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Development of Efficient Organic Synthetic Reactions via Novel Activation of Unsaturated Hydrocarbons

不飽和炭化水素の新規活性化に伴う 高効率有機合成反応の開発

January 2017
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Graduate School of Engineering
Nagasaki University
長崎大学大学院工学研究科

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General Introduction

Unsaturated hydrocarbons, (such as alkenes, alkynes, conjugated dienes, and conjugated enynes), are useful carbon sources for modern organic synthesis. They are useful for important intermediates in organic synthesis because many of them are commercially available and various kind of synthetic methods have been known. As for the reactivities, it is well known that unsaturated hydrocarbons react with various compounds such as hydrogen halides, alcohols, amines, and halogens to form C–X (X = H, N, O, Cl, Br, etc.) bonds.

Transition-metal catalysts are so effective for C–C bond formation reactions of unsaturated hydrocarbons. Especially, a nickel is one of the most useful transition-metals for coupling reactions with unsaturated hydrocarbons. For example, the nickel catalysis applies for the oligomerization, polymerization, and cycloaddition of alkenes, alkynes, and conjugated dienes. Furthermore, the notable feature of nickel catalyst is to promote the coupling reactions of unsaturated hydrocarbons and carbonyl compounds. Recently, it has been revealed that a combination of a nickel catalyst and an organometallic reagent can promote the regio- and stereoselective coupling reactions of unsaturated hydrocarbons, carbonyl compounds, and organometallic reagents. In this case, it is noteworthy that unsaturated hydrocarbons react with carbonyl compounds selectively to form C–C bonds, and serve as more reactive nucleophiles than organometallic reagents in the presence of a nickel catalyst.
Unsaturated hydrocarbons behave as nucleophiles for coupling reactions with carbonyl compounds via the formation of oxanickellacycles by oxidative cyclization of unsaturated hydrocarbons and carbonyl compounds in the presence of nickel(0) species. It has been found that the oxanickellacycles undergo transmetallation with organometallic reagents, followed by reductive elimination to give three-component adducts and nickel(0) species. Additionally, in the case of conjugated dienes as unsaturated hydrocarbons, nucleophilic allylnickel species are formed via oxidative cyclization of two molecules of conjugated dienes or hydronickelation of conjugated dienes. These species also react with carbonyl compounds to participate in the C−C bond formations.

In author's group, the coupling reactions of unsaturated hydrocarbons, carbonyl compounds, and organometallic reagents by using nickel catalysis and specific reactivities of organozincs and organoboranes via oxanickellacycles have been developed. Especially, author's group has focused on conjugated dienes as nucleophiles. For example, Ni-catalyzed three-component coupling reaction of conjugated dienes, aldehydes, and dimethylzinc was developed. The reaction provided homoallylic alcohols high regio- and stereoselectively. Moreover, the reaction was expanded to five-component coupling reactions involving alkynes and amines. When triphenylphosphine was used as a ligand in the reaction, the dimerization of conjugated dienes proceeded to give six-component coupling products with high regio- and stereoselectivities. On the other hand, in the case of diethylzinc and triethylborane as organometallic reagents having β-hydrogens, reductive coupling reactions proceed. For example, Ni-catalyzed reductive coupling reaction of conjugated dienes and
aldehydes by using triethylborane was developed.\textsuperscript{6a} In the case of aldimes as electrophiles, diethyzinc was a best reducing agent in the reductive coupling reactions.\textsuperscript{6e}

The purpose of this study is to develop the efficient organic synthetic reactions via novel activation of unsaturated hydrocarbons by using a nickel catalysis and a specific reactivity of organometallic reagent. In particular, the Ni-Zn and Ni-Al catalytic systems for activation of conjugated enynes, conjugated dienes, and alkenes as nucleophiles for coupling reactions with aldehydes and carbon dioxide are developed. This thesis consists of the following four chapters.

In chapter 1, remarkably selective formation of allenyl and dienyl alcohols via Ni-catalyzed three-component coupling reaction of conjugated enynes, aldehydes, and organozinc reagents is described (Scheme 1). Ligand effects dramatically controlled the chemo- and regioselectivities of the products depending on the stability of oxanickellacycle intermediates. In the absence of a ligand, the three-component coupling reaction proceeded via 1,4-addition of aldehydes and alkyl groups of organozinc reagents to the enynes to give allenyl alcohols with high regio- and stereoselectivities. On the other hand, in the presence of a ligand, a similar coupling reaction of conjugated enynes, aldehydes, and organozinc reagents proceeded via 3,4-addition of aldehydes and alkyl groups of organozinc reagents to the enynes to afford dienyl alcohols.
Scheme 1. Ni-Catalyzed Three-Component Coupling Reaction of Conjugated Enynes, Aldehydes, and Organozinc Reagents

In chapter 2, Ni-catalyzed multicomponent coupling reaction of alkyne, 1,3-butadiene, and dimethylzinc under carbon dioxide is described (Scheme 2). This reaction proceeded via bis(allyl)nickel intermediate, which was generated through oxidative cyclization of two equivalents of dienes to a Ni catalyst. The bis(allyl)nickel species could react with carbon dioxide regioselectively at C3 position to form oxanickellacycle intermediate, followed by alkyne insertion and transmetallation, and then provided trienylcarboxylic acids. On the other hand, in the case of diethylzinc, the reductive coupling proceeded without insertion of alkyne to give dienylcarboxylic acids instead of trienylcarboxylic acids.

Scheme 2. Ni-Catalyzed Coupling Reaction of Alkyne, 1,3-Butadiene, and Organozinc Reagent under Carbon Dioxide
In chapter 3, Ni-catalyzed reductive coupling reaction of carbon dioxide with conjugated diene promoted by diisobutylaluminum hydride (DIBAL-H) is described (Scheme 3). In this case, one equivalent of conjugated diene reacted with carbon dioxide to give the β,γ-unsaturated carboxylic acids without dimerization and oligomerization of conjugated diene under the Ni-catalytic conditions. The Ni-DIBAL-H catalysis showed different reaction feature in contrast to the results of Ni-Et₂Zn catalysis in Chapter 2.

![Scheme 3](image)

**Scheme 3.** Ni-Catalyzed Reductive Coupling Reaction of Carbon Dioxide with Conjugated Diene and DIBAL-H

In chapter 4, Ni-catalyzed three-component coupling reaction of monosubstituted alkene, carbon dioxide, and organoaluminum reagent is described (Scheme 4). The reaction provided the homoallylic alcohol with high regio- and stereoselectivities. The first step in the reaction, carbon dioxide reacted with organoaluminum to form ketone, and then formal carbonyl-ene type reaction of alkene with ketone provided the homoallylic alcohol.

![Scheme 4](image)

**Scheme 4.** Ni-Catalyzed Three-Component Coupling Reaction of Alkene, Carbon Dioxide, and Organoaluminum Reagent
References


5. Ni-catalyzed multicomponent coupling reaction of conjugated dienes, carbonyl compounds, and organometallic reagents, see:


6. Ni-catalyzed reductive coupling reaction of conjugated dienes, carbonyl compounds, see:


Chapter 1

Ni-Catalyzed Three-Component Coupling Reaction of Conjugated Enyne, Aldehyde, and Organozinc Reagent

Summary: Nickel catalyst promoted three-component coupling reaction of conjugated enyne, aldehyde, and organozinc reagent. In the absence of a ligand, the three-component coupling reaction proceeded via 1,4-addition of aldehydes and alkyl groups of organozinc reagents to the enynes to give allenyl alcohols with high regio- and stereoselectivities. On the other hand, in the presence of a ligand, a similar coupling reaction of conjugated enynes, aldehydes, and organozinc reagents proceeded via 3,4-addition of aldehydes and alkyl groups of organozinc reagents to the enynes to afford dienyl alcohols.
Introduction

C–C bond transformations are among the most important and fundamental processes in organic synthesis. Especially, multi-component reactions (MCRs) can be significantly straightforward synthetic utilities for multiple C–C bond formations in a single manipulation.\(^1\) Kimura has developed the examples of the highly regio- and stereoselective Ni-catalyzed MCRs of butadiene, aldehydes, and dimethylzinc providing 3-hexenyl alcohols (Scheme 1).\(^2\) In this case, 1,4-butadiene can serve as the C4 unit for elongation of carbon chains for the useful unsaturated alcohols.

\[
\text{Scheme 1. Three-Component Coupling Reaction of Conjugated Diene, Aldehydes, and Me}_2\text{Zn}
\]

Montgomery has reported the MCRs of alkynes, carbonyls, and organozinc reagents to provide an efficient entry to allylic alcohols.\(^3\) In this case, highly chemo-, regio-, and stereoselective additions of alkynes, carbonyls, and organozinc reagents directly afforded the stereodefined allylic alcohols (Scheme 2). Furthermore, Jamison has reported the similar MCRs of alkynes with organoboranes, such as triethylborane, and aldehydes or aldimines in the presence of Ni-catalyst.\(^4\) These methodologies are extremely effective and useful synthetic methods for preparation of unsaturated alcohols involving oxidative coupling reactions of alkynes and carbonyls via oxanickelacycles.
Scheme 2. Three-Component Coupling Reaction of Conjugated Diene, Aldehydes, and Me$_2$Zn

Furthermore, Kimura has developed the MCRs with alkyne, conjugated dienes, carbonyls, and dimethylzinc in the presence of Ni-catalyst to provide 3,6-octadienyl alcohols with high regio- and stereoselectivities (Scheme 3). In this case, alkynes were incorporated as the alkenyl skeletons as well as the ligand for stabilization of nickelacycle intermediates.

Scheme 3. Ni-Catalyzed Multi-Component Coupling Reaction of Alkyne, Conjugated Diene, Aldehydes, and Me$_2$Zn

Conjugated enynes are also useful and versatile feedstocks in modern organic syntheses. Regio- and stereoselective formations of polysubstituted benzenes by cycloaddition of conjugated enynes, intermolecular [2+2] cycloadditions of conjugated enynes with alkenes, and cycloisomerizations of aryl substituted enynes are efficient synthetic strategies for preparation of cyclic hydrocarbons and benzannulation products. Although the coupling reactions of conjugated enynes with a wide variety of carbonyl
compounds using transition-metal catalysts are applicable to provide unsaturated alcohols, it has not been reported so much as to construct the cyclized hydrocarbon units.

Herein, the author would like to disclose that the Ni-catalyzed three-component coupling reactions of conjugated enynes, aldehydes, and dimethylzinc leads to the selective formation of allenic alcohols and conjugated dienyl alcohols. In the absence of ligand, the three-component coupling reaction proceeds by 1,4-addition manner of aldehyde and methyl group of dimethylzinc toward the enynes to afford the tetrasubstituted allenyl alcohols with high regio- and stereoselectivities. Whereas, in the presence of ligands, the similar MCRs of conjugated enyne, aldehyde, and dimethylzinc proceeds to provide the dienyl alcohols with high regio- and stereoselectivities. In this case, aldehyde and methyl group tend to add to the enynes on 3,4-addition manner (Scheme 4).

Scheme 4. Ni-Catalyzed Coupling Reaction of Conjugated Enyne, Aldehydes, and Me₂Zn to Form Allenyl Alcohols and Dienyl Alcohols
**Results and Discussion**

The reaction was undertaken in the presence of Ni(cod)$_2$ catalyst by exposing dimethylzinc to the THF solution of a mixture of conjugated enyne and aldehyde under nitrogen atmosphere. The results using 2-methyl-1-hexen-3-yne and benzaldehyde are summarized in Table 1. 1.2 equivalent of enyne and 2.4 equivalents of dimethylzinc based on benzaldehyde provided the tetrasubstituted allenic alcohol 4a in 34% yield as a mixture of diastereomeric isomers in a 83:17 ratio (entry 1, Table 1). After investigation of various amounts of enyne and dimethylzinc, both of 2.4 equivalents of enyne and dimethylzinc based on benzaldehyde provided the best results of the formation of 4a (entry 3, Table 1). Aprotic polar solvents, such as THF and DMA, gave the higher diastereoselectivities compared to the non-polar solvents such as toluene and $n$-hexane.
Table 1. Optimization of Reaction Conditions for Ni-Catalyzed Three-Component Coupling Reaction of Conjugated Enyne, Benzaldehyde, and Me₂Zn

\[
\begin{align*}
1a & \\
\text{entry} & \text{enyne (mmol)} & \text{Me}_2\text{Zn (mmol)} & \text{solvent} & \text{yield (\%)} \text{ of } 4a \ [\text{dr}^b] \\
1 & 0.6 & 1.2 & \text{THF} & 34 \ [83/17] \\
2 & 1.2 & 0.6 & \text{THF} & 53 \ [75/25] \\
3 & 1.2 & 1.2 & \text{THF} & 66 \ [83/17] \\
4 & 1.2 & 1.2 & \text{toluene} & 62 \ [67/33] \\
5 & 1.2 & 1.2 & n\text{-hexane} & 56 \ [67/33] \\
6 & 1.2 & 1.2 & \text{DMA} & 57 \ [88/12] \\
\end{align*}
\]

\[a\] The reaction was undertaken in the presence of Ni(cod)\(_2\) (0.05 mmol), enyne (indicated amount; mmol), benzaldehyde (0.5 mmol), dimethylzinc (indicated amount; mmol) in solvent (1.5 mL) at r.t. for 24 h under N\(_2\).  

\[b\] Diastereomeric ratio.

Next the various kinds of aldehydes are examined, and the results are exemplified in Table 2.  As for the aromatic aldehydes, such as benzaldehyde, \(p\)-anisaldehyde, \(p\)-chlorobenzaldehyde, and mesityl aldehyde, the expected C–C bond formation proceeded to afford the corresponding allenyl alcohols 4 in good to moderate yields (entries 1-4, Table 2).  In particular, mesityl aldehyde provided the corresponding allenyl alcohol 4d with higher diastereoselectivity (entry 4, Table 2).  Aliphatic aldehydes, such as \(n\)-
hexanal, cyclohexanecarbaldehyde, and pivalaldehyde gave the desired allenyl alcohols 4e–g in reasonable yields with high diastereoselectivities (entries 5-7, Table 2).

**Table 2.** Ni-Catalyzed Three-Component Coupling Reaction of Conjugated Enyne, Various Aldehydes, and Me₂Zn to Form Allenyl Alcohols

<table>
<thead>
<tr>
<th>entry</th>
<th>RCHO (2)</th>
<th>time (h)</th>
<th>yield (%) [dr]</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCHO (2a)</td>
<td>24</td>
<td>4a: 66 [83/17]</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>p-MeOC₆H₄CHO (2b)</td>
<td>48</td>
<td>4b: 63 [75/25]</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>p-ClC₆H₄CHO (2c)</td>
<td>48</td>
<td>4c: 54 [83/17]</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>MesCHO (2d)</td>
<td>72</td>
<td>4d: 58 [96/4]</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>n-C₅H₁₁CHO (2e)</td>
<td>72</td>
<td>4e: 32 [83/17]</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>CyCHO (2f)</td>
<td>72</td>
<td>4f: 54 [88/12]</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>t-BuCHO (2g)</td>
<td>72</td>
<td>4g: 61 [91/9]</td>
<td></td>
</tr>
</tbody>
</table>

*a The reaction was undertaken in the presence of Ni(cod)₂ (0.05 mmol), enyne (1.2 mmol), aldehyde (0.5 mmol), dimethylzinc (1.2 mmol) in THF (1.5 mL) at r.t. under N₂.  
* Diastereomeric ratio.

Next, the author developed the similar coupling reaction with a wide variety of enynes and organozinc reagents in the presence of Ni-catalyst and benzaldehyde under optimized conditions of Table 1. The results are summarized in Table 3. 4-n-Butyl and 4-phenyl
substituted enynes could be also utilized in the coupling reaction to give the desired allenyl alcohols 4h and 4i in reasonable yields (entries 1 and 2, Table 3). 4-Trimethylsilyl-substituted enyne could give the corresponding product 4j in moderate yield (entry 3, Table 3). In place of dimethylzinc, diethylzinc served as ethylating agent for similar coupling reaction to give the tetrasubstituted allenyl alcohol 4k. If the organozinc reagents which are prepared from ZnCl₂ and the Grignard reagents can participate in the desired reactions, high potential synthetic utilities might be tolerated. However, dibenzylzinc and t-butylzinc bromide prepared from the corresponding Grignard reagents and ZnCl₂ provided no expected coupling products, instead, homopropargyl alcohols were obtained in modest yields by 1,2-addition reaction of benzyl or t-butyl group with aldehyde at the alkene moieties.
**Table 3.** Ni-Catalyzed Three-Component Coupling Reaction of Various Conjugated Enynes, Benzaldehyde, and Organozinc Reagents to Form Allenyl Alcohols<sup>a</sup>

![Reaction Scheme](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>enyne</th>
<th>zinc</th>
<th>time (h)</th>
<th>yield (%) [dr]&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-Bu</td>
<td>Me (1b)</td>
<td>Me (3a)</td>
<td>24</td>
</tr>
<tr>
<td>2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Ph</td>
<td>Me (1c)</td>
<td>Me (3a)</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>Me&lt;sub&gt;3&lt;/sub&gt;Si</td>
<td>Me (1d)</td>
<td>Me (3a)</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td>Et</td>
<td>Me (1a)</td>
<td>Et (3b)</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>Et</td>
<td>Me (1a)</td>
<td>Ph (3c)</td>
<td>48</td>
</tr>
<tr>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Et</td>
<td>Me (1a)</td>
<td>Bn (3d)</td>
<td>72</td>
</tr>
<tr>
<td>7</td>
<td>Et</td>
<td>Me (1a)</td>
<td>t-Bu (3e)</td>
<td>72</td>
</tr>
</tbody>
</table>

<sup>a</sup> The reaction was undertaken in the presence of Ni(cod)<sub>2</sub> (0.05 mmol), enyne (1.2 mmol), benzaldehyde (0.5 mmol), organozinc reagent (1.2 mmol) in THF (1.5 mL) at r.t. under N<sub>2</sub>.  
<sup>b</sup> Diastereomeric ratio.  
<sup>c</sup> Ph<sub>2</sub>Zn and Bn<sub>2</sub>Zn were prepared from ZnCl<sub>2</sub> with 2 equivalent of PhMgBr and BnMgCl, respectively.
The structure of allenyl alcohol 4a was determined on the basis of transformation to give 5,6-dihydropyran via 6-endo cycloisomerization of β-hydroxyallene promoted by Au(I)-catalyst (Scheme 5).\textsuperscript{11} The cyclized products, dihydropyran 5a and 5b, were unequivocally characterized by NOE experimental analytical data and the coupling constant of the $^1$H NMR spectral data (Figure 1).

**Scheme 5.** Au-Catalyzed Transformation of 4a to 5a and 5b

**Figure 1.** Structure Determination of 5a by $^1$H NMR spectra and NOE experiment
According to the results of structural determination, a plausible reaction mechanism can be shown in Scheme 6. Oxidative cyclization of enyne and aldehyde involving a Ni(0) species proceeds to form oxanickelacycle intermediate I via addition of the carbonyl group of the aldehyde to olefinic termini of the enyne exclusively. In this case, aldehydes place at the quasi-equatorial position to avoid the steric repulsion between R and R² substituents. Alkyne coordinated nickelacycle I might accelerate the 1,3-shift migration at the γ-position of the propargylnickel moiety with retention of configuration to afford the stereodefined 7-membered allenynickel species II. And then, the methyl group transfer from dimethylzinc to the nickelacycle metal center provides an allenyl methyl nickel intermediate, followed by formation of the tetrasubstituted allenyl alcohols through reductive elimination with liberating active Ni(0) species.

**Scheme 6.** Plausible Reaction Mechanism for Ni-Catalyzed Coupling Reaction of Conjugated Enyne, Aldehyde, and Me₂Zn
The similar reductive coupling of conjugated enyne, aldehyde with triethylborane using nickel catalyst and phosphine ligand has been previously reported by Jamison.\textsuperscript{12} In this case, triethylborane serves as a reducing agent and the regioselectivity is opposite that observed by Montgomery in intramolecular aldehyde-ene coupling.\textsuperscript{13} Based on these results of the MCRs, the author explored the ligand effects of the selective construction of tetrasubstituted allenyl alcohol 4 and conjugated dienyl alcohols 6 using a wide variety of ligands. The results are summarized in Table 4. When the monodentate phosphine ligands such as PPh\textsubscript{3}, P(n-Bu)\textsubscript{3}, PPh\textsubscript{2}Cy, PCy\textsubscript{3}, and P(t-Bu)\textsubscript{3} were loaded, the diastereomeric ratios of allenyl alcohol 4a to dienyl alcohol 6a decreased, although dienyl alcohol 6a was obtained with high regio- and stereoselectivities (entries 2-6, Table 4). In the cases of PCy\textsubscript{3} and P(t-Bu)\textsubscript{3}, dienyl alcohol 6a were obtained as a major product or as equal the amount of allenyl alcohol (entries 5 and 6, Table 4). Bulkier phosphine ligands tend to take advantage of the formation of dienyl alcohol 6a. Furthermore, N-heterocyclic carbene ligands such as IrBu, IMes, SIMes, ICy, IPr, and SIPr were examined (entries 7-13, Table 4). Especially, IPr was most effective for the coupling reaction giving rise to the dienyl alcohol 6a in good yields with high regioselectivities (entry 11, Table 4). These results seem to suggest that the balance of the steric bulkiness and the electron donation of ligands is important for selective formations of dienyl alcohols in three-component coupling reactions.\textsuperscript{14}
Table 4. Ligand Effects on Ni-Catalyzed Coupling Reaction of Conjugated Enyne, Aldehyde, and Me$_2$Zn$^a$

![Chemical Reaction Diagram]

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand (mmol)</th>
<th>yield (%)</th>
<th>4a [dr]$^b$</th>
<th>6a [ratio]$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>66 [83/17]</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Ph$_3$P (0.1)</td>
<td>12 [67/33]</td>
<td>2 [97/3]</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>n-Bu$_3$P (0.1)</td>
<td>21 [67/33]</td>
<td>11 [99/1]</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Ph$_2$CyP (0.1)</td>
<td>20 [67/33]</td>
<td>17 [97/3]</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Cy$_3$P (0.1)</td>
<td>14 [67/33]</td>
<td>31 [97/3]</td>
<td></td>
</tr>
<tr>
<td>6$^d$</td>
<td>t-Bu$_3$P·HBF$_4$ (0.1)</td>
<td>39 [50/50]</td>
<td>39 [96/4]</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Ir-Bu (0.05)</td>
<td>22 [67/33]</td>
<td>10 [96/4]</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>IMes (0.05)</td>
<td>10 [67/33]</td>
<td>25 [96/4]</td>
<td></td>
</tr>
<tr>
<td>9$^e$</td>
<td>SIMes·HCl (0.05)</td>
<td>24 [60/40]</td>
<td>27 [97/3]</td>
<td></td>
</tr>
<tr>
<td>10$^e$</td>
<td>ICy·HCl (0.05)</td>
<td>16 [50/50]</td>
<td>7 [99/1]</td>
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<td>11</td>
<td>IPr (0.05)</td>
<td>4 [67/33]</td>
<td>55 [96/4]</td>
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<tr>
<td>12</td>
<td>SIPr (0.05)</td>
<td>5 [60/40]</td>
<td>36 [79/21]</td>
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</tr>
<tr>
<td>13$^e$</td>
<td>IPr$^*$·HCl (0.05)</td>
<td>24 [67/33]</td>
<td>25 [99/1]</td>
<td></td>
</tr>
</tbody>
</table>
The reaction was undertaken in the presence of Ni(cod)$_2$ (0.05 mmol), enyne (1.2 mmol), benzaldehyde (0.5 mmol), Me$_2$Zn (1.2 mmol) in THF (1.5 mL) at r.t. under N$_2$.  

$^b$ Diastereomeric ratio.  

$^c$ Regioisomeric ratio.  

$^d$ i-Pr$_2$NEt (0.1 mmol) was added.  

$^e$ t-BuOK (0.05 mmol) was added.

The reaction conditions of three-component coupling reaction to give dienyl alcohol 6a were optimized. These results using 2-methyl-1-hexen-3-yne and benzaldehyde are summarized in Table 5. 1.2 mmol of enyne and 0.5 mmol of benzaldehyde provided the tetrasubstituted allenyl alcohol 4a along with the dienyl alcohol 6a in 4% and 55% yield, respectively, with high regio- and stereoselectivities (entry 1, Table 5). Interestingly, 0.5 mmol of enyne and 1.2 mmol of benzaldehyde provided the dienyl alcohol 6a in 68% as a sole product (entry 3, Table 5). Non-polar solvent such as $n$-hexane gave the expected product with higher regio- and stereoselectivities (entries 4 and 5, Table 5). The reaction in $n$-hexane at 50 °C gave the best result, as the non-polar solvent was so effective to stabilize the formation of oxanickelacylce intermediate to afford dienyl alcohol 6a with excellent regioselectivities.
Table 5. Ni-Catalyzed Coupling Reaction of Conjugated Enyne, Aldehyde, and Me₂Zn to Form Dienyl Alcohol\(^a\)

\[
\begin{align*}
\text{entry} & \quad \text{enyne (mmol)} & \quad \text{aldehyde (mmol)} & \quad \text{yield (%)} \\
1 & 1.2 & 0.5 & 4 \ [67/33] & 55 \ [96/4] \\
2 & 0.5 & 0.5 & 3 \ [50/50] & 67 \ [96/4] \\
3 & 0.5 & 1.2 & 0 & 68 \ [96/4] \\
4 & 0.5 & 1.2 & 7 \ [67/33] & 73 \ [98/2] \\
5 & 0.5 & 1.2 & 4 \ [50/50] & 82 \ [97/3] \\
\end{align*}
\]

\(^a\) The reaction was undertaken in the presence of Ni(cod)\(_2\) (0.05 mmol), IPr (0.05 mmol), enyne (indicated amount; mmol), benzaldehyde (indicated amount; mmol), Me₂Zn (1.2 mmol) in THF (1.5 mL) at r.t. under N\(_2\).

\(^b\) Diastereomeric ratio.

\(^c\) Regioisomeric ratio.

\(^d\) n-Hexane was used instead of THF as solvent.

\(^e\) At 50 °C.

A wide variety of aldehydes were examined, and the results are depicted in Table 6. As for the aromatic aldehydes, such as benzaldehyde, \(p\)-anisaldehyde, and \(p\)-chlorobenzaldehyde, these MCRs proceeded to give the corresponding dienyl alcohols in good to reasonable yields with excent regioselectivities (entries 1-4, Table 6). In the
case of mesityl aldehyde, although the yield decreased to 21%, the regioselectivity increased and the desired product 6d was obtained as a sole product (entry 4, Table 6). Aliphatic aldehydes, such as n-hexanal, cyclohexanecarbaldehyde, and pivalaldehyde gave the dienyl alcohols 6e-g in reasonable yields with high regioselectivities (entries 5-7, Table 6).

Table 6. Ni-Catalyzed Three-Component Coupling Reaction of Conjugated Enyne, Various Aldehydes, and Me₂Zn to Form Dienyl Alcohols

<table>
<thead>
<tr>
<th>entry</th>
<th>RCHO (2)</th>
<th>time (h)</th>
<th>yield (%) [ratio]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCHO (2a)</td>
<td>24</td>
<td>6a: 82 [97/3]</td>
</tr>
<tr>
<td>2</td>
<td>p-MeOC₆H₄CHO (2b)</td>
<td>24</td>
<td>6b: 46 [95/5]</td>
</tr>
<tr>
<td>3</td>
<td>p-ClC₆H₄CHO (2c)</td>
<td>24</td>
<td>6c: 57 [95/5]</td>
</tr>
<tr>
<td>4</td>
<td>MesCHO (2d)</td>
<td>72</td>
<td>6d: 28 [&gt;99/1]</td>
</tr>
<tr>
<td>5c</td>
<td>n-C₅H₁₁CHO (2e)</td>
<td>72</td>
<td>6e: 68 [97/3]</td>
</tr>
<tr>
<td>6c</td>
<td>CyCHO (2f)</td>
<td>72</td>
<td>6f: 49 [93/7]</td>
</tr>
<tr>
<td>7c</td>
<td>t-BuCHO (2g)</td>
<td>72</td>
<td>6g: 53 [97/3]</td>
</tr>
</tbody>
</table>

a The reaction was undertaken in the presence of Ni(cod)₂ (0.05 mmol), IPr (0.05 mmol), enyne (0.5 mmol), aldehyde (1.2 mmol), dimethylzinc (1.2 mmol) in n-hexane (1.5 mL) at 50 °C. under N₂.

b Regioisomeric ratio.  c THF was used instead of n-hexane as solvent.
Finally, the similar coupling reaction with a variety of enynes with organozinc reagents was developed. The results are summarized in Table 7. 4-n-Butyl- and 4-phenyl substituted enynes could be used in the coupling reaction to give the desired dienyl alcohols 6 in reasonable yields (entries 1 and 2, Table 7). 4-Trimethylsilyl substituted enyne gave the corresponding product 6j in moderate yield (entry 3, Table 7). In the case of diethylzinc could not take part in the coupling reaction as an ethylating agent, instead, a complex mixture of reductive coupling products was obtained (entry 6, Table 7). Diphenylzinc could serve as a phenylating agent for the similar coupling reaction to give tetrasubstituted dienyl alcohol 6m in modest yield (entry 7, Table 7).
Table 7. Ni-Catalyzed Three-Component Coupling Reaction of Various Conjugated Enynes, Benzaldehyde, and Organozinc Reagents to Form Dienyl Alcohols

![Chemical Structure]

<table>
<thead>
<tr>
<th>entry</th>
<th>enyne</th>
<th>zinc</th>
<th>time (h)</th>
<th>yield (%) [dr]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-Bu Me (1b)</td>
<td>Me (3a)</td>
<td>24</td>
<td>6h: 73 [98/2]</td>
</tr>
<tr>
<td>2c</td>
<td>Ph Me (1c)</td>
<td>Me (3a)</td>
<td>72</td>
<td>6i: 69 [&gt;99/1]</td>
</tr>
<tr>
<td>3</td>
<td>Me₃Si Me (1d)</td>
<td>Me (3a)</td>
<td>72</td>
<td>6j: 40 [&gt;99/1]</td>
</tr>
<tr>
<td>4</td>
<td>n-Bu H (1e)</td>
<td>Me (3a)</td>
<td>24</td>
<td>6k: 36 [&gt;99/1]</td>
</tr>
<tr>
<td>5</td>
<td>Ph H (1f)</td>
<td>Me (3a)</td>
<td>48</td>
<td>6l: 38 [50/50]</td>
</tr>
<tr>
<td>6</td>
<td>Et Me (1a)</td>
<td>Et (3b)</td>
<td>72</td>
<td>complex mixture</td>
</tr>
<tr>
<td>7c</td>
<td>Et Me (1a)</td>
<td>Ph (3c)</td>
<td>72</td>
<td>6m: 2 [&gt;99/1]</td>
</tr>
</tbody>
</table>

*a* The reaction was undertaken in the presence of Ni(cod)₂ (0.05 mmol), IPr (0.05 mmol), enyne (0.5 mmol), benzaldehyde (1.2 mmol), organozinc reagent (1.2 mmol) in n-hexane (1.5 mL) at 50 °C. under N₂.

*b* Regioisomeric ratio.  
*c* Ph₂Zn was prepared from ZnCl₂ with 2 equivalent of PhMgBr and BnMgCl, respectively.
A plausible reaction mechanism was shown in Scheme 7. In the presence of ligand, the repulsion between ligand (L = IPr) and the substituent on the acetylenic carbon atom prevents the oxidative cyclization shown in Scheme 6, instead, causes to the alternative orientation for the oxidative cyclization of enyne and carbonyl group. The alkyne moiety of enyne and carbonyl groups of aldehyde predominantly react with the Ni(0) species to form the oxanickelacyclopentene intermediate III. Then, the methyl group transfer from dimethylzinc to the nickelacycle readily provides an allenyl methyl nickel species, followed by formation of the dienyl alcohols through the reductive elimination with liberating Ni(0) active species.

Scheme 7. Plausible Reaction Mechanism for Ni-Catalyzed Coupling Reaction of Conjugated Enyne, Aldehyde, and Me₂Zn in the presence of Ligand
In conclusion, the author developed the Ni-catalyzed three-component coupling reaction of dimethylzinc, conjugated enyne, and aldehyde to afford the allenyl alcohols and dienyl alcohols. Ligand effect dramatically controlled the chemo and regioselectivities to lead to the selective formation of allenyl alcohols and dienyl alcohols depending on the stability of oxanickellacycle key intermediates. In the absence of ligand, the three-component coupling reaction proceeded on 1,4-addition manner of aldehyde and methyl group of dimethylzinc toward the enynes to afford the tetrasubstituted allenyl alcohols with high regio- and stereoselectivities. Whereas, in the presence of ligands, such as IPr, IPr*, SIMes, the similar coupling reaction of conjugated enyne, aldehyde, and dimethylzinc proceeded to provide the dienyl alcohols with high regio- and stereoselectivities. In this case, aldehyde and methyl group added to the enynes on 3,4-addition manner.
**Experimental Section**

Reactions employed oven-dried glassware unless otherwise noted. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator (Merck Silica gel 60F254). Flash chromatography columns were packed with 230-400 mesh silica gel as a slurry in hexane. Gradient flash chromatography was conducted eluting with a continuous gradient from hexane to the indicated solvent. Proton and carbon NMR data were obtained with a JEOL JNM-AL400 with tetramethylsilane as an internal standard. Chemical shift values were given in ppm downfield from the internal standard. Infrared spectra were recorded with a JASCO A-100 FT-IR spectrophotometer. High resolution mass spectra (HRMS) were measured with a JEOL JMS-700N. Distillation were carried out in a Kugelrohr apparatus (SIBATA glass tube oven GTO-350RG). Boiling points are meant to refer to the oven temperature (± 1 °C).

**Solvents and Reagents**

Tetrahydrofuran, N,N-dimethylacetamide (DMA), toluene, and n-hexane were dried and distilled from benzophenone-sodium immediately prior to use under nitrogen atmosphere. Dichloromethane was dried and distilled from CaH2 immediately prior to use under nitrogen atmosphere. Dimethylzinc, diethylzinc (1 M hexane, KANTO Kagaku), Ni(cod)2 (KANTO Kagaku), P(n-Bu)3, PPh3, PPh2Cy, IPr, SiMes·HCl, IMes, IrBu, and ICy·HCl (Tokyo Kasei Kogyo Co., Ltd), t-BuOK (99.99%), PCy3, P(t-Bu)3·HBF4, SIPr, and AuCl (Aldrich) were used without further purification. IPr*·HCl was
furnished by the known procedures. Dibenzylzinc and diphenylzinc were prepared from ZnCl$_2$ with 2-equivalents of benzylmagnesium chloride and phenylmagnesium bromide, respectively. $t$-BuZnBr (Aldrich) were used without further purification. Benzaldehyde, $p$-anisaldehyde, mesitylaldehyde, hexanal, cyclohexanecarbaldehyde, and pivaldehyde (Tokyo Kasei Kogyo Co., Ltd) were purchased and distilled via Kugelrohl apparatus under reduced pressure prior to use. $p$-Chlorobenzaldehyde (Tokyo Kasei Kogyo Co., Ltd) was purchased and used without further purification. $N,N$-Diisopropylethylamine (Tokyo Kasei Kogyo Co., Ltd) and 2-Methyl-1-hexen-3-yne (Aldrich) were purchased and distilled via Kugelrohl apparatus under reduced pressure prior to use. Other conjugated enynes were prepared by Sonogashira cross-coupling of terminal alkyne and alkenylbromide. Spectral data of the enynes were consistent with literature data. The NHCs employed in this paper are as follows: IPr, 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene; SIPr, 1,3-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene; IPr* · HCl, 1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazolium Chloride; IMes, 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene; SIMes · HCl, 1,3-bis(2,4,6-trimethylphenyl)imidazolinium Chloride; ICy · HCl, 1,3-dicyclohexylimidazolium Chloride; IrBu, 1,3-di-$t$-butylimidazol-2-ylidene.

**Preparation of diphenylzinc and dibenzylzinc reagents**

A 50 mL Schlenk flask equipped with a rubber septum was charged with ZnCl$_2$ solution (2 mL of 1 M ethyl ether, 2 mmol) under nitrogen atmosphere. A solution of phenyl magnesium bromide (4 mL of 1 M THF, 4 mmol) or benzyl magnesium chloride (4.5 mL
of 0.9 M THF, 4 mmol) was added to the ZnCl₂ solution via syringe at 0 °C, and then was diluted with THF solvent to 0.25 M solution. The reaction mixture was stirred at room temperature for 12 hours. Thus, diphenylzinc and dibenzylzinc reagents were freshly prepared prior to use.

**Typical procedure for the three-component coupling reaction of aldehydes, en-yne, and Me₂Zn to give allenyl alcohol** (entry 3, Table 1)

The reaction was undertaken as follows: Into a nitrogen-purged flask with Ni(cod)₂ (13.8 mg, 0.05 mmol) was introduced successively THF (1.5 mL), benzaldehyde (53.1 mg, 0.5 mmol), 2-methyl-1-hexen-3-yne (113 mg, 1.2 mmol), and dimethylzinc (1.2 mL of 1 M hexanes, 1.2 mmol) via syringe. The homogeneous mixture was stirred at room temperature for 24 h, during which the reaction was monitored by TLC. After dilution with ethyl acetate (30 mL), the mixture was washed successively with 2 N-HCl, sat. NaHCO₃, and brine, and then dried (MgSO₄) and concentrated in vacuo. The residual oil was subjected to column chromatography over silica gel (hexane/ethyl acetate = 20/1, v/v) to give 4a (71.4 mg, 66%) in 83:17 ratio.

**3,5-dimethyl-1-phenylhepta-3,4-dien-1-ol (4a):** a mixture of diastereomers in a ratio of 83:17

R₇ = 0.50 (hexane-EtOAc, 4:1)

IR (neat): 3356 (m), 3065 (w), 3030 (w), 2964 (s), 2897 (s), 2849 (s), 1750 (w), 1495 (w), 1454 (s), 1367 (m), 1047 (m), 1018 (m), 756 (m), 700 (m) cm⁻¹.
$^1$H NMR (400 MHz, CDCl$_3$, major isomer): $\delta$ 0.96 (t, $J = 7.3$ Hz, 3 H), 1.66 (s, 3 H), 1.70 (s, 3 H), 1.92 (q, $J = 7.3$ Hz, 2 H), 2.33-2.38 (m, 3 H), 4.77-4.81 (m, 1 H), 7.22-7.38 (m, 5 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 12.3, 19.5, 19.9, 27.4, 44.9, 72.1, 95.9, 101.5, 125.7, 127.2, 128.1, 143.8, 198.6.

$^1$H NMR (400 MHz, CDCl$_3$, minor isomer): $\delta$ 0.98 (t, $J = 7.3$ Hz, 3 H), 1.65 (s, 3 H), 1.70 (s, 3 H), 1.94 (q, $J = 7.3$ Hz, 2 H), 2.33-2.41 (m, 3 H), 4.77-4.83 (m, 1 H), 7.22-7.38 (m, 5 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, minor isomer): $\delta$ 12.4, 19.2, 19.9, 27.5, 44.8, 72.1, 96.0, 101.5, 125.8, 127.2, 128.1, 143.8, 198.6.

HRMS: $m/z$ (M$^+$) calcd for C$_{15}$H$_{20}$O: 216.1514; found 216.1496.

1-(4-methoxyphenyl)-3,5-dimethylhepta-3,4-dien-1-ol (4b): a mixture of diastereomers in a ratio of 75:25

$R_f$ = 0.35 (hexane-EtOAc, 4:1)

IR (neat): 3452 (m), 3040 (w), 2976 (s), 2939 (s), 2837 (s), 1751 (w), 1612 (s), 1514 (s), 1456 (s), 1248 (s), 1038 (s), 831 (m) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$, major isomer): $\delta$ 0.96 (t, $J = 7.3$ Hz, 3 H), 1.65 (s, 3 H), 1.69 (s, 3 H), 1.92 (q, $J = 7.3$ Hz, 2 H), 2.28-2.40 (m, 3 H), 3.80 (s, 3 H), 4.72-4.77 (m, 1 H), 6.85-7.30 (m, 4 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 12.3, 19.5, 19.9, 27.4, 44.8, 55.2, 71.8, 95.9, 101.4, 113.6, 127.0, 136.1, 158.8, 198.6.
\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, minor isomer): \(\delta 0.98\ (t, J = 7.6 Hz, 3 H), 1.65\ (s, 3 H), 1.69\ (s, 3 H), 1.93\ (q, J = 7.6 Hz, 2 H), 2.28-2.40\ (m, 3 H), 3.80\ (s, 3 H), 4.72-4.77\ (m, 1 H), 6.85-7.30\ (m, 4 H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}, minor isomer): \(\delta 12.4, 19.2, 19.9, 27.5, 44.7, 55.2, 71.8, 96.1, 101.7, 113.6, 127.0, 136.1, 158.8, 198.4.\)

HRMS: \(m/z\ (M^+)\) calcd for C\textsubscript{16}H\textsubscript{22}O\textsubscript{2}: 246.1620; found 246.1606.

\textbf{1-(4-chlorophenyl)-3,5-dimethylhepta-3,4-dien-1-ol (4c):} a mixture of diastereomers in a ratio of 83:17

\(R_f = 0.45\) (hexane-EtOAc, 4:1)

IR (neat): 3435 (m), 3065 (w), 3030 (w), 2964 (s), 2930 (s), 2901 (s), 1718 (m) 1493 (s), 1445 (w), 1092 (s), 1015 (s), 829 (m), 779 (w) cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, major isomer): \(\delta 0.96\ (t, J = 7.3 Hz, 3 H), 1.66\ (s, 3 H), 1.70\ (s, 3 H), 1.93\ (q, J = 7.3 Hz, 2 H), 2.28-2.41\ (m, 3 H), 4.75-4.79\ (m, 1 H), 7.28-7.33\ (m, 4 H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}, major isomer): \(\delta 12.3, 19.5, 19.9, 27.4, 44.9, 71.5, 95.7, 101.8, 127.1, 128.3, 132.8, 142.3, 198.6.\)

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}, minor isomer): \(\delta 0.98\ (t, J = 7.6 Hz, 3 H), 1.65\ (s, 3 H), 1.69\ (s, 3 H), 1.94\ (q, J = 7.6 Hz, 2 H), 2.28-2.41\ (m, 3 H), 4.75-4.79\ (m, 1 H), 7.28-7.33\ (m, 4 H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}, minor isomer): \(\delta 12.4, 19.2, 19.9, 27.5, 44.8, 71.5, 95.8, 102.0, 127.1, 128.2, 132.8, 142.3, 198.6.\)
1-mesityl-3,5-dimethylhepta-3,4-dien-1-ol (4d): a mixture of diastereomers in a ratio of 96:4

R_f = 0.60 (hexane-EtOAc, 4:1)

IR (neat): 3445 (m), 3005 (w), 3030 (w), 2964 (s), 2932 (s), 2874 (s), 1722 (w) 1612 (w), 1445 (s), 1038 (m), 1016 (m), 851 (s), 785 (w) cm⁻¹.

¹H NMR (400 MHz, CDCl₃, major isomer): δ 0.99 (t, J = 7.3 Hz, 3 H), 1.71 (s, 3 H), 1.73 (s, 3 H), 1.96 (q, J = 7.3 Hz, 2 H), 2.08 (d, J = 2.4 Hz, 1 H), 2.20 (dd, J = 3.4, 15.1 Hz, 1 H), 2.23 (s, 3 H), 2.39 (s, 6 H), 2.59 (dd, J = 10.2, 15.1 Hz, 1 H), 5.24 (ddd, J = 2.4, 3.4, 10.2 Hz, 1 H), 6.79 (s, 2 H).

¹³C NMR (100 MHz, CDCl₃, major isomer): δ 12.4, 19.5, 19.7, 20.7, 20.7, 27.5, 41.3, 69.6, 96.4, 101.4, 129.9, 135.8, 136.1, 136.1, 198.5.

¹H NMR (400 MHz, CDCl₃, minor isomer): δ 1.01 (t, J = 7.3 Hz, 3 H), 1.70 (s, 3 H), 1.73 (s, 3 H), 1.95 (q, J = 7.3 Hz, 2 H), 2.08 (d, J = 2.4 Hz, 1 H), 2.20 (dd, J = 3.4, 15.1 Hz, 1 H), 2.23 (s, 3 H), 2.38 (s, 6 H), 2.59 (dd, J = 10.2, 15.1 Hz, 1 H), 5.24 (ddd, J = 2.4, 3.4, 10.2 Hz, 1 H), 6.79 (s, 2 H).

¹³C NMR (100 MHz, CDCl₃, minor isomer): δ 12.4, 19.3, 19.7, 20.7, 20.7, 27.5, 41.0, 69.6, 96.4, 101.4, 129.8, 135.8, 136.1, 136.1, 198.5.

HRMS: m/z (M⁺) calcd for C₁₆H₂₆O: 258.1984; found 258.1996.

8,10-dimethyldodeca-8,9-dien-6-ol (4e): a mixture of diastereomers in a ratio of 83:17
**1-cyclohexyl-3,5-dimethylhepta-3,4-dien-1-ol (4f):** a mixture of diastereomers in a ratio of 88:12

\[ R_f = 0.70 \text{ (hexane-EtOAc, 4:1)} \]

**IR (neat):** 3441 (m), 2959 (s), 2932 (s), 2860 (s), 1715 (m), 1373 (m), 1086 (w), 1016 (w) cm\(^{-1}\).

\(^1^H\) NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta\) 0.89 (t, \(J = 7.3\) Hz, 3 H), 0.98 (t, \(J = 7.3\) Hz, 3 H), 1.26-1.50 (m, 8 H), 1.68 (s, 3 H), 1.68 (s, 3 H), 1.94 (q, \(J = 7.3\) Hz, 2 H), 1.99-2.11 (m, 3 H), 3.67-3.73 (m, 1 H).

\(^1^C\) NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta\) 12.3, 14.0, 19.6, 20.0, 22.6, 25.5, 27.4, 32.0, 36.8, 42.8, 69.7, 96.2, 101.1 198.3.

\(^1^H\) NMR (400 MHz, CDCl\(_3\), minor isomer): \(\delta\) 0.89 (t, \(J = 7.3\) Hz, 3 H), 0.99 (t, \(J = 7.3\) Hz, 3 H), 1.26-1.50 (m, 8 H), 1.68 (s, 3 H), 1.68 (s, 3 H), 1.94 (q, \(J = 7.3\) Hz, 2 H), 1.99-2.11 (m, 3 H), 3.67-3.73 (m, 1 H).

\(^1^C\) NMR (100 MHz, CDCl\(_3\), minor isomer): \(\delta\) 12.4, 14.0, 19.3, 20.0, 22.6, 25.5, 27.5, 32.0, 36.8, 42.6, 69.7, 96.3, 101.1 198.2.

HRMS: \(m/z\) (M\(^+\)) calcd for C\(_{14}\)H\(_{26}\)O: 210.1984; found 210.1953.

**1-cyclohexyl-3,5-dimethylhepta-3,4-dien-1-ol (4f):** a mixture of diastereomers in a ratio of 88:12

\[ R_f = 0.70 \text{ (hexane-EtOAc, 4:1)} \]

**IR (neat):** 3474 (m), 2964 (m), 2928 (s), 2853 (s), 1726 (w), 1450 (m), 1371 (m), 1101 (w), 1086 (w), 893 (w) cm\(^{-1}\).

\(^1^H\) NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta\) 0.98 (t, \(J = 7.3\) Hz, 3 H), 1.02-1.30 (m, 5 H), 1.38 (dm, \(J = 5.4\) Hz, 1 H), 1.64-1.79 (m, 5 H), 1.68 (s, 3 H), 1.68 (s, 3 H), 1.84 (br
s, 1 H), 1.94 (q, $J = 7.3$ Hz, 2 H), 2.00 (dd, $J = 9.5$, 14.6 Hz, 1 H), 2.13 (dd, $J = 3.2$, 14.6 Hz, 1 H), 3.47 (ddd, $J = 3.2$, 5.4, 9.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 12.4, 19.6, 19.9, 26.3, 26.4, 26.6, 27.4, 28.2, 29.3, 39.8, 43.1, 73.5, 96.4, 101.0, 198.3.

$^1$H NMR (400 MHz, CDCl$_3$, minor isomer): $\delta$ 0.98 (t, $J = 7.3$ Hz, 3 H), 1.02-1.30 (m, 5 H), 1.34-1.43 (m, 1 H), 1.64-1.79 (m, 5 H), 1.68 (s, 3 H), 1.68 (s, 3 H), 1.87 (br s, 1 H), 1.94 (q, $J = 7.3$ Hz, 2 H), 2.00 (dd, $J = 9.8$, 14.9 Hz, 1 H), 2.15 (dd, $J = 2.9$, 14.9 Hz, 1 H), 3.49 (ddm, $J = 2.9$, 9.8 Hz, 1 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, minor isomer): $\delta$ 12.5, 19.3, 19.9, 26.3, 26.4, 26.6, 27.5, 28.1, 29.3, 39.6, 43.1, 73.5, 96.5, 101.3, 198.3.

HRMS: $m/z$ (M$^+$) calcd for C$_{15}$H$_{26}$O: 222.1984; found 222.1971.

2,2,5,7-tetramethylnona-5,6-dien-3-ol (4g): a mixture of diastereomers in a ratio of 91:9

R$_f$ = 0.70 (hexane-EtOAc, 4:1)

IR (neat): 3558 (m), 2963 (m), 2910 (s), 2872 (s), 1718 (w) 1460 (w), 1364 (m), 1072 (w), 1009 (w), 897 (w) cm$^{-1}$.

$^1$H NMR (400 MHz, C$_6$D$_6$, major isomer): $\delta$ 0.99 (t, $J = 7.3$ Hz, 3 H), 1.00 (s, 9 H), 1.59 (s, 3 H), 1.66 (s, 3 H), 1.83 (q, $J = 7.3$ Hz, 2 H), 2.01 (dd, $J = 10.5$, 14.4 Hz, 1 H), 2.02 (m, 1 H), 2.10 (dd, $J = 2.0$, 14.4 Hz, 1 H), 3.45 (ddm, $J = 2.0$, 10.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 12.3, 19.7, 19.7, 25.8, 25.9, 27.4, 34.3, 37.7, 96.8, 101.1, 198.3.
$^1$H NMR (400 MHz, C$_6$D$_6$, minor isomer): $\delta$ 0.95 (s, 9 H), 0.99 (t, $J = 7.3$ Hz, 3 H), 1.60 (s, 3 H), 1.66 (s, 3 H), 1.83 (q, $J = 7.3$ Hz, 2 H), 1.95-2.12 (m, 3H), 3.46-3.49 (m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$, minor isomer): $\delta$ 12.5, 19.7, 19.7, 25.7, 25.8, 27.5, 34.4, 37.4, 96.8, 101.1, 198.3.

HRMS: $m/z$ (M$^+$) calcd for C$_{13}$H$_{24}$O: 196.1827; found 196.1826.

3,5-dimethyl-1-phenynona-3,4-dien-1-ol (4h): a mixture of diastereomers in a ratio of 83:17

$R_f = 0.55$ (hexane-EtOAc, 4:1)

IR (neat): 3410 (m), 3074 (w), 3032 (w), 2953 (s), 2930 (s), 2860 (s), 1718 (w) 1452 (m), 1369 (w), 1043 (m), 1026 (m), 756 (m), 700 (m) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$, major isomer): $\delta$ 0.89 (t, $J = 7.3$ Hz, 3 H), 1.28-1.38 (dm, $J = 7.3$ Hz, 4 H), 1.65 (s, 3 H), 1.69 (s, 3 H), 1.91 (t, $J = 7.3$ Hz, 2 H), 2.34-2.36 (dm, $J = 7.8$ Hz, 2 H), 4.77-4.81 (dm, $J = 7.8$ Hz, 1 H), 7.22-7.38 (m, 5 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 13.9, 19.5, 19.8, 22.3, 29.8, 34.1, 44.9, 72.1, 95.0, 99.7, 125.8, 127.2, 128.1, 143.8, 199.1.

$^1$H NMR (400 MHz, CDCl$_3$, minor isomer): $\delta$ 0.90 (t, $J = 7.3$ Hz, 3 H), 1.28-1.38 (dm, $J = 7.6$ Hz, 4 H), 1.62 (s, 3 H), 1.68 (s, 3 H), 1.90 (t, $J = 7.6$ Hz, 2 H), 2.34-2.36 (dm, $J = 7.8$ Hz, 2 H), 4.77-4.81 (dm, $J = 7.8$ Hz, 1 H), 7.22-7.38 (m, 5 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, minor isomer): $\delta$ 14.0, 19.6, 19.8, 22.3, 29.9, 34.2, 44.7, 72.2, 95.1, 99.9, 125.8, 127.2, 128.1, 143.8, 199.1.

HRMS: $m/z$ (M$^+$) calcd for C$_{17}$H$_{24}$O: 244.1827; found 244.1830.
3-methyl-1,5-diphenylhexa-3,4-dien-1-ol (4i): a mixture of diastereomers in a ratio of 67:33

R<sub>f</sub> = 0.60 (hexane-EtOAc, 4:1)

IR (neat): 3395 (m), 3090 (m), 3028 (m), 2980 (m), 2903 (m), 2864 (m), 1950 (w), 1597 (m) 1493 (s), 1445 (s), 1047 (m), 1026 (m), 760 (s), 696 (s) cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, major isomer): δ 1.82 (s, 3 H), 2.02 (s, 3 H), 2.13 (br s, 1 H), 2.49 (dd, <i>J</i> = 5.1, 15.1 Hz, 1 H), 2.53 (dd, <i>J</i> = 8.1, 15.1 Hz, 1 H), 4.83 (dd, <i>J</i> = 5.1, 8.1 Hz, 1 H), 7.12-7.36 (m, 10 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, major isomer): 17.3, 19.3, 44.3, 72.4, 98.3, 100.4, 125.5, 125.8, 126.3, 127.4, 128.2, 128.3, 137.5, 143.7, 202.0.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, minor isomer): δ 1.82 (s, 3 H), 1.98 (s, 3 H), 2.16 (br s, 1 H), 2.55 (dd, <i>J</i> = 6.8, 14.4 Hz, 2 H), 4.84 (t, <i>J</i> = 6.8 Hz, 1 H), 7.12-7.36 (m, 10 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>, minor isomer): 17.1, 19.3, 44.3, 72.4, 98.0, 100.4, 125.5, 125.8, 126.3, 127.3, 128.2, 128.2, 137.8, 143.7, 202.0.

HRMS: <i>m/z</i> (M<sup>+</sup>) calcd for C<sub>19</sub>H<sub>20</sub>O: 264.1514; found 264.1517.

3-methyl-5-(trimethylsilyl)-1-phenylhexa-3,4-dien-1-ol (4j): a mixture of diastereomers in a ratio of 50:50

R<sub>f</sub> = 0.60 (hexane-EtOAc, 4:1)

IR (neat): 3447 (m), 3065 (w), 2957 (m), 2899 (m), 2860 (w), 1940 (m) 1713 (m), 1450 (m), 1248 (s), 1047 (m), 839 (m), 754 (m), 700 (m) cm<sup>-1</sup>.
\[ {^1}H \text{ NMR (400 MHz, CDCl}_3, \text{ one isomer): } \delta \ 0.07 (s, 9 \text{ H}), 1.66 (s, 3 \text{ H}), 1.70 (s, 3 \text{ H}), 2.29-2.39 (m, 2 \text{ H}), 2.31 (dm, J = 4.4 \text{ Hz}, 1 \text{ H}), 4.75 (dm, J = 4.4 \text{ Hz}, 1 \text{ H}), 7.24-7.40 (m, 5 \text{ H}). \]

\[ {^{13}}C \text{ NMR (100 MHz, CDCl}_3, \text{ one isomer): } \delta \ -1.8, 16.1, 18.7, 44.8, 71.8, 89.2, 91.8, 125.9, 127.4, 128.3, 144.0, 204.6. \]

\[ {^1}H \text{ NMR (400 MHz, CDCl}_3, \text{ the other isomer): } \delta \ 0.09 (s, 9 \text{ H}), 1.64 (s, 3 \text{ H}), 1.67 (s, 3 \text{ H}), 2.29-2.39 (m, 2 \text{ H}), 2.31 (dm, J = 4.6 \text{ Hz}, 1 \text{ H}), 4.80 (dm, J = 4.6 \text{ Hz}, 1 \text{ H}), 7.24-7.40 (m, 5 \text{ H}). \]

\[ {^{13}}C \text{ NMR (100 MHz, CDCl}_3, \text{ the other isomer): } \delta \ -1.7, 15.8, 19.0, 44.1, 72.4, 89.4, 92.2, 125.8, 127.3, 128.3, 144.0, 204.3. \]

HRMS: \( m/z (M^+) \) calcd for \( C_{16}H_{24}OSi \): 260.1596; found 260.1591.

5-ethyl-3-methyl-1-phenylhepta-3,4-dien-1-ol (4k)

\( R_f = 0.50 \) (hexane-EtOAc, 4:1)

IR (neat): 3379 (m), 3063 (w), 3030 (w), 2964 (s), 2932 (s), 2876 (s), 1717 (w) 1493 (w), 1454 (s), 1373 (m), 1028 (m), 756 (m), 700 (m) cm\(^{-1}\).

\[ {^1}H \text{ NMR (400 MHz, CDCl}_3): \delta \ 0.98 (t, J = 7.6 \text{ Hz}, 6 \text{ H}), 1.72 (s, 3 \text{ H}), 1.95 (q, J = 7.6 \text{ Hz}, 4 \text{ H}), 2.37-2.40 (br s, 1 \text{ H}), 2.38 (d, J = 6.6 \text{ Hz}, 2 \text{ H}) 4.82 (t, J = 6.6 \text{ Hz}, 1 \text{ H}), 7.24-7.39 (m, 5 \text{ H}). \]

\[ {^{13}}C \text{ NMR (100 MHz, CDCl}_3): \delta \ 12.4, 12.5, 20.0, 26.0, 26.0, 45.0, 72.2, 98.2, 108.5, 125.7, 127.1, 128.1, 143.9, 197.8. \]

HRMS: \( m/z (M^+) \) calcd for \( C_{16}H_{22}O \): 230.1671; found 230.1671.
3-methyl-1,5-diphenylepta-3,4-dien-1-ol (4l): a mixture of diastereomers in a ratio of 50:50

Rf = 0.60 (hexane-EtOAc, 4:1)

IR (neat): 3410 (m), 3028 (m), 2964 (m), 2910 (m), 2874 (m), 1950 (w), 1597 (m) 1493 (s), 1454 (s), 1367 (m), 1055 (m), 1030 (m), 754 (s), 696 (s) cm⁻¹.

¹H NMR (400 MHz, CDCl₃, one isomer): δ 1.08 (t, J = 7.3 Hz, 3 H), 1.85 (s, 3 H), 2.37 (br s, 1 H), 2.39 (q, J = 7.3 Hz, 2 H), 2.53 (d, J = 6.1 Hz, 2 H), 4.86 (t, J = 6.1 Hz, 1 H), 7.14-7.37 (m, 10 H).

¹³C NMR (100 MHz, CDCl₃, one isomer): δ 11.5, 18.4, 22.3, 43.6, 71.4, 99.4, 106.4, 124.7, 124.8, 125.3, 126.3, 127.2, 127.2, 136.7, 142.7, 200.5.

¹H NMR (400 MHz, CDCl₃, the other isomer): δ 1.09 (t, J = 7.3 Hz, 3 H), 1.85 (s, 3 H), 2.37 (br s, 1 H), 2.41 (q, J = 7.3 Hz, 2 H), 2.53 (d, J = 6.1 Hz, 2 H), 4.86 (t, J = 6.1 Hz, 1 H), 7.14-7.37 (m, 10 H).

¹³C NMR (100 MHz, CDCl₃, the other isomer): δ 11.7, 18.4, 22.3, 43.4, 71.4, 99.1, 106.6, 124.7, 124.8, 125.3, 126.3, 127.2, 127.2, 136.3, 142.7, 200.3.

HRMS: m/z (M⁺) calcd for C₂₀H₂₂O: 278.1671; found 278.1668.

Typical procedure for the three-component coupling reaction of aldehydes, en-yne, and Me₂Zn to give dienyl alcohol (entry 1, Table 6)

The reaction was undertaken as follows: Into a nitrogen-purged flask with Ni(cod)₂ (13.8 mg, 0.05 mmol) and IPr (19.5 mg, 0.05 mmol) was introduced successively n-
hexane (1.5 mL), benzaldehyde (127.3 mg, 1.2 mmol), 2-methyl-1-hexen-3-yne (47.1 mg, 0.5 mmol), and dimethylzinc (1.2 mL of 1M hexanes, 1.2 mmol) via syringe. The homogenous mixture was stirred at 50 °C for 24 h, during which the reaction was monitored by TLC. After dilution with ethyl acetate (30 mL), the mixture was washed successively with 2 N-HCl, sat. NaHCO₃, and brine, and then dried (MgSO₄) and concentrated in vacuo. The residual oil was subjected to column chromatography over silica gel (hexane/ethyl acetate = 20/1, v/v) to give 2a (88.7 mg, 82%) in 97:3 ratio.

(E)-2-ethyl-3,4-dimethyl-1-phenylpenta-2,4-dien-1-ol (6a): a mixture of regioisomers in a ratio of 97:3

R_f = 0.50 (hexane-EtOAc, 4:1)

IR (neat): 3409 (br), 2964 (s), 2932 (s), 2873 (s), 1691 (w), 1630 (w), 1448 (s) 1371 (w), 1028 (s), 1003 (m), 748 (m), 700 (m) cm⁻¹.

¹H NMR (400 MHz, CDCl₃, major isomer): δ 0.81 (t, J = 7.3 Hz, 3 H), 1.78 (s, 1H), 1.85 (t, J = 1.5 Hz, 3 H), 1.87 (s, 3 H), 1.94 (dq, J = 7.3, 14.0 Hz, 1 H), 2.13 (dq, J = 7.3, 14.0 Hz, 1 H), 4.71 (dq, J = 0.98, 1.5 Hz, 1 H), 4.88 (dq, J = 0.98, 1.5 Hz, 1 H), 5.77 (s, 1 H), 7.21-7.39 (m, 5 H).

¹³C NMR (100 MHz, CDCl₃, major isomer): δ 15.8, 18.4, 22.1, 22.2, 72.7, 111.8, 125.7, 126.8, 128.2, 136.2, 137.1, 143.3, 147.7.

HRMS: m/z (M⁺) calcd for C₁₅H₂₀O: 216.1514; found: 216.1512.
NOE experimental data of product 6a (major isomer)

**[(E)-2-ethyl-1-(4-methoxyphenyl)-3,4-dimethylpenta-2,4-dien-1-ol (6b)]**: a mixture of regioisomers in a ratio of 95:5

R_f = 0.35 (hexane-EtOAc, 4:1)

IR (neat): 3422 (br), 2936 (s), 2914 (s), 2874 (w), 1612 (m), 1510 (s), 1443 (w), 1248 (w), 1171 (m), 1038 (m), 895 (w), 833 (w) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta =\)

- 0.83 (t, \(J = 7.3\) Hz, 3 H)
- 1.84 (t, 1.5 Hz, 3 H)
- 1.84 (s, 3H)
- 1.96 (dq, \(J = 7.3, 14.0\) Hz, 1 H)
- 2.01 (s, 1H)
- 2.12 (dq, \(J = 7.3, 14.0\) Hz, 1 H)
- 3.79 (s, 3 H)
- 4.70 (dq, \(J = 0.98, 1.5\) Hz, 1 H)
- 4.88 (dq, \(J = 0.98, 1.5\) Hz, 1 H)
- 5.71 (s, 1 H)
- 6.83-6.89 (m, 2 H)
- 7.26-7.32 (m, 2 H).

\(^13\)C NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta =\)

- 15.8, 18.2, 22.0, 22.1, 55.1, 72.2, 111.6,
- 113.5, 126.8, 135.3, 136.1, 136.5, 147.7, 158.4.

HRMS: m/z (M⁺) calcd for C\(_{16}\)H\(_{22}\)O\(_2\): 246.1620; found: 246.1621.

**[(E)-1-(4-chlorophenyl)-2-ethyl-3,4-dimethylpenta-2,4-dien-1-ol (6c)]**: a mixture of regioisomers in a ratio of 95:5

R_f = 0.45 (hexane-EtOAc, 4:1)
IR (neat): 3402 (br), 3074 (w), 2966 (s), 2934 (s), 2973 (s), 1631 (m) 1489 (s), 1448 (m), 1091 (s), 1014 (s), 897 (m), 783 (m) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$, major isomer): \(\delta\) 0.81 (t, \(J = 7.3\) Hz, 3 H), 1.85 (t, \(J = 1.5\) Hz, 3 H), 1.87 (s, 3 H), 1.89 (s, 1 H), 1.90 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 2.10 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 4.70 (dq, \(J = 0.98, 1.5\) Hz, 1 H), 4.89 (dq, \(J = 0.98, 1.5\) Hz, 1 H), 5.73 (s, 1 H), 7.28-7.33 (m, 4 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): \(\delta\) 15.8, 18.4, 22.1, 22.1, 72.0, 111.9, 127.1, 128.3, 132.5, 135.9, 137.5, 141.8, 147.4.

HRMS: \(m/z\) (M$^+$) calcd for C$_{15}$H$_{19}$ClO: 250.1124; found: 250.1121.

**\((E)-2\)-ethyl-1-mesityl-3,4-dimethylpenta-2,4-dien-1-ol (6d):** a mixture of regioisomers in a ratio of $\geq$99:1

\(R_f = 0.60\) (hexane-EtOAc, 4:1)

IR (neat): 3418 (br), 3074 (w), 2968 (s), 2934 (s), 2871 (s), 1610 (m) 1447 (s), 1036 (s), 853 (m), 799 (m) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$, major isomer): \(\delta\) 0.86 (t, \(J = 7.3\) Hz, 3 H), 1.60 (s, 3 H), 1.81 (s, 3 H), 2.21 (dq, \(J = 7.3, 14.6\) Hz, 1 H), 2.23 (dq, \(J = 7.3, 14.6\) Hz, 1 H), 2.24 (s, 1H), 2.25 (s, 3 H), 2.37 (s, 6 H), 4.65 (m, 1 H), 4.84 (m, 1 H), 5.88 (s, 1 H), 6.81 (s, 2 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): \(\delta\) 16.0, 18.3, 20.7, 21.0, 22.2, 33.4, 71.4, 111.2, 130.1, 135.1, 136.2, 136.4, 136.4, 136.7, 148.5.

HRMS: \(m/z\) (M$^+$) calcd for C$_{18}$H$_{26}$O: 258.1984; found: 250.1988.
(E)-4-ethyl-2,3-dimethyldeca-1,3-dien-5-ol (6e): a mixture of regioisomers in a ratio of 97:3

R_f = 0.70 (hexane-EtOAc, 4:1)
IR (neat): 3368 (br), 2961 (s), 2934 (s), 2873 (s), 2860 (s) 1629 (m), 1456 (m), 1371 (m), 895 (s), 735 (s) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta\) 0.89 (m, 3 H), 1.02 (t, \(J = 7.3\) Hz, 3 H), 1.21-1.72 (m, 8 H), 1.57 (s, 1 H) 1.75 (s, 3 H), 1.80 (t, \(J = 1.5\) Hz, 3 H), 2.04 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 2.15 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 4.56 (dd, \(J = 5.9, 8.3\) H, 1 H), 4.64 (dq, \(J = 0.98, 1.5\) H, 1 H), 4.84 (dq, \(J = 0.98, 1.5\) Hz, 1 H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta\) 13.9, 16.1, 17.7, 21.2, 22.1, 22.6, 25.8, 31.8, 35.8, 71.7, 111.3, 135.3, 136.5, 148.0.


(E)-1-cyclohexyl-2-ethyl-3,4-dimethylpenta-2,4-dien-1-ol (6f): a mixture of regioisomers in a ratio of 93:7

R_f = 0.70 (hexane-EtOAc, 4:1)
IR (neat): 3443 (br), 2928 (s), 2853 (s), 1703 (m), 1631 (w), 1450 (s) 1371 (w), 1001 (m), 893 (m), 790 (w) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta\) 0.78-1.04 (m, 2 H), 1.03 (t, \(J = 7.3\) Hz, 3 H), 1.10-1.32 (m, 3 H), 1.35-1.75 (m, 6 H), 1.76 (s, 3 H), 1.82 (t, \(J = 1.5\) Hz, 3 H), 2.02 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 2.12 (s, 1H), 2.14 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 4.21 (d, \(J = 9.8, 1\) H), 4.65 (dq, \(J = 0.98, 1.5\) Hz, 1 H), 4.85 (dq, \(J = 0.98, 1.5\) Hz, 1 H).
\(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta\) 16.2, 18.2, 21.6, 22.2, 26.0, 26.1, 26.5, 29.1, 30.2, 42.2, 76.4, 111.4, 135.1, 136.9, 148.2.

HRMS: \(m/z\) (M\(^+\)) calcd for C\(_{15}\)H\(_{26}\)O: 222.1984; found: 222.1985.

\((E)\)-4-ethyl-2,2,5,6-tetramethylhepta-4,6-dien-3-ol (6g): a mixture of regioisomers in a ratio of 97:3

\(R_f = 0.70\) (hexane-EtOAc, 4:1)

IR (neat): 3504 (br), 2966 (s), 2874 (s), 2249 (w), 1732 (m), 1697 (w), 1464 (m) 1364 (m), 1259 (m), 1047 (m), 1002 (m), 910 (s), 732 (s) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta\) 0.95 (s, 9 H), 1.01 (t, \(J = 1.5\) Hz, 3 H) 1.41 (d, \(J = 4.4\) Hz, 1 H), 1.76 (s, 3 H), 1.85 (t, \(J = 1.5\) Hz, 3 H), 2.09 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 2.18 (dq, \(J = 7.3, 14.0\) Hz, 1 H), 4.36 (d, \(J = 4.4\) Hz, 1 H), 4.69 (dq, \(J = 0.98, 1.5\) Hz, 1 H), 4.86 (dq, \(J = 0.98, 1.5\) Hz, 1 H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta\) 16.5, 19.8, 22.3, 22.5, 26.9, 37.6, 78.5, 111.6, 135.4, 137.2, 148.4.

HRMS: \(m/z\) (M\(^+\)) calcd for C\(_{13}\)H\(_{24}\)O: 196.1827; found: 196.1827.

\((E)\)-2-(3-methylbut-3-en-2-ylidene)-1-phenylhexan-1-ol (6h): a mixture of regioisomers in a ratio of 98:2

\(R_f = 0.55\) (hexane-EtOAc, 4:1)

IR (neat): 3410 (br), 3069 (w), 2959 (s), 2932 (s), 2872 (s), 2860 (s), 1691 (m) 1450 (s), 1375 (w), 1007 (m), 895 (m), 700 (s) cm\(^{-1}\).
$^1$H NMR (400 MHz, CDCl$_3$, major isomer): $\delta$ 0.75 (t, $J = 7.3$ Hz, 3 H), 0.98-1.39 (m, 4 H), 1.84 (s, 3 H), 1.87 (s, 3 H), 1.87 (dt, $J = 4.4$, 12.0 Hz, 1 H), 1.88 (s, 1 H) 2.07 (dt, 4.4, 12.0 Hz, 1 H), 4.69 (d, $J = 0.98$ Hz, 1 H), 4.88 (d, $J = 0.98$ Hz, 1 H), 5.75 (s, 1 H), 7.18-7.43 (m, 5 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 13.7, 18.4, 22.1, 23.3, 29.2, 33.2, 72.6, 111.7, 125.7, 126.7, 128.1, 135.1, 137.1, 142.6, 147.6.

HRMS: $m/z$ (M$^+$) calcd for C$_{17}$H$_{24}$O: 244.1827; found: 244.1831.

(*E*)-3,4-dimethyl-1,2-diphenylpenta-2,4-dien-1-ol (6i): a mixture of regioisomers in a ratio of >99:1

$R_f$ = 0.60 (hexane-EtOAc, 4:1)

IR (neat): 3417 (br), 3059 (m), 3028 (m), 2914 (m), 1633 (m), 1601 (m), 1493 (s), 1448 (s), 1011 (m), 894 (m), 700 (s) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$, major isomer): $\delta$ 1.62 (s, 3 H), 1.85 (d, $J = 7.3$ Hz, 1 H), 2.10 (s, 3 H), 4.54 (s, 1 H), 4.67 (s, 1 H), 5.96 (d, $J = 7.3$ Hz, 1 H), 6.80-6.93 (m, 2 H), 7.06-7.37 (m, 8 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 18.8, 22.3, 72.1, 114.2, 125.8, 126.6, 126.9, 127.4, 128.1, 130.4, 136.8, 138.1, 138.3, 142.8, 147.0.

HRMS: $m/z$ (M$^+$) calcd for C$_{19}$H$_{20}$O: 264.1514; found: 264.1518.

(*Z*)-3,4-dimethyl-2-(trimethylsilyl)-1-phenylpenta-2,4-dien-1-ol (6j): a mixture of regioisomers in a ratio of >99:1
\( R_f = 0.60 \) (hexane-EtOAc, 4:1)

IR (neat): 3458 (br), 3069 (w), 2952 (m), 2897 (m), 1638 (m), 1597 (m) 1492 (m), 1448 (m), 1245 (s), 1020 (m), 840 (s), 760 (m), 701 (s) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \( \delta \) 0.00 (s, 9 H), 1.83 (s, 3 H), 1.92 (s, 3 H), 1.92 (d, \( J = 3.4 \) Hz, 1 H), 4.83 (s, 1 H), 4.86 (s, 1 H), 5.76 (d, \( J = 3.4 \) Hz, 1 H), 7.19-7.38 (m, 5 H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer): \( \delta \) 2.4, 19.9, 22.4, 74.0, 113.5, 125.8, 126.6, 128.1, 136.8, 143.5, 149.7, 153.4.

HRMS: \( m/z \) (M\(^+\)) calcd for C\(_{16}\)H\(_{24}\)OSi: 260.1596; found: 260.1597.

\((E)-2-(\text{but-3-en-2-ylidene})-1\text{-phenylhexan-1-ol (6k)}\): a mixture of regioisomers in a ratio of >99:1

\( R_f = 0.55 \) (hexane-EtOAc, 4:1)

IR (neat): 3369 (br), 2957 (s), 2933 (s), 2871 (m), 1602 (w), 1492 (w) 1450 (m), 1153 (w), 1018 (s), 900 (s), 734 (m), 700 (s) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \( \delta \) 0.80 (t, \( J = 7.3 \) Hz, 3 H), 0.81-1.43 (m, 4 H), 1.79 (d, \( J = 3.4 \) Hz, 1 H), 1.97 (s, 3 H), 2.05 (dt, \( J = 4.9, 12.8 \) Hz, 1 H), 2.20 (dt, 4.9, 12.8 Hz, 1 H), 5.16 (d, \( J = 10.7 \) Hz, 1 H), 5.32 (d, \( J = 17.1 \) Hz, 1 H), 5.95 (d, \( J = 3.4 \) Hz, 1 H), 6.80 (dd, \( J = 10.7, 17.1 \) Hz, 1H), 7.24-7.36 (m, 5 H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer): \( \delta \) 13.6, 13.7, 23.3, 27.4, 33.6, 72.9, 114.1, 125.7, 127.0, 128.2, 129.5, 136.0, 140.7, 141.1.

HRMS: \( m/z \) (M\(^+\)) calcd for C\(_{16}\)H\(_{22}\): 230.1671; found: 230.1662.
NOE experimental data of product 2k (major isomer)

\((\textit{E})\)-3-methyl-1,2-diphenylpenta-2,4-dien-1-ol (6l): a mixture of regioisomers in a ratio of >99:1

\(R_f = 0.60\) (hexane-EtOAc, 4:1)

IR (neat): 3416 (br), 3059 (m), 3026 (m), 2928 (m), 1811 (w), 1684 (m), 1601 (m), 1493 (s), 1448 (s), 997 (s), 905 (m), 752 (m), 700 (s) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta\) 1.88 (m, 1 H), 2.12 (s, 3 H), 4.98 (d, \(J = 10.7\) Hz, 1 H), 5.30 (d, \(J = 16.9\) Hz, 1 H), 6.08 (m, 1 H), 6.22 (dd, \(J = 10.7, 16.9\) Hz, 1 H), 6.83 (m, 2 H), 7.17-7.34 (m, 8 H).

\(^13\)C NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta\) 13.8, 72.5, 114.3, 125.9, 127.0, 127.1, 127.8, 128.1, 130.6, 131.7, 137.2, 137.7, 141.7, 142.5.

HRMS: \(m/z\) (M\(^+\)) calcd for C\(_{18}\)H\(_{18}\)O: 250.1358; found: 250.1364.

\((\textit{Z})\)-2-ethyl-4-methyl-1,3-diphenylpenta-2,4-dien-1-ol (6m): a mixture of regioisomers in a ratio of >99 : 1

\(R_f = 0.60\) (hexane-EtOAc, 4:1)

IR (neat) 3398 (m), 3074 (m), 3024 (m), 2966 (s), 2933 (m), 2874 (m), 1601 (w), 1491 (m) 1448 (s), 1024 (m), 764 (m), 702 (s) cm\(^{-1}\).
$^1$H NMR (400 MHz, CDCl$_3$, major isomer): $\delta$ 0.89 (t, $J = 7.3$ Hz, 3 H), 1.71 (br s, 1 H), 1.75 (s, 3 H), 2.02 (dq, $J = 15.1$, 7.3 Hz, 1 H), 2.33 (dq, $J = 15.1$, 7.3 Hz, 1 H), 4.99 (m, 2 H), 5.47 (s, 1 H), 7.19-7.38 (m, 10 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, major isomer): $\delta$ 15.9, 21.4, 21.4, 73.5, 113.4, 125.6, 126.7, 126.9, 128.1, 128.3, 128.8, 139.0, 140.5, 143.1, 144.2, 145.8.

HRMS: $m/z$ (M$^+$) calcd for C$_{20}$H$_{22}$O: 278.1671; found 278.1674.

**Procedure for Au-Catalyzed cyclization of allenyl alcohol** (Scheme 5)

The reaction was undertaken as follows: Into a nitrogen-purged flask with AuCl (11.6 mg, 0.05 mmol) was introduced successively dichloromethane (10 mL) and allenyl alcohol 1a (216 mg, 1 mmol) via syringe. The homogeneous mixture was stirred at room temperature for 4 days, during which the reaction was monitored by TLC. The reaction mixture was concentrated in vacuo, then the residual oil was subjected to column chromatography over silica gel (hexane/ethyl acetate = 50/1, v/v) to give 5a (169 mg, 78%) in 83:17 diastereomeric ratio.

**2-ethyl-5,6-dihydro-2,4-dimethyl-6-phenyl-2H-pyran (5a, 5b):** a mixture of diastereomers 3a, 3b in a ratio of 83:17

$R_f = 0.70$ (hexane-EtOAc, 4:1)

IR (neat): 3089 (w), 3053 (w), 2968 (s), 2928 (s), 2887 (m), 1680 (w) 1495 (w), 1450 (s), 1377 (m), 1200 (m), 1096 (m), 752 (s), 698 (s) cm$^{-1}$. 

50
$^1$H NMR (400 MHz, C$_6$D$_6$, 3a): $\delta$ 1.02 (t, $J$ = 7.3 Hz, 3 H), 1.22 (s, 3 H), 1.55 (s, 3 H), 1.72 (q, $J$ = 7.3 Hz, 2 H), 1.79 (dd, $J$ = 3.2, 16.6 Hz, 1 H), 2.04 (dd, $J$ = 10.7, 16.6 Hz, 1 H), 4.66 (dd, $J$ = 3.2, 10.7 Hz, 1 H), 5.16 (s, 1 H), 7.10-7.45 (m, 5 H).

$^{13}$C NMR (100 MHz, C$_6$D$_6$, 3a): $\delta$ 8.4, 23.0, 24.9, 35.7, 38.4, 70.7, 75.6, 126.1, 127.8, 128.0, 128.2, 131.4, 144.1.

$^1$H NMR (400 MHz, C$_6$D$_6$, 3b): $\delta$ 0.90 (t, $J$ = 7.3 Hz, 3 H), 1.30 (s, 3 H), 1.53 (s, 3 H), 1.75 (q, $J$ = 7.3 Hz, 2 H), 1.81 (dd, $J$ = 3.4, 16.8 Hz, 1 H), 2.08 (dd, $J$ = 10.7, 16.8 Hz, 1 H), 4.64 (dd, $J$ = 3.4, 10.7 Hz, 1 H), 5.34 (s, 1 H), 7.10-7.45 (m, 5 H).

$^{13}$C NMR (100 MHz, C$_6$D$_6$, 3b): $\delta$ 8.4, 23.0, 26.2, 31.3, 38.0, 70.4, 75.3, 127.1, 128.0, 128.4, 128.8, 130.2, 143.9.

HRMS: m/z (M$^+$) calcd for C$_{15}$H$_{20}$O: 216.1514; found 216.1522.
References


14. Electronic and steric parameters of NHC ligands are reported:


Chapter 2

Ni-Catalyzed Multicomponent Coupling Reaction of Alkyne, Buta-1,3-diene, and Dimethylzinc under Carbon Dioxide

\[
\begin{align*}
\text{R}_1^1 \quad & + \quad \text{R}_2^2 \quad \text{CO}_2 \quad \xrightarrow{\text{Ni-catalyst Me}_2\text{Zn}} \quad \text{R}_1^1 \quad \text{Me} \quad \text{R}_2^2 \quad \text{CO}_2\text{H}
\end{align*}
\]

Summary: Nickel catalyst promoted multicomponent coupling reaction of alkyne, 1,3-butadiene, and dimethylzinc under carbon dioxide. Various kind of alkyne could be used in this coupling reaction. On the other hand, in the case of diethylzinc, the reductive coupling proceeded without insertion of alkyne to give dienylcarboxylic acids instead of trienylcarboxylic acids.
Introduction

Multi-component coupling reactions are among the most efficient strategies for C–C bond transformations in a single step.\textsuperscript{1} This strategy is especially convenient and straightforward for coupling reactions involving alkyne insertion to prepare unsaturated hydrocarbons, alcohols, amines, and carboxylic acids.\textsuperscript{2} Therefore, alkynes can serve as important carbon skeletons for the synthesis of useful physiologically active molecules and fine chemicals.\textsuperscript{3}

\textbf{Scheme 1.} Ni-Catalyzed Four Component Coupling Reactions of Alkyne, 1,3-Butadiene, Aldehyde, and Dimethylzinc

The Ni-catalyzed multi-component coupling reaction of alkynes, conjugated dienes, and carbonyls in the presence of dimethylzinc to form 3,6-octadienyl alcohols as a sole product with excellent regio- and stereoselectivities has been reported previously (Scheme 1).\textsuperscript{4} This type of transformation occurs via oxanickelacycle intermediates through the oxidative coupling of alkynes, dienes, and carbonyls with a Ni(0) catalyst.
Scheme 2. Ni-Catalyzed Five Component Coupling Reactions of Alkyne, 1,3-Butadiene, Aldimine, and Dimethylzinc

These coupling reaction also can be applied to a similar coupling reaction with aldimines, prepared from an amine and carbonyls in situ, to construct dienylamines and trienylamines depending on the nature of the amine and ligands (Scheme 2).\(^5\) Both of these transformations using aldehydes and aldimines are achieved via a C-C bond coupling reaction of conjugated dienes with alkynes to form linear carbon chain frameworks with high regio- and stereoselectivities.

The present study describes the Ni-catalyzed four-component coupling reaction of alkyne, 1,3-butadiene, and dimethylzinc under carbon dioxide to provide 2-vinyl-5\(E\),8\(Z\)-decadienoic acid in high regio- and stereoselectivities (Scheme 3).

Scheme 3. Ni-Catalyzed Coupling Reaction of Alkyne, 1,3-Butadiene, and Organozinc Reagent under Carbon Dioxide
Results and Discussion

Initially, the reaction was performed in the presence of 0.1 mmol Ni catalyst, 1.0 mmol 3-hexyne, 2.5 mmol 1,3-butadiene, and 1.2 mmol dimethylzinc under 1 atm carbon dioxide. Results using various ligands and solvents are summarized in Table 1. In the absence of a ligand, a complex mixture was obtained. This result was complementary to the multi-component coupling of aldehydes or aldimines under a nitrogen atmosphere (entry 1, Table 1). In experiments involving mono- and bidentate phosphine ligands, and NHC ligands, Ph$_3$P ligand was the best choice for providing the expected product 3aa in 91% yield (entry 3, Table 1). The most effective solvent was tetrahydrofuran.
Table 1. Optimization of Reaction Conditions for Ni-Catalyzed Coupling Reaction of Alkyne, 1,3-Butadiene, and Organozinc Reagent under Carbon Dioxide

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand (mmol)</th>
<th>solvent</th>
<th>yield of 3aa (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>THF</td>
<td>complex mixture</td>
</tr>
<tr>
<td>2</td>
<td>$n$-Bu$_3$P (0.2)</td>
<td>THF</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>Ph$_3$P (0.2)</td>
<td>THF</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>Ph$_3$P (0.2)</td>
<td>DMSO</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>Ph$_3$P (0.2)</td>
<td>toluene</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>Ph$_3$P (0.2)</td>
<td>Et$_2$O</td>
<td>35</td>
</tr>
<tr>
<td>7</td>
<td>Ph$_3$P (0.2)</td>
<td>CH$_2$Cl$_2$</td>
<td>complex mixture</td>
</tr>
<tr>
<td>8</td>
<td>dppf (0.1)</td>
<td>THF</td>
<td>51</td>
</tr>
<tr>
<td>9</td>
<td>Xantphos (0.1)</td>
<td>THF</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>IPr (0.1)</td>
<td>THF</td>
<td>complex mixture</td>
</tr>
</tbody>
</table>

*The reaction was undertaken in the presence of Ni(cod)$_2$ (0.1 mmol), ligand (0.1-0.2 mmol), 3-hexyne (1 mmol), 1,3-butadiene (2.5 mmol), dimethylzinc (1.2 mmol) in THF (2 mL) at r.t. for 24 h under carbon dioxide (1 atm). dppf: 1,1’-bis(diphenylphosphino)ferrocene. Xantphos: 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene. IPr: 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene.*
Next, a similar coupling reaction using a wide variety of alkynes under optimized conditions was investigated (Table 1, entry 3) and the results are summarized in Table 2. Methyl- and \( n \)-propyl-substituted alkynes participated in the coupling reaction to provide 2-vinyl-5,8-decadienoic acid analogs as a single product with excellent regio- and stereoselectivities (entries 1 and 2, Table 2). A diphenyl-substituted alkyne also was used in the coupling reaction to provide diphenyl-substituted decadienoic acid \( 3\text{da} \) in reasonable yield (entry 3, Table 2). Unsymmetrical substituted alkynes also were investigated and results showed that regioselectivity depended on the type of the substituent. For example, 1-phenyl-1-butyne and 2-methyl-1-buten-3-yne yielded the expected products \( 3\text{ea} \) and \( 3\text{fa} \) with high regioselectivities (entries 4 and 5, Table 2).\(^7\) The less sterically hindered carbon atoms of the alkynes tended to combine to form dimerized butadienes. Although an unsymmetrical alkyne with a trimethylsilyl group could participate in the coupling reaction, regioselectivity with respect to the alkyne was moderate, irrespective of the type of the substituent such as methyl and phenyl groups (entries 6 and 7, Table 2).
**Table 2.** Ni-Catalyzed Coupling Reaction of Various Alkyne, 1,3-Butadiene, and Organozinc Reagent under Carbon Dioxide$^a$

![Reaction Scheme]

<table>
<thead>
<tr>
<th>entry</th>
<th>$R^1$</th>
<th>$R^2$ (1)</th>
<th>yield of 3 (%)</th>
<th>ratio$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>Me (1b)</td>
<td>3ba : 94</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>$n$-Pr</td>
<td>$n$-Pr (1c)</td>
<td>3ca : 64</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>Ph (1d)</td>
<td>3da : 74</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>Ph</td>
<td>Et (1e)</td>
<td>3ea : 73</td>
<td>6:1</td>
</tr>
<tr>
<td>5</td>
<td>isopropenyl</td>
<td>Et (1f)</td>
<td>3fa : 72</td>
<td>10:1</td>
</tr>
<tr>
<td>6</td>
<td>TMS</td>
<td>Me (1g)</td>
<td>3ga : 35</td>
<td>3:1</td>
</tr>
<tr>
<td>7</td>
<td>TMS</td>
<td>Ph (1h)</td>
<td>3ha : 31</td>
<td>3:1</td>
</tr>
</tbody>
</table>

$^a$ The reaction was undertaken in the presence of Ni(cod)$_2$(0.1 mmol), Ph$_3$P (0.2 mmol), Alkyne (1 mmol), 1,3-butadiene (2.5 mmol), dimethylzinc (1.2 mmol) in THF (2 mL) at r.t. for 24 h under carbon dioxide (1 atm).  

$^b$ Regioisomeric ratio.

A wide variety of organozinc reagents, along with trimethylborane and trimethylaluminum in place of dimethylzinc, were investigated (Table 3). Dibenzylzinc, prepared from zinc chloride and two equivalents of benzylmagnesium bromide, participated in the expected coupling reaction to afford unsaturated carboxylic acid 3ab in good yield with high region- and stereoselectivities (entry 1, Table 3). Diethylzinc and
di(isopropyl)zinc provided the 2-vinylheptenoic acids 4 and 5 without producing the expected dienyl carboxylic acids 3 (entries 2 and 3, Table 3). These organozinc reagents served as hydrogen transfer agents, not to promote the insertion of alkynes, but in the reductive coupling reaction of butadiene and carbon dioxide. Diphenyl and divinylzinc provided phenyl- and vinyl-substituted 2-vinylheptenoic acids, respectively, and the desired coupling product 3 was not produced (entries 4 and 5, Table 3). Trimethylborane and trimethylaluminum induced a similar four-component coupling reaction with dimethylzinc to afford 3aa as a sole product in reasonable yield (entries 6 and 7, Table 4).
Table 3. Ni-Catalyzed Coupling Reaction of Alkyne, 1,3-Butadiene, and Various Organometallic Reagent under Carbon Dioxide

<table>
<thead>
<tr>
<th>entry</th>
<th>RnM (2)</th>
<th>yield of 3, 4, 5 (%) [ratio]b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bn₂Zn (2b)</td>
<td>3ab : 82</td>
</tr>
<tr>
<td>2</td>
<td>Et₂Zn (2c)</td>
<td>4c : 49 (R = H), 5c : 49 (R = H)</td>
</tr>
<tr>
<td>3</td>
<td>i-Pr₂Zn (2d)</td>
<td>4c : 48 (R = H), 5c : 48 (R = H)</td>
</tr>
<tr>
<td>4</td>
<td>Ph₂Zn (2e)</td>
<td>4e : 80, 5e : 19 [1:1]</td>
</tr>
<tr>
<td>5</td>
<td>(CH₂CH)₂Zn (2f)</td>
<td>4f : 85 (R = H), 5f : 14 (R = H)</td>
</tr>
<tr>
<td>6</td>
<td>Me₃B (2g)</td>
<td>3aa : 50</td>
</tr>
<tr>
<td>7</td>
<td>Me₃Al (2h)</td>
<td>3aa : 70</td>
</tr>
</tbody>
</table>

a The reaction was undertaken in the presence of Ni(cod)₂ (0.1 mmol), Ph₃P (0.2 mmol), 3-hexyne (1 mmol), 1,3-butadiene (2.5 mmol), RnM (1.2 mmol) in THF (2 mL) at r.t. for 24 h under carbon dioxide (1atm).

b Diastereomeric ratio.

A plausible reaction mechanism for the Ni-catalyzed four-component coupling reaction of alkyne, 1,3-butadiene, and dimethylzinc under carbon dioxide is shown in Scheme 4. Oxidative cyclization of two equivalents of 1,3-butadiene accompanying dimerization promoted by Ni(0) catalyst proceeds to form the bis-π-allylnickel complex I, which is in
equilibrium with the $\sigma$-allyl-$\pi$-allylnickel species $\text{II}$.\textsuperscript{8} Because $\sigma$-allyl-$\pi$-allylnickel $\text{II}$ possesses greater nucleophilicity on the $\sigma$-allylnickel moiety,\textsuperscript{9} carbon dioxide can react at the $\sigma$-allylic carbon atom to provide the oxa-$\pi$-allylnickel species $\text{III}$ with coordination of the alkynes as spectator ligands. Alkyne insertion proceeded smoothly following carbonickelation to form oxanickelacycle $\text{IV}$, which then underwent transmetallation with dimethylzinc to provide the branched unsaturated carboxylic acid predominantly, similarly to the multi-component coupling reaction with the aldimines that produced the straight-chain compound.

Scheme 4. Plausible Reaction Mechanism of Ni-Catalyzed Coupling Reaction of Alkyne, 1,3-Butadiene, and Organozinc Reagent under Carbon Dioxide
In summary, a Ni-catalyzed multi-component coupling reaction involving alkyne 1,3-butadiene, dimethylzinc, and carbon dioxide was developed that provided 2-vinyl-5\textit{E},8\textit{Z}-decadienoic acid in excellent yield with high region- and stereoselectivities. These transformations can be applied to the synthesis of terpenes and physiologically active molecules involving carbon dioxide as a carbon source, and are currently under investigation.
Experimental Section

Reactions employed oven-dried glassware unless otherwise noted. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator (Merck Silica gel 60F$_{254}$). Flash chromatography columns were packed with 230-400 mesh silica gel as a slurry in hexane. Gradient flash chromatography was conducted eluting with a continuous gradient from hexane to the indicated solvent. Proton and carbon NMR data were obtained with a JEOL JNM-AL400 with tetramethylsilane as an internal standard. Chemical shift values were given in ppm downfield from the internal standard. Infrared spectra were recorded with a JASCO A-100 FT-IR spectrophotometer. High resolution mass spectra (HRMS) were measured with a JEOL JMS-700N. Distillation were carried out in a Kugelrohr apparatus (SIBATA glass tube oven GTO-350RG). Boiling points are meant to refer to the oven temperature ($\pm$ 1 °C).

Solvents and Reagents

Tetrahydrofuran, toluene, and diethyl ether were dried and distilled from benzophenone-sodium immediately prior to use under nitrogen atmosphere. DMSO and dichloromethane were distilled over calcium hydride. Dimethylzinc, diethylzinc (1 M hexane), trimethylaluminum (1.0 M in hexane), Ni(cod)$_2$ (KANTO Kagaku), PPh$_3$, $n$-Bu$_3$P, dppf, Xantphos (Aldrich) IPr NHC ligand (Tokyo Kasei Kogyo Co., Ltd) were used without further purification. Dibenzylzinc, diisopropylzinc, diphenylzinc, and divinylzinc were prepared from ZnCl$_2$ with 2-equivalents of benzyl, phenyl, isopropyl,
and vinylmagnesium bromide, respectively. Trimethylborane was prepared from trichlororborane (1 M in hexane, Aldrich) and 3-equi valents of methyl lithium (1 M in hexane, KANTO Kagaku). 3-Hexyne, 4-octyne, diphenylacetylene, 1-phenyl-1-butyne, 2-methyl-1-hexen-3-yne, 1-trimethylsilylpropyne, 1-phenyl-2-trimethylsilylacet ylene (Tokyo Kasei Kogyo Co., Ltd) were purchased and distilled prior to use. 1,3-Butadiene (Tokyo Kasei Kogyo Co., Ltd) was purchased, and was liquefied by cooling at -78 °C (dry ice/isopropanol) prior to use under argon atmosphere. 1,3-Butadiene could be measured by syringe kept cool in the freezer as well beforehand, and then was introduced into the reaction mixture at room temperature.

**Preparation of diisopropylzinc, diphenylzinc, divinylzinc, and dibenzylzinc reagent:**

A 100 mL Schlenk flask equipped with a rubber septum was charged with ZnCl₂ solution (2 mL of 1 M in ethyl ether, 2 mmol, Tokyo Kasei Kogyo Co., Ltd) under nitrogen atmosphere. A solution of isopropyl magnesium bromide (4 mL of 1 M in THF, 4 mmol, Aldrich) was added to the ZnCl₂ solution via syringe at 0 °C and diluted with 2 mL of THF. The reaction mixture was stirred at room temperature for 12 hours. Thus, diisopropylzinc solution (0.25 M) was prepared prior to use. Diphenylzinc (0.25 M), divinylzinc (0.25 M), and dibenzylzinc (0.25 M) were prepared following the above procedure from phenyl magnesium bromide (4 mL of 1 M in THF, 4 mmol, KANTO Kagaku), vinyl magnesium bromide (4 mL of 1 M in THF, 4 mmol, Aldrich), and benzyl magnesium chloride (4.5 mL of 0.9 M in THF, 4.05 mmol, Tokyo Kasei Kogyo Co., Ltd), respectively.
Preparation of trimethylborane reagent

A 100 mL Schlenk flask equipped with a rubber septum was charged with BCl$_3$ solution (2 mL of 1 M in hexane, 2 mmol, Aldrich) under nitrogen atmosphere. A solution of methyl lithium (6 mL of 1 M in hexane, 6 mmol, KANTO Kagaku) was added to the BCl$_3$ solution via syringe at 0 °C. The reaction mixture was stirred at room temperature for 12 hours. Thus, trimethylborane (0.25 M solution) reagents were prepared prior to use.

Typical procedure for the four-component coupling reaction of 3-hexyne, 1,3-butadiene, Me$_2$Zn under carbon dioxide (entry 3, Table 1)

The reaction was undertaken as follows: Into a carbon dioxide-purged flask with Ni(cod)$_2$ (27.5 mg, 0.1 mmol) and PPh$_3$ (52.5 mg, 0.2 mmol), was introduced successively THF (2 mL), 3-hexyne (82.2 mg, 1 mmol), 1,3-butadiene (220 μL, 2.5 mmol), and dimethylzinc (1.2 mL of 1 M hexanes, 1.2 mmol) via syringe. The homogeneous mixture was stirred at room temperature for 24 h, during which the reaction was monitored by TLC. After dilution with ethyl acetate (30 mL), the mixture was washed successively with 2 M-HCl and brine, and then dried (MgSO$_4$) and concentrated in vacuo. The residual oil was subjected to column chromatography over silica gel (hexane/ethyl acetate = 4/1, v/v) to give 1a (227.8 mg, 91%) as a single isomer.
**(5E,8E)-8-Ethyl-9-methyl-2-vinylundeca-5,8-dienoic acid (3aa)**

\[ R_f = 0.30 \text{ (hexane-EtOAc, 4:1)} \]

IR (neat): 3075 (s), 2960 (s), 2872 (s), 2660 (br m), 1708 (s), 1639 (m), 1412 (m), 1373 (m), 1151 (m) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)): \( \delta = 0.97 \) (t, \( J = 7.6 \) Hz, 3 H), 0.98 (t, \( J = 7.6 \) Hz, 3 H), 1.53 (ddt, \( J = 13.2, 8.5, 5.9 \) Hz, 1 H), 1.62 (s, 3 H), 1.83 (ddt, \( J = 13.2, 8.5, 6.6 \) Hz, 1 H), 1.90 – 1.98 (m, 2 H), 2.01 (q, \( J = 7.6 \) Hz, 2 H), 2.07 (q, \( J = 7.6 \) Hz, 2 H), 2.72 (d, \( J = 5.9 \) Hz, 2 H), 3.00 (q, \( J = 8.5 \) Hz, 1 H), 4.94 (dd, \( J = 10.1, 1.2 \) Hz, 1 H), 5.00 (dd, \( J = 17.1, 1.2 \) Hz, 1 H), 5.31 (dt, \( J = 15.1, 6.3 \) Hz, 1 H), 5.39 (dt, \( J = 15.1, 5.9 \) Hz, 1 H), 5.74 (ddd, \( J = 17.1, 10.1, 8.5 \) Hz, 1 H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 13.2, 13.6, 17.4, 24.7, 27.0, 29.6, 29.7, 35.0, 48.8, 117.5, 128.2, 129.3, 130.5, 131.3, 135.0, 177.6.\)

HRMS: \( m/z \) (M\(^+\)) calcd for C\(_{16}\)H\(_{26}\)O\(_2\): 250.1933; found: 250.1917.

**\((E)\)-8,9-Dimethyl-2-vinyldeca-5,8-dienoic acid (3ba)**

\[ R_f = 0.30 \text{ (hexane-EtOAc, 4:1)} \]

IR (neat): 3065 (m), 2920 (s), 2860 (m), 2658 (br m), 1709 (s), 1639 (m), 1414 (m), 1373 (m), 1153 (m) cm\(^{-1}\).
1H NMR (400 MHz, C6D6): δ = 1.61 (s, 3H), 1.63 (ddt, J = 13.2, 7.7, 6.6 Hz, 1 H), 1.65 (s, 6 H), 1.86 (ddt, J = 13.2, 8.5, 6.6 Hz, 1 H), 1.96 – 2.11 (m, 2 H), 2.70 (d, J = 5.9 Hz, 2 H), 3.05 (q, J = 8.5 Hz, 1 H), 4.94 (dd, J = 9.4, 1.1 Hz, 1 H), 5.00 (dd, J = 17.1, 1.2 Hz, 1 H), 5.29 (dt, J = 15.2, 6.1 Hz, 1 H), 5.37 (dt, J = 15.2, 5.9 Hz, 1 H), 5.74 (ddd, J = 17.1, 9.4, 8.5 Hz, 1 H).

13C NMR (100 MHz, CDCl3): δ = 18.2, 20.1, 20.6, 29.8, 31.7, 37.7, 49.0, 117.7, 124.6, 125.8, 128.8, 129.1, 135.2, 178.0.

HRMS: m/z (M+) calcd for C14H22O2: 222.1620; found: 222.1626.

(5E,8E)-9-Methyl-8-propyl-2-vinyldodeca-5,8-dienoic acid (3ca)

RF = 0.30 (hexane-EtOAc, 4:1)

IR (neat): 2959 (br s), 2932 (s), 2872 (m), 2665 (br m), 1709 (s), 1638 (m), 1452 (m), 1420 (m), 1286 (m), 991 (m), 968 (m), 922 (m) cm⁻¹.

1H NMR (400 MHz, CDCl3): δ = 0.86 (t, J = 7.6 Hz, 3 H), 0.89 (t, J = 7.6 Hz, 3 H), 1.34 (tq, J = 7.8, 7.6 Hz, 2 H), 1.37 (tq, J = 7.8, 7.6 Hz, 2 H), 1.56 – 1.65 (m, 1 H), 1.61 (s, 3 H), 1.81 – 1.87 (m, 1 H), 1.94 – 2.05 (m, 2 H), 1.98 (q, J = 7.8 Hz, 2 H), 1.99 (q, J = 7.8 Hz, 2 H), 2.68 (d, J = 4.5 Hz, 2 H), 3.04 (q, J = 8.8 Hz, 1 H), 5.13 (d, J = 10.5 Hz, 1 H), 5.16 (d, J = 17.6 Hz, 1 H), 5.32 – 5.38 (m, 2 H), 5.80 (ddd, J = 17.6, 10.5, 8.8 Hz, 1 H).

13C NMR (100 MHz, CDCl3): δ = 14.1, 14.3, 17.9, 21.7, 22.1, 29.7, 31.7, 34.2, 35.5, 36.3, 49.1, 117.7, 128.4, 129.5, 129.7, 130.8, 135.2, 179.3.
HRMS: $m/z$ ($M^+$) calcd for $C_{18}H_{30}O_2$: 278.2246; found: 278.2246.

![Chemical Structure](image)

**(5E,8Z)-8,9-Diphenyl-2-vinyldeca-5,8-dienoic acid (3da)**

$R_f = 0.40$ (hexane-EtOAc, 4:1)

IR (neat): 3030 (m), 2932 (s), 2858 (m), 2664 (br m), 1705 (s), 1637 (m), 1599 (m), 1490 (m), 1443 (m), 1373 (m), 764 (s), 700 (s) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.58$ (ddt, $J = 13.2, 8.5, 6.8$ Hz, 1 H), 1.83 (ddt, $J = 13.2, 8.5, 6.8$ Hz, 1 H), 1.97 − 2.07 (m, 2 H), 2.03 (s, 3 H), 2.98 (q, $J = 8.5$ Hz, 1 H), 3.24 (d, $J = 4.2$ Hz, 2 H), 5.11 (d, $J = 9.8$ Hz, 1 H), 5.14 (d, $J = 17.1$ Hz, 1 H), 5.42 (dt, $J = 15.1, 5.4$ Hz, 1 H), 5.47 (dt, $J = 15.2, 4.2$ Hz, 1 H), 5.77 (ddd, $J = 17.1, 9.8, 8.5$ Hz, 1 H), 6.92 − 7.08 (m, 10 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 21.1, 29.7, 31.6, 38.3, 48.9, 117.8, 125.4, 125.5, 127.3, 127.4, 128.0, 129.0, 129.4, 129.5, 134.1, 135.1, 135.4, 143.3, 144.3, 178.8.

HRMS: $m/z$ ($M^+$) calcd for $C_{24}H_{26}O_2$: 346.1933; found: 346.1935.

![Chemical Structure](image)

**(5E,8E)-8-Ethyl-9-phenyl-2-vinyldeca-5,8-dienoic acid (3ea):** a mixture of regioisomers in a 6 : 1 ratio

$R_f = 0.40$ (hexane-EtOAc, 4:1)
IR (neat): 3025 (s), 2970 (s), 2932 (s), 2654 (br m), 1705 (s), 1639 (m), 1599 (w), 1491 (m), 1286 (m), 968 (m), 924 (m), 766 (s), 702 (s) cm⁻¹.

¹H NMR (400 MHz, CDCl₃, major isomer): δ = 0.90 (t, J = 7.6 Hz, 3 H), 1.66 (ddt, J = 13.2, 9.0, 6.6 Hz, 1 H), 1.85 – 1.90 (m, 1 H), 1.88 (q, J = 7.6 Hz, 2 H), 1.92 (s, 3 H), 2.04 – 2.13 (m, 2 H), 2.83 (d, J = 5.9 Hz, 2 H), 3.05 (q, J = 8.6 Hz, 1 H), 5.15 (d, J = 10.0 Hz, 1 H), 5.19 (d, J = 17.1 Hz, 1 H), 5.44 (dt, J = 15.1, 5.6 Hz, 1 H), 5.46 (dt, J = 15.1, 6.0 Hz, 1 H), 5.80 (ddd, J = 17.1, 10.0, 8.6 Hz, 1 H), 7.11 (dd, J = 7.3, 1.6 Hz, 1 H), 7.25 – 7.30 (m, 4 H).

¹³C NMR (100 MHz, CDCl₃, major isomer): δ = 13.4, 20.9, 26.1, 29.8, 31.7, 34.2, 49.1, 117.8, 125.7, 127.9, 128.0, 128.9, 129.0, 131.6, 135.0, 135.2, 145.1, 178.7.

¹H NMR (400 MHz, CDCl₃, minor isomer): δ = 0.92 (t, J = 7.6 Hz, 3 H), 1.60 – 1.64 (m, 1 H), 1.78 (s, 3 H), 1.82 – 1.90 (m, 3 H), 1.95 – 2.00 (m, 2 H), 2.83 (d, J = 5.9 Hz, 2 H), 3.00 (q, J = 8.6 Hz, 1 H), 5.09 (d, J = 10.0 Hz, 1 H), 5.11 (d, J = 17.1 Hz, 1 H), 5.29 – 5.33 (m, 2 H), 5.77 (m, 1 H), 7.07 (dd, J = 7.3, 1.6 Hz, 1 H), 7.16 – 7.20 (m, 4 H).

¹³C NMR (100 MHz, CDCl₃, minor isomer) δ = 13.2, 17.0, 28.5, 29.6, 31.6, 38.0, 48.8, 117.8, 125.7, 127.7, 128.4, 128.6, 129.0, 131.6, 135.0, 135.2, 143.9, 178.7.

HRMS: m/z (M⁺) calcd for C₂₀H₂₆O₂: 298.1933; found: 298.1943.

NOE experimental data of product 3ea
(5E,8E)-8-Ethyl-9,10-dimethyl-2-vinylundeca-5,8,10-trienoic acid (3fa): a mixture of regioisomers in a 10:1 ratio

\[ R_f = 0.40 \text{ (hexane-EtOAc, 4:1)} \]

IR (neat): 2950 (br s), 2878 (s), 2669 (br m), 1709 (s), 1638 (m), 1375 (m), 1192 (m), 970 (m), 922 (m) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer): \(\delta = 0.92 \) (t, \(J = 7.6 \text{ Hz}, 3 \text{ H}\), 1.57 – 1.66 (m, 1 H), 1.69 (s, 3 H), 1.78 (dd, \(J = 1.2, 1.0 \text{ Hz}, 3 \text{ H}\), 1.86 (ddt, \(J = 13.2, 8.8, 6.8 \text{ Hz}, 1 \text{ H}\), 2.00 – 2.16 (m, 2 H), 2.03 (q, \(J = 7.6 \text{ Hz}, 2 \text{ H}\), 2.72 (d, \(J = 5.1 \text{ Hz}, 2 \text{ H}\), 3.06 (q, \(J = 8.8 \text{ Hz}, 1 \text{ H})\), 4.59 (dq, \(J = 1.5, 1.0 \text{ Hz}, 1\text{H}\), 4.81 (dq, \(J = 1.5, 1.2 \text{ Hz}, 1\text{H}\), 5.13 (dd, \(J = 9.8, 1.2 \text{ Hz}, 1 \text{ H}\), 5.17 (dd, \(J = 17.6, 1.2 \text{ Hz}, 1 \text{ H}\), 5.31 – 5.41 (m, 2 H), 5.80 (ddd, \(J = 17.6, 9.8, 8.8 \text{ Hz}, 1 \text{ H}\).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta = 13.9, 17.9, 22.4, 25.9, 29.8, 31.8, 33.7, 49.2, 111.0, 117.6, 128.8, 129.0, 132.5, 131.1, 135.4, 148.1, 179.9.

\(^1\)H NMR (400 MHz, CDCl\(_3\), minor isomer): \(\delta = 0.89 \) (t, \(J = 7.6 \text{ Hz}, 3 \text{ H}\), 1.57 – 1.66 (m, 1 H), 1.63 (s, 3 H), 1.74 (dd, \(J = 1.2, 1.0 \text{ Hz}, 3 \text{ H}\), 1.81 – 1.90 (m, 1 H), 2.00 – 2.16 (m, 2 H), 2.03 (q, \(J = 7.6 \text{ Hz}, 2 \text{ H}\), 2.75 (d, \(J = 4.7 \text{ Hz}, 2 \text{ H}\), 3.06 (q, \(J = 8.8 \text{ Hz}, 1 \text{ H})\), 4.52 (dq, \(J = 1.5, 1.0 \text{ Hz}, 1\text{H}\), 4.83 (dq, \(J = 1.5, 1.2 \text{ Hz}, 1\text{H}\), 5.13 (dd, \(J = 9.8, 1.2 \text{ Hz}, 1 \text{ H})\), 5.17 (dd, \(J = 17.6, 1.2 \text{ Hz}, 1 \text{ H}\), 5.31 – 5.41 (m, 2 H), 5.80 (ddd, \(J = 17.6, 9.8, 8.8 \text{ Hz}, 1 \text{ H}\).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\), minor isomer): \(\delta = 13.7, 16.5, 23.1, 25.9, 28.4, 29.7, 34.9,
HRMS: $m/z$ (M$^+$) calcd for $\text{C}_{17}\text{H}_{26}\text{O}_2$: 262.1933; found: 262.1906.

**NOE experimental data of product 3fa**

(5E,8E)-8-Methyl-9-(trimethylsilyl)-2-vinyldeca-5,8-dienoic acid (3ga): a mixture of regioisomers in a 3:1 ratio

$R_f = 0.40$ (hexane-EtOAc, 4:1)

IR (neat): 2950 (br s), 2932 (s), 2660 (br m), 1709 (s), 1639 (m), 1418 (m), 1175 (m), 968 (m), 922 (m) cm$^{-1}$.

$^1\text{H NMR}$ (400 MHz, CDCl$_3$, major isomer): $\delta$ = 0.14 (s, 9 H), 1.56 - 1.67 (m, 1 H), 1.67 (s, 3 H), 1.78 (s, 3 H), 1.81 - 1.90 (m, 1 H), 2.00 - 2.12 (m, 2 H), 2.79 (d, $J = 5.1$ Hz, 2 H), 3.05 (q, $J = 8.5$ Hz, 1 H), 5.16 (d, $J = 10.5$ Hz, 1 H), 5.20 (d, $J = 16.8$ Hz, 1 H), 5.32 - 5.40 (m, 2 H), 5.82 (ddd, $J = 16.8$, 10.5, 8.5 Hz, 1 H).

$^{13}\text{C NMR}$ (100 MHz, CDCl$_3$, major isomer): $\delta$ = 0.025, 17.0, 22.5, 29.3, 31.2, 37.8, 48.5, 117.2, 127.5, 127.8, 129.6, 134.5, 143.1, 177.5.

$^1\text{H NMR}$ (400 MHz, CDCl$_3$, minor isomer): $\delta$ = 0.13 (s, 9 H), 1.56 - 1.67 (m, 1 H), 1.71 (s, 3 H), 1.86 (s, 3 H), 1.81 - 1.90 (m, 1 H), 2.00 - 2.12 (m, 2 H), 2.79 (d, $J = 5.1$ Hz, 2
H), 3.05 (q, J = 8.5 Hz, 1 H), 5.16 (d, J = 10.5 Hz, 1 H), 5.20 (d, J = 16.8 Hz, 1 H), 5.21 – 5.30 (m, 2 H), 5.82 (ddd, J = 16.8, 10.5, 8.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, CDCl$_3$, minor isomer): \( \delta = 0.34, 20.6, 24.8, 29.4, 31.4, 34.1, 48.5, 117.1, 127.4, 128.4, 129.6, 134.6, 143.4, 177.5. \)

HRMS: m/z (M$^+$) calcd for C$_{16}$H$_{28}$O$_2$Si: 280.1859; found: 280.1861.

NOE experimental data of product 3ga

(5E,8Z)-9-(Trimethylsilyl)-8-phenyl-2-vinyldeca-5,8-dienoic acid (3ha): a mixture of regioisomers in a 3:1 ratio

$R_f = 0.43$ (hexane-EtOAc, 4:1)

IR (neat): 2950 (br s), 2878 (s), 2671 (br m), 1705 (s), 1495 (w), 1418 (m), 1221 (m), 922 (m), 837 (m), 764 (s), 702 (s) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$, major isomer): \( \delta = -0.25 \) (s, 9 H), 1.65 (ddt, J = 13.4, 8.5, 6.6 Hz, 1 H), 1.90 (ddt, J = 13.4, 8.5, 6.6 Hz, 1 H), 1.99 (s, 3 H), 2.05 – 2.16 (m, 2 H), 2.96 (d, J = 4.6 Hz, 2 H), 3.05 (q, J = 8.8 Hz, 1 H), 5.13 (d, J = 10.0 Hz, 1 H), 5.17 (d, J = 17.5 Hz, 1 H), 5.40 (dt, J = 15.4, 4.6 Hz, 1 H), 5.45 (dt, J = 15.4, 5.6 Hz, 1 H), 5.83 (ddd, J = 17.5, 10.0, 8.8 Hz, 1 H), 7.10 (dd, J = 6.8, 1.7 Hz, 2 H), 7.19 – 7.29 (m, 3 H).
\(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer): \(\delta = 0.53, 22.6, 29.9, 31.8, 34.7, 49.0, 117.6, 126.2, 127.5, 128.0, 128.4, 129.5, 133.9, 135.0, 146.7, 149.3, 178.3\).

\(^1\)H NMR (400 MHz, CDCl\(_3\), minor isomer): \(\delta = -0.25 \text{ (s, 9 H)}, 1.56 - 1.60 \text{ (m, 1 H)}, 1.79 - 1.84 \text{ (m, 1 H)}, 1.83 \text{ (s, 3 H)}, 1.95 - 2.02 \text{ (m, 2 H)}, 2.96 \text{ (d, } J = 4.6 \text{ Hz, 2 H)}, 3.05 \text{ (q, } J = 8.8 \text{ Hz, 1 H)}, 5.12 \text{ (d, } J = 17.5 \text{ Hz, 1 H)}, 5.15 \text{ (d, } J = 10.0 \text{ Hz, 1 H)}, 5.38 - 5.49 \text{ (m, 2 H)}, 5.74 \text{ (ddd, } J = 17.5, 10.0, 8.8 \text{ Hz, 1 H)}, 7.05 \text{ (dd, } J = 6.3, 1.7 \text{ Hz, 2 H)}, 7.19 - 7.29 \text{ (m, 3 H)}\).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\), minor isomer): \(\delta = -0.18, 17.7, 29.6, 31.5, 39.1, 48.7, 117.5, 126.1, 127.3, 128.0, 128.7, 129.3, 132.7, 135.0, 145.4, 149.0, 178.3\).

HRMS: \(m/\text{z (M}^+\text{)}\) calcd for C\(_{21}\)H\(_{30}\)O\(_2\)Si: 342.2015; found: 342.2022.

![3ha (major isomer)]

NOE experimental data of product 3ha

(5E,8Z)-9-Benzyl-8-ethyl-2-vinylundeca-5,8-dienoic acid (3ab)

R\(_f\) = 0.40 (hexane-EtOAc, 4:1)

IR (neat): 3020 (s), 2932 (s), 2872 (s), 2662 (br m), 1705 (s), 1638 (m), 1602 (w), 1495 (m), 1454 (m), 1288 (m), 993 (m), 918 (m), 750 (m), 729 (s) cm\(^{-1}\).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 0.92 \text{ (t, } J = 7.6 \text{ Hz 3 H)}, 1.01 \text{ (t, } J = 7.6 \text{ Hz 3 H)}, 1.60...
(ddt, $J = 13.7, 8.5, 6.6$ Hz, 1 H), 1.84 (ddt, $J = 13.7, 8.5, 6.6$ Hz, 1 H), 1.95 – 2.16 (m, 2 H), 1.98 (q, $J = 7.6$ Hz, 2 H), 2.10 (q, $J = 7.6$ Hz, 2 H), 2.79 (d, $J = 5.1$ Hz, 2 H), 3.04 (q, $J = 8.5$ Hz, 1 H), 3.40 (s, 2 H), 5.13 (dd, $J = 10.5, 0.98$ Hz, 1 H), 5.16 (dd, $J = 16.8, 0.98$ Hz, 1 H), 5.33 (dt, $J = 15.1, 5.6$ Hz, 1 H), 5.38 (dt, $J = 15.1, 5.1$ Hz, 1 H), 5.80 (ddd, $J = 16.8, 10.5, 8.5$ Hz, 1 H), 7.12 – 7.17 (m, 3 H), 7.22 – 7.28 (m, 2 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 13.6, 13.6, 24.5, 24.6, 29.8, 31.7, 34.9, 36.6, 49.1, 117.7, 125.5, 128.0, 128.3, 129.0, 129.6, 133.5, 134.4, 135.2, 140.8, 179.0.

HRMS: $m/z$ (M$^+$) calcd for C$_{22}$H$_{30}$O$_2$: 326.2246; found: 326.2259.

\[
\text{(E)-2-Vinylhept-5-enoic acid (4c)}
\]

$R_f = 0.30$ (hexane-EtOAc, 4:1)

IR (neat): 2962 (br s), 2934 (s), 2874 (s), 2660 (br m), 1705 (s), 1639 (m), 1418 (m), 1375 (m), 1286 (m), 1234 (m), 993 (m), 920 (m), 837 (m) cm$^{-1}$.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 1.54 – 1.65$ (m, 1 H), 1.64 (d, $J = 6.1$ Hz, 3 H), 1.85 (ddd, $J = 13.4, 7.8, 6.6$ Hz, 1 H), 1.94 – 2.10 (m, 2 H), 3.05 (q, $J = 7.8$ Hz, 1 H), 5.17 (dd, $J = 11.0, 1.2$ Hz, 1 H), 5.17 (dd, $J = 17.6, 1.2$ Hz, 1 H), 5.37 (dq, $J = 15.4, 6.3$ Hz, 1 H), 5.46 (dt, $J = 15.4, 6.1$ Hz, 1 H), 5.82 (ddd, $J = 17.6, 11.0, 7.8$ Hz, 1 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 26.2, 29.8, 31.6, 49.8, 117.7, 126.0, 129.7, 135.1, 179.6.$

HRMS: $m/z$ (M$^+$) calcd for C$_9$H$_{14}$O$_2$: 154.0994; found: 154.0993.
2-Vinylhept-6-enoic acid (5c)

R_f = 0.30 (hexane-EtOAc, 4:1)

IR (neat): 2962 (br s), 2934 (s), 2874 (s), 2660 (br m), 1705 (s), 1639 (m), 1418 (m), 1375 (m), 1286 (m), 1234 (m), 993 (m), 920 (m), 837 (m) cm^{-1}.

^1^H NMR (400 MHz, CDCl_3): δ = 1.35 – 1.50 (m, 2 H), 1.54 – 1.65 (m, 1 H), 1.80 (ddd, J = 13.2, 7.8, 6.6 Hz, 1 H), 2.07 (q, J = 7.3 Hz, 2 H), 3.03 (q, J = 7.8 Hz, 1 H), 4.96 (dd, J = 10.0, 1.7 Hz, 1 H), 5.01 (dd, J = 17.1, 1.7 Hz, 1 H), 5.17 (dd, J = 17.6, 1.2 Hz, 1 H), 5.17 (dd, J = 11.0, 1.2 Hz, 1 H), 5.78 (ddt, J = 17.1, 10.0, 7.3 Hz, 1 H), 5.79 (dd, J = 17.6, 11.0, 7.8 Hz, 1 H).

^13^C NMR (100 MHz, CDCl_3): δ = 17.8, 31.4, 33.3, 49.2, 114.7, 117.7, 135.2, 138.0, 179.6.

HRMS: m/z (M^+ ) calcd for C_9H_{14}O_2: 154.0994; found: 154.0993.

(E)-7-Phenyl-2-vinylhept-5-enoic acid (4e)

R_f = 0.32 (hexane-EtOAc, 4:1)

IR (neat): 3028 (s), 2927 (s), 2660 (br m), 1705 (s), 1637 (m), 1602 (w), 1495 (m), 1452 (m), 1418 (m), 1286 (m), 1223 (m), 970 (m), 923 (m), 746 (m), 698 (s) cm^{-1}.

^1^H NMR (400 MHz, CDCl_3): δ = 1.64 (ddt, J = 13.4, 8.8, 6.8 Hz, 1 H), 1.88 (ddt, J = 13.4, 8.8, 6.8 Hz, 1 H), 2.00 – 2.20 (m, 2 H), 3.03 (q, J = 8.8 Hz, 1 H), 3.32 (d, J = 6.6 Hz, 2
H), 5.14 (d, J = 11.0 Hz, 1 H), 5.16 (d, J = 17.5 Hz, 1 H), 5.45 (dt, J = 15.1, 6.6 Hz, 1 H),
5.60 (dt, J = 15.1, 6.8 Hz, 1 H), 5.82 (ddd, J = 17.5, 11.0, 8.8 Hz, 1 H), 7.15 – 7.33 (m, 5 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 29.7, 31.5, 39.0, 49.2, 117.8, 125.8, 128.2, 128.3, 130.1,
130.1, 135.0, 140.6, 179.2.

HRMS: $m/z$ (M$^+$) calcd for C$_{15}$H$_{18}$O$_2$: 230.1307; found: 230.1308.

![5-Phenyl-2-vinylhept-6-enoic acid (5e): a mixture of diastereo isomers in a 1:1 ratio](image)

R$_f$ = 0.32 (hexane-EtOAc, 4:1)

IR (neat): 3028 (s), 2927 (s), 2660 (br m), 1705 (s), 1637 (m), 1602 (w), 1495 (m), 1452
(m), 1418 (m), 1286 (m), 1223 (m), 970 (m), 923 (m), 746 (m), 698 (s) cm$^{-1}$.

$^1$H NMR (400 MHz, C$_6$D$_6$, one isomer): $\delta$ = 1.43 – 1.51 (m, 1 H), 1.72 – 1.82 (m, 3 H),
2.99 (q, J = 7.6 Hz, 1 H), 3.22 (q, J = 7.6 Hz, 1 H), 5.03 (dd, J = 17.6, 1.5 Hz, 1 H), 5.03
(dd, J = 10.0, 1.5 Hz, 1 H), 5.14 (d, J = 10.0 Hz, 1 H), 5.15 (d, J = 17.6, Hz, 1 H), 5.76
(ddd, J = 17.6, 10.0, 7.6 Hz, 1 H), 5.92 (ddd, J = 17.5, 10.0, 7.6 Hz, 1 H), 7.15 – 7.33 (m, 5 H).

$^{13}$C NMR (100MHz, CDCl$_3$, one isomer): $\delta$ = 29.9, 32.7, 39.0, 49.8, 114.3, 126.2, 128.3,
128.4, 130.0, 135.0, 141.6, 143.9, 179.1.

$^1$H NMR (400 MHz, C$_6$D$_6$, the other isomer): $\delta$ = 1.43 – 1.51 (m, 1 H), 1.72 – 1.82 (m, 3 H),
2.99 (q, J = 7.6 Hz, 1 H), 3.22 (q, J = 7.6 Hz, 1 H), 5.03 (dd, J = 17.6, 1.5 Hz, 1 H),

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5.03 (dd, $J = 10.0$, 1.5 Hz, 1 H), 5.14 (d, $J = 10.0$ Hz, 1 H), 5.15 (d, $J = 17.6$, Hz, 1 H),
5.76 (dd, $J = 17.6$, 10.0, 7.6 Hz, 1 H), 5.92 (ddd, $J = 17.5$, 10.0, 7.6 Hz, 1 H), 7.15 –
7.33 (m, 5 H).

$^{13}$C NMR (100MHz, CDCl$_3$, the other isomer): $\delta = 29.7$, 32.7, 39.0, 49.7, 114.3, 127.4,
128.3, 128.4, 130.0, 135.0, 141.6, 143.9, 179.2.

HRMS: $m/z$ (M$^+$) calcd for C$_{15}$H$_{18}$O$_2$: 230.1307; found: 230.1308.

(E)-2-Vinylnona-5,8-dienoic acid (4f)

R$_f$ = 0.30 (hexane-EtOAc, 4:1)

IR (neat): 2970 (br s), 2920 (s), 2660 (br m), 1710 (s), 1412 (m), 1180 (m), 974 (m), 918
(m) cm$^{-1}$.

$^1$H NMR (400 MHz, C$_6$D$_6$): $\delta = 1.62$ (ddt, $J = 13.4$, 8.5, 6.6 Hz, 1 H), 1.86 (ddt, $J = 13.4$,
8.5, 6.6 Hz, 1 H), 1.98 – 2.09 (m, 2 H), 2.72 (dd, $J = 7.5$, 6.3 Hz, 2 H), 3.03 (q, $J = 8.5$
Hz, 1 H), 4.97 (dd, $J = 10.0$, 1.7 Hz, 1 H), 5.02 (dd, $J = 17.1$, 1.7 Hz, 1 H), 5.16 (dd, $J$
= 11.0, 0.9 Hz, 1 H), 5.19 (dd, $J = 17.1$, 0.9 Hz, 1 H), 5.40 (dt, $J = 15.4$, 6.3 Hz, 1 H), 5.46
(dt, $J = 15.4$, 5.4 Hz, 1 H), 5.77 (ddt, $J = 17.1$, 11.0, 7.5 Hz, 1 H), 5.83 (ddd, $J = 17.1$,
10.0, 8.5 Hz, 1 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 29.8$, 31.5, 36.6, 49.2, 114.8, 117.7, 128.9, 129.8,
135.1, 136.9, 180.0.

HRMS: $m/z$ (M$^+$) calcd for C$_{11}$H$_{16}$O$_2$: 180.1150; found: 180.1146.
2,5-Divinylhept-6-enoic acid (5f)

R$_f$ = 0.30 (hexane-EtOAc, 4:1)

IR (neat): 2970 (br s), 2920 (s), 2660 (br m), 1710 (s), 1412 (m), 1180 (m), 974 (m), 918 (m) cm$^{-1}$.

$^1$H NMR (400 MHz, C$_6$D$_6$): $\delta$ = 1.40 – 1.48 (m, 1 H), 1.70 – 1.81 (m, 1 H), 1.98 – 2.09 (m, 2 H), 2.64 – 2.79 (m, 1 H), 3.02 (q, $J$ = 8.5 Hz, 1 H), 4.96 – 5.04 (m, 4 H), 5.16 (d, $J$ = 11.0 Hz, 1 H), 5.19 (d, $J$ = 17.1 Hz, 1 H), 5.64 – 5.74 (m, 3 H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 29.5, 31.5, 47.5, 49.9, 114.4, 117.7, 135.2, 140.5, 180.0.

HRMS: $m/z$ (M$^+$) calcd for C$_{11}$H$_{16}$O$_2$: 180.1150; found: 180.1146.
References


   (c) Gu, Z.; Vollhardt, K. P. C. Synthesis 2013, 45, 2469.


7. See experimental section.


Chapter 3

Ni-Catalyzed Reductive Coupling Reaction of Carbon Dioxide with Conjugated Diene Promoted by Diisobutylaluminum Hydride

**Summary:** Ni-Catalyzed reductive coupling reaction of carbon dioxide with conjugated dienes promoted by diisobutylaluminum hydride proceeds to give allylic carboxylic acids. In this case, one-to-one coupling reaction of conjugated dienes and carbon dioxide occurs without dimerization of conjugated dienes.
Introduction

Carbon dioxide (CO$_2$) is a non-toxic, inexpensive, and abundant resource. Thus, it is important to use CO$_2$ as a C1 source in organic synthesis. In particular, C–C bond formation reaction of CO$_2$ with carbon nucleophiles is an efficient synthetic method to give valuable carboxylic acids. As for the classical coupling reactions, it has been known that high reactive organometallic reagents such as organolithium and Grignard reagent react with CO$_2$ smoothly to give carboxylic acids. Recently, transition-metal catalysis has allowed low reactive organic compounds such as unsaturated hydrocarbons to react with carbon dioxide under mild conditions.$^1$

Reductive coupling reaction of CO$_2$ with conjugated dienes is useful synthetic method to give unsaturated carboxylic acids. One-to-one reductive coupling reaction of conjugated dienes and CO$_2$ in the presence of a stoichiometric amount of Ni(0) complex have been developed (Scheme 1).$^2$

\[
\begin{align*}
\text{Ph}-\underset{\text{(1 atm)}}{\text{C=C}} + \text{CO}_2 & \quad \overset{\text{Ni(cod)$_2$ (1 eq.)}}{\text{DBU (2 eq.)}} \quad \overset{\text{H}^+}{\rightarrow} \\
\text{Ph}-\underset{\text{CO}_2\text{H}}{\text{C=C}} + \quad \text{Ph}-\underset{\text{CO}_2\text{H}}{\text{C=C}}
\end{align*}
\]

**Scheme 1.** Stoichiometric One-to-One Coupling Reaction of Conjugated Diene and CO$_2$

As for the catalytic reaction, dimerization of conjugated dienes proceeds to give bis(allyl)nickel species, which react with CO$_2$ to afford unsaturated carboxylic acids
In this case, one-to-one coupling of dienes and CO$_2$ does not proceed at all. The catalytic reaction of one-to-one reductive coupling reaction of conjugated dienes and CO$_2$ by using a nickel complex has been a challenging reaction.\textsuperscript{4}

\begin{align*}
\text{Scheme 2. Catalytic Two-to-One Coupling Reaction of Conjugated Diene and CO}_2
\end{align*}

Herein, the author would like to introduce Ni-catalyzed one-to-one reductive coupling reaction of conjugated dienes and CO$_2$ to give $\beta,\gamma$-unsaturated carboxylic acids (Scheme 3).

\begin{align*}
\text{Scheme 3. Catalytic One-to-One Coupling Reaction of Conjugated Diene and CO}_2
\end{align*}
Results and Discussion

The reaction was performed in the presence of Ni(cod)$_2$ (0.05 mmol), myrcene (4 mmol), organometallic reagent (1 mmol) at room temperature for 24 h under 1 atm of carbon dioxide. Table 1 summarizes the results obtained from using various organometallic reagents and solvents. The reaction using Et$_3$B as an organometallic reagent in 1,4-dioxane provided a complex mixture (entry 1, Table 1). In the cases of Et$_2$Zn and Et$_3$Al, the reactions were also complicated (entries 2 and 3, Table 1). The reaction using DIBAL-H proceeded to furnish β,γ-unsaturated carboxylic acid in 50% yield with a mixture of 2a and 3a as regioisomers in 3:1 (entry 4, Table 1). In the cases of 9-BBN-H and Et$_3$SiH, the reactions did not proceed at all (entries 5 and 6, Table 1). n-Hexane instead of 1,4-dioxane as a solvent provided the carboxylic acids in 69% yield with a mixture of regioisomers in 3:1 (entry 7, Table 1). The use of toluene also gave the desired product in moderate yield (entry 8, Table 1). In the case of THF as a solvent, a complex mixture was observed (entry 9, Table 1). In the absence of a nickel catalyst, the reaction did not proceed at all (entry 10, Table 1).
Table 1. Optimization of Reaction Conditions for Ni-Catalyzed Reductive Coupling Reaction of Carbon Dioxide with Conjugated Diene Promoted by Diisobutylaluminum Hydride$^a$

![Chemical Structure](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>organometal</th>
<th>solvent</th>
<th>yield (%) [2a/3a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et$_3$B</td>
<td>1,4-dixane</td>
<td>complex mixture</td>
</tr>
<tr>
<td>2</td>
<td>Et$_2$Zn</td>
<td>1,4-dixane</td>
<td>complex mixture</td>
</tr>
<tr>
<td>3</td>
<td>Et$_3$Al</td>
<td>1,4-dixane</td>
<td>complex mixture</td>
</tr>
<tr>
<td>4</td>
<td>DIBAL-H</td>
<td>1,4-dixane</td>
<td>50 [3/1]</td>
</tr>
<tr>
<td>5</td>
<td>9-BBN-H</td>
<td>1,4-dixane</td>
<td>complex mixture</td>
</tr>
<tr>
<td>6</td>
<td>Et$_3$SiH</td>
<td>1,4-dixane</td>
<td>complex mixture</td>
</tr>
<tr>
<td>7</td>
<td>DIBAL-H</td>
<td>$n$-hexane</td>
<td>69 [3/1]</td>
</tr>
<tr>
<td>8</td>
<td>DIBAL-H</td>
<td>toluene</td>
<td>47 [3/1]</td>
</tr>
<tr>
<td>9</td>
<td>DIBAL-H</td>
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<tr>
<td>10$^b$</td>
<td>DIBAL-H</td>
<td>$n$-hexane</td>
<td>complex mixture</td>
</tr>
</tbody>
</table>

$^a$ The reaction was undertaken in the presence of Ni(cod)$_2$ (0.05 mmol), myrcene (4.0 mmol), organometallic reagent (1.0 mmol) in solvent (2 mL) for 24 h under carbon dioxide (1 atm).

$^b$ In the absence of Ni(cod)$_2$. 
Next, various kind of conjugated dienes were examined, and these results are summarized in Table 2. 1,3-Butadiene provided corresponding carboxylic acid 2b in good yield as a single isomer (entry 1, Table 2). Isoprene could be used in this coupling reaction to give 2c and 3c in good yield in 3:1 (entry 2, Table 2). Interestingly, n-octyl substituted conjugated diene 1d provided the carboxylic acid 2d in reasonable yields as a single isomer (entry 3, Table 2). In the case of (p-MeO)Ph substituted conjugated diene 1e, the reaction proceeded to provide carboxylic acids 2e and 3e in reasonable yield with a mixture of regioisomer in 3:1 (entry 4, Table 2). 2,3-Dimethyl-1,3-butadiene provided corresponding carboxylic acids 2f in moderate to good yield as a single isomer (entry 5, Table 2). In the case of 2-methyl-1,3-pentadiene, the coupling reaction proceeded regioselectively to give carboxylic acid 2g in good yield as a single isomer (entry 6, Table 2). As for 2,4-disubstituted conjugated diene 1h, the reaction proceeded to give 2h and 3h in 6:1 (entry 7, Table 2). Furthermore, in the case of 3-methyl-1,3-pentadiene, the coupling reaction underwent to afford 2i in good yield as a single isomer (entry 8, Table 2). Among these results, the regioselectivity of this coupling reaction was extremely different from previous Mori's work, which is nickel promoted one-to-one coupling reaction of carbon dioxide with conjugated dienes.2
Table 2. Scope of Ni-Catalyzed Reductive Coupling Reaction of Carbon Dioxide with Conjugated Diene Promoted by Diisobutylaluminum Hydride$^a$

<table>
<thead>
<tr>
<th>entry</th>
<th>conjugated diene</th>
<th>products, yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^{a}$Synthesis performed under 1 atm (1 atm) with Ni-catalyst DIBAL-H.
The reaction was undertaken in the presence of Ni(cod)$_2$ (0.05 mmol), conjugated diene (4.0 mmol), DIBAL-H (1.0 mmol) in n-hexane (2 mL) for 24 h under carbon dioxide (1 atm). $^b$ (E)-Stereoisomere was observed. $^c$ E/Z = 1/1.

A plausible reaction mechanism are shown in Scheme 4. At first, oxidative addition of a nickel(0) species upon H-Al bond of DIBAL-H proceeds to give H-Ni-Al(i-Bu)$_2$ (I) species.$^5$ Then, hydronickelation of conjugated diene occurs to give π-allylnickel species (II).$^6$ After that, the reductive elimination proceeds the least steric hindered π-allylnickel species (II) to give allylaluminum (III) species and an Ni(0) species. The allylaluminum species (III) can react with carbon dioxide smoothly at γ-position to give carboxylate complex (IV).$^7$ After hydrolysis, the corresponding carboxylic acid 2 is formed.

In the cases of R$_3^3$=H or Ar, the regioisomer of π-allylnickel species (V) is formed because the stability of π-allylnickel species (V) is similar to another π-allylnickel species (II). And then, the reductive elimination proceeds to give the allylaluminum species (VI). As a result, the corresponding carboxylic acid 3 is obtained.
Scheme 4. Plausible Reaction Mechanism of Ni-Catalyzed Reductive Coupling Reaction of Carbon Dioxide with Conjugated Diene Promoted by Diisobutylaluminum Hydride
In conclusion, Ni-catalyzed reductive coupling reaction of carbon dioxide with conjugated dienes promoted by diisobutylaluminum hydride to give allylic carboxylic acids in moderate to good yields. The coupling reaction was one-to-one coupling reaction of conjugated dienes with carbon dioxide. Various kind of conjugated dienes could be used in the coupling reaction. The regioselectivity might depend on the reductive elimination step, which proceeded the least steric hindered π-allylnickel species to give allylaluminum species.
Experimental Section

Reactions employed oven-dried glassware unless otherwise noted. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator (Merck Silica gel 60F\textsubscript{254}). Flash chromatography columns were packed with 230-400 mesh silica gel as a slurry in hexane. Gradient flash chromatography was conducted eluting with a continuous gradient from hexane to the indicated solvent. Proton and carbon NMR data were obtained with a JEOL JNM-AL400 with tetramethylsilane as an internal standard. Chemical shift values were given in ppm downfield from the internal standard. Infrared spectra were recorded with a JASCO A-100 FT-IR spectrophotometer. High resolution mass spectra (HRMS) were measured with a JEOL JMS-700N. Distillation were carried out in a Kugelrohr apparatus (SIBATA glass tube oven GTO-350RG). Boiling points are meant to refer to the oven temperature (± 1 °C).

Solvents and Reagents

Tetrahydrofuran, N,N-dimethylacetoamide (DMA), toluene, and \(n\)-hexane, \(n\)-octane were dried and distilled from benzophenone-sodium immediately prior to use under nitrogen atmosphere. Ni(cod)\textsubscript{2}, diisobuthyl aluminium hydride (1 M hexane, KANTO Kagaku) were used without further purification. 1,3-cyclohexadiene, 3-phenylpropionaldehyde, citral, trans-2-undecenal, (Tokyo Kasei Kogyo Co., Ltd), Myrcene, (Aldrich), cinnamaldehyde, benzalacetone (nakarai) were purchased and distilled via Kugelrohl apparatus under reduced pressure prior to use. 1,3-butadiene,
Isoprene, 2,3-dimethyl-1,3-butadiene, 2,4-hexadiene, 2-methyl-1,3-pentadiene, Methyltriphenylphosphonium bromide, 4-methoxycinnamaldehyde (Tokyo Kasei Kogyo Co., Ltd), 3-methyl-1,3-pentadiene (Aldrich) were purchased and used without further purification. Other conjugated dienes were prepared by Wittig reaction of aldehyde and Methyltriphenylphosphonium bromide.

**Typical procedure for the Ni-Catalyzed Reductive Coupling Reaction of Carbon Dioxide with Conjugated Diene Promoted by Diisobutylaluminum Hydride** (entry 7, Table 1)

The reaction was undertaken as follows: Into a carbon dioxide-purged flask with Ni(cod)$_2$ (13.8 mg, 0.05 mmol) was introduced successively $n$-hexane (2 mL), myrcene (545 mg, 4.0 mmol), and DIBAL-H (1.0 mL of 1M hexanes, 1.0 mmol) via syringe. The homogeneous mixture was stirred at room temperature for 24 h, during which the reaction was monitored by TLC. After dilution with diethyl ether (30 mL), the mixture was washed successively with 2 N-HCl, brine, and then dried (MgSO$_4$) and concentrated in vacuo. The residual oil was subjected to column chromatography over silica gel (hexane/ethyl acetate = 4/1, v/v) to give 2a and 3a (125 mg, 69%) in 3:1 ratio.
2,7-dimethyl-3-methyleneoct-6-enoic acid: (a mixture of regioisomers in a ratio of 3:1): IR (neat) 3100 (br), 2860 (br), 2638 (br), 1711 (s), 1645 (m), 1414 (m), 1286 (m) 1231 (m), 1092 (w), 901 (m), 833 (w) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\), major isomer) \(\delta\) 1.31 (d, \(J = 6.8\) Hz, 3 H), 1.61 (s, 3 H), 1.69 (s, 3 H), 2.08-2.17 (m, 4 H), 3.17 (q, 6.8 Hz, 1 H), 4.95 (s, 1 H), 5.00 (s, 1 H); 5.08-5.13 (m, 1 H) \(^{13}\)C NMR (100 MHz, CDCl\(_3\), major isomer) \(\delta\) 16.1, 17.7, 25.6, 26.3, 34.6, 45.6, 111.5, 123.7, 132.0, 147.4, 181.1; \(^1\)H-NMR (400 MHz, CDCl\(_3\), minor isomer) \(\delta\) 1.31 (s, 3 H), 1.58 (s, 3 H), 1.59-1.64 (m, 1 H), 1.67 (s, 3 H), 1.72-1.79 (m, 1 H), 1.92-1.99 (m, 2 H), 5.08-5.13 (m, 1 H), 5.14 (d, 17.6 Hz, 1 H), 5.15 (d, 10.7 Hz, 1 H), 6.04 (dd, 10.7, 17.6 Hz, 1 H); \(^{13}\)C-NMR (100 MHz, CDCl\(_3\), minor isomer) \(\delta\) 17.6, 20.2, 23.3, 25.6, 38.9, 48.3, 114.1, 123.6, 132.1, 140.9, 182.6, High-resolution MS, calcd for C\(_{11}\)H\(_{18}\)O\(_2\): 182.1307. Found \(m/z\) (relative intensity): 183 (M\(^+\)+1, 4), 182.1310 (M\(^+\), 28), 167 (4), 137 (14).

2-vinylundecanoic acid (2d): IR (neat): 3090 (br), 2925 (s), 2856 (s), 2662 (br), 1709 (s), 1639 (w), 1466 (m), 1414 (m), 1379 (w), 1286 (m), 1221 (m), 991 (m), 920 (s), 735 (s) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 0.88 (t, \(J = 6.8\) Hz, 3 H), 1.27 (m, 14 H), 1.54-1.58 (m, 1 H), 1.73-1.79 (m, 2 H), 3.01 (q, \(J = 7.8\) Hz, 1 H), 5.16 (dd, \(J = 6.8, 10.2, 1\) H),
5.17 (dd, \( J = 6.8, 17.1 \) Hz, 1 H), 5.81 (ddd, \( J = 6.8, 10.2, 17.1 \) Hz, 1 H); \(^{13}\text{C} \) NMR (400 MHz, CDCl\(_3\)): \( \delta \) 4.3, 14.1, 22.7, 27.0, 29.3, 29.4, 29.5, 31.9, 32.0, 50.1, 117.6, 135.5, 180.6; High-resolution MS, calcd for C\(_{13}\)H\(_{24}\)O\(_2\): 212.1776. Found \( m/z \) (relative intensity): 217.1775 (M\(^+\), 100), 197 (24), 194 (25), 184 (13).
References


4. Pd-Catalyzed one-to-one coupling of 1,3-diene with carbon dioxide, see:


6. Hydronickelation of alkyne, see:

Chapter 4

Ni-Catalyzed Three-Component Coupling Reaction of Alkene, Carbon Dioxide, and Organoaluminum Reagent

Summary: Ni-Catalyzed three-component coupling reaction of simple alkenes, carbon dioxide, and organoaluminum reagents proceeded to give homoallylic alcohols with high regio- and stereoselectivities. The first step in the reaction, carbon dioxide reacted with an organoaluminum reagent to form a ketone, and then formal carbonyl ene type reaction of an alkene with the ketone provided a homoallylic alcohol.
Introduction

The carbonyl-ene reaction (Prins Reaction) is so important to form C–C bond between alkenes and carbonyl compounds in organic synthesis. In general, electron rich alkenes (such as 1,1-disubstituted alkenes and trisubstituted alkenes) and electron deficient carbonyl compounds (such as α-ketoaldehydes and α-ketoesters) are effective for the carbonyl-ene reaction.\(^1\) Recently, Jamison reported carbonyl-ene type reaction of monosubstituted alkenes with aromatic and aliphatic aldehydes under nickel catalysis (Scheme 1).\(^2\) However, the reactions were not applicable to non-activated ketones like acetone as electrophiles. Consequently, the carbonyl-ene reaction of monosubstituted alkenes and non-activated ketones has been a challenging issue.\(^3\)

![Scheme 1. Ni-Catalyzed Carbonyl-Ene Type Reactions of Mono-Substituted Alkenes](image)

Nickel-catalyzed C–C bond formation reaction is one of the useful synthetic method to provide complex molecules in organic chemistry.\(^4\) Kimura has reported Ni-catalyzed multi-component coupling reaction of unsaturated hydrocarbons (such as conjugated diene and enyne), and carbonyl compound with organometallic reagent as alkyl, aryl, and hydride sources to give unsaturated alcohols in a single manipulation.\(^5\)

Herein, the author would like to introduce the Ni-catalyzed three-component coupling reaction of monosubstituted alkenes, carbon dioxide, and organoaluminum reagents to
give homoallylic alcohols (Scheme 2). This reaction shown that formal carbonyl ene
type reaction of simple alkenes and ketones proceeded.⁶

Scheme 2. Ni-Catalyzed Three-Component Coupling Reaction of Alkene, CO₂, and Organoaluminum Reagent
Results and Discussion

The reaction was underwent in the presence of a catalytic amount of Ni(cod)$_2$ and PCy$_3$ by exposing Me$_3$Al to the 1,4-dioxane solution of allylbenzene under carbon dioxide (1 atm). At first, the amount of Me$_3$Al and reaction temperature were examined (Table 1). The coupling reaction using 1.0 mmol of Me$_3$Al at room temperature proceeded to give the homoallylic alcohol 3aa in 40% yield with high regio- and stereoselectivities (entry 1, Table 1). After investigation of various amount of Me$_3$Al and reaction temperature, the reaction using 1.5 mmol of Me$_3$Al at 40 °C gave the best result (entry 5, Table 1). Higher temperature was not effective for this reaction (entry 6, Table 1). Ni(acac)$_2$ could be used in this reaction but the yield was slightly low (entry 7, Table 1).
Table 1. Optimization of Reaction Conditions for Ni-Catalyzed Three-Component Coupling Reaction of Alkene, CO$_2$, and Organoaluminum Reagent$^a$

<table>
<thead>
<tr>
<th>entry</th>
<th>Me$_3$Al (mmol)</th>
<th>temperature ($^\circ$C)</th>
<th>yield (%) [3aa/4aa]$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td>r.t.</td>
<td>40 [&gt;99/1]</td>
</tr>
<tr>
<td>2</td>
<td>1.5</td>
<td>r.t.</td>
<td>54 [&gt;99/1]</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>r.t.</td>
<td>55 [&gt;99/1]</td>
</tr>
<tr>
<td>4</td>
<td>3.0</td>
<td>r.t.</td>
<td>49 [&gt;99/1]</td>
</tr>
<tr>
<td>5</td>
<td>1.5</td>
<td>40</td>
<td>73 [&gt;99/1]</td>
</tr>
<tr>
<td>6</td>
<td>1.5</td>
<td>50</td>
<td>61 [&gt;99/1]</td>
</tr>
<tr>
<td>7$^c$</td>
<td>1.6</td>
<td>40</td>
<td>65 [&gt;99/1]</td>
</tr>
</tbody>
</table>

$^a$ The reaction was undertaken in the presence of Ni(cod)$_2$ (0.05 mmol), PCy$_3$ (0.1 mmol), allylbenzene (0.5 mmol), trimethylaluminum (indicated amount; 1 M in hexanes solution) in 1,4-dioxane (4 mL) for 24 h under carbon dioxide (1 atm). $^b$ (E)-Stereoisomerues were formed respectively. $^c$ Ni(acac)$_2$ was used instead of Ni(cod)$_2$.

Next, the effect of solvents was investigated in the coupling reaction (Table 2). The reaction using 1,4-dioxane proceeded to give the product in good yield (entry 1, Table 2). The reactions in THF and CPME also underwent to furnish the homoallylic alcohol 3aa in moderate yields (entries 2 and 3, Table 2). Polar solvent such as DMA, DMF and
DMSO did not provide the product at all (entries 4-6, Table 2). Non polar solvent were ineffective for the coupling reaction (entries 7 and 8, Table 2).

**Table 2.** Effect of Solvents for Ni-Catalyzed Three-Component Coupling Reaction of Alkene, CO₂, and Organoaluminum Reagent

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>yield (%) [3aa/4aa] b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,4-dioxane</td>
<td>73 [&gt;99/1]</td>
</tr>
<tr>
<td>2</td>
<td>THF</td>
<td>41 [&gt;99/1]</td>
</tr>
<tr>
<td>3</td>
<td>CPME</td>
<td>31 [98/2]</td>
</tr>
<tr>
<td>4</td>
<td>DMA</td>
<td>not observed</td>
</tr>
<tr>
<td>5</td>
<td>DMF</td>
<td>not observed</td>
</tr>
<tr>
<td>6</td>
<td>DMSO</td>
<td>not observed</td>
</tr>
<tr>
<td>7</td>
<td>n-hexane</td>
<td>13 [96/4]</td>
</tr>
<tr>
<td>8</td>
<td>toluene</td>
<td>24 [95/5]</td>
</tr>
</tbody>
</table>

a The reaction was undertaken in the presence of Ni(cod)₂ (0.05 mmol), PCy₃ (0.1 mmol), allylbenzene (0.5 mmol), trimethylaluminum (1.5 mmol; 1 M in hexanes solution) in solvent (4 mL) at 40 °C for 24 h under carbon dioxide (1 atm). b (E)-Stereoisomers were formed respectively.

CPME: cyclopentyl methyl ether
Next, the effect of ligands was investigated in this coupling reaction (Table 3). Monodentate triarylphosphine and monoalkyldiarylphosphine were ineffective for the coupling reactions (entries 1-3, Table 3). Trialkylphosphine such as PMe$_3$ did not provide desired product at all (entry 4, Table 3). However, in the cases of P($n$-Bu)$_3$ and PCyp$_3$, the three-component coupling reaction proceeded to give the homoallylic alcohol 3aa in moderate yield with high regio- and stereoselectivities (entries 5 and 6, Table 3). In these cases, trace amount of allylic alcohol 4aa was observed. Interestingly, PCy$_3$ gave homoallylic alcohol in good yield as a sole product (entry 7, Table 3). In the cases of P($t$-Bu)$_3$ and Xphos, the three-component coupling reaction did not proceed (entries 8 and 9, Table 3). Bidentate phosphine ligands, phenanthroline ligands, and $N$-heterocyclic carbene ligands were not effective for the coupling reaction at all (entries 10-20, Table 3).
Table 3. Effect of Ligands for Ni-Catalyzed Three-Component Coupling Reaction of Alkene, CO₂, and Organoaluminum Reagent

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand (mmol)</th>
<th>yield (%) [3aa/4aa]&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PPh₃ (0.1)</td>
<td>not observed</td>
</tr>
<tr>
<td>2</td>
<td>P(4-Me₂NPh)₃ (0.1)</td>
<td>not observed</td>
</tr>
<tr>
<td>3</td>
<td>PCyPh₂ (0.1)</td>
<td>not observed</td>
</tr>
<tr>
<td>4</td>
<td>PMe₃ (0.1)</td>
<td>not observed</td>
</tr>
<tr>
<td>5</td>
<td>P(n-Bu)₃ (0.1)</td>
<td>27 [94/6]</td>
</tr>
<tr>
<td>6</td>
<td>PCyp₃ (0.1)</td>
<td>37 [95/5]</td>
</tr>
<tr>
<td>7</td>
<td>PCys (0.1)</td>
<td>73 [&gt;99/1]</td>
</tr>
<tr>
<td>8&lt;sup&gt;c&lt;/sup&gt;</td>
<td>P(t-Bu)₃·HBF₄ (0.1)</td>
<td>not observed</td>
</tr>
<tr>
<td>9</td>
<td>Xphos (0.1)</td>
<td>not observed</td>
</tr>
<tr>
<td>10</td>
<td>dCype (0.05)</td>
<td>not observed</td>
</tr>
<tr>
<td>11</td>
<td>dppe (0.05)</td>
<td>not observed</td>
</tr>
<tr>
<td>12</td>
<td>dppf (0.05)</td>
<td>not observed</td>
</tr>
<tr>
<td>13</td>
<td>Xantphos (0.05)</td>
<td>not observed</td>
</tr>
<tr>
<td>14</td>
<td>1,10-phen (0.05)</td>
<td>no reaction</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: Ph, CO₂ (1 atm), Me₃Al, cat. Ni(cod)₂/ligand. 
<sup>b</sup> 1,4-dioxane as solvent (1 mL), room temperature, 18 h. 
<sup>c</sup> Reactions were carried out in the presence of HBF₄·Et₂O (1.0 equiv).
<table>
<thead>
<tr>
<th></th>
<th>Reaction Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>2,9-Me\textsubscript{2}-1,10-phen (0.05) not observed</td>
</tr>
<tr>
<td>16</td>
<td>3,4,7,8-Me\textsubscript{4}-1,10-phen (0.05) not observed</td>
</tr>
<tr>
<td>17\textsuperscript{d}</td>
<td>IDM·HCl (0.05) not observed</td>
</tr>
<tr>
<td>18\textsuperscript{d}</td>
<td>ICy·HCl (0.05) not observed</td>
</tr>
<tr>
<td>19\textsuperscript{d}</td>
<td>IMes·HCl (0.05) no reaction</td>
</tr>
<tr>
<td>20\textsuperscript{d}</td>
<td>IPr·HCl (0.05) not observed</td>
</tr>
</tbody>
</table>

\textsuperscript{a} The reaction was undertaken in the presence of Ni(cod)\textsubscript{2} (0.05 mmol), ligand (0.05-0.1 mmol), allylbenzene (0.5 mmol), trimethylaluminum (1.5 mmol; 1 M in hexanes solution) in 1,4-dioxane (4 mL) at 40 °C for 24 h under carbon dioxide (1 atm). \textsuperscript{b} (E)-Stereoisomers were formed respectively. \textsuperscript{c} 0.1 mmol of NEt(i-Pr)\textsubscript{2} was added. \textsuperscript{d} 0.05 mmol of KOr-Bu was added.

A wide variety of 1-alkenes were examined in the three-component coupling reaction under the optimized condition. The results were summarized in Table 4. 1-Allyl-2-methylbenzene (1b), 4-allyltoluene (1c), and 4-allylanisole (1d) gave the corresponding products in good yields with high regio- and stereoselectivities (entries 2-4, Table 4). 1-Allyl-4-fluorobenzene (1e) provided higher yields (entry 5, Table 4). As for 1-allylnaphtharene (1f) and 3-allylindole (1g), the three-component coupling reaction proceeded to give the corresponding homoallylic alcohols in moderate to high yields (entries 6 and 7, Table 4). Interestingly, simple alkenes such as 1-octene (1h) could be used in the three component coupling reaction (entry 8, Table 4). 4-Phenyl-1-butene (1i), 5-hexen-1-ol (1j), and methyl 5-hexenoate (1k) gave the corresponding products in moderate yields with high regio- and stereoselectivities (entries 9-11, Table 4). In the
cases of 3,3-diphenyl-1-propene (11) and vinylcyclohexane (1m), the three-component coupling reaction proceeded to afford the homoallylic alcohols in low yields (entries 12 and 13, Table 4). 4-(4-tert-Butyl)phenyl-3-methyl-1-butene (1n) gave the mixture of stereoisomers as a 5:1 (E/Z) (entry14, Table 4). As for 1,1- and 1,2-disubstituted alkenes, three-component coupling reaction did not proceed at all.
Table 4. Scope of the Ni-Catalyzed Three-Component Coupling Reaction of Alkene 1, CO₂, and Organoaluminum Reagent

<table>
<thead>
<tr>
<th>entry</th>
<th>R¹</th>
<th>R² (1)</th>
<th>yield of 3 (%) [E/Z]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>H (1a)</td>
<td>3aa : 73 [E only]</td>
</tr>
<tr>
<td>2</td>
<td>(2-Me)Ph</td>
<td>H (1b)</td>
<td>3ba : 64 [E only]</td>
</tr>
<tr>
<td>3</td>
<td>(4-Me)Ph</td>
<td>H (1c)</td>
<td>3ca : 68 [E only]</td>
</tr>
<tr>
<td>4</td>
<td>(4-MeO)Ph</td>
<td>H (1d)</td>
<td>3da : 70 [E only]</td>
</tr>
<tr>
<td>5</td>
<td>(4-F)Ph</td>
<td>H (1e)</td>
<td>3ea : 77 [E only]</td>
</tr>
<tr>
<td>6</td>
<td>1-Naphtyl</td>
<td>H (1f)</td>
<td>3fa : 54 [E only]</td>
</tr>
<tr>
<td>7</td>
<td>3-Indolyl</td>
<td>H (1g)</td>
<td>3ga : 86 [E only]</td>
</tr>
<tr>
<td>8</td>
<td>CH₃(CH₂)₄-</td>
<td>H (1h)</td>
<td>3ha : 54 [E only]</td>
</tr>
<tr>
<td>9</td>
<td>Ph(CH₂)₂-</td>
<td>H (1i)</td>
<td>3ia : 42 [E only]</td>
</tr>
<tr>
<td>10</td>
<td>HO(CH₂)₃-</td>
<td>H (1j)</td>
<td>3ja : 30 [E only]</td>
</tr>
<tr>
<td>11</td>
<td>MeO₂C(CH₂)₃-</td>
<td>H (1k)</td>
<td>3ka : 24 [E only]</td>
</tr>
<tr>
<td>12</td>
<td>Ph</td>
<td>Ph (1l)</td>
<td>3la : 24</td>
</tr>
<tr>
<td>13</td>
<td>-(CH₂)₅- (1m)</td>
<td></td>
<td>3ma : 22</td>
</tr>
<tr>
<td>14</td>
<td>(4-t-Bu)PhCH₂-</td>
<td>Me (1n)</td>
<td>3na : 49 [5/1]</td>
</tr>
</tbody>
</table>
The reaction was undertaken in the presence of Ni(cod)$_2$ (0.05 mmol), PCy$_3$ (0.1 mmol), alkene (0.5 mmol), trimethylaluminum (1.5 mmol; 1 M in hexanes solution) in 1,4-dioxane (4 mL) at 40 °C for 24 h under carbon dioxide (1 atm).  

Next, various kind of organoaluminum reagents were examined in this reaction.  The results were summarized in Table 5.  In this reaction, other organometallic reagents such as MeLi, MeMgBr, Me$_2$Zn, Me$_3$B did not provide the homoallylic alcohol at all.  Me$_3$Al provided homoallylic alcohol 3aa in good yield with high regio- and stereoselectivities (entry 1, Table 5).  As for Et$_3$Al (2b), (CH$_2$CHCH$_2$)Et$_2$Al (2c), (PhCH$_2$)Et$_2$Al (2d), three-component coupling reaction did not proceed (entries 2-4, Table 5).  However, in the cases of (CH$_2$CHCH$_2$)Et$_2$Al (2c) and (PhCH$_2$)Et$_2$Al (2d), 4-allylhepta-1,6-dien-4-ol (5c) and 2-benzyl-1,3-diphenylpropan-2-ol (5d) were observed respectively.  The reactions forming 5c and 5d proceeded in the absence of Ni(cod)$_2$ and PCy$_3$ (entries 5 and 6, Table 5).
Table 5. Scope of the Ni-Catalyzed Three-Component Coupling Reaction of Alkene, CO$_2$, and Organoaluminum Reagent 2$^a$

<table>
<thead>
<tr>
<th>entry</th>
<th>organoaluminum</th>
<th>yield of 3 and 5 (%) [E/Z]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me$_3$Al (2a)</td>
<td>3aa : 73 [E only]</td>
</tr>
<tr>
<td>2</td>
<td>Et$_3$Al (2b)</td>
<td>not observed</td>
</tr>
<tr>
<td>3$^b$</td>
<td>(CH$_2$CHCH$_2$)Et$_2$Al (2c)</td>
<td>5c : 51 (R = CH$_2$CHCH$_2$)</td>
</tr>
<tr>
<td>4$^b$</td>
<td>(PhCH$_2$)Et$_2$Al (2d)</td>
<td>5d : 34 (R = PhCH$_2$)</td>
</tr>
<tr>
<td>5$^{b,c}$</td>
<td>(CH$_2$CHCH$_2$)Et$_2$Al (2c)</td>
<td>5c : 51 (R = CH$_2$CHCH$_2$)</td>
</tr>
<tr>
<td>6$^{b,c}$</td>
<td>(PhCH$_2$)Et$_2$Al (2d)</td>
<td>5d : 35 (R = PhCH$_2$)</td>
</tr>
</tbody>
</table>

$^a$ The reaction was undertaken in the presence of Ni(cod)$_2$ (0.05 mmol), PCy$_3$ (0.1 mmol), alkene (0.5 mmol), organoaluminum (1.5 mmol) in 1,4-dioxane (4 mL) at 40 °C for 24 h under carbon dioxide (1 atm).

$^b$ Organoaluminum reagent 2c and 2d was prepared from Et$_2$AlCl (1 M in hexanes solution) and (CH$_2$CHCH$_2$)MgBr (1 M in diethyl ether solution) and PhCH$_2$MgBr (0.9 M in THF solution) respectively.

$^c$ The reaction was undertaken in the absence of Ni(cod)$_2$ and PCy$_3$.

To reveal the reaction mechanism, some reactions were examined. At first, trans-styrylacetic acid was used as a substrate in the presence of a catalytic amount of Ni(cod)$_2$, PCy$_3$ and 1.5 mmol of Me$_3$Al under nitrogen atmosphere (Eq. 1). The reaction did not proceed to give the homoallylic alcohol. Next, acetone was used as a substrate instead of carbon dioxide. The coupling reaction of allylbenzene and acetone underwent to
furnish the desired homoallylic alcohol (3aa) in 30% yield with high regio- and stereoselectivities (Eq. 2). The reaction of allylbenzene with acetone did not proceed at all in the absence of a nickel catalyst and Me₃Al. To confirm the formation of acetone, the reaction was examined without allylbenzene under a standard condition (Eq. 3). As a result, acetone was detected by gas chromatography and mass spectrometry.

\[
\begin{align*}
\text{Ph} &- \text{CH} & \text{CO}_2\text{H} & \xrightarrow{\text{Ni(cod)}_2 (0.05 \text{ mmol})} \text{Me}_3\text{Al (1.5 mmol)} & \xrightarrow{\text{PCY}_3 (0.1 \text{ mmol})} & \text{Me}_3\text{Al (1.5 mmol)} \\
6 : 0.5 \text{ mmol} & \xrightarrow{1,4\text{-dioxane (4 mL) \ 40^\circ\text{C, 24 h}}} & \text{3aa : not observed} \\
\end{align*}
\]

\[
\begin{align*}
\text{Ph} &- \text{CH} & \text{OH} & \xrightarrow{\text{Ni(cod)}_2 (0.05 \text{ mmol})} \text{Me}_3\text{Al (1.5 mmol)} & \xrightarrow{\text{PCY}_3 (0.1 \text{ mmol})} & \text{Me}_3\text{Al (1.5 mmol)} \\
1\text{a} : (0.5 \text{ mmol}) & + & \text{Me} & - \text{CO} & \xrightarrow{1,4\text{-dioxane (4 mL) \ 40^\circ\text{C, 24 h}}} & \text{3aa : 30% [E only]} \\
7 : (0.5 \text{ mmol}) & & & & & \\
\end{align*}
\]

\[
\begin{align*}
\text{CO}_2 & \xrightarrow{\text{Ni(cod)}_2 (0.05 \text{ mmol})} \text{Me}_3\text{Al (1.5 mmol)} & \xrightarrow{\text{PCY}_3 (0.1 \text{ mmol})} & \text{Me}_3\text{Al (1.5 mmol)} \\
(1 \text{ atm}) & \xrightarrow{1,4\text{-dioxane (4 mL) \ 40^\circ\text{C, 24 h}}} & \text{detected by GC and MS} \\
& & & & \\
\end{align*}
\]
A plausible reaction mechanism are shown in Scheme 3. At first, carbon dioxide reacts with Me₃Al to give acetone. Then, oxidative cyclization of Ni(0) across alkene and acetone proceeds to give oxanickellacycle intermediate I with high regioselectivity. The intermediate I might be stable in the case of anti conformation of methylene group and R¹ to avoid the steric repulsion between methylene group and R¹ (R¹>R²). Thus, stereoselective β-hydrogen elimination undergoes to give intermediate II. Finally, transmetallation proceeds to give III and hydride methyl nickel species IV, followed by generation of Ni(0) active species through reductive elimination.

![Scheme 2. Plausible Reaction Mechanism of Ni-Catalyzed Three-Component Coupling Reaction of Alkene, CO₂, and Me₃Al](image)
In conclusion, the author succeeded to find a Ni-catalyzed multicomponent coupling reaction of monosubstituted alkenes, carbon dioxide, and organoaluminum reagents provides homoallylic alcohols with high regio- and stereoselectivities. The reactions could be considered that carbon dioxide reacted with organoaluminum to form ketone at the first step in the reaction, and then formal carbonyl-ene type reaction of alkene with the ketone provided the homoallylic alcohol. Actually, when ketones were used instead of carbon dioxide, the coupling reaction of alkenes and ketones proceeded to give the homoallylic alcohols. The notable features of this multicomponent coupling reaction are that it achieves not only C–C bond formation by monosubstituted alkenes and carbon dioxide but also transformation of carbon dioxide to unsaturated alcohols.
Experimental Section

Reactions employed oven-dried glassware unless otherwise noted. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator (Merck Silica gel 60F254). Flash chromatography columns were packed with 230-400 mesh silica gel as a slurry in hexane. Gradient flash chromatography was conducted eluting with a continuous gradient from hexane to the indicated solvent. Proton and carbon NMR data were obtained with a JEOL JNM-AL400 with tetramethylsilane as an internal standard. Chemical shift values were given in ppm downfield from the internal standard. Infrared spectra were recorded with a JASCO A-100 FT-IR spectrophotometer. High resolution mass spectra (HRMS) were measured with a JEOL JMS-700N. Distillation were carried out in a Kugelrohr apparatus (SIBATA glass tube oven GTO-350RG). Boiling points are meant to refer to the oven temperature (± 1 °C).

Solvents and Reagents

Tetrahydrofuran (KANTO Kagaku), 1,4-dioxane, CPME [cyclopentyl methyl ether], DMA [N, N-dimethylacetamide], DMF [N, N-dimethylformamide], DMSO [dimethyl sulfoxide], n-hexane and toluene (Wako Chemicals) were purchased as anhydrous solvents and used without further purification. Ni(cod)₂ (KANTO Kagaku), PPh₃, P(4-Me₂NPh)₃, PCyPh₂, P(n-Bu)₃, PCyp₃, Xantphos, 1,10-phen, 2,9-Me₂-1,10-phen, 3,4,7,8-Me₄-1,10-phen, IDM∙HCl, ICy∙HCl IMes∙HCl, IPr∙HCl (Tokyo Kasei Kogyo Co., Ltd), Ni(acac)₂, PMe₃ (1.0 M in THF), PCy₃, P(t-Bu)₃∙HBF₄, Xphos, dCype, dppe, dppf
Trimethylaluminum (1 M in n-hexane) and triethylaluminum reagents (1 M in n-hexane, KANTO Kagaku) were purchased and used without further purification. Benzyldiethylaluminium and Allyldiethylaluminium were prepared from diethylaluminium chloride (1 M in n-hexane, KANTO Kagaku) with benzylmagnesium bromide (0.9 M in THF, Tokyo Kasei Kogyo Co., Ltd) and allylmagnesium bromide (1 M in diethyl ether, Aldrich), respectively. Allylbenzene, 1-allylnaphthalene, 1-octene, 4-phenyl-1-butene, 5-hexen-1-ol, methyl 5-hexenoate, vinylcyclohexane (Tokyo Kasei Kogyo Co., Ltd), 1-allyl-2-methylbenzene, 4-allyltoluene, 4-allylanisole, and 1-allyl-4-fluorobenzene (Sigma-Aldrich) were purchased and and distilled via Kugelrohr apparatus under reduced pressure prior to use. 3-Allylindole, 3,3-diphenyl-1-propene, 3-methyl-4-(4-tert-butylphenyl)-1-butene were prepared by literature methods. Acetone (Tokyo Kasei Kogyo Co., Ltd) were purchased and and distilled via Kugelrohr apparatus under reduced pressure prior to use. trans-Styrylacetic acid (Sigma-Aldrich) was purchased and used without further purification.

Preparation of benzyldiethylaluminium and allyldiethylaluminium solution

A 100 mL Schlenk flask equipped with a rubber septum was charged with Et₂AlCl (4.5 mL of 1 M in n-hexane, 4.5 mmol) under nitrogen atmosphere. A solution of PhCH₂MgBr (5 mL of 0.9 M in THF, 4.5 mmol) was added to the Et₂AlCl via syringe at 0 °C. The reaction mixture was stirred at room temperature for 12 hours. Thus, benzyldiethylaluminium solution (0.47 M) was prepared prior to use.
(CH₂CHCH₂)₂Et₂Al (0.5 M) was prepared following the above procedure from (CH₂CHCH₂)MgBr (4.5 mL of 1 M in diethyl ether, 4.5 mmol).

**Typical procedure for the Ni-catalyzed three-component coupling reaction of alkene, CO₂, organoaluminum reagent** (entry 5, Table 1)

The reaction was undertaken as follows: Into a carbon dioxide-purged flask with Ni(cod)₂ (13.8 mg, 0.05 mmol) and PCy₃ (28.1 mg, 0.1 mmol) were introduced successively 1,4-dioxane (4 mL), allylbenzene (59.1 mg, 0.5 mmol), and Me₃Al (1.5 mL of 1 M in n-hexanes, 1.5 mmol) via syringe. The homogeneous mixture was stirred at 40 °C for 24 h, during which the reaction was monitored by TLC. Then the mixture was quenched by adding 2 N HCl (10 ml) and extracted with ethyl acetate three times. The combined organic extracts were washed with sat. NaHCO₃, brine, and then dried (MgSO₄) and concentrated in vacuo. The residual oil was subjected to column chromatography over silica gel (hexane/ethyl acetate = 4/1, v/v) to give 3aa (64.3 mg, 73%).
(E)-2-methyl-5-phenylpent-4-en-2-ol (3aa): IR (neat) 3387 (m), 3059 (m), 2970 (s), 1599 (s), 1497 (m), 1377 (s), 1140 (s), 968 (s), 692 (s) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.27 (s, 6 H), 1.54 (br, 1 H), 2.39 (d, \(J = 7.6\) Hz, 2 H), 6.28 (dt, \(J = 15.9, 7.6\) Hz, 1 H), 6.46 (d, \(J = 15.9\) Hz, 1 H), 7.21 (t, \(J = 7.3\) Hz, 1 H), 7.30 (t, \(J = 7.3\) Hz, 2 H), 7.34 (d, \(J = 7.3\) Hz, 2 H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 29.3, 47.4, 70.9, 125.7, 126.1, 127.2, 128.5, 133.6, 137.3; High-resolution MS, calcd for C\(_{12}\)H\(_{16}\)O: 176.1201. Found m/z (relative intensity): 176.1203 (M\(^+\), 9), 118 (100).

(E)-2-methyl-5-o-tolylpent-4-en-2-ol (3ba): IR (neat) 3364 (m), 3020 (w), 2970 (s), 2923 (s), 1602 (w), 1489 (s), 1142 (s), 968 (s), 741 (m) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.28 (s, 6 H), 1.57 (br, 1 H), 2.34 (s, 3 H), 2.41 (d, \(J = 7.8\) Hz, 2 H), 6.15 (dt, \(J = 15.6, 7.8\) Hz, 1 H), 6.66 (d, \(J = 15.6\) Hz, 1 H), 7.13-7.18 (m, 3 H), 7.42-7.44 (m, 1 H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 19.8, 29.2, 47.6, 70.8, 125.6, 126.0, 127.2, 130.2, 131.7, 135.1, 136.6; High-resolution MS, calcd for C\(_{13}\)H\(_{18}\)O: 190.1358. Found m/z (relative intensity): 190.1353 (M\(^+\), 59), 157 (100).

(E)-2-methyl-5-p-tolylpent-4-en-2-ol (3ca): IR (neat) 3379 (br), 3021 (m), 2970 (s), 1514 (m), 1377 (m), 1138 (m), 800 (m) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.27 (s, 6
H), 1.53 (br, 1 H), 2.33 (s, 3 H), 2.37 (d, \( J = 7.8 \) Hz, 2 H), 6.23 (dt, \( J = 15.6, 7.8 \) Hz, 1 H), 6.43 (d, \( J = 15.6 \) Hz, 1 H), 7.11 (d, \( J = 7.6 \) Hz, 2 H), 7.27 (d, \( J = 7.6 \) Hz, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 21.1, 29.2, 47.4, 70.9, 124.7, 126.0, 129.2, 133.6, 134.4, 137.0; High-resolution MS, calcd for C\(_{13}\)H\(_{18}\)O: 190.1358. Found \( m/z \) (relative intensity): 190.1367 (M\(^+\), 6), 132 (100).

\( \text{(E)} \)-5-(4-methoxyphenyl)-2-methylpent-4-en-2-ol (3da): IR (neat) 3386 (br), 3030 (m), 2968 (s), 2931 (m), 1608 (s), 1510 (s), 1249 (s), 1174 (s), 1035 (m), 970 (m) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 1.26 (s, 6 H), 1.59 (br, 1 H), 2.35 (d, \( J = 7.8 \) Hz, 3 H), 3.80 (s, 3 H), 6.13 (dt, \( J = 15.6, 7.8 \) Hz, 1 H), 6.40 (d, \( J = 15.6 \) Hz, 1 H), 6.84 (d, \( J = 8.8 \) Hz, 2 H), 7.30 (d, \( J = 8.8 \) Hz, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 29.2, 47.3, 55.3, 70.8, 114.0, 123.5, 127.2, 130.2, 133.1, 159.0; High-resolution MS, calcd for C\(_{13}\)H\(_{18}\)O\(_2\): 206.1307. Found \( m/z \) (relative intensity): 206.1311 (M\(^+\), 100), 191 (28).

\( \text{(E)} \)-5-(4-fluorophenyl)-2-methylpent-4-en-2-ol (3ea): IR (neat) 3394 (br), 3031 (w), 2972 (m), 2929 (w), 2893 (w), 1600 (m), 1508 (s), 1228 (s), 970 (m) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 1.27 (s, 6 H), 1.63 (br, 1 H), 2.37 (d, \( J = 7.8 \) Hz, 2 H), 6.20 (dt, \( J = 15.8, 7.8 \) Hz, 1 H), 6.42 (d, \( J = 15.8 \) Hz, 1 H), 6.90-7.02 (m, 2 H), 7.30-7.32 (m, 2 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 29.3, 47.3, 70.9, 115.4 (d, \( J = 21.5 \)), 125.6, 127.6 (d, \( J = 7.5 \)), 132.4,
133.6 (d, \( J = 3.3 \)), 162.1 (d, \( J = 245.8 \)); High-resolution MS, calcd for \( C_{12}H_{15}FO: 190.1107 \). Found m/z (relative intensity): 194.1103 (M\(^+\), 76), 179 (100).

(E)-2-methyl-5-(naphthalen-5-yl)pent-4-en-2-ol (3fa): IR (neat) 3361 (br), 3045 (w), 2970 (m), 2927 (w), 1589 (w), 1508 (w), 1377 (m), 1143 (m), 970 (s), 796 (s), 777 (s) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 1.30 (s, 6 H), 2.51 (d, \( J = 7.8 \) Hz, 2 H), 6.30 (dt, \( J = 15.1, 7.8 \) Hz, 1 H), 7.20 (d, \( J = 15.1 \) Hz, 1 H), 7.42-7.53 (m, 3 H), 7.58 (d, \( J = 6.8 \) Hz, 1 H), 7.76 (d, \( J = 8.3 \) Hz, 1 H), 7.83-7.85 (m, 1 H), 8.12 (d, \( J = 7.8 \) Hz, 1 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 29.3, 47.8, 70.9, 123.7, 123.8, 125.6, 125.7, 126.0, 127.7, 128.5, 129.2, 131.0, 131.1, 133.6, 135.2; High-resolution MS, calcd for \( C_{16}H_{18}O: 226.1358 \). Found m/z (relative intensity): 226.1358 (M\(^+\), 100).

(E)-5-(1H-indol-3-yl)-2-methylpent-4-en-2-ol (3ga): IR (neat) 3402 (br), 3269 (br), 3045 (w), 2970 (m), 2927 (w), 1531 (w), 1412 (m), 740 (s) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 1.30 (s, 6 H), 1.68 (br, 1 H), 2.41 (d, \( J = 7.8 \) Hz, 2 H), 6.24 (dt, \( J = 15.6, 7.8 \) Hz, 1 H), 6.64 (d, \( J = 15.6 \) Hz, 1 H), 7.15-7.24 (m, 3 H), 7.35 (d, \( J = 7.8 \) Hz, 1 H), 7.85
(d, J = 7.6 Hz, 1 H), 8.19 (br, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 29.2, 48.0, 70.9, 111.3, 115.3, 120.0, 120.2, 122.4, 122.5, 122.8, 125.6, 126.5, 136.7; High-resolution MS, calcd for C$_{14}$H$_{17}$NO: 215.1310. Found m/z (relative intensity): 215.1309 (M$^+$, 100), 200 (25).

(E)-2-methyldec-4-en-2-ol (3ha): IR ( neat) 3361 (br), 2962 (s), 2927 (s), 2856 (m), 1497 (w), 1377 (w), 1151 (w), 972 (w) cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.89 (t, J = 6.8 Hz, 3 H), 1.20 (s, 6 H), 1.26-1.41 (m, 6 H), 1.50 (br, 1 H), 2.03 (q, J = 7.3 Hz, 2 H), 2.16 (d, J = 6.8 Hz, 2 H), 5.46 (dt, J = 15.1, 7.3 Hz, 1 H), 5.53 (dt, J = 15.1, 6.8 Hz, 1 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.0, 22.5, 29.0, 29.2, 31.4, 32.7, 47.0, 70.4, 125.2, 135.4; High-resolution MS, calcd for C$_{11}$H$_{22}$O: 170.1671. Found m/z (relative intensity): 170.1668 (M$^+$, 14 ), 155 (100).

(E)-2-methyl-6-phenylhex-4-en-2-ol (3ia): IR ( neat) 3367 (br), 3028 (w), 2972 (s), 2856 (m), 1497 (w), 1377 (w), 1151 (w), 972 (w) cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.21 (s, 6 H), 1.57 (br, 1 H), 2.20 (d, J = 6.8 Hz, 2 H), 3.38 (d, J = 6.3 Hz, 2 H), 5.58 (dt, J = 15.6, 6.8 Hz, 1 H), 5.69 (dt, J = 15.6, 6.3 Hz, 1 H), 7.17-7.30 (m, 5 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 29.1, 39.2, 46.9, 70.5, 126.0, 127.0, 128.4, 128.5, 133.3, 140.6; High-resolution MS, calcd for C$_{13}$H$_{18}$O: 190.1358. Found m/z (relative intensity): 190.1353 (M$^+$,26 ), 175 (100).
(E)-7-methyloct-4-ene-1,7-diol (3ja): IR (neat) 3357 (br), 2968 (s), 2933 (s), 2875 (m), 1456 (w), 1377 (m), 1265 (s), 1058 (m), 740 (s) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.21 (s, 6 H), 1.67 (tt, \(J = 6.8, 6.3\) Hz, 2 H), 1.68 (br, 1 H), 1.78 (br, 1 H), 2.15 (dt, \(J = 6.8, 6.3\) Hz, 2 H), 2.17 (d, \(J = 5.9\) Hz, 2 H), 3.67 (t, \(J = 6.3\) Hz, 2 H), 5.52 (dt, \(J = 15.6, 6.3\) Hz, 1 H), 5.56 (dt, \(J = 15.6, 5.9\) Hz, 1 H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 29.0, 29.2, 32.2, 46.8, 62.4, 70.5, 125.9, 134.3; High-resolution MS, calcd for C\(_9\)H\(_{18}\)O\(_2\): 158.1307. Found \(m/z\) (relative intensity): 158.1312 (M\(^+\), 4), 143 (53).

(E)-methyl 7-hydroxy-7-methyloct-4-enoate (3ka): IR (neat) 3423 (br,), 2970 (s), 2931 (s), 1737 (s), 1676 (m), 1438 (m), 1170 (m), 974 (m) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.20 (s, 6 H), 1.72 (br, 1 H), 2.16 (d, \(J = 5.9\) Hz, 2 H), 2.38 (t, \(J = 5.9\) Hz, 2 H), 2.39 (dt, \(J = 6.8, 5.9\) Hz, 2 H), 3.67 (s, 3 H), 5.51 (dt, \(J = 15.6, 5.9\) Hz, 1 H), 5.56 (dt, \(J = 15.6, 6.8\) Hz, 1 H); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 28.0, 29.0, 33.9, 46.7, 51.6, 70.3, 126.9, 132.6, 173.6; High-resolution MS, calcd for C\(_{10}\)H\(_{18}\)O\(_3\): 186.1256. Found \(m/z\) (relative intensity): 186.1329 (M\(^+\), 10), 139 (100).

2-methyl-5,5-diphenylpent-4-en-2-ol (3ma): IR (neat) 3373 (br), 3052 (s), 3024 (s),
2970 (s), 2891 (s), 1599 (s), 1495 (m), 1142 (m), 754 (m) cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.23 (s, 6 H), 1.64 (br, 1 H), 2.32 (d, \(J = 7.8\) Hz, 2 H), 6.23 (t, \(J = 7.8\) Hz, 1 H), 7.17-7.39 (m, 10 H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 29.4, 43.5, 71.4, 124.9, 127.0, 127.0, 127.2, 128.1, 128.2, 129.9, 140.0, 142.6, 144.0; High-resolution MS, calcd for C\(_{18}\)H\(_{20}\)O: 252.1514. Found \(m/z\) (relative intensity): 252.1512 (M\(^+\), 0.3), 194 (100).

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\text{4-cyclohexylidene-2-methylbutan-2-ol (3la): IR (neat) 3373 (s), 2926 (s), 2855 (s), 1447 (s), 1375 (s), 905 (m) cm}^{-1}; \ ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 1.21 (s, 6 H), 1.47-1.56 (m, 7 H), 2.14-2.20 (m, 4 H), 2.18 (d, \(J = 8.3\) Hz, 2 H) 5.18(t, \(J = 8.3, 7.3\), 1 H); \ ^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } \delta 26.9, 27.9, 28.7, 28.8, 29.0, 37.6, 41.0, 71.2, 116.1, 143.7; \text{High-resolution MS, calcd for C}_{11}\text{H}_{20}\text{O: 168.1514. Found } m/z \text{ (relative intensity): 168.1514 (M}^+\text{, 1.7), 135 (100).}
\]

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(E)-6-(4-\text{tert-butylphenyl)}-2,5\text{-dimethylhex-4-en-2-ol (3na): (a mixture of stereoisomers in a ratio of 5 : 1): IR (neat) 3362 (br, s), 3024 (w), 2959 (s), 1514 (m), 1464 (s), 1047 (s), 908 (w), 735 (s) cm}^{-1}; \ ^1\text{H NMR (400 MHz, CDCl}_3\text{, major isomer): } \delta 1.23 (s, 6 H), 1.31 (s, 9 H), 1.53 (br, 1 H), 1.58 (s, 3 H), 2.23 (d, \(J = 7.8\) Hz, 2 H), 3.31 (s, 2 H), 5.39 (t, \(J = 7.8\) Hz, 1 H), 7.10 (d, \(J = 8.3\) Hz, 2 H), 7.30 (d, \(J = 8.3\) Hz, 2 H); \ ^{13}\text{C...}
\]
NMR (100 MHz, CDCl$_3$, major isomer) $\delta$ 16.1, 29.1, 31.4, 34.4, 42.1, 46.1, 71.5, 121.5, 125.2, 128.4, 137.1, 138.4, 148.9; $^1$H NMR (400 MHz, CDCl$_3$, minor isomer): $\delta$ 1.25 (s, 6 H), 1.31 (s, 9 H), 1.53 (br, 1 H), 1.69 (s, 3 H), 2.34 (d, $J$ = 7.8 Hz, 2 H), 3.37 (s, 2 H), 5.42 (t, $J$ = 7.8 Hz, 1 H), 7.10 (d, $J$ = 8.3 Hz, 2 H), 7.30 (d, $J$ = 8.3 Hz, 2 H); $^{13}$C NMR (100 MHz, CDCl$_3$, minor isomer) $\delta$ 23.8, 29.1, 31.4, 34.3, 37.3, 42.2, 71.1, 121.4, 125.2, 128.1, 136.7, 137.6, 148.8; High-resolution MS, calcd for C$_{18}$H$_{28}$O: 260.2140. Found $m/z$ (relative intensity): 260.2133(M$^+$, 43).

NOE experimental data of product 3na (major isomer and minor isomer)

4-allylhepta-1,6-dien-4-ol (5c): IR (neat) 3431 (br,), 3076 (m), 2979 (m), 2931 (m), 1639 (s), 1440 (m), 997 (s), 914 (s) cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.73 (br, 1 H), 2.24 (d, $J$ = 7.3 Hz, 6 H), 5.12 (dd, $J$ = 17.6, 1.5 Hz, 3 H), 5.16 (dd, $J$ = 10.2, 1.5 Hz, 3 H), 5.87 (ddt, $J$ = 17.6, 10.2, 7.3 Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 43.6, 73.0, 118.7, 133.6; High-resolution MS, calcd for C$_{10}$H$_{16}$O: 152.1201. Found $m/z$ (relative intensity): 152.1199 (M$^+$, 1), 120 (100).
2-benzyl-1,3-diphenylpropan-2-ol (5d): IR (neat) 3090 (br), 2926 (s), 1600 (m), 1495 (m), 1265 (m), 1030 (w), 739 (s) cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 2.92 (s, 6 H), 4.16 (s, 1 H), 7.18-7.30 (m, 15 H); ¹³C NMR (100 MHz, CDCl₃): δ 37.9, 67.9, 125.9, 128.3, 128.4, 141.8; High-resolution MS, calcd for C₂₂H₂₂O: 302.1671. Found m/z (relative intensity): 171 (100).

1-tert-butyl-4-(2-methylbut-3-enyl)benzene (1n): IR (neat) 3074 (m), 2964 (s), 2925 (s), 2868 (s), 1458 (m), 1363 (s), 910 (m) cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 0.98 (d, J = 5.9 Hz, 3H), 1.31 (s, 9H), 2.39-2.52 (m, 2H), 2.62-2.70 (m, 1H), 4.92 (d, J = 10.2 Hz, 1H), 4.96 (d, J = 17.1 Hz, 1H), 5.82 (ddd, J = 6.4, 10.2, 17.1 Hz, 1H), 7.08 (d, J = 7.8 Hz, 2H), 7.29, (d, J = 7.8 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 19.3, 31.4, 34.3, 39.1, 42.7, 112.5, 125.0, 128.8, 137.6, 144.2, 148.5; High-resolution MS, calcd for C₁₃H₁₈: 202.1722. Found m/z (relative intensity): 202.1725 (M⁺, 78), 187 (100).
References


3. The reaction of di-substituted alkene with non-activated ketone such as cyclohexanone, see:


6. Ni-catalyzed intramolecular coupling reaction of alkenes and ketones has been reported, see:


Preface

The study presented in this thesis has been carried out under the direction of Professor Dr. Masanari Kimura at the Graduate School of Engineering, Nagasaki University during 2012 to 2017. This thesis describes the development of efficient organic synthetic reactions via novel activation of unsaturated hydrocarbons.

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January 2017

Yasuyuki Mori
Publication List

Chapter 1
“Ni-Catalyzed Three-component Coupling Reaction of Conjugated Enyne, Carbonyls, and Dimethylzinc to Construct Allenyl Alcohols”

“Remarkably Selective Formation of Allenyl and Dienyl Alcohols via Ni-Catalyzed Coupling Reaction of Conjugated Enyne, Aldehyde, and Organozinc Reagents”

Chapter 2
“Nickel-Catalyzed Multicomponent Coupling of Alkyne, Buta-1,3-diene, and Dimethylzinc under Carbon Dioxide”

Chapter 3
Manuscript in Preparation

Chapter 4
Manuscript in Preparation

Other related publications
“Nickel-Catalyzed Regioselective 1,4-Addition of Organozinc Reagents and Aldehydes across 1,3-Conjugated Diynes”
Y. Ohira, Y. Mori, G. Onodera, M. Kimura
DOI: 10.1002/adsc.201601309