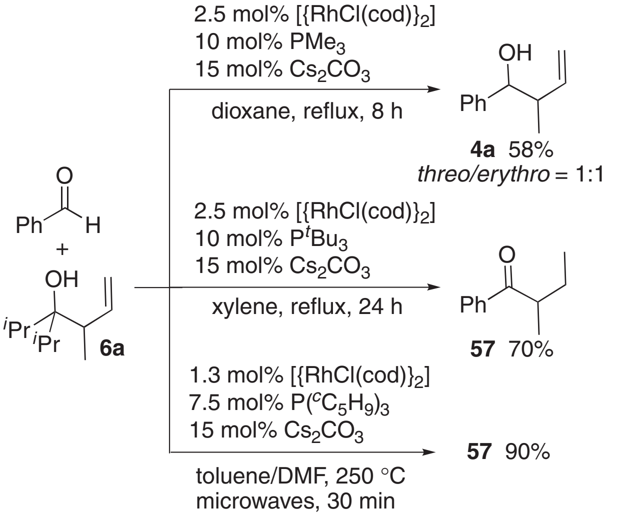
Although many allylmetal reagents are used for the allylation of carbonyl compounds, rhodium-mediated or -catalyzed carbonyl allylation is quite rare.[29] We established a new method for the generation of nucleophilic allylrhodium reagents from homoallyl alcohols via retro-allylation and applied them to the allylation of carbonyl compounds.[30,31] The [{RhCl(cod)}$_2$]/PMe$_3$-catalyzed reaction of benzaldehyde with **6a** in dioxane at 100 °C effected the crotylation of the aldehyde (Scheme 19). Unfortunately, no stereoselectivity was observed in the crotylation reaction due to the rapid σ–π isomerization of allylrhodium species. Interestingly, a similar reaction with the aid of [{RhCl(cod)}$_2$]/P^{t}Bu$_3$ in xylene at



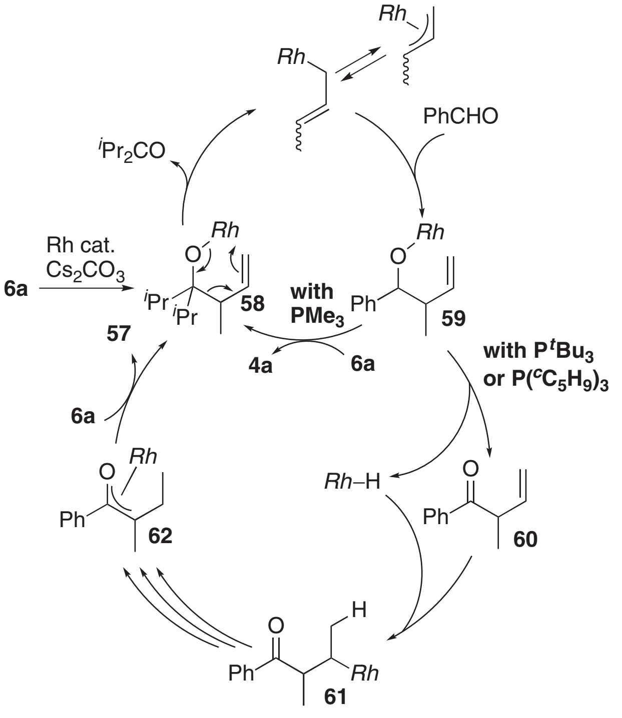
Scheme 17. Plausible reaction mechanism.



Scheme 18. Nickel- or palladium-catalyzed selective preparation of vinylsilane or allylsilane.



Scheme 19. Rhodium-catalyzed allyl transfer.

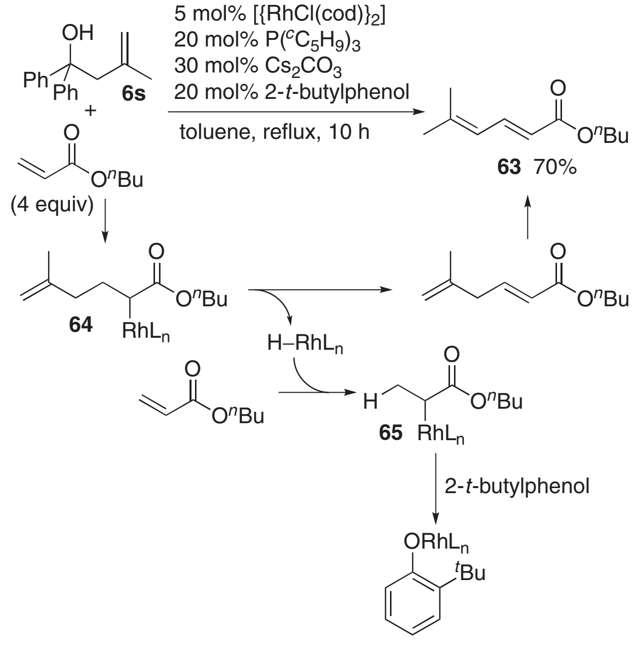


Scheme 20. Plausible mechanism.

reflux afforded saturated ketone **57**. Under microwave irradiation at 250 °C, ketone **57** was obtained in high yield within 30 min.

Alkoxide–chloride exchange between the rhodium catalyst and **6a** should occur with the aid of cesium carbonate to yield **58** (Scheme 20). Retro-allylation of **58** would initially provide σ-crotylrhodium, which can be in fast equilibrium with π-crotylrhodium. The allylrhodium would react with benzaldehyde to yield the rhodium alkoxide **59**. When **59** bears trimethylphosphine as a ligand, protonolysis of **59** with **6a** would proceed smoothly to yield **4a** and **58**. In the event that the ligand is bulky like P^tBu_3, the protonolysis of **59** with **6a** would be so suppressed that β-hydride elimination would occur to yield **60** and rhodium hydride. Hydrorhodation of **60** at the olefinic moiety should afford **61**. The subsequent iterative β-elimination/hydrorhodation would generate oxa-π-allylrhodium **62**, which should be protonated by **6a** to complete the catalytic cycle.

Rhodium also catalyzed allyl transfer from homoallyl alcohol **6s** to butyl acrylate in a 1,4-fashion (Scheme 21). Rhodium enolate **64** would undergo β-hydrogen elimination followed by isomerization to afford $\alpha,\beta,\gamma,\delta$-unsaturated ester



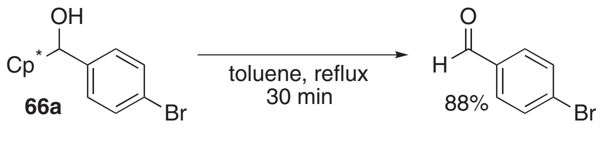
Scheme 21. Rhodium-catalyzed allyl transfer to acrylate ester.

63. The rhodium hydride generated by the β-hydrogen elimination would react with remaining butyl acrylate to afford enolate **65**. Enolate **65** should react with 2-*t*-butylphenol to form rhodium phenoxide. The rhodium phenoxide would participate in smooth ligand exchange to yield the rhodium alkoxide of **6s** which is ready for retro-allylation.

8. Cp*H in Organic Synthesis

Pentamethylcyclopentadienide (Me$_5$C$_5$$^-$, Cp^{*-}) is an extremely important "ligand" in transition-metal chemistry because of its unique structure and electronic properties. However, there are few reports of using Cp^{*-} itself as a reagent in organic synthesis.[32] Keeping in mind that Cp^{*-} is an allylic anion (Figure 3), we explored the utility of Cp^{*-} in organic synthesis. We thus found some interesting organic reactions by using Cp^{*-}.[33]

Treatment of 4-bromobenzaldehyde with [Li(Cp*)] in THF at −20 °C for 1 h provided the corresponding adduct **66a** in excellent yield (Table 14, Entry 1, from aldehyde to **66**). The reaction was so chemoselective that keto (Entries 3 and 6), ester (Entry 4), and cyano (Entry 5) moieties were compatible. Interestingly, alcohols **66** were sensitive to acids and were exposed to a catalytic amount of trichloroacetic acid in dichloromethane at 25–30 °C to provide the parent aldehydes in good yields (from **66** to aldehyde). Notably, in polar coordinating solvents such as THF and methanol, the acid-catalyzed cleavage was not observed. Similar carbon–carbon bond cleavage occurred when alcohol **66** was simply heated in toluene without any acids (eq 3).



(3)

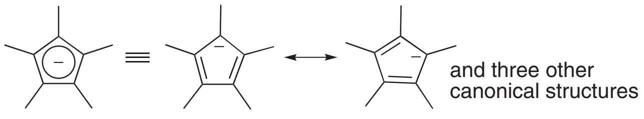
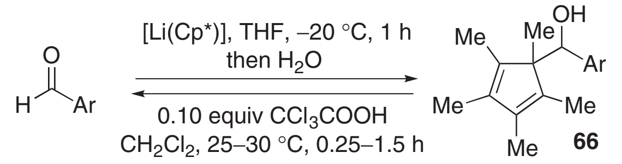
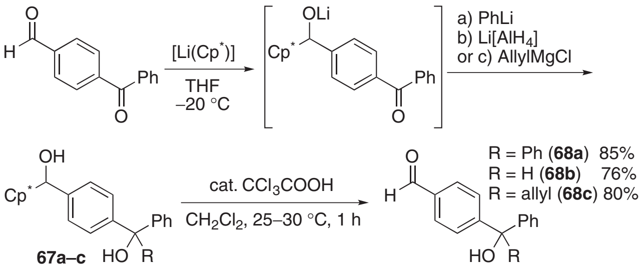


Figure 3. Resonance and canonical structures of Cp^{*-}.

Table 14. Nucleophilic Addition of [Li(Cp*)] to Aromatic Aldehydes and Carbon–Carbon Bond Cleavage of the Adducts Affording the Parent Aldehydes



Entry	Ar	66	From aldehyde to 66/%	From 66 to aldehyde/%
1	4-BrC$_6$H$_4$	**66a**	95	92
2	2-C$_{10}$H$_7$	**66b**	88	87
3	4-PhCOC$_6$H$_4$	**66c**	85	87
4	4-MeO$_2$CC$_6$H$_4$	**66d**	87	91
5	4-NCC$_6$H$_4$	**66e**	95	79
6	4-^{i}PrCOC$_6$H$_4$	**66f**	84	93
7	2-MeOC$_6$H$_4$	**66g**	97	69



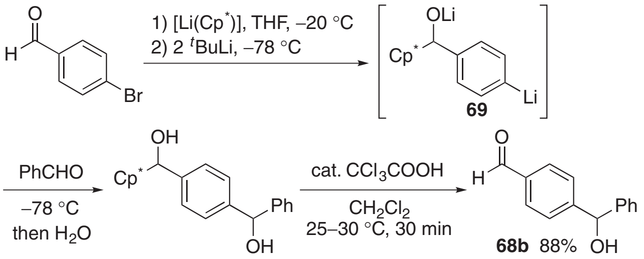
Scheme 22. Keto-selective nucleophilic addition by protection of formyl group with Cp*.

The formation and cleavage of the Cp*–carbon bonds reminded us of utilizing Cp* as a protective group (Scheme 22). After the formyl group of 4-formylbenzophenone was masked with [Li(Cp*)], the keto group was subjected to several nucleophilic addition reactions. The crude alcohols **67** were exposed to the acidic conditions to produce hydroxy aldehydes **68** in high overall yields. All the reactions proceeded so cleanly that no purification of intermediate **67** was necessary. The protective method allowed for preparation of a formyl-substituted phenyllithium equivalent **69** (Scheme 23).

The reaction of [Li(Cp*)] with aliphatic aldehyde failed to yield the corresponding adduct since [Li(Cp*)] served as a bulky base to generate the lithium enolate of the aldehyde. Fortunately, chlorodimethylaluminum proved to promote the addition of Cp^{*-} to a wide range of aliphatic aldehydes (Table 15, from aldehyde to **70**). Chlorodimethylaluminum is likely to activate the carbonyl group as a Lewis acid. However, contrary to the instability of aromatic alcohols **66** under acidic or thermal conditions, alcohols **70** were stable toward acids or high temperature. We found that a catalytic amount of 2,3-

dichloro-5,6-dicyanobenzoquinone (DDQ) alternatively induces smooth carbon–carbon bond cleavage to produce the parent aldehyde and Cp*H (from **70** to aldehyde).

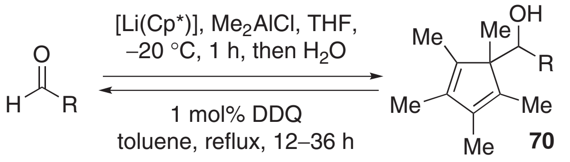
Under thermal conditions, elimination of Cp*H from **66** is likely to take place through a retro-carbonyl–ene mechanism (Scheme 24). Under the acid-catalyzed conditions, protonation at the Cp* group in nonpolar dichloromethane would facilitate the carbon–carbon bond cleavage. The protonation would promote release of the steric hindrance and recovery of a stabilized conjugated diene and eventually lead to carbon–carbon bond cleavage. The mechanism of the DDQ-promoted cleavage is not clear. Initially, oxidative cleavage could occur to afford very unstable pentamethylcyclopentadienyl cation. The cyclic 4π-electronic cation Cp^{*+} would be a strong hydride acceptor and able to abstract hydride from **70** via **71** to produce the protonated aldehyde, tetramethylfulvene, and Cp*H. Proton transfer from the protonated aldehyde to tetramethylfulvene would regenerate Cp^{*+} to complete the catalytic cycle.



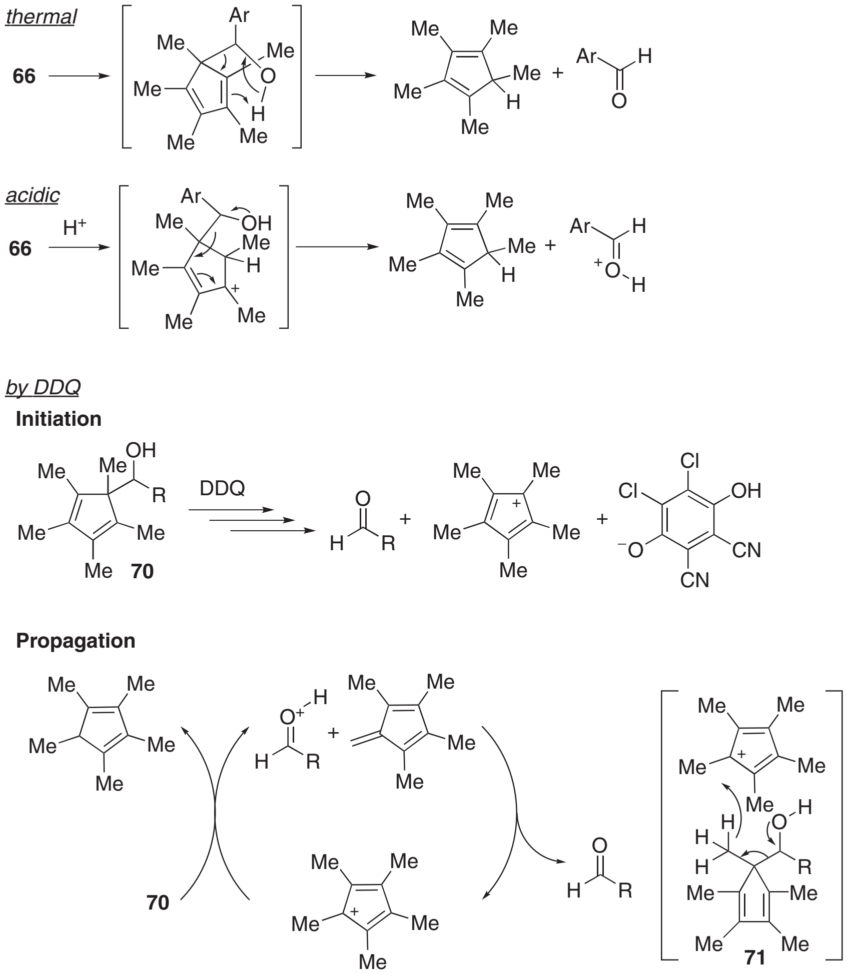
Scheme 23. Generation of aryllithium bearing protected formyl group.

The reaction of methyl cinnamate with lithium pentamethylcyclopentadienide in the presence of chlorodiethylaluminum

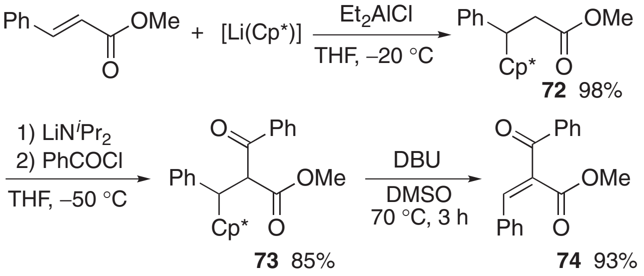
Table 15. Addition of [Li(Cp*)] to Aliphatic Aldehydes and Cp*–Carbon Bond Cleavage of the Adducts



Ar	**70**	From aldehyde to **70**/%	From **70** to aldehyde/%
$C_{11}H_{23}$	**70a**	92	92
$^{c}C_6H_{11}$	**70b**	97	82
$NC(CH_2)_5$	**70c**	89	75
$Cl(CH_2)_9$	**70d**	93	95
$MeO_2C(CH_2)_4$	**70e**	82	81



Scheme 24. Plausible mechanisms for Cp*–carbon bond cleavage.



Scheme 25. α-Acylation of methyl cinnamate through formation and cleavage of Cp*–carbon bond.

provided the corresponding 1,4-adduct **72** in good yield (Scheme 25). The adduct **72** underwent α-acylation reaction upon sequential treatment with lithium diisopropylamide and benzoyl chloride. DBU-mediated removal of the pentamethylcyclopentadienyl group from **73** afforded methyl α-benzoylcinnamate (**74**). Interestingly, the α-benzoylation process accompanied the inversion of the stereochemistry of the alkene moiety. The overall transformation utilizes the strong nucleophilicity and proper leaving ability of Cp^{*-}.

9. Conclusion

We have developed several new transformations by using metal-assisted retro-allylation of homoallyl alcohols. Among them, retro-allylation mediated by gallium and palladium has emerged as a useful method for highly stereo- and regioselective preparation of the corresponding σ-allylmetals that are otherwise difficult to prepare. In the cases of rhodium and nickel, the initially formed σ-allylmetals are prone to isomerize. We should hence work on either to freeze or utilize the isomerization. Extension of the retro-allylation to other metals such as copper would be fruitful. The use of homoallyl alcohols as allylmetal equivalents will facilitate invention of new preparations of well-defined homoallyl alcohols. Learning much about retro-allylation from the rich chemistry of allylation, we hope that retro-allylation will achieve a position for preparing allylmetals as significant as the Barbier/Grignard reaction and transmetalation.

The invaluable contributions of co-workers whose names appear in the references are greatly acknowledged. This work was supported by Grants-in-Aid for Scientific Research and GCOE Research from JSPS. H.Y. is grateful for financial support from Eisai and Kyoto University. We are grateful to Professor Masaki Shimizu in the same department for his help with X-ray crystallographic analysis to determine the relative stereochemistry of homoallyl alcohols.

References

1 a) Y. Yamamoto, N. Asao, *Chem. Rev.* **1993**, *93*, 2207. b) S. E. Denmark, J. Fu, *Chem. Rev.* **2003**, *103*, 2763. c) J. W. J. Kennedy, D. G. Hall, *Angew. Chem., Int. Ed.* **2003**, *42*, 4732. d) E. J. Thomas, *Chem. Rec.* **2007**, *7*, 115.

2 a) *Comprehensive Organic Synthesis*, ed. by B. M. Trost, I. Fleming, S. L. Schreiber, Pergamon Press, New York, **1991**, Vol. 1, Chap. 1. b) *Organometallics in Synthesis*, ed. by M. Schlosser, John Wiley & Sons, Chichester, UK, **2002**. c) J. Tsuji, *Transition Metal Reagents and Catalysts*, John Wiley & Sons, Chichester, UK, **2000**, Chap. 4.

3 K. Fujita, H. Yorimitsu, K. Oshima, *Chem. Rec.* **2004**, *4*, 110.

4 Concerning Li, K, Mg, Zn, or Al: a) R. A. Benkeser, W. E. Broxterman, *J. Am. Chem. Soc.* **1969**, *91*, 5162. b) P. Miginiac, *Bull. Chim. Soc. Fr.* **1970**, 1077. c) P. F. Gerard, P. Miginiac, *Bull. Chim. Soc. Fr.* **1974**, 1924. d) F. Gerard, P. Miginiac, *Bull. Chim. Soc. Fr.* **1974**, 2527. e) R. A. Benkeser, M. P. Siklosi, *J. Org. Chem.* **1976**, *41*, 3212. f) T. Holm, *Acta Chem. Scand., Ser. B* **1976**, *30*, 985. g) F. Barbot, P. Miginiac, *Bull. Chim. Soc. Fr.* **1977**, 113. h) F. Barbot, P. Miginiac, *J. Organomet. Chem.* **1977**, *132*, 445. i) R. A. Benkeser, M. P. Siklosi, E. C. Mozdzen, *J. Am. Chem. Soc.* **1978**, *100*, 2134. j) R. L. Snowden, K. H. Schulte-Elte, *Helv. Chim. Acta* **1981**, *64*, 2193.

5 A crotylzinc reagent generated by retro-allylation reacted with aldehydes to yield the corresponding *threo*-homoallyl alcohols selectively: a) P. Jones, N. Millot, P. Knochel, *Chem. Commun.* **1998**, 2405. b) P. Jones, P. Knochel, *Chem. Commun.* **1998**, 2407. c) P. Jones, P. Knochel, *J. Org. Chem.* **1999**, *64*, 186. d) N. Millot, P. Knochel, *Tetrahedron Lett.* **1999**, *40*, 7779.

6 Organostannane-mediated retro-allylation: a) V. Peruzzo, G. Tagliavini, *J. Organomet. Chem.* **1978**, *162*, 37. b) A. Gambaro, D. Marton, V. Peruzzo, G. Tagliavini, *J. Organomet. Chem.* **1981**, *204*, 191. c) A. Yanagisawa, T. Aoki, T. Arai, *Synlett* **2006**, 2071.

7 Pioneering work about transition-metal-catalyzed retro-allylation and its application to organic synthesis: a) T. Kondo, K. Kodoi, E. Nishinaga, T. Okada, Y. Morisaki, Y. Watanabe, T. Mitsudo, *J. Am. Chem. Soc.* **1998**, *120*, 5587. b) T. Kondo, T. Mitsudo, *Chem. Lett.* **2005**, *34*, 1462.

8 A part of this Account is described in Japanese. H. Yorimitsu, K. Oshima, *J. Synth. Org. Chem., Jpn.* **2008**, *66*, 332.

9 K. Fujita, H. Yorimitsu, H. Shinokubo, S. Matsubara, K. Oshima, *J. Am. Chem. Soc.* **2001**, *123*, 12115.

10 K. Fujita, H. Yorimitsu, H. Shinokubo, K. Oshima, *J. Org. Chem.* **2004**, *69*, 3302.

11 The unambiguous erythro/threo nomenclature is used throughout the manuscript: R. Noyori, I. Nishida, J. Sakata, *J. Am. Chem. Soc.* **1981**, *103*, 2106.

12 For convenience, throughout the manuscript, crotylation, methallylation, and prenylation are defined as introductions of 1-methyl-2-propenyl, 2-methyl-2-propenyl, and 1,1-dimethyl-2-propenyl groups, respectively, into a carbonyl group. On the other hand, crotyl, methallyl, and prenyl groups denote herein 2-butenyl, 2-methyl-2-propenyl, and 3-methyl-2-butenyl groups, respectively.

13 a) M. Chino, T. Matsumoto, K. Suzuki, *Synlett* **1994**, 359. b) Y. Yamamoto, K. Maruyama, *Tetrahedron Lett.* **1981**, *22*, 2895.

14 a) S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *Org. Lett.* **2005**, *7*, 3577. b) S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *J. Organomet. Chem.* **2007**, *692*, 505.

15 a) T. Hiyama, Y. Hatanaka, *Pure Appl. Chem.* **1994**, *66*, 1471. b) Y. Obora, Y. Tsuji, M. Kobayashi, T. Kawamura, *J. Org. Chem.* **1995**, *60*, 4647. c) Y. Yamamoto, S. Takada, N. Miyaura, *Chem. Lett.* **2006**, *35*, 704. d) Y. Yamamoto, S. Takada, N. Miyaura, *Chem. Lett.* **2006**, *35*, 1368. e) Y. Yamamoto, S. Takada, N. Miyaura, T. Iyama, H. Tachikawa, *Organometallics* **2009**, *28*, 152.

16 a) Y. Terao, H. Wakui, T. Satoh, M. Miura, M. Nomura, *J. Am. Chem. Soc.* **2001**, *123*, 10407. b) Y. Terao, H. Wakui, M. Nomoto, T. Satoh, M. Miura, M. Nomura, *J. Org. Chem.* **2003**, *68*, 5236. c) H.-F. Chow, C.-W. Wan, K.-H. Low, Y.-Y. Yeung, *J. Org. Chem.* **2001**, *66*, 1910. d) T. Nishimura, S. Uemura, *J. Am. Chem.*

Soc. **1999**, *121*, 11010. Reviews: e) J. Muzart, *Tetrahedron* **2005**, *61*, 9423. f) T. Satoh, M. Miura, *J. Synth. Org. Chem., Jpn.* **2006**, *64*, 1199.

17 a) S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2006**, *128*, 2210. b) M. Iwasaki, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2007**, *129*, 4463.

18 M. Iwasaki, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *Tetrahedron* **2007**, *63*, 5200.

19 M. Iwasaki, H. Yorimitsu, K. Oshima, *Bull. Chem. Soc. Jpn.* **2009**, *82*, 249.

20 S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2007**, *129*, 12650.

21 S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2008**, *130*, 5048.

22 J. Imoto, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *Bull. Chem. Soc. Jpn.* **2009**, *82*, 393.

23 Similar palladium-catalyzed reactions of aryl halides with 3,4-alkadien-1-ols were reported. However, the scope of the reactions was limited, and the proposed mechanism is different from our working hypothesis. C. H. Oh, S. H. Jung, S. Y. Bang, D. I. Park, *Org. Lett.* **2002**, *4*, 3325.

24 a) M. Murakami, R. Minamida, K. Itami, M. Sawamura, Y. Ito, *Chem. Commun.* **2000**, 2293. b) K. Kumar, R. S. Jolly, *Tetrahedron Lett.* **1998**, *39*, 3047. c) M. Lautens, W. Klute, W. Tam, *Chem. Rev.* **1996**, *96*, 49.

25 M. Suginome, A. Yamamoto, M. Murakami, *J. Am. Chem. Soc.* **2003**, *125*, 6358.

26 T. Ohmura, T. Awano, M. Suginome, H. Yorimitsu, K. Oshima, *Synlett* **2008**, 423.

27 T. Niwa, H. Yorimitsu, K. Oshima, *Angew. Chem., Int. Ed.* **2007**, *46*, 2643.

28 Y. Sumida, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *Org. Lett.* **2008**, *10*, 1629.

29 a) M. Shi, G.-X. Lei, Y. Masaki, *Tetrahedron: Asymmetry* **1999**, *10*, 2071. b) Y. Masuyama, Y. Kaneko, Y. Kurusu, *Tetrahedron Lett.* **2004**, *45*, 8969.

30 a) Y. Takada, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *Org. Lett.* **2006**, *8*, 2515. b) Y. Sumida, Y. Takada, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *Chem. Asian J.* **2008**, *3*, 119. c) M. Jang, S. Hayashi, K. Hirano, H. Yorimitsu, K. Oshima, *Tetrahedron Lett.* **2007**, *48*, 4003.

31 Rh-catalyzed deallylation was recently reported. a) P. Zhao, C. D. Incarvito, J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 3124. b) R. Shintani, K. Takatsu, T. Hayashi, *Org. Lett.* **2008**, *10*, 1191.

32 a) F. X. Kohl, P. Jutzi, *Chem. Ber.* **1987**, *120*, 1539. b) H.-A. Brune, P. Lach, G. Schmidtberg, *Chem. Ber.* **1985**, *118*, 2671. c) H.-A. Brune, P. Lach, G. Schmidtberg, *Chem. Ber.* **1985**, *118*, 2681. d) H. Otto, H. Werner, *Chem. Ber.* **1987**, *120*, 97. e) P. Jutzi, K.-H. Schwartzen, A. Mix, *Chem. Ber.* **1990**, *123*, 837. f) U. Burger, R. Etienne, *Helv. Chim. Acta* **1984**, *67*, 2057. g) P. Jutzi, K.-H. Schwartzen, A. Mix, H.-G. Stammler, B. Neumann, *Chem. Ber.* **1993**, *126*, 415. h) R. F. Childs, M. Zeya, *J. Am. Chem. Soc.* **1974**, *96*, 6418. i) M. Maeda, S. Fujiwara, T. Shin-ike, N. Kambe, N. Sonoda, *J. Am. Chem. Soc.* **1996**, *118*, 8160. j) S. Fujiwara, H. Maeda, T. Matsuya, T. Shin-ike, N. Kambe, N. Sonoda, *J. Org. Chem.* **2000**, *65*, 5022.

33 a) K. Yagi, H. Yorimitsu, K. Oshima, *Tetrahedron Lett.* **2005**, *46*, 4831. b) M. Uemura, H. Yorimitsu, K. Oshima, *Tetrahedron Lett.* **2006**, *47*, 163. c) M. Uemura, K. Yagi, M. Iwasaki, K. Nomura, H. Yorimitsu, K. Oshima, *Tetrahedron* **2006**, *62*, 3523. d) M. Uemura, H. Yorimitsu, K. Oshima, *Chem. Lett.* **2006**, *35*, 408. e) M. Iwasaki, E. Morita, M. Uemura, H. Yorimitsu, K. Oshima, *Synlett* **2007**, 167. f) M. Uemura, M. Iwasaki, E. Morita, H. Yorimitsu, K. Oshima, *Bull. Chem. Soc. Jpn.* **2007**, *80*, 2400.

Hideki Yorimitsu was born in Kochi, Japan, in 1975. He obtained his B.S. and Ph.D. in 1997 and in 2002, respectively, from Kyoto University under the supervision of Professor Oshima. He then served as a JSPS postdoctoral fellow, working with Professor Eiichi Nakamura at the University of Tokyo. He became an Assistant Professor at Kyoto University in 2003 and has been an Associate Professor since 2008. His research program focuses on the development of new organic reactions useful for synthesizing biologically interesting compounds, novel coordinating structures, and organometallic compounds. He received the Chemical Society of Japan Award for Young Chemists for 2008.

Koichiro Oshima was born in Hyogo, Japan, in 1947. He graduated from Kyoto University in 1970 and obtained his Ph.D. in 1975 under the guidance of Professor Hitosi Nozaki. He then spent two and a half years as a postdoctoral fellow with Professor Barry Sharpless at MIT and became an Assistant Professor at Kyoto University in 1977. He was promoted to Lecturer in 1984, Associate Professor in 1986, and Professor in 1993. His current research interests include the development of new synthetic methods via radical reactions and organometallic reagents. He received the Award for Young Chemists of the Society of Synthetic Organic Chemistry, Japan in 1983, the Japan Synthetic Organic Chemistry Award in 2004, and the Chemical Society of Japan Award for 2006.