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Tetrahedron
Tetrahedron 61 (2005) 3709–3718

# Pd-catalyzed nucleophilic allylic alkylation of aliphatic aldehydes by the use of allyl alcohols

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Received 28 December 2004; revised 4 February 2005; accepted 4 February 2005

**Abstract**—Under catalysis of $Pd(OAc)_2$-(P-*n*-$Bu)_3$, $Et_2Zn$ promotes a variety of allyl alcohols to undergo nucleophilic allylation of aliphatic aldehydes and ketones at room temperature and provides homoallyl alcohols in 60–90 and ca. 60% isolated yield, respectively. The reaction is irreversible and kinetically controlled, and unique regio- and stereoselectivities observed for the allylation with unsymmetrically substituted allyl alcohols are discussed.


## 1. Introduction

Nucleophilic alkylation of aldehydes and ketones is among the most fundamental and useful methods to elaborate molecules, and many methodologies, especially allylation using a variety of allyl metals (Li, Mg, etc.) and metalloids (B, Si, Sn, etc.), have been explored.[1] Allylating agents are basically prepared from allyl halides derived from allyl alcohols by treatment with a stoichiometric amount of hazardous hydrogen halides or anhydrides of hydrogen halides–organic and inorganic acids. As allyl metalloids, despite their toxicity and instability, allylstannanes have been most widely studied and utilized owing to their good performance in reactivity and selectivity.[2]

Needless to say, the use of allyl alcohols themselves as allylation agents has many advantages from an economical and environmental points of view: no need for additional steps to convert to other allylating agents and production of water instead of strong acids as a side-product. Furthermore, from a practical point of view, ready availability of a wide structural variety, moderate stability withstanding purification by distillation and storage, and wide abundance in nature, all combine to make allyl alcohols suitable and ideal for small- to large-scale experiments.

## 2. Results and discussion

The allylation with allyl alcohols was first realized and studied extensively by Masuyama et al.,[3] who used a Pd–$SnCl_2$ catalytic system. At a first glance, heterolytic cleavage of the C–O bond of an allyl alcohol to generate an allyl anion and a hydroxy cation species ($CH_2{=}CHCH_2OH \rightarrow CH_2{=}CHCH_2^- + OH^+$) may seem to be unrealistic; however, this task could be realized by virtue of capability of a palladium(0) species to undergo oxidative addition upon an allyl alcohol, probably being activated by coordination to a Lewis acid, to form a π-allylpalladium species ($CH_2{=}CHCH_2OH + Pd(0) \rightarrow CH_2{=}CHCH_2Pd^+OH^-$) and capability of $SnCl_2$ to reduce a cationic π-allylpalladium species to an anionic allylstannane species ($CH_2{=}CHCH_2Pd^+OH^- + Sn^{2+}Cl_2 \rightarrow CH_2{=}CHCH_2Sn^{4+}Cl_2OH + Pd(0)$). From an environmental view point, however, this method suffers from hazardous nature of hydrogen chloride, ultimately formed by hydrolysis of chlorostannanes used in an excess amount.

Recently, we have disclosed that nucleophilic allylation of aromatic aldehydes can be successfully performed by using allyl alcohols under a Pd–$Et_3B$ catalytic system, where $Et_3B$ not only serves as a Lewis acid to activate an allyl alcohol, but it reacts with a π-allylpalladium intermediate to exchange the ethyl and allyl ligands to each other to give a nucleophilically active allylborane species and an unstable ethylpalladium(II) species, which might readily decompose in many ways, e.g. via β-hydrogen elimination generating ethylene and water molecules together with a catalytically active Pd(0) species (Scheme 1a).[4] Unfortunately, however,

*Keywords*: Palladium; Allyl alcohols; Allylation; Aldehydes; Ketones.
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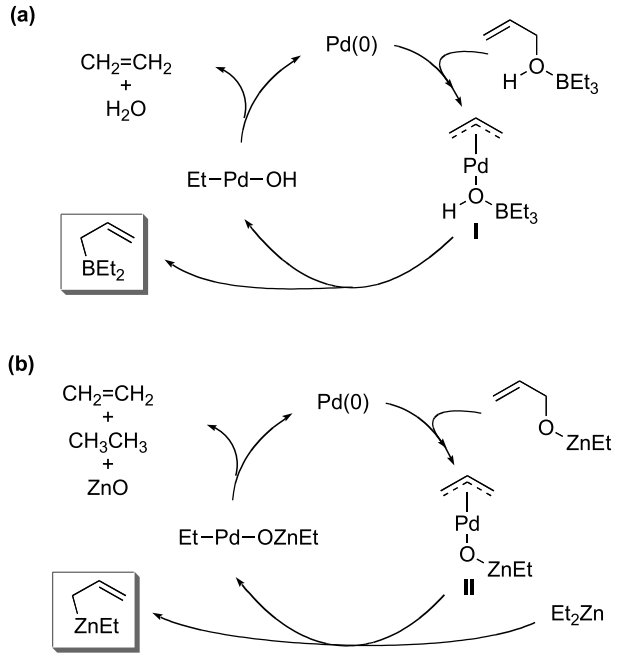
doi:10.1016/j.tet.2005.02.005




**Scheme 1.** Catalytic cycles for the generation of allylborane (a) and allylzinc (b) from allyl alcohol in the presence of a palladium(0) species.

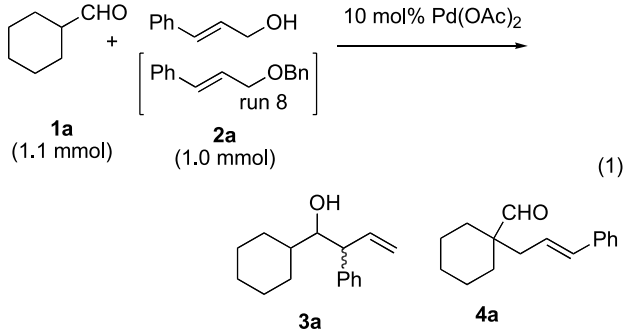
the reaction was not applicable to aliphatic aldehydes; nucleophilic allylation was accompanied by electrophilic allylation at the α-carbons of aliphatic aldehydes.[5]

For example, under the catalysis of Pd(0)–$Et_3B$, the reaction of cyclohexanecarboxaldehyde (**1a**) and cinnamyl alcohol (**2a**) provided a mixture of **3a** and **4a** in almost equal amounts (Eq. 1 and runs 1, Table 1) or **4a** selectively (run 2). The selective α-allylation giving rise to **4a** could be realized by using LiCl (facilitating the exchange of the counter ion of **I**: $Et_3BOH^-$ to $Cl^-$) and $Et_3N$ (increasing the concentration of an aldehyde enolate) as additives.[5] However, we have not been successful yet to modify the reaction to selectively undergo nucleophilic allylation at the carbonyl carbons of aldehydes.

Our working hypothesis (Scheme 1) suggested that organometallic species of higher migratory aptitude might promote the allyl–ethyl exchange process and hence facilitate the generation of an allylmetal species. Accordingly, we reexamined the reaction of **1a** and **2a** using $Et_2Zn$ in place of $Et_3B$ (Scheme 1b).[6] As was expected, **4a** was eliminated completely (run 3, Table 1); however, the reaction was very sluggish (45% conversion, 20 h at room temperature) and provided the expected **3a**, albeit in low yield. Application of *n*-$Bu_3P$, in place of $Ph_3P$, dramatically increased not only the yield of **3a**, but the reaction rate (run 4). Interestingly, non-polar solvents seemed to give the better results (runs 5 and 7). The solvent system in these reactions is rather unique and consists of non-polar solvents: toluene (0.5 mL) and *n*-hexane (3.6 mL, the solvent of $Et_2Zn$) for a 1 mmol scale reaction. The amount of toluene was set as small as possible to make the initial reaction mixture homogeneous at 0 °C (Section 4). Loading of 4 equiv of *n*-$Bu_3P$ relative to $Pd(OAc)_2$ brought about higher diastereoselectivity (runs 5 and 7).

The diastereoselectivity is largely affected by the amount and the kind of phosphine ligands as well as by the solvent systems. In *n*-hexane–toluene solvent, there seems to be a

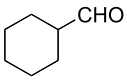
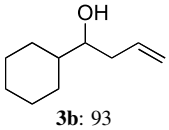
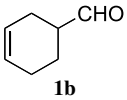
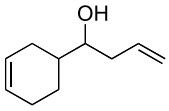
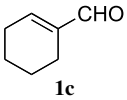
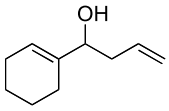
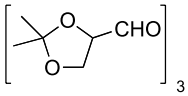
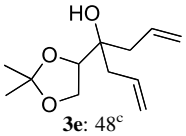
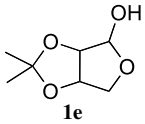
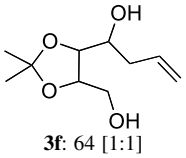
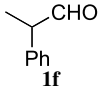
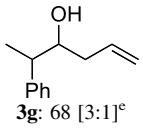
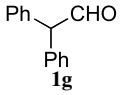
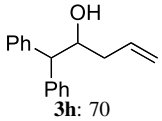
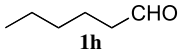
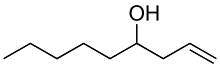
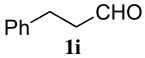
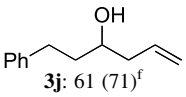
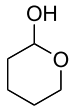
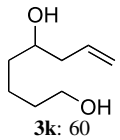
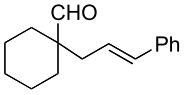
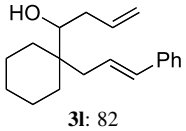
**Table 1**. Effects of organometallics (RM), ligands, and solvents on the Pd-catalyzed allylation of **1a** with allyl alcohol[a]




| Run | RM (mol%) | Phosphine (mol%) | Solvent (ml) | Time (h) | % Yield [*anti*:*syn*][b] | |
|---|---|---|---|---|---|---|
| | | | | | **3a** | **4a** |
| 1 | $Et_3B$ (240) | $PPh_3$(20) | THF (5) | 4 | 39 [–] | 30[c] |
| 2 | $Et_3B$ (240) | P(*n*-Bu)$_3$(20) | THF (5) | 23 | 21 [18:1] | 51 |
| 3 | $Et_2Zn$ (360) | $PPh_3$(20) | THF (5) | 20[d] | 18 [7:1] | 0 |
| 4 | $Et_2Zn$ (360) | P(*n*-Bu)$_3$(20) | THF (5) | 10 | 53 [14:1] | 0 |
| 5 | $Et_2Zn$ (360) | P(*n*-Bu)$_3$(20) | Tol (0.5)[e] | 30 | 72 [2:1] | 0[c] |
| 6 | $Et_2Zn$ (360) | $PPh_3$(20) | Tol (0.5) | 20 | 63 [1:1] | 0 |
| 7 | $Et_2Zn$ (360) | P(*n*-Bu)$_3$(40) | Tol (0.5) | 6 | 75 [18:1] | 0 |
| 8[f] | $Et_2Zn$ (360) | P(*n*-Bu)$_3$(40) | Tol (0.5) | 1 | 93 [10:1] | 0 |

[a] Reaction conditions: cinnamyl alcohol (**2a**) (1.0 mmol), cyclohexanecarboxaldehyde (1.2 mmol), $Pd(OAc)_2$ (10 mol%), $Et_3B$ or $Et_2Zn$ (indicated amount), phosphine (indicated amount) at room temperature under $N_2$.
[b] Yields refer to the isolated spectroscopically homogeneous materials. The diastereomer ratios were determined on the basis of $^1H$ NMR (400 MHz).
[c] 1,4-Diphenyl-1,5-hexadiene was isolated in 20% (run 1) and 10% yields (run 5), respectively.
[d] 45% conversion.
[e] tol = dry toluene.
[f] Benzyl cinnamyl ether was used in place of **2a**.

**Table 2**. Allylation of a variety of aldehydes **1** with allyl alcohol **2b**[a]

| Run | Aldehyde | Time (h) | % isolated yield[b] |
|---|---|---|---|
| 1 |  **1a** | 6 |  **3b**: 93 |
| 2 |  **1b** | 8 |  **3c**: 74 |
| 3 |  **1c** | 6 |  **3d**: 73 |
| 4 |  **1d** | 10 |  **3e**: 48[c] |
| 5[d] |  **1e** | 20 |  **3f**: 64 [1:1] |
| 6 |  **1f** | 7 |  **3g**: 68 [3:1][e] |
| 7 |  **1g** | 6 |  **3h**: 70 |
| 8 |  **1h** | 8 |  **3i**: 78 |
| 9 |  **1i** | 6 |  **3j**: 61 (71)[f] |
| 10[d] |  **1j** | 18 |  **3k**: 60 |
| 11 |  **1k** | 8 |  **3l**: 82 |

[a] Reaction conditions: allyl alcohol (**2b**) (1.0 mmol), an aldehyde (1.2 mmol), $Pd(OAc)_2$ (10 mol%), $Et_2Zn$ (3.6 mmol, 1M *n*-hexane solution), P(*n*-Bu)$_3$ (40 mol%) at room temperature under $N_2$.
[b] Yields refer to the isolated spectroscopically homogeneous materials.
[c] Yield is based on allyl alcohol, hence 0.24 mmol of **3e** was isolated.
[d] $Et_2Zn$ (4.6 mmol) was used.
[e] Diastereomer ratio of *syn* to *anti*.
[f] Under the conditions of run 4 (Table 1); rt., 10 h.

general trend that the more electron donating and the more the amounts of the phosphine ligands, the higher the *anti*-selectivities (runs 5∼7). This may be accounted for as follows. The polarity of the solvent system is such that allylzinc would form aggregate with itself or with other zinc species (e.g., $Et_2Zn$, zinc alkoxide); hence, it hardly forms a putative six-membered chair-like transition state leading to an *anti*-isomer (vide infra, cf. **VI**, Scheme 3). In the presence of *n*-$Bu_3P$, on the other hand, it may loosen the aggregate to form an allylzinc monomer by coordination to $Zn^{2+}$; hence, a monomeric allylzinc species may participate in the reaction and undergo allylation via a transition state like **VI**, resulting in increasing the *anti*-selectivity.

Under the same conditions as run 7, using 1 mol% of $Pd(OAc)_2$ and 4 mol% of *n*-$Bu_3P$, one tenth of the amounts of the standard conditions (room temperature for 22 h), **3a** was obtained in 55% isolated yield as a mixture with 1-cyclohexylpropanol (14%).

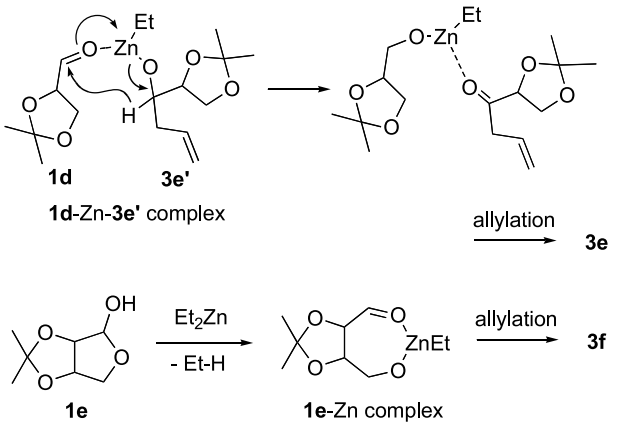
With respect to the chemical yields of homoallyl alcohols, it is apparently better to use allyl ethers (run 8, Table 1) or acid esters (e.g., acetate, benzoate, or phosphate) of allyl alcohols;[7] however, as mentioned above, there are many beneficial aspects for using allyl alcohols themselves.[8] In this paper, we disclose a full scope of the nucleophilic allylation of aliphatic aldehydes and ketones promoted by a Pd–$Et_2Zn$ catalytic system.

### 2.1. Allylation of aliphatic aldehydes with allyl alcohol promoted by Pd–$Et_2Zn$

Table 2 reveals that allyl alcohol itself can be used as an allyl anion equivalent for a variety of aliphatic aldehydes encompassing primary (runs 8–10), secondary (runs 1–7) and tertiary aldehydes (run 11). All reactions were undertaken uniformly under the conditions established in run 7 of Table 1 (footnote a, Table 2). The yields range within a level of practical use (more than 60–70%) for all aldehydes examined except for **1d**, which produced an unexpected diallylation product **3e** (run 4) in modest yield.

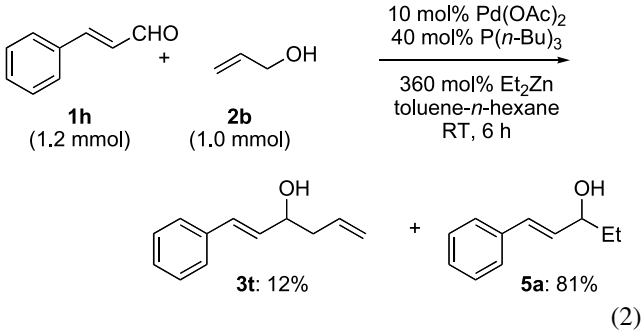
The formation of **3e** may be rationalized supposing the Meerwein–Pondorf–Verley (M–P–V) oxidation[9] of the primary allylic alkylation product **3e′** with the starting aldehyde **1d** (Scheme 2). The special feature about this substrate may be primarily attributed to the enhanced electrophilic reactivity of **1d** caused by the electron-withdrawing inductive effects by both the α- and β-oxygens.[10] In this context, the usual reactivity observed for **1e** (run 5) may deserve some comments. For the reactions of cyclic hemiacetals **1e** and **1j**, an additional 1 equiv $Et_2Zn$ is used, since 1 equiv $Et_2Zn$ is consumed to convert acidic hydroxy group into its zinc salt. Under such conditions, **1e** and **1j** might form a seven- and an eight-membered cyclic intermediate, respectively (e.g., **1e**-Zn complex, Scheme 2). The carbonyl oxygen of **1e**-Zn complex might be so weakly Lewis basic that it were no longer capable of forming such a complex like **1d**-**Zn**-**3e′**, being essential for the M–P–V reaction to proceed.

The reaction feature of α,β-unsaturated aldehyde **1c** (run 3) is in sharp contrast to those of cinnamaldehyde (Eq. 2) and

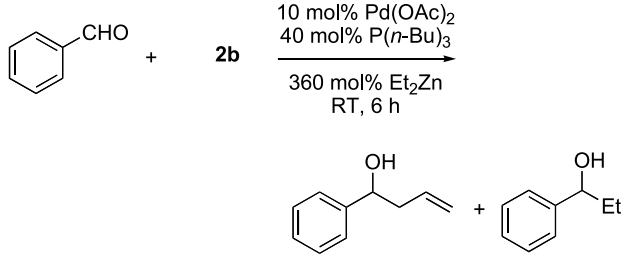



**Scheme 2.** Contrasting reactivity of **1d** and **1e**. The former undergoes M–P–V reduction through a complex **1d**-**Zn**-**3e**′.

benzaldehyde (Eq. 3). While the latter two react directly with $Et_2Zn$ and provide the ethylation products, **5a** and **5b**, respectively, as major products, **1c** selectively undergoes allylation and provides no ethylation product at all.




(2)




| | | |
|---|---|---|
| toluene (0.5 ml)-*n*-hexane (3.6 ml) | **3u**: 29% | **5b**: 66% |
| THF (5 ml)-*n*-hexane (3.6 ml) | **3u**: 80% | **5b**: 0% |

(3)

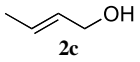
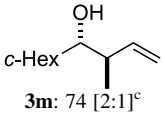
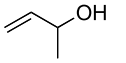
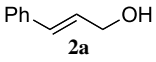
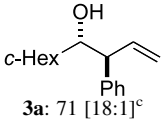
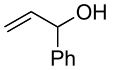
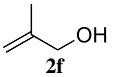
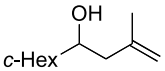
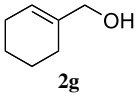
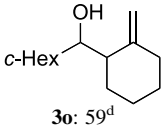
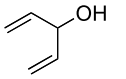
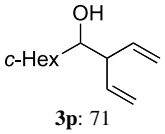
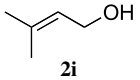
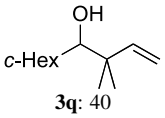
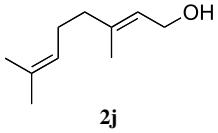
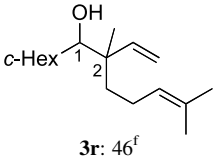
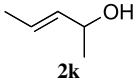
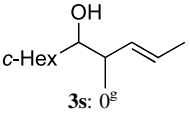
The allylation–ethylation competition seems to be a subject of large solvent effects, and the reaction of benzaldehyde and allyl alcohol in THF-*n*-hexane furnished an allylation product **3u** exclusively in 80% isolated yield (Eq. 3).

It is worth noting that, despite in situ formation of zinc alkoxides, no aldol-, Cannizzaro-, or Tischchenko-type products were detected at all in these reactions.

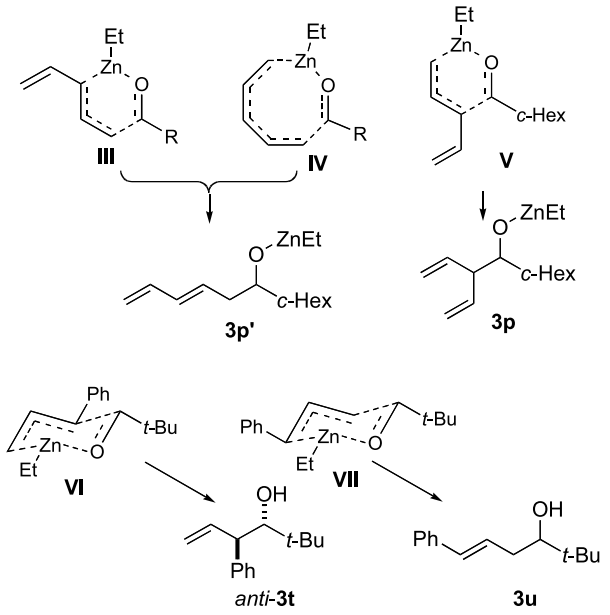
## 2.2. Allylation of cyclohexanecarboxaldehyde (1a) with a variety of allyl alcohols 2a–k promoted by Pd–$Et_2Zn$

Next, the reaction scope with respect to the structural variation of allyl alcohols was examined and the results examined using cyclohexanecarboxaldehyde as a probe are summarized in Table 3. Generally, unsymmetrically substituted allyl alcohols underwent C–C bond formation at the most substituted allylic termini, giving rise to branched homoallyl alcohols exclusively. All these results, particularly the results of run 7, strongly suggest that 1) allylzincs

**Table 3**. Allylation of cyclohexanecarboxaldehyde (**1a**) with substituted allyl alcohols **2**[a]

| Run | Allylic alcohol **2** | Time (h) | % Isolated yield[b] |
|---|---|---|---|
| 1 |  **2c** | 6 |  **3m**: 74 [2:1][c] |
| 2 |  **2d** | 6 | **3m**: 78 [2:1] |
| 3 |  **2a** | 6 |  **3a**: 71 [18:1][c] |
| 4 |  **2e** | 6 | **3a**: 71 [12:1][c] |
| 5 |  **2f** | 8 |  **3n**: 68 |
| 6 |  **2g** | 11 |  **3o**: 59[d] |
| 7 |  **2h** | 8 |  **3p**: 71 |
| 8 |  **2i** | 38[e] |  **3q**: 40 |
| 9 |  **2j** | 48[e] |  **3r**: 46[f] |
| 10 |  **2k** | 6 |  **3s**: 0[g] |

[a] Reaction conditions: an allyl alcohol (1.0 mmol), **1a** (1.2 mmol), $Pd(OAc)_2$ (10 mol%), $Et_2Zn$ (3.6 mmol, 1 M *n*-hexane solution), P (*n*-Bu)$_3$ (40 mol%) at room temperature under $N_2$.
[b] Yields refer to the isolated spectroscopically homogeneous materials.
[c] Diastereomer ratio of *anti* to *syn*.
[d] Single diastereomer, the stereochemistry unknown.
[e] At 50 °C.
[f] (1*S*′,2*S*′):(1*R*′,2*S*′)=5:1.
[g] 1-Cyclohexylpropanol (59%) was isolated.



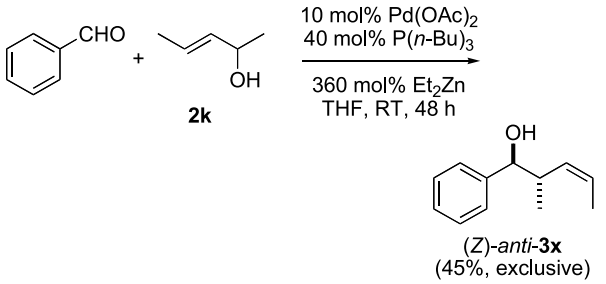

**Scheme 3.** Transition state models rationalizing regio- and stereoselectivities observed for the allylation of aldehydes with unsymmetrically substituted allyl alcohols.

are fluxional and 2) the allylzinc species with C–Zn σ-bonds bound to the least substituted allylic carbons participates in the reactions through a six-membered chair-like transition state **V** (Scheme 3). An isomeric product **3p′**, which might be derived through transition states **III** (characterized by an allylzinc bearing a *sec*-C–Zn bond) or **IV** (characterized by an eight-membered cyclic structure), was not detected at all.

The yields turned out to be dependent on the substitution patterns of allyl alcohols. The α-(runs 2, 4, 7), β-(run 5), γ-mono-substituted (runs 1, 3), and β,γ-disubstituted allyl alcohols (run 6), all recorded yields at an acceptable level; however, γ,γ-disubstituted allyl alcohols (runs 8 and 9) showed apparently diminished yields and reactivities, and for complete disappearance of the starting alcohols, heating for a long period of time was required. α,γ-Disubstituted allyl alcohols, **2k** and 2-cyclohexenol, did not participate in the reaction at all and ethylation with $Et_2Zn$ was only the reaction detected, furnishing 1-cyclohexylpropanol in 59% (run 10).

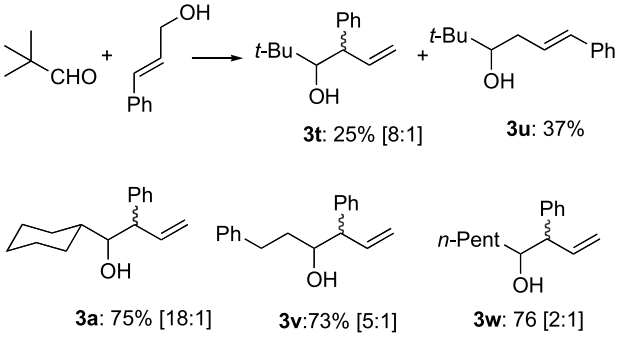
In order to address the possibility that **2k** might inhibit or retard generation of an active Pd(0) species, we examined the reaction of run 10 using a small amount of allyl alcohol (**2b**) (0.1 mmol) as an initiator; however, only **3b** and 1-cyclohexylpropanol were formed and no expected **3s** was detected at all, indicating **2k** being intrinsically unreactive toward aliphatic aldehydes under the conditions.

It should be noted that **2k** is reactive toward benzaldehyde, though requiring a long period of reaction time, and provides an allylation product **3x** as a single stereoisomer, the stereochemistry being *anti* with respect to the C1–C2 stereocenters and *Z* with respect to the double bond (Eq. 4).



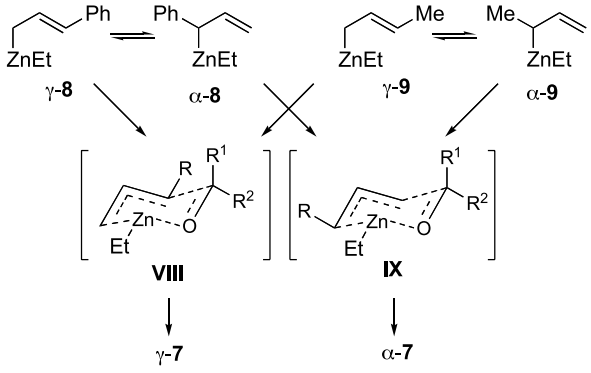

(4)

The same ratio of stereoisomers of **3m** was observed for the reactions with γ-methyl- (**2c**) and α-methylallyl alcohols (**2d**) (runs 1 and 2, Table 3). The phenyl analogues, **2a** and **2e**, provided **3a** in somewhat different ratios, but with much higher diastereoselectivity, furnishing *anti*-**3a** as a major product (12–18:1, runs 3 and 4). As is expected, the diastereoselectivity is a subject of the steric size of aldehydes and decreases as the size becomes small. In Scheme 4 are shown the results examined with cyclohexanecarbaldehyde, dihydrocinnamaldehyde and hexanal together with those examined with pivalaldehyde.




**Scheme 4.** Regio- and diastereoselectivities observed for the allylation of aliphatic aldehydes of different steric bulk with *trans*-cinnamyl alcohol under the conditions shown in footnote a in Table 2. In blankets are indicated isomer ratios of *anti* to *syn*.

Interestingly, pivalaldehyde turned out to be exceptional with respect to both regioselectivity and stereoselectivity; cinnamyl alcohol reacted to provide an expected isomer **3t** as a minor product together with its regioisomer **3u** as a major product. Furthermore, the stereoselectivity of **3t** was apparently lower than that of **3a**. These results may be rationalized by a close analysis of a transition state **VI**




**Scheme 5.** Fluxional behavior of allylzincs **8** and **9** and regioselectivity for the allylation of ketones.

(Scheme 3), otherwise being the most favored and responsible for the formation of *anti*-**3t**. For the particular case of pivalaldehyde, a gauche repulsion between Ph and *t*-Bu is such that preference of a transition state **VI** over others might be diminished, resulting in a low diastereoselectivity. In addition, in order to circumvent steric repulsion, an otherwise unstable allylzinc species (α-phenylallylzinc, cf., α-**8** in Scheme 5, vide infra) participates in the reaction to provide **3u** as a major product through a transition state **VII**. The trans structure of **3u** was determined on the basis of $^1$H NMR and IR spectra.

### 2.3. Allylation of aliphatic ketones with allyl alcohols 2 promoted by Pd–$Et_2Zn$

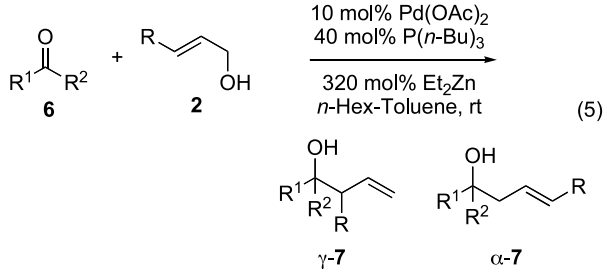
In Table 4 are summarized the results for the reactions of aliphatic ketones with allyl alcohols **2a–c**, performed under the identical conditions to those indicated in footnote a, Table 2. For reference, alkyl aryl and diaryl ketones were also examined under the identical conditions (runs 8–14). For the all combinations of ketones and allyl alcohols, the yields are modest and range from 50 to 70%, irrespective of the kinds of ketones, either aliphatic or aromatic.

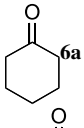
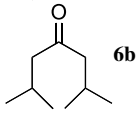
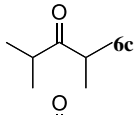
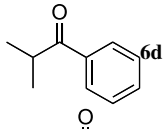
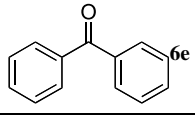
Interestingly, the regioselectivity (α- vs. γ-allylation) depends on the steric bulk of substituents of ketones and the kind of allylating agents. Cinnamyl alcohol undergoes nucleophilic addition to cyclohexanone (**6a**) at the most substituted allylic terminus to furnish γ-**7a** exclusively (run 1, Table 4), while it reacts with di-isobutyl ketone (**6b**) and di-isopropyl ketone (**6c**) at the least substituted allylic terminus, giving rise to α-**7d** and α-**7f**, respectively (runs 4 and 6). Similar, but less drastic change in the regioselectivity was observed for the reaction of crotyl alcohol with **6a–6c** (runs 2, 5, and 7).

The fact that cinnamyl alcohol tends to give the α-**7** isomers, while crotyl alcohol does the γ-**7** isomers might be partly ascribed to a larger steric repulsion that a phenyl group of **8** experiences against $R^1$ and $R^2$ than a methyl group of **9** does in a transition state **VIII** (Scheme 5), which might guide **8** to react with a ketone through a transition state **IX**. Another factor may be due to a higher population of α-**8** in an equilibrium between α-**8** and γ-**8**, as compared with α-**9** in an equilibrium between α-**9** and γ-**9**, owing to delocalization stabilization of the anionic charge on the carbon bearing Zn by a phenyl group.

Very clear-cut and contrasting results were observed for the allylation of aromatic ketones; cinnamyl alcohol provided exclusively α-**7**, while crotyl alcohol furnished the other regioisomers γ-**7** exclusively for the reactions with

**Table 4**. Allylation of ketone with allyl alcohols **2a–c**[a]




| Run | Ketone **8** | **2** | Time (h) | % Isolated yield[b] | |
|---|---|---|---|---|---|
| | | | | γ-**7** | α-**7** |
| 1 |  **6a** | **2a**: R=Ph | 6 | γ-**7a**: 58 | α-**7a**: 0 |
| 2 | | **2c**: R=Me | 7 | γ-**7b**: 52 | α-**7b**: 0 |
| 3 |  **6b** | **2b**: R=H | 8 | **7c**: 58 | |
| 4 | | **2a**: R=Ph | 8 | γ-**7d**: 0 | α-**7d**: 52 |
| 5 | | **2c**: R=Me | 9 | γ-**7e**: 53 | α-**7e**: 5 |
| 6 |  **6c** | **2b**: R=Ph | 6 | γ-**7f**: 0 | α-**7f**: 52 |
| 7 | | **2c**: R=Me | 7 | γ-**7g**: 10 | α-**7g**: 54 |
| 8 |  **6d** | **2b**: R=H | 6 | **7h**: 66 | |
| 9 | | **2a**: R=Ph | 8 | γ-**7i**: 0 | α-**7i**: 55 |
| 10 | | **2c**: R=Me | 6 | γ-**7j**: 55[c] | α-**7j**: 0 |
| 11 |  **6e** | **2b**: R=H | 4 | **7k**: 70 | |
| 12 | | **2a**: R=Ph | 6 | γ-**7l**: 0 | α-**7l**: 50 |
| 13 | | **2c**: R=Me | 9 | γ-**7m**: 53 | α-**7m**: 0 |
| 14 | | **2c**: R=Me | 32 | γ-**7m**: 54 | α-**7m**: 0 |

[a] Reaction conditions: an allyl alcohol (1.0 mmol), a ketone (1.2 mmol), $Pd(OAc)_2$ (10 mol%), $Et_2Zn$ (3.6 mmol, 1 M *n*-hexane solution), P (*n*-Bu)$_3$ (40 mol%) at room temperature under $N_2$.
[b] Yields refer to the isolated spectroscopically homogeneous materials.
[c] A mixture of diastereomers (1:1).

isopropyl phenyl ketone (runs 9 and 10) and benzophenone (runs 12 and 13).

Finally, it should be noted that the reactions compiled in runs 1–13 are irreversible, and α- and γ-**7** are kinetically controlled products. This was confirmed by exposing the kinetic product γ-**7m** under the conditions for a long period of time (run 14), where no thermodynamic product α-**7m** was produced at all. This is primarily due to the low polarity of the solvents used in these reactions. In polar solvents, crotyl and cinnamylzincs react with sterically congested ketones reversibly and selectively provide γ-**7** under kinetic control and α-**7** under thermodynamic control.[11]

## 3. Conclusion

A variety of allyl alcohols, except for 1,3-disubstituted ones (e.g., 1,3-dimethylallyl alcohol and 2-cyclohexenol), serve as nucleophilic allylating agents for the allylation of aliphatic aldehydes and aliphatic ketones under the catalysis of $Pd(OAc)_2$ (10 mol%) -P(*n*-Bu)$_3$ (40 mol%) in the presence of $Et_2Zn$ (360 mol%). The isolated yields of allylation products of primary, secondary, and tertiary aldehydes range from 60 to 90% and those of ketones about 60%. Almost all reactions proceed at room temperature and attain completion within 10 h. 1,3-Disubstituted allyl alcohols failed to react with aliphatic aldehydes.

Allylzinc intermediates, e.g. **8** and **9**, are fluxional and equilibrate between α- and γ-isomers (Scheme 5) and react with aldehydes, except for pivalaldehyde, through α-isomers to give rise to branched homoallyl alcohols exclusively with diastereomeric ratios (2:1–18:1), providing *anti*-isomers preferentially over *syn*-isomers. Cyclohexanone selectively reacts with **8** and **9** through the α-isomers to furnish branched homoallyl alcohols γ-**7**, while sterically more congested ketones tend to react with **8** and **9** through the γ-isomers giving rise to straight-chain homoallyl alcohols α-**7**. Pivalaldehyde behaves like sterically congested ketones and provides a mixture of straight-chain and branched homoallyl alcohols.

The synthetic utility of the reaction presented here may be augmented by 1) the ease with which the reactions can be performed, 2) ready availability and stability of allyl alcohols of a wide structural variety, 3) production of no hazardous side products, and 4) the catalytic nature of the reaction with respect to palladium.

## 4. Experimental

### 4.1. Solvents and reagents

Tetrahydrofuran was dried and distilled from benzophenone and sodium immediately prior to use under nitrogen atmosphere. Toluene was distilled over calcium hydride. $Pd(OAc)_2$ (purity 97.0%, Nakarai), $Ph_3P$ (purity 97+%, Wako Pure Chemical Industries, Ltd), *n*-$Bu_3P$ (purity 90.0+%, Tokyo Kasei Kogyo Co., Ltd), 2,3-*O*-isopropylidene-D-erythronolactone (Aldrich), $Et_3B$ (1.0 M hexane solution, KANTO CHEMIKAL Co., INC.) and $Et_2Zn$ (1.0 M hexane solution, KANTO), DIBAL (1.0 M hexane solution, KANTO) were purchased and used as received. The following allyl alcohols, aldehydes, and ketones were purchased and distilled prior to use by Kugelrohr apparatus: cinnamyl alcohol, allyl alcohol, crotyl alcohol, but-3-en-2-ol, α-phenylallyl alcohol, 2-methyl-2-propen-1-ol, divinylcarbinol, prenyl alcohol, geraniol, 2-cyclohexenol, 3-penten-2-ol, cyclohexanecarboxaldehyde, hexanal, dihydrocinnamaldehyde, α-phenylpropionaldehyde, diphenylacetaldehyde, 3-cyclohexenecarboxaldehyde, 1-cyclohexenecarboxaldehyde, pivalaldehyde, cyclohexanone, di-isobutyl ketone, di-isopropyl ketone, isopropyl phenyl ketone, benzophenone.

**4.1.1. 2,2-Dimethyl-1,3-dioxolane-4-carboxaldehyde unsymmetric trimer (1d).** To a solution of 2,2-dimethyl-1,3-dioxolane-4-methanol (1.32 g, 10 mmol) in $CH_2Cl_2$ (10 mL) was added pyridinium chlorochromate (4.33 g, 20 mmol) and sodium acetate (0.66 g, 8 mmol), each in one portion, at room temperature. After stirring for 12 h at room temperature, the mixture was extracted with ether (2× 100 mL). The combined extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by means of column chromatography over silica gel (eluent; hexane/ethyl acetate=4:1) to give **1d** in 34% yield. IR (neat) 2986, 2939, 2885, 1759, 1458, 1373, 1211, 1103, 842 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 1.36 (s, 3H), 1.41 (s, 3H), 1.43 (s, 3H), 1.51 (s 3H), 3.76 (ddd, 8.0, 5.8, 1.9 Hz, 1H), 4.06–4.30 (m, 5H), 4.34 (quint, $J$=5.8 Hz, 1H), 4.63 (dt, $J$=1.9, 5.8 Hz, 1H).

**4.1.2. 2,3-*O*-Isopropylidene-D-erythronolactol (1e).** A solution of DIBAL (40.7 mmol, 1.0 M toluene solution) was added dropwise into a well-stirred solution of 2,3-*O*-isopropylidene-D-erythronolactone (3.0 g, 19 mmol) in $CH_2Cl_2$ (60.0 mL) kept at −78 °C over 0.5 h. After the mixture was stirred for 4 h at −78 °C, methanol (15 mL) and then water (15 mL) were added dropwise. After being allowed to warm to room temperature, ether (150 mL) and $MgSO_4$ were added into the mixture containing white precipitate. The mixture was filtrated and the filter cake was washed with ether (60 mL). The extracts were concentrated in vacuo and the residue was purified by means of a column chromatography over silica gel (AcOEt–hexane, 1/16 v/v) to give **1e** in 81% yield. IR (neat) 3425, 2986, 2947, 2885, 1458, 1380, 1335, 1211, 1165, 1072, 987, 910, 856 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 1.33 (s, 3H), 1.47 (s, 3H), 3.53 (br, 1H), 4.02 (d, $J$=10.2 Hz, 1H), 4.07 (dd, $J$=10.2, 3.3 Hz, 1H), 4.57 (d, $J$=5.8 Hz, 1H), 4.84 (dd, $J$=5.8, 3.3 Hz, 1H), 5.42 (s, 1H).

**4.1.3. Tetrahydro-2*H*-pyran-2-ol (1j).** To a solution of 3,4-dihydro-2*H*-pyran (8.28 g, 100 mmol) in water (90 mL) was added 2 M—HCl (1.7 mL, 20 mmol) at 0 °C over 30 min period. The mixture was allowed to warm to room temperature and stirred for an additional 1 h. Then the reaction mixture was neutralized with satd $NaHCO_3$ and extracted with $CH_2Cl_2$ (20 mL). The extract was dried ($MgSO_4$), filtered, and concentrated in vacuo, and the residue was purified by Kugelrohr distillation (80 °C/2.0 mm Hg) to give **1j** in 93% yield. IR (neat) 3387, 2939, 2855, 1736, 1442, 1358, 1272, 1196, 1080, 1026, 979, 903, 864 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 1.29–1.55 (m,

4H), 1.58–1.88 (m, 2H), 3.44 (dt, $J$=6.0, 5.5 Hz, 1H), 3.94 (m, 1H), 4.05 (s, 1H), 4.81 (s, 1H).

**4.1.4. 1-(*trans*-Cinnamyl)cyclohexanecarbaldehyde (1k).**[5] To a solution of $Pd(OAc)_2$ (43.2 mg, 0.2 mmol), $Ph_3P$ (116.0 mg, 0.4 mmol) and LiCl (88.0 mg, 2.0 mmol) in dry THF (10 mL) were successively added cyclohexanecarboxaldehyde (249.2 mg, 2.2 mmol), cinnamyl alcohol (268.3 mg, 2.0 mmol), triethylamine (249.8 mg, 2.4 mmol), and triethylborane (4.8 mmol, 1.0 M hexane solution) via syringe at ambient temperature under $N_2$. The mixture was stirred at ambient temperature for 48 h. The mixture was washed with satd $NaHCO_3$ and then brine, and the organic phase was dried ($MgSO_4$) and concentrated in vacuo to give an yellow oil, which was purified by means of column chromatography over silica gel (AcOEt–hexane, 1/30 v/v) to give **1k** in 78% yield.

**4.1.5. (1-Cyclohexenyl)methanol (2g).** To a solution of lithium aluminum hydride (0.23 g, 6 mmol) in dry ether (20 mL) was added 1-cyclohexenecarboxaldehyde (1.10 g, 10 mmol) at 0 °C over 10 min. The mixture was stirred under nitrogen at room temperature for 5 h. After addition of $H_2O$ (20 mL) and removal of white solid by filtration, the filtrate was concentrated in vacuo and the residue was purified by means of column chromatography over silica gel (hexane/ethyl acetate=7:1) to give **2g** in 97% yield. IR (neat) 3325, 2924, 2862, 1142, 1011, 918, 802 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 1.21–1.34 (m, 1H), 1.69–1.84 (m, 3H), 1.90–2.14 (m, 4H), 3.52 (s, 2H), 5.68 (s, 1H).

The following products were characterized by comparison of $^1H$ NMR spectral data with those of literature: 1-cyclohexyl-2-phenyl-3-buten-1-ol (**3a**),[5] 1-cyclohexyl-3-buten-1-ol (**3b**),[5] 1-(3-cyclohexenyl)-3-buten-1-ol (**3c**),[12] 2-phenyl-5-hexen-3-ol (**3g**),[13] 1,1-diphenyl-4-penten-2-ol (**3h**),[14] 1-nonen-4-ol (**3i**),[15] 6-phenyl-1-hexen-4-ol (**3j**),[16] 7-octene-1,5-diol (**3k**),[6] 1-cyclohexyl-2-methyl-3-buten-1-ol (**3m**),[16] 1-cyclohexyl-3-methyl-3-buten-1-ol (**3n**),[17] 1-cyclohexyl-2-vinyl-3-buten-1-ol (**3p**),[18] 1-cyclohexyl-2,2-dimethyl-3-buten-1-ol (**3q**),[17] 1-cyclohexyl-2,6-dimethyl-2-vinyl-5-hepten-1-ol (**3r**),[19] 1-phenyl-1,5-hexadien-3-ol (**3t**),[20] 1-phenyl-3-buten-1-ol (**3u**),[21] 1,4-diphenyl-5-hexen-3-ol (**3v**),[22] 3-phenyl-1-nonen-4-ol (**3w**),[22] (*Z*)-*anti*-2-methyl-1-phenyl-3-pentenol (**3x**), (*E*)-1-phenyl-1-penten-3-ol (**5a**),[5] 1-phenylpropan-1-ol (**5b**),[21] 1-(1-phenylallyl)cyclohexanol ($\gamma$-**7a**),[21] 1-(1-methylallyl)cyclohexanol ($\gamma$-**7b**),[21] (*E*)-3-isopropyl-2-methyl-6-phenyl-5-hexen-3-ol ($\alpha$-**7f**),[23] 3-isopropyl-2,4-dimethyl-5-hexen-3-ol ($\gamma$-**7g**),[23] (*E*)-3-isopropyl-2-methyl-5-hepten-3-ol ($\alpha$-**7g**),[23] 5-methyl-4-phenyl-1-hexen-4-ol (**7h**),[24] 2,4-dimethyl-3-phenyl-5-hexen-3-ol ($\gamma$-**7j**),[23] 1,1-diphenyl-3-buten-1-ol (**7k**).[25]

### 4.2. General procedure: allylation of cyclohexanecarboxaldehyde with *trans*-cinnamyl alcohol (run 3, Table 3)

Diethylzinc (3.2 mmol, 1.0 M *n*-hexane solution) and cinnamyl alcohol (1.0 mmol) was added successively by syringe to a homogeneous solution of $Pd(OAc)_2$ (22.6 mg, 0.1 mmol), *n*-$Bu_3P$ (98 μl, 0.4 mmol) and cyclohexanecarboxaldehyde (1.1 mmol) in toluene (0.5 mL) at 0 °C under nitrogen. After completion of addition, the mixture was allowed to warm to room temperature and stirred for an additional 2 h, during which time a copious amount of a white precipitate appeared and the reaction mixture became sludgy. The mixture was diluted with EtOAc and washed with HCl (0.2 M), satd $NaHCO_3$, and brine, and then the organic phase was dried ($MgSO_4$) and concentrated in vacuo to give an yellow oil, which was purified by column chromatography over silica gel (AcOEt/hexane, 1/30 v/v) to give **3a** in 75% isolated yield.

**4.2.1. 1-(1-Cyclohexenyl)-3-buten-1-ol (3d).** IR (neat) 3361, 2930, 2858, 2837, 1641, 1436, 1138, 989, 914, 842 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.48–1.71 (m, 6H), 1.85–2.10 (m, 3H), 2.29 (ddd, $J$=14.0, 5.2, 7.4 Hz, 1H), 2.33 (ddd, $J$=14.0, 7.4. 5.2 Hz, 1H), 4.01 (s, 1H), 5.10 (dd, $J$=10.2, 1.7 Hz, 1H), 5.12 (dd, $J$=17.0, 1.7 Hz, 1H), 5.68 (s, 1H), 5.78 (ddt, $J$=17.0, 10.2, 7.4 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 22.6, 22.7, 23.9, 24.9, 39.8, 75.2, 117.4, 122.9, 134.8, 139.1; HRMS calcd for $C_{10}H_{16}O$ 152.1201, found *m*/*z* (relative intensity): 152.1175 ($M^+$, 49), 151 (16), 140 (92), 136 (27), 135 (100).

**4.2.2. 4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1,6-heptadien-4-ol (3e).** IR (neat) 3481, 3076, 2983, 2935, 2900, 1639, 1438, 1371, 1217, 1070, 999, 916, 864, 796, 661 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 1.36 (s, 3H), 1.43 (s, 3H), 2.06 (s, 1H), 2.10 (dd, $J$=14.4, 8.0 Hz, 1H), 2.27 (dd, $J$=13.9, 6.8 Hz, 1H), 2.32 (dd, $J$=13.9, 6.8 Hz, 1H), 2.37 (dd, $J$=13.9, 8.0 Hz, 1H), 3.89 (t, $J$=7.8 Hz, 1H), 3.95 (dd, $J$=7.8, 6.3 Hz, 1H), 4.03 (t, $J$=7.8, 6.3 Hz, 1H), 5.09 (d, $J$=10.7 Hz, 1H), 5.11 (d, $J$=15.7 Hz, 1H), 5.12 (d, $J$=15.7 Hz, 1H),5.14 (d, $J$=10.7 Hz, 1H), 5.88 (dddd, $J$=15.7, 10.7, 8.0, 6.8 Hz, 1H); HRMS calcd for $M^+-OH$ $C_{12}H_{19}O_3$ 195.1390, found *m*/*z* (relative intensity): 195.1367 ($M^+-OH$, 100), 172 (10), 171 (95), 141 (13).

**4.2.3. 1-[5-(Hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-buten-1-ol (3f, 1:1 mixture of diastereomers).** IR (neat) 3396, 3078, 2986, 2937, 2359, 2341, 1643, 1456, 1380, 1246, 1217, 1167, 1042, 918, 874, 797 $cm^{-1}$; One isomer: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 1.38 (s, 3H), 1.52 (s, 3H), 2.29–2.45 (m, 2H), 2.82–2.92 (br, 2H), 3.78–3.99 (m, 3H), 4.11 (dd, $J$=6.9, 3.0 Hz, 1H), 4.23 (dt, $J$=6.9, 5.0 Hz, 1H), 5.13 (dd, $J$=10.2, 1.4 Hz, 1H), 5.16 (dd, $J$=17.3, 1.4 Hz, 1H), 5.86 (ddt, $J$=17.3, 10.2, 7.1 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 25.02, 27.24, 39.58, 61.26, 68.58, 77.30, 78.39, 108.36, 118.05, 134.28 (C2); the other isomer: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$1.36 (s, 3H), 1.41 (s, 3H), 2.21 (dt, $J$=14.3, 8.4 Hz, 1H), 2.60–2.66 (m, 2H), 2.80 (br, 1H), 3.76 (ddd, $J$=11.7, 7.0, 5.1 Hz, 1H), 3.81–3.90 (m, 2H), 3.99 (dd, $J$=9.2, 5.1 Hz, 1H), 4.32 (dt, $J$=8.1, 5.1 Hz, 1H), 5.20 (dd, $J$=14.7, 1.5 Hz, 1H), 5.21 (dd, $J$=11.7, 1.5 Hz, 1H), 5.86 (dddd, $J$=14.7, 11.7, 8.4, 6.2 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 25.34, 27.95, 38.84, 61.03, 68.54, 77.41, 79.36, 108.39, 119.21, 133.93; HRMS calcd for $C_{10}H_{19}O_4$ 203.1302, found *m*/*z* (relative intensity): 203.1283 ($M^+$, 3), 188 (10), 187 (100), 171 (23), 169 (1).

**4.2.4. 1-[(1-Cinnamyl)cyclohexyl]-3-buten-1-ol (3l).** IR (neat) 3463, 3024, 2923, 2862, 1643, 1596, 1497, 1389, 1281, 1041, 972, 910, 856, 748, 694 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 1.27–1.58 (m, 11H), 2.06–2.17 (m, 1H), 2.28 (dd, $J$=14.1, 7.4 Hz, 1H), 2.40–2.45 (m, 1H),

2.46 (dd, $J=14.1$, 7.4 Hz, 1H), 3.52 (ddd, $J=10.5$, 4.0, 1.9 Hz, 1H), 5.13 (d, $J=10.0$ Hz, 1H), 5.14 (d, $J=16.8$ Hz, 1H), 5.86 (dddd, $J=16.8$, 10.0, 8.5, 5.9 Hz, 1H), 6.30 (dt, $J=15.9$, 7.3 Hz, 1H), 6,41 (d, $J=15.9$ Hz, 1H), 7.18–7.36 (m, 5H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta=21.4$, 21.5, 26.2, 30.9, 31.4, 35.8, 36.0, 40.5, 75.4, 117.6, 125.9, 126.8, 127.5, 128.3, 131.8, 136.6, 137.7; HRMS calcd $C_{19}H_{26}O$ 270.1984, found *m/z* (relative intensity): 270.1978 ($M^+$, 100), 269 (2), 268 (7).

**4.2.5. Cyclohexyl (2-methylenecyclohexyl)methanol (3o).** IR (neat) 3489, 3069, 2852, 2795, 1643, 1448, 1390, 1259, 1085, 980, 893, 866, 682, 642 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 1.19–1.78 (m, 18H), 2.17–2.29 (m, 3H), 3.60 (d, $J=9.9$ Hz, 1H), 4.77 (s, 1H), 4.85 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 22.3, 24.2, 26.4, 26.6, 27.0, 28.1, 28.8, 31.2, 32.7, 38.9, 46.5, 72.5, 109.9, 150.1; HRMS calcd $C_{14}H_{24}O$ 208.1827, found *m/z* (relative intensity): 208.1788 ($M^+$, 20), 207 (11), 206 (53), 191 (61), 190 (100).

**4.2.6. Mixture of 2,2-dimethyl-4-phenyl-5-hexen-3-ol (3t) and (*E*)-2,2-dimethyl-6-phenyl-5-hexen-3-ol (3u).** IR (neat) 3456, 3024, 2955, 2869, 2361, 1597, 1474, 1366, 1180, 1072, 1011, 972, 918, 741, 694 cm$^{-1}$; $^1$H NMR (**3t**, 300 MHz, $CDCl_3$): $\delta$ 0.93 (s, 9H, *anti*-isomer), 0.97 (s, 9H, *syn*-isomer), 1.45 (d, $J=4.1$ Hz, 1H, *syn*–isomer), 1.75 (d, $J=4.6$ Hz, 1H, *anti*-isomer), 3.53–3.66 (m, 2H, *anti*+*syn*-isomers), 5.03 (d, $J=10.2$ Hz, 1H, *syn*-isomer), 5.06 (d, $J=17.6$ Hz, 1H, *syn*-isomer), 5.12 (d, $J=17.6$ Hz, 1H, *anti*-isomer), 5.18 (d, $J=10.3$ Hz, 1H, *anti*-isomer), 6.16 (ddd, $J=17.6$, 10.2, 8.2 Hz, 1H, *syn*-isomer), 6.31 (ddd, $J=17.6$, 10.3, 8.2 1H, *anti*-isomer), 7.18–7.39 (m, 5H, *anti*+*syn*-isomers); $^{13}$C NMR (**3t**, 100 MHz, $CDCl_3$): $\delta$ 26.6 (*anti*-isomer), 26.7 (*syn*-isomer), 35.6 (*anti*-isomer), 35.8 (*syn*-isomer), 52.7 (*anti*-isomer), 53.7 (*syn*-isomer), 81.3 (*syn*-isomer), 81.4 (*anti*-isomer), 114.6 (*syn*-isomer), 117.0 (*anti*-isomer), 126.1 (*anti*-isomer), 126.5 (*syn*-isomer), 127.7 (*anti*-isomer), 128.2 (*syn*-isomer), 128.3 (*anti*-isomer), 128.7 (*syn*-isomer), 138.6 (*anti*+*syn*-isomers), 141.3 (*syn*-isomer), 144.2 (*anti*-isomer); $^1$H NMR (**3u**, 300 MHz, $CDCl_3$): $\delta$ 1.00 (s, 9H), 1.67 (s, 1H), 2.21 (dddd, $J=14.2$, 10.5, 8.3, 1.4 Hz, 1H), 2.55 (ddt, $J=14.2$, 6.1, 1.4 1H), 3.38 (d, $J=10.5$ Hz, 1H), 6.31 (ddd, $J=15.9$, 8.3, 6.1 1H), 6.53 (d, $J=15.9$ Hz, 1H), 7.23–7.41 (m, 5H); $^{13}$C NMR (**3u**, 100 MHz, $CDCl_3$): $\delta$ 25.8, 34.7, 35.7, 78.6, 125.9, 127.0, 127.9, 128.4, 132.6, 137.1; HRMS calcd $C_{14}H_{20}O$ 204.1514, found *m/z* (relative intensity): 204.1516 ($M^+$, 26), 129 (6), 119 (36), 118 (100), 117 (43).

**4.2.7. 4-Isobutyl-6-methylhept-1-en-4-ol (7c).** IR (neat) 3485, 3076, 2954, 2927, 2869, 1709, 1639, 1468, 1367, 1261, 1097, 1018, 914, 866, 804, 661 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 0.90 (d, $J=6.6$, 6H), 0.91 (d, $J=6.6$, 6H), 1.23 (s, 1H), 1.36 (d, $J=6.6$, 4H), 1.75 (sept, $J=6.6$, 2H), 2.21 (d, $J=7.4$, 2H), 5.05 (d, $J=17.2$ Hz, 1H), 5.07 (d, $J=10.4$ Hz, 1H), 5.77 (ddt, $J=17.2$, 10.4, 7.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 23.9, 24.7. 24.8, 44.8, 48.4, 75.1, 118.5, 134.2; HRMS calcd $C_{12}H_{24}O$ 184.1827, found *m/z* (relative intensity): 184.1792 ($M^+$, 4), 169 (3), 157 (18), 143 (100).

**4.2.8. 4-Isobutyl-6-methyl-1-phenylhept-1-en-4-ol (α-7d).** IR (neat) 3487, 3024, 2955, 2360, 1466, 1366, 964, 740, 694 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 0.92 (d, $J=6.6$ Hz, 6H, *Z*-isomer), 0.93 (d, $J=6.6$ Hz, 6H, *Z*-isomer), 0.98 (d, $J=6.6$ Hz, 6H, *E*-isomer), 0.99 (d, $J=6.6$ Hz, 6H, *E*-isomer), 1.43 (d, $J=6.6$ Hz, 4H), 1.85 (sept, $J=6.6$ Hz, 2H, *E*-isomer), 2.42 (d, $J=7.4$ Hz, 2H, *E*-isomer), 2.56 (dd, $J=7.4$, 1.9 Hz, 2H, *Z*-isomer), 5.74 (dt, $J=11.5$, 7.4 Hz, 1H, *Z*-isomer), 6.23 (dt, $J=15.9$, 7.4 Hz, 1H, *E*-isomer), 6.45 (d, $J=15.7$ Hz, *E*-isomer), 6.56 (d, $J=11.5$ Hz, 1H, *Z*-isomer); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 23.9, 24.8, 24.9, 44.1, 48.6, 75.6, 125.8, 125.9, 127.0, 128.4, 133.4, 137.3; HRMS calcd for $C_{18}H_{28}O$ 260.2140, found *m/z* (relative intensity): 260.2087 ($M^+$, 1), 245 (1), 243 (4), 204 (16), 203 (100).

**4.2.9. Mixture of 4-Isobutyl-3,6-dimethyl-1-hepten-4-ol (γ-7e) and (*E*)-4-isobutyl-2-methyl-6-octen-4-ol (α-7e).** IR (neat) 3495, 3070, 2951, 2933, 2859, 1729, 1640, 1469, 1261, 1108, 914, 804, 722, 668 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.79 (d, $J=6.3$ Hz, 3H, α-isomer), 0.80 (d, $J=6.3$ Hz, 3H, α-isomer), 0.81 (d, $J=6.3$ Hz, 3H, α-isomer), 0.82 (d, $J=6.3$ Hz, 3H, α-isomer), 0.83 (d, $J=6.3$ Hz, 3H, α-isomer), 0.88 (d, $J=6.8$ Hz, 3H), 0.89 (d, $J=6.8$ Hz, 3H), 0.90 (d, $J=6.8$ Hz, 3H), 0.91 (d, $J=6.8$, 3H), 0.92 (d, $J=6.8$ Hz, 3H), 1.20 (s, 1H), 1.21 (dd $J=14.4$, 6.8 Hz, 1H), 1.29 (dd $J=14.4$, 6.8 Hz, 1H), 1.30 (dd $J=14.4$, 6.8 Hz, 1H), 1.37 (dd $J=14.4$, 6.8 Hz, 1H), 1.56–1.65 (m, 2H, α-isomer), 1.75 (sept, $J=6.8$ Hz, 1H), 1.76 (sept, $J=6.8$ Hz, 1H), 2.15–2.23 (m, 2H, α-isomer), 2.36 (dq, $J=8.3$, 6.8 Hz, 1H), 5.01 (dd, $J=10.5$, 1.9 Hz, 1H), 5.02 (dt, $J=17.1$, 1.9 Hz, 1H), 5.31–5.40 (m, 1H, α-isomer), 5.55 (dt, $J=17.3$ Hz, 1H), 5.76 (ddd, $J=17.1$, 10.5, 1.9 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 13.9, 22.5, 22.6, 23.5, 23.6, 23.7, 24.1, 44.1, 44.2, 45.0, 75.5, 115.2, 139.5; HRMS calcd for $M^+-Me_2$ $C_{11}H_{21}O$ 169.1590, found *m/z* (relative intensity): 169.1590 ($M^+-Me_2$, 5), 167 (4), 143 (100), 141 (8).

**4.2.10. (*E*)-2-Methyl-3,6-diphenylhex-5-en-3-ol (α-7i).** IR (neat) 3560, 3487, 3058, 3026, 2964, 2875, 2795, 1598, 1495, 1447, 1384, 1238, 1173, 1003, 970, 891, 764, 746, 702 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 0.79 (d, $J=6.8$ Hz, 3H), 0.97 (d, $J=6.8$ Hz, 3H), 1.95 (s, 1H), 2.07 (sept, $J=6.8$ Hz, 1H), 2.70 (dd, $J=14.0$, 9.3 Hz, 1H), 2.93 (ddd, $J=14.0$, 5.6, 1.7 Hz, 1H), 5.86 (ddd, $J=15.6$, 9.3, 5.6 Hz, 1H), 6.46 (d, $J=15.6$ Hz, 1H), 7.15–7.41 (m, 10H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 16.8, 17.6, 37.8, 43.2, 78.2, 125.2, 125.9, 126.0, 126.3, 127.2, 127.9, 128.3, 134.3, 136.9, 144.9; HRMS calcd for $C_{19}H_{22}O$ 266.1671, found *m/z* (relative intensity): 266.1646 ($M^+$, 19), 251 (3), 248 (3), 224 (19), 223 (100).

**4.2.11. (*E*)-1,1,4-Triphenyl-3-buten-1-ol (α-7l).** IR (KBr) 3541, 3456, 3021, 2839, 1596, 1488, 1357, 1203, 1057, 972, 910, 748, 694 cm$^{-1;}$ $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.60 (s, 1H), 3.21 (d, $J=7.4$ Hz, 2H), 6.04 (dt, $J=15.9$, 7.4 Hz, 1H), 6.56 (d, $J=15.9$ Hz, 1H), 7.20–7.49 (m, 15H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 46.1, 77.4, 124.5, 126.0, 126.2, 126.9, 127.5, 128.2, 128.4, 135.3, 136.8, 146.4; HRMS calcd for $C_{22}H_{20}O$ 300.1514, found *m/z* (relative intensity): 300.1498 ($M^+$, 10), 283 (85), 282 (100).

**4.2.12. 2-Methyl-1,1-diphenyl-3-buten-1-ol (γ-7m).** IR (neat) 3514, 3058, 2977, 1598, 1578, 1493, 1448, 1319, 1278, 1153, 1001, 941, 810, 766, 748, 702 cm$^{-1}$; $^1$H NMR

(300 MHz, $CDCl_3$): $\delta$ 0.99 (d, $J=6.6$ Hz, 3H), 2.27 (s, 1H), 3.54 (quint, $J=6.6$ Hz, 1H), 5.12 (dd, $J=10.7$, 1.7 Hz, 1H), 5.17 (dd, $J=17.3$, 1.7 Hz, 1H), 5.86 (ddd, $J=17.3$, 10.7, 6.6 Hz, 1H), 7.14–7.60 (m, 10H); $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 13.4, 44.3. 79.2, 117.1, 125.5, 125.7, 126.3, 126.4, 127.9, 128.0,128.1, 129.9,132.2, 139.1, 145.6, 146.6; HRMS calcd for $C_{17}H_{18}O$ 238.1358, found *m/z* (relative intensity): 238.1329 ($M^+$, 2), 221 (100), 206 (15).

## Acknowledgements

We thank Dr. Kazufumi Shibata for his helpful discussions and Mr. Y. Ohhama for his NMR measurements. Financial support by the Ministry of Education, Culture, Sports, Science, and Technology, Japanese Government is gratefully acknowledged.

## References and notes

1. (a) Puentes, C. O.; Kouznetsov, V. J. *Heterocycl. Chem.* **2002**, *39*, 595. (b) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VHC: Weinheim, 2000. (c) Chemler, S. R.; Roush, R. W. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VHC: Weinheim, 2000. (d) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069.
2. (a) Dubost, C.; Leroy, B.; Marko, I. E.; Tinant, B.; Declercq, J.-P.; Bryans, J. *Tetrahedron* **2004**, *60*, 7693. (b) Yanagisawa, A.; Nakamura, Y.; Arai, T. *Tetrahedron: Asymmetry* **2004**, *15*, 1909. (c) Solin, N.; Kjellgren, J.; Szabo, K. J. *J. Am. Chem. Soc.* **2004**, *126*, 7026. (d) Wallner, O. A.; Szabo, K. J. *Org. Lett.* **2004**, *6*, 1829. (e) Shibata, I.; Kato, H.; Kanazawa, N.; Yasuda, M.; Baba, A. *J. Am. Chem. Soc.* **2004**, *126*, 466. (f) Kobayashi, S.; Ogawa, C.; Konishi, H.; Sugiura, M. *J. Am. Chem. Soc.* **2003**, *125*, 6610. (g) Yadav, J. S.; Reddy, B. V. S.; Raju, A. K. *Synthesis* **2003**, 883. (h) Choudary, B. M.; Chidara, S.; Sekhar, C. V. R. *Synlett* **2002**, 1694. (i) Yadav, J. S.; Reddy, B. V. S.; Reddy, P. S. R.; Rao, M. S. *Tetrahedron Lett.* **2002**, *43*, 6245. (j) Yasuda, M.; Hirata, K.; Nishino, A.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 13442.
3. (a) Takahara, J. P.; Masuyama, Y.; Kurusu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577. For reviews, see: (b) Masuyama, Y. In Liebeskind, L. S., Ed.; Advances in Metal-Organic Chemistry; JAI: Creenwith, CT, 1994; Vol. 3, p 255. (c) Tamaru, Y. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley: New York, 2002; Vol. 3, p 1917.
4. Tamaru, Y.; Horino, Y.; Araki, M.; Tanaka, S.; Kimura, M. *Tetrahedron Lett.* **2000**, *41*, 5705.
5. Mukai, R.; Horino, Y.; Tanaka, S.; Tamaru, Y.; Kimura, M. *J. Am. Chem. Soc.* **2004**, *126*, 11138.
6. Kimura, M.; Shimizu, M.; Shibata, K.; Tazoe, M.; Tamaru, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 3392.
7. Nucleophilic allylation with allyl alcohol derivatives (ethers, thioethers, carboxylic acid esters): (a) Kimura, M.; Kiyama, I.; Tomizawa, T.; Horino, Y.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1999**, *40*, 6795. (b) Kimura, M.; Ogawa, Y.; Shimizu, M.; Sueishi, M.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1998**, *39*, 6903. (c) Shimizu, M.; Kimura, M.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1998**, *39*, 609. (d) Tamaru, Y.; Tanaka, A.; Yasui, K.; Goto, S.; Tanaka, S. *Angew. Chem., Int. Ed.* **1995**, *34*, 787.
8. Nucleophilic allylation of aldehydes with allyl alcohols:[3,4,6] (a) Masuyama, Y.; Kaneko, Y.; Kurusu, Y. *Tetrahedron Lett.* **2004**, *45*, 8969. (b) Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, *2*, 847. (c) Mereno-Manas, M.; Trius, A. *Tetrahedron Lett.* **1981**, *22*, 3109.
9. Smith, M. B.; March, J. *Marche's Advanced Organic Chemistry*, 5th ed.; Wiley: Tront, 2001; p 1199.
10. Exner, O.; Böhm, S. *Chem. Eur. J.* **2002**, *8*, 5147.
11. (a) Millot, N.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7779. (b) Gerard, F.; Miginiac, Ph. *Bull. Soc. Chim. Fr.* **1974**, 2527.
12. Borthwick, A. D.; Caddick, S.; Parsons, P. J. *Tetrahedron Lett.* **1990**, *31*, 6911.
13. (a) Smith, K.; Lock, S.; El-Hiti, G. A.; Wada, M.; Miyoshi, N. *Org. Biomol. Chem.* **2004**, *2*, 935. (b) Kojima, S.; Kondoh, F.; Kawakami, J.; Yamamoto, Y.; Akiba, K. *Heteroatom Chem.* **2001**, *12*, 424.
14. Harada, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn* **1993**, *66*, 882.
15. Akiyama, T.; Iwai, J.; Sugano, M. *Tetrahedron.* **1999**, *55*, 7499.
16. Tan, K.-T.; Chng, S.-S.; Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 2958.
17. McCluskey, A.; Muderawan, I. W.; Muntari; Young, D. J. *J. Org. Chem.* **2001**, *66*, 7811.
18. Nishigaichi, Y.; Fujimoto, M.; Takuwa, A. *Synlett* **1994**, 731.
19. Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S. *J. Am. Chem. Soc.* **1998**, *120*, 6609.
20. Shibata, I.; Yoshimura, N.; Yabu, M.; Baba, A. *Eur. J. Org. Chem.* **2001**, 3207.
21. Durandetti, M.; Meignein, C.; Périchon, J. *J. Org. Chem.* **2003**, *68*, 3121.
22. Yang, X.-W.; Sheng, J.-H.; Da, C.-S.; Wang, H.-S.; Su, W.; Wang, R.; Chan, A. S. C. *J. Org. Chem.* **2000**, *65*, 295.
23. Benkeser, R. A.; Siklosi, M. P.; Mozdzen, E. C. *J. Am. Chem. Soc.* **1978**, *100*, 2134.
24. Uccello-Barretta, G.; Bernardini, R.; Lazzaroni, R.; Salvadori, P. *J. Organomet. Chem.* **2000**, *598*, 174.
25. Okuma, K.; Kamahori, Y.; Tsubakihara, K.; Yoshihara, K.; Tanaka, Y.; Shioji, K. *J. Org. Chem.* **2002**, *67*, 7355.