DOI: 10.1002/ejoc.200700550

Cationic $P(OPh)_3$- or PPh_3-Rhodium(I) Complex-Catalyzed Isomerizations of 5-Alkynals to δ-Alkynyl Ketones, Cyclopent-1-enyl Ketones, and Cyclohexenones

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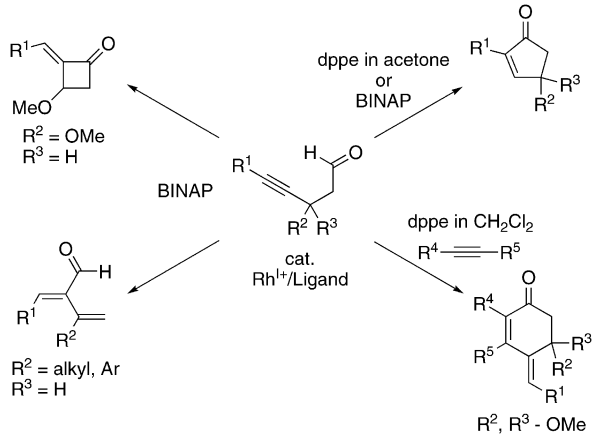
Keywords: Aldehydes / Ketones / Alkynes / Rhodium / Catalysis

We have developed catalytic isomerizations of 5-alkynals to γ-alkynyl ketones and cyclopent-1-enyl ketones using $[Rh\{P(OPh)_3\}_2]BF_4$ as a catalyst. $Cu(OTf)_2$ and $AgBF_4$ are also effective catalysts for the formation of γ-alkynyl ketones. The substituents at the 4-positions in 5-alkynals play important roles in the selection of two different isomerization pathways. The first catalytic *endo*/*trans* hydroacylation of acyclic 5-alkynals leading to cyclohexenones was also developed with $[Rh(PPh_3)_2]BF_4$ as a catalyst. Crossover deuterium-labeling studies indicated that these isomerization reactions proceed intramolecularly.

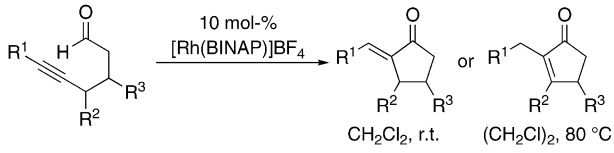
Introduction

Rhodium-catalyzed intramolecular hydroacylation of 4-alkenals, first discovered by Sakai and co-workers in 1972, is well established method for the preparation of cyclopentanones.[1–3] However, the intramolecular hydroacylation of 5-alkenals to generate cyclohexanones is not a general method, being restricted to cyclic substrates.[4,5] In 2001, the corresponding reactions of 4-alkynals to generate cyclopentenones through intramolecular *endo*/*trans* hydroacylation were developed using a cationic dppe-rhodium(I) complex in acetone [dppe = 1,2-bis(diphenylphosphanyl)-ethane, see Scheme 1].[6a] The effects of ligands and substituents on the cationic rhodium(I) complex-catalyzed transformations of 4-alkynals were then thoroughly examined, which revealed that the use of dppe as a ligand furnishes cyclopentenones[6a] or [4+2] annulation products[6b] depending on the solvents used, and that the use of BINAP [2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl] as a ligand furnishes cyclopentenones,[6c,6d] cyclobutanones,[6d] or dienals,[6e] depending on the substituents at the 3-positions (Scheme 1).[6]



Scheme 1. Effect of ligands and substituents on cationic rhodium(I) complex-catalyzed transformations of 4-alkynals.

Unlike that of 5-alkenals, the intramolecular *exo*/*cis* hydroacylation of 5-alkynals to generate α-alkylidenecyclopentanones can proceed at room temp. in high yield through the use of a cationic rhodium(I)/BINAP complex as a catalyst (Scheme 2).[7,8] At elevated temperature (80 °C), a tandem *exo*/*cis* hydroacylation-double bond migration to generate cyclopentenones proceeds in high yield (Scheme 2).



Scheme 2. Rh^{I+}/BINAP-catalyzed reactions of 5-alkynals.

However, the effects of ligands and substituents on the cationic rhodium(I) complex-catalyzed transformations of 5-alkynals have not been thoroughly examined. In this paper, we describe cationic $P(OPh)_3$- or PPh_3-rhodium(I) complex-catalyzed isomerizations of 5-alkynals to γ-alkynyl

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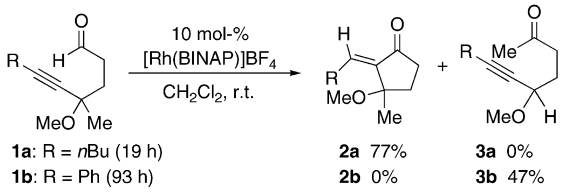
ketones, cyclopent-1-enyl ketones, and cyclohexenones, revealing that the substituents at the 4-positions and the choice of ligands determine the selectivity among the three products.[9]

Results and Discussion

Cationic $P(OPh)_3$-Rhodium(I) Complex-Catalyzed Isomerization of 5-Alkynals to δ-Alkynyl Ketones

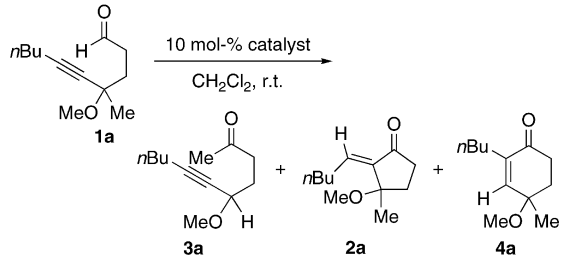
In order to examine the effects of substituents at the 4-positions of 5-alkynals in cationic rhodium(I)/BINAP complex-catalyzed intramolecular hydroacylation, the reaction of 6-alkyl-4-methoxy-5-alkynal **1a** with 10 mol-% [Rh(BINAP)]BF_4 in CH_2Cl_2 at room temp. was conducted, furnishing the corresponding *exo*/*cis* hydroacylation product **2a** in 77% yield (Scheme 3). To our surprise, though, the reaction of 6-phenyl-4-methoxy-5-alkynal **1b** provided not the expected α-alkylidenecyclopentanone **2b**, but γ-alkynyl ketone **3b** in 47% yield (Scheme 3).



Scheme 3. Rh^{I+}/BINAP-catalyzed reactions of 4-methoxy-5-alkynals.

The use of various cationic rhodium(I)/phosphane catalysts to promote the isomerization of **1a** to γ-alkynyl ketone **3a** was examined, as shown in Table 1. The use of bidentate phosphane ligands did not furnish **3a** at all (Entries 1–3). On the other hand, the use of 10 mol-% [$Rh(PPh_3)_2$]BF_4 catalyzed *endo*/*trans* hydroacylation of **1a** to give cyclohexenone **4a** in 30% yield (Entry 4). Fortunately, a cationic rhodium(I)/electron-deficient monodentate phosphane or phosphite complex catalyzed the isomerization of **1a** to **3a** (Entries 5 and 6). Especially, the use of 10 mol-% [$Rh(P(OPh)_3)_2$]BF_4 gave **3a** in 77% yield (Entry 6). We anticipated that this isomerization reaction might proceed through activation of alkynes and aldehydes by complexation to electrophilic transition metal complexes. Indeed, catalytic cycloisomerizations of alkynyl carbonyl compounds leading to a variety of cyclic compounds through the use of a range of electrophilic transition metal complexes have been developed.[10–12] However, the corresponding reactions of γ-alkynyl carbonyl compounds, including 5-alkynals, have hardly been explored.[13] Accordingly, other electrophilic transition metal complexes, which are frequently used for activation of alkynyl carbonyl compounds, were also examined. Although the use of 10 mol-% $PdCl_2$,[11c,12l–12o] $PtCl_2$,[12c] and SbF_5[14a] led to unidentified mixtures (Entries 7–9), the use of 10 mol-% $Cu(OTf)_2$[12i,12j] and $AgBF_4$[15a] gave **3a** in 69% and 70% yields, respectively (Entries 10 and 11). Among the silver(I) salts examined (Entries 11–15), $AgBF_4$ showed the highest catalytic activity (Entry 11). Brønsted acids did not catalyze this isomerization reaction at all (Entries 16 and 17).

Table 1. Screening of catalysts for isomerization of 5-alkynal **1a** to γ-alkynyl ketone **3a**.



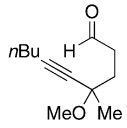
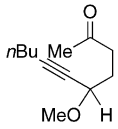
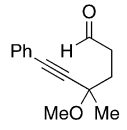
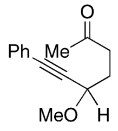
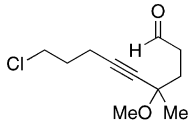
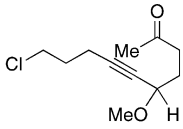
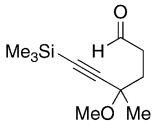
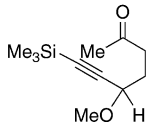
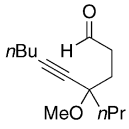
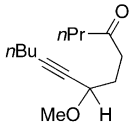
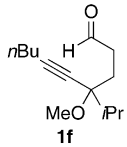
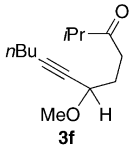
Entry	Catalyst[a]	Time [h]	Yield [%][b] 3a	2a	4a
1	[Rh(BINAP)]BF_4	19	0	77	0
2	[Rh(dppe)]BF_4	16	0	0	0
3	[Rh($(C_6F_5)_2PCH_2CH_2P(C_6F_5)_2$)]$BF_4$	16	0	0	0
4	[$Rh(PPh_3)_2$]BF_4	85	0	<5	30
5	[Rh($(p\text{-}F_3CC_6H_4)_3P)_2$]$BF_4$	16	57	0	0
6	[$Rh(P(OPh)_3)_2$]BF_4	16	77	0	0
7[c]	$PdCl_2$	16	<2	0	0
8[c]	$PtCl_2$	16	<2	0	0
9	SbF_5	16	0	0	0
10[c]	$Cu(OTf)_2$	16	69	0	0
11	$AgBF_4$	16	70	0	0
12	$AgPF_6$	16	66	0	0
13	$AgSbF_6$	16	53	0	0
14	$AgClO_4$	16	0	0	0
15	AgOTf	16	0	0	0
16	CF_3CO_2H	16	0	0	0
17	CF_3SO_3H	16	0	0	0

[a] Rh catalysts were generated in situ from [$Rh(cod)_2$]BF_4 or [$Rh(nbd)_2$]BF_4, ligand, and H_2. [b] Isolated yield. [c] Solvent: CH_3CN.

The reactions of a series of 4-alkyl-4-methoxy-5-alkynals were investigated in the presence of 10 mol-% [$Rh(P(OPh)_3)_2$]BF_4, $Cu(OTf)_2$, or $AgBF_4$ at room temp. as shown in Table 2. The 6-alkyl- and 6-phenyl-5-alkynals **1a**–**c** all cleanly afforded the corresponding γ-alkynyl ketones **3a**–**c** in good yields (Entries 1, 3, 5, 7, and 8). Although the yield of the ketone **3a** was reduced, 5 mol-% Rh, Cu, or Ag catalyst can be used (Entries 2, 4, and 6). Although the reaction of 6-trimethylsilyl-5-alkynal **1d** in the presence of [$Rh(P(OPh)_3)_2$]BF_4 did not proceed even at elevated temperature (80 °C, Entry 9), the use of $Cu(OTf)_2$ or $AgBF_4$ at 80 °C gave the desired ketone **3d** in low yields (Entries 10 and 11). The scope of 4-alkyl substituents was also investigated. Not only methyl-, but also *n*-propyl- and isopropyl-substituted 5-alkynals **1e** and **1f** can be used for this reaction (Entries 12 and 13).

In order to clarify the stereochemical course of this isomerization, the reactions of enantioenriched 4-methoxy-5-alkynals were examined. The reaction of enantioenriched 4-methoxy-5-alkynal (–)-**1b** (18% *ee*), prepared through the kinetic resolution of racemic **1b** by treatment with 10 mol-% [Rh((*R*)-BINAP)]BF_4 at room temp.,[16] proceeded in the presence of 10 mol-% [$Rh(P(OPh)_3)_2$]BF_4 at room temp. to

Table 2. $Rh^{I+}/P(OPh)_3$, $Cu(OTf)_2$, or $AgBF_4$-catalyzed isomerization of 5-alkynals to γ-alkynylketones.[a]

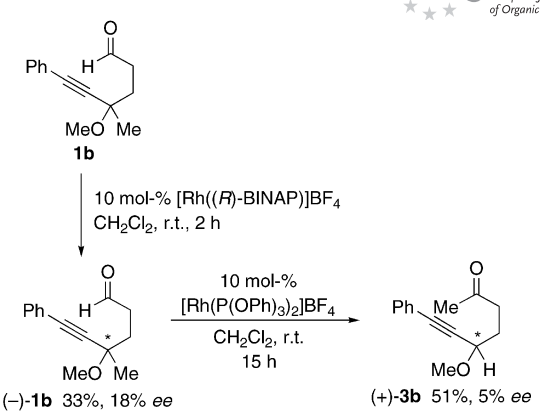
Entry	Substrate	Time [h]	Product	Yield [%][b]
				
1	**1a**	16	**3a**	77
2[c]	**1a**	40	**3a**	64
3[d]	**1a**	15	**3a**	69
4[c,d]	**1a**	16	**3a**	66
5[e]	**1a**	14	**3a**	64
6[c,e]	**1a**	16	**3a**	44
				
7	**1b**	16	**3b**	71
				
8	**1c**	39	**3c**	74
				
9[f]	**1d**	91	**3d**	<1
10[d,f]	**1d**	110	**3d**	24
11[e,f]	**1d**	49	**3d**	13
				
12	**1e**	82	**3e**	43
				
13	**1f**	16	**3f**	57

[a] Reactions were conducted with $[Rh(P(OPh)_3)_2]BF_4$ (0.050 mmol), **1** (0.50 mmol), and CH_2Cl_2 (2.0 mL) at room temp. [b] Isolated yield. [c] Catalyst: 5 mol-%. [d] Catalyst: $Cu(OTf)_2$. Solvent: CH_3CN. [e] Catalyst: $AgBF_4$ (0.030 mmol), **1** (0.30 mmol). [f] At 80 °C.

give (+)-**3b** with 5% *ee*, which revealed that the partial racemization of the stereocenter occurs during the isomerization (Scheme 4).

Although the isomerization of 4-methoxy-5-alkynals to γ-alkynyl ketones proceeds in good yield, the corresponding reactions of a 5-methoxy-6-alkynal, a 3-methoxy-4-alkynal, and a 3-oxa-5-alkynal in the presence of 10 mol-% $[Rh(P(OPh)_3)_2]BF_4$ at room temp. led to mixtures of unidentified products (Figure 1).

The existence of an alkyne moiety is essential for the isomerization. The reaction of 4-methoxyaldehyde **5** in the



Scheme 4. $Rh^{I+}/P(OPh)_3$-catalyzed isomerization of enantio-enriched 4-methoxy-5-alkynal (–)-**1b** to γ-alkynyl ketone (+)-**3b**.

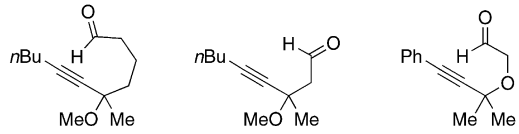
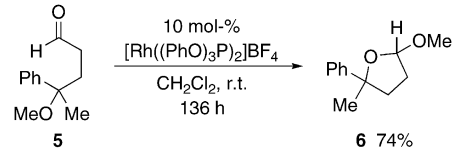


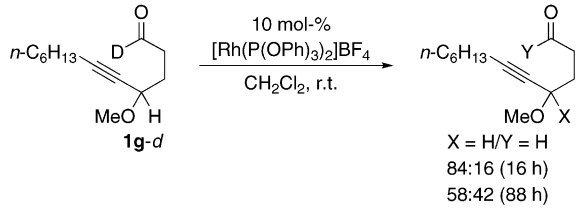
Figure 1. Unsuitable alkynals for $Rh^{I+}/P(OPh)_3$-catalyzed isomerization to alkynyl ketones.

presence of 10 mol-% $[Rh(P(OPh)_3)_2]BF_4$ at room temp. led to the corresponding cyclic acetal **6** in 74% yield (Scheme 5).



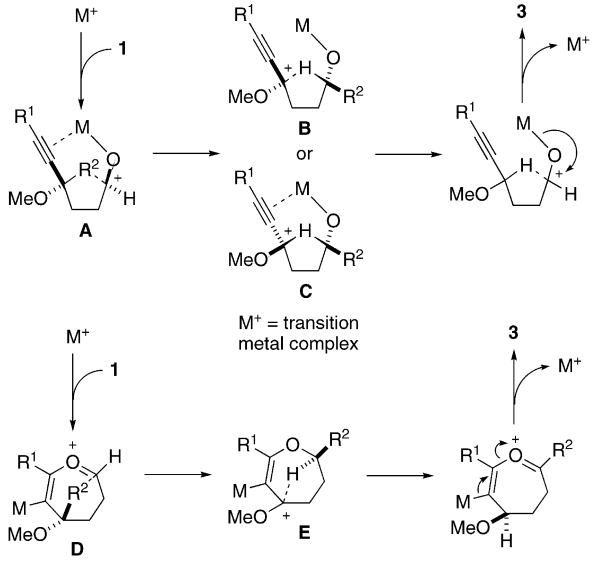
Scheme 5. $Rh^{I+}/P(OPh)_3$-catalyzed reaction of 4-methoxyaldehyde **5** to give cyclic acetal **6**.

Although no reaction was observed when 4-methoxydodec-5-ynal (**1g**) was treated in the presence of 10 mol-% $[Rh(P(OPh)_3)_2]BF_4$ at room temp., we anticipated that an exchange reaction between formyl hydrogen and propargylic hydrogen might proceed in place of that between formyl hydrogen and propargylic alkyl group. Indeed, deuterium–hydrogen exchange between formyl deuterium and propargylic hydrogen proceeded slowly in the reaction of 1-deuteriated 4-methoxydodec-5-ynal ([D]-**1g**, Scheme 6).



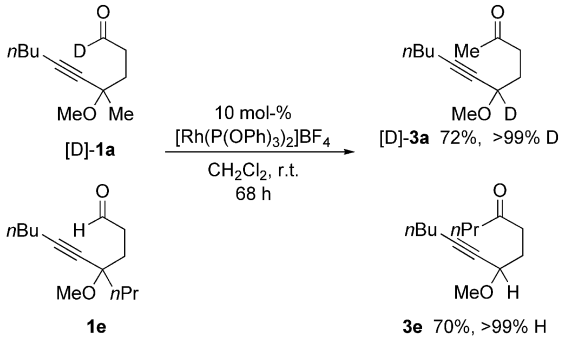
Scheme 6. $Rh^{I+}/P(OPh)_3$-catalyzed deuterium–hydrogen exchange reaction.

Scheme 7 depicts a possible mechanism for the formation of γ-alkynyl ketone **3**. We believe that the coordination of a transition metal complex could lead to acyclic cationic intermediate **A**. An exchange reaction between alkyl group (R^2) and formyl hydrogen would proceed via either the monocoordinated intermediate **B** or the biscoordinated intermediate **C** to form γ-alkynyl ketone **3** and regenerate the transition metal complex. Alternatively, the coordination of an electrophilic transition metal complex could induce an attack of a carbonyl oxygen onto an alkyne through an *endo* pathway, leading to cyclic vinylmetal complex **D**.[17] An exchange reaction between R^2 and formyl hydrogen would then proceed via the oxygen-stabilized cationic intermediate **E** to form the γ-alkynyl ketone **3**. The intermediate **C** may be partially involved in this isomerization, which would account for the partial racemization of the stereocenter.



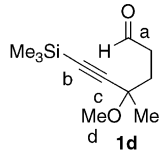
Scheme 7. Possible mechanism for isomerization of 4-methoxy-5-alkynals **1** to γ-alkynyl ketones **3**.

Consistently with this pathway, a crossover deuterium-labeling experiment of a 1:1 mixture of deuterated 5-alkynal [D]-**1a** and nondeuterated 5-alkynal **1e** in the presence of 10 mol-% $[Rh(P(OPh)_3)_2]BF_4$ revealed that the deuterium in [D]-**1a** was stereospecifically incorporated into the propargylic position of γ-alkynylketone [D]-**3a**, while no deuterium crossover between γ-alkynyl ketones [D]-**3a** and **3e** was observed (Scheme 8).



Scheme 8. Crossover deuterium-labeling experiment.

In order to confirm the activation of alkynes and aldehydes by complexation to electrophilic transition metal complexes, ^{13}C NMR spectroscopic analysis of 5-alkynal **1d** in the presence of $AgBF_4$ was investigated. In the presence of 50 mol-% $AgBF_4$ at room temp., both carbonyl and alkyne carbon signals disappeared, but the methoxy carbon signal was unchanged.[18] In the presence of 100 mol-% $AgBF_4$ at room temp., complete isomerization to γ-alkynyl ketone **3d** took place (Figure 2). These results demonstrated that transition metal complexes may activate both carbonyl and triple bond in the isomerization reaction.



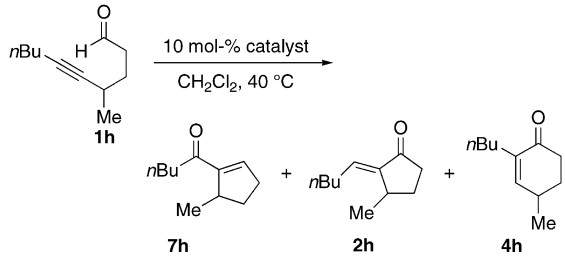
	^{13}C NMR [ppm]			
$AgBF_4$	a	b	c	d
0 mol-%	202.0	105.4	90.6	51.4
50 mol-%	–	–	–	51.4
100 mol-%	(208.1)	(103.6)	(91.1)	(56.4)

Figure 2. ^{13}C NMR spectroscopic analysis of 5-alkynal **1d** in the presence of $AgBF_4$ (numbers in parentheses are the chemical shifts of the isomerization product **3d**).

Cationic $P(OPh)_3$-Rhodium(I) Complex-Catalyzed Isomerization of 5-Alkynals to Cyclopent-1-enyl Ketones

As cationic rhodium(I)/electron-deficient monodentate phosphane complexes catalyze the isomerization of 4-meth-

Table 3. Screening of catalysts for isomerization of 5-alkynal **1h** to cyclopent-1-enyl ketone **7h**.



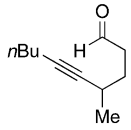
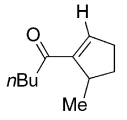
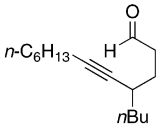
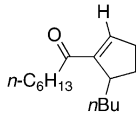
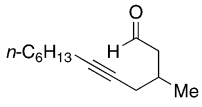
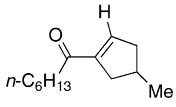
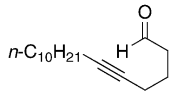
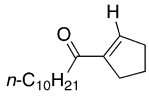
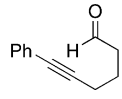
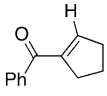
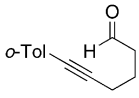
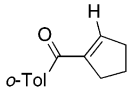
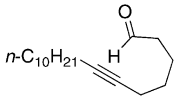
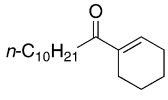
Entry	Catalyst[a]	Time [h]	Yield [%][b] 7h	2h	4h
1	$[Rh(P(OPh)_3)_2]BF_4$	18	58	0	0
2	$[Rh((p\text{-}F_3CC_6H_4)_3P)_2]BF_4$	18	11	0	0
3	$[Rh(PPh_3)_2]BF_4$	64	0	18[c]	19[c]
4	$[Rh(BINAP)]BF_4$	1	0	84[c]	0
5	$[Rh(dppe)]BF_4$	18	0	0	0
6	$[Rh((C_6F_5)_2PCH_2CH_2P(C_6F_5)_2)]BF_4$	18	0	0	0
8[d]	$PdCl_2$	18	0	0	0
10[d]	$PtCl_2$	18	0	0	0
11[d]	SbF_5	18	0	0	0
12[d]	$Cu(OTf)_2$	18	<1	0	0
13	$AgBF_4$	18	0	0	0
14	CF_3CO_2H	18	0	0	0
15	CF_3SO_3H	18	<1	0	0

[a] Rh catalysts were generated in situ from $[Rh(cod)_2]BF_4$ or $[Rh(nbd)_2]BF_4$, ligand, and H_2. [b] NMR yield. [c] Isolated yield. [d] Solvent: CH_3CN.

oxy-5-alkynals to γ-alkynyl ketones, the reaction of 5-alkynal **1h**, bearing no methoxy group at the 4-position, in the presence of 10 mol-% $[Rh(P(OPh)_3)_2]BF_4$ was also examined. Interestingly, the intramolecular addition of aldehyde to alkyne proceeded in CH_2Cl_2 at 40 °C to give cyclopent-1-enyl ketone **7h** in moderate yield (Table 3, Entry 1).[14,15] The use of $(p\text{-}F_3CC_6H_4)_3P$ as a ligand decreased the yield of **7h** (Entry 2). The use of PPh_3 and BINAP as ligands furnished *endo*/*trans* and *exo*/*cis* hydroacylation products **4h** and **2h**, which was similar to the reactions of 4-methoxy-5-alkynals (Entries 3 and 4). Other electrophilic transition metal complexes and Brønsted acids were also examined, but none was effective (Entries 8–15). Although SbF_5[14a] and Ag^I salts[15a] are known to catalyze the addition of aldehyde to alkyne, they did not catalyze the isomerization of **1h** to **7h** (Entries 11 and 13).

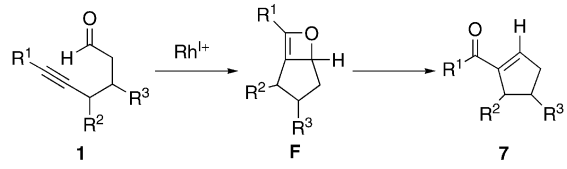
Thus, the reactions of a series of 5-alkynals in the presence of 10 mol-% $[Rh(P(OPh)_3)_2]BF_4$ were investigated as shown in Table 4. 4-Alkyl-5-alkynals **1h** and **1i** afforded the corresponding cyclopent-1-enyl ketones **7h** and **7i** in good yields (Entries 1 and 2), but 3-alkyl-5-alkynal **1j** and 5-alkynals **1k**–**m**, bearing no substituents at either 3- or 4-positions, afforded the corresponding cyclopent-1-enyl ketones **7j**–**m** in low to moderate yields (Entries 3–6). Not only 5-alkynals **1h**–**m**, but also 6-alkynal **8** could also cyclize to give cyclohex-1-enyl ketone **9**, although the yield was low (Entry 7).

Table 4. $Rh^{I+}/P(OPh)_3$-catalyzed isomerizations of 5- and 6-alkynals to 1-cycloalkenyl ketones.[a]

Entry	Substrate	Time [h]	Product	Yield [%][b]
1	 **1h**	72	 **7h**	62
2	 **1i**	40	 **7i**	71
3	 **1j**	72	 **7j**	47
4	 **1k**	72	 **7k**	43
5[c]	 **1l**	44	 **7l**	28
6[c]	 **1m**	72	 **7m**	39
7[c]	 **8**	72	 **9**	19

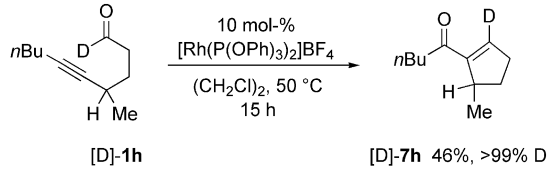
[a] Reactions were conducted with $[Rh(P(OPh)_3)_2]BF_4$ (0.050 mmol) and either **1** or **8** (0.50 mmol), in $(CH_2Cl)_2$ (2.0 mL) at 50 °C. [b] Isolated yield. [c] At 80 °C.

Scheme 9 depicts a possible mechanism for the rhodium-catalyzed intramolecular addition of aldehyde to alkyne. We believe that the formation of cyclopent-1-enyl ketone **7** may proceed through an oxete intermediate **F**, as has also been proposed in the case of previously reported metal-catalyzed inter- and intramolecular addition of aldehydes to alkynes.[14,15]



Scheme 9. Possible mechanism for isomerization of 5-alkynals to cyclopent-1-enyl ketones.

The reaction of 1-deuteriated 5-alkynal [D]-**1h** led to stereospecific incorporation of the deuterium into the vinylic position of cyclopent-1-enyl ketone [D]-**7h**, which is consistent with the mechanism proposed above (Scheme 10).



Scheme 10. Deuterium labeling study.

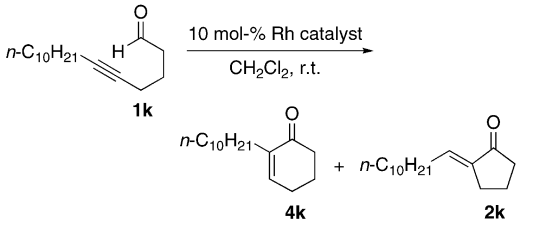
Cationic PPh_3-Rhodium(I) Complex-Catalyzed Isomerization of 5-Alkynals to Cyclohexenones

As shown in Table 1 and Table 3, the combined use of a cationic rhodium catalyst with PPh_3 and BINAP as ligands could furnish *endo*/*trans* and *exo*/*cis* hydroacylation products. As an example of intramolecular *endo*/*trans* hydroacylation of a 5-alkynal to generate a cyclohexenone, Nicolaou and co-workers observed an unexpected hydroacylation of a tricyclic 5-alkynal to generate a tetracyclic cyclohexenone (78% yield based on 50% conversion) while attempting to decarbonylate an aldehyde in the presence of a stoichiometric amount of $RhCl(PPh_3)_3$.[19] However, rigidity of the substrates is crucial for the success of their reaction and the method cannot be applicable to acyclic 5-alkynals.

Accordingly, we thoroughly examined the reaction of acyclic 5-alkynal **1k**, bearing no substituent at either 3- or 4-positions, in the presence of 10 mol-% cationic rhodium(I)/phosphane complexes at room temp. to promote the *endo*/*trans* hydroacylation (Table 5). The use of PPh_3 as a

ligand furnished both *endo*/*trans* and *exo*/*cis* hydroacylation products **4k** and **2k**, with **4k** being obtained as the major product (Entry 1). The use of 3 equiv. of PPh_3 relative to rhodium lowered the yield of **4k** (Entry 2). Other monodentate phosphane ligands with different electronic and steric characters, such as *o*-Tol_3P, (*p*-$F_3CC_6H_4)_3P$, (*p*-$MeOC_6H_4)_3P$, and *n*Bu_3P, also lowered the yield of **4k**. The use of bisphosphane ligands [dppm: bis(diphenylphosphanyl)methane, dppe, and dppp: 1,3-bis(diphenylphosphanyl)propane], which have small P–M–P natural bite angles, furnished no hydroacylation products (Entries 3–5). On the other hand, the use of bisphosphane ligands [dppb: 1,4-bis(diphenylphosphanyl)butane, dppf: 1,1′-bis(diphenylphosphanyl)ferrocene, and BINAP], which have large P–M–P natural bite angles, furnished *exo*/*cis* hydroacylation product **2k**, but no *endo*/*trans* hydroacylation product **4k** was obtained (Entries 6–8).

Table 5. Screening of catalysts for isomerization of 5-alkynal **1k** to cyclohexenone **4k**.



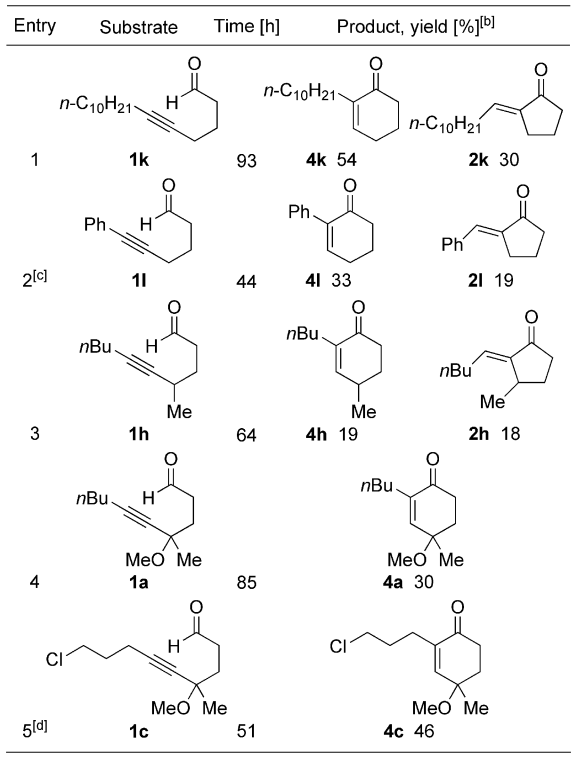
Entry	Catalyst[a]	Time [h]	Yield [%][b] 4k	2k
1	$[Rh(PPh_3)_2]BF_4$	16	54[c]	30[c]
2	$[Rh(PPh_3)_3]BF_4$	16	15	15
3	$[Rh(dppm)]BF_4$	16	0	0
4	$[Rh(dppe)]BF_4$	16	0	0
5	$[Rh(dppp)]BF_4$	16	0	0
6	$[Rh(dppb)]BF_4$	0.7	0	60
7	$[Rh(dppf)]BF_4$	93	0	59
8	$[Rh(BINAP)]BF_4$	16	0	94[c]

[a] Rh catalysts were generated in situ from $[Rh(cod)_2]BF_4$ or $[Rh(nbd)_2]BF_4$, ligand, and H_2. [b] NMR yield. [c] Isolated yield.

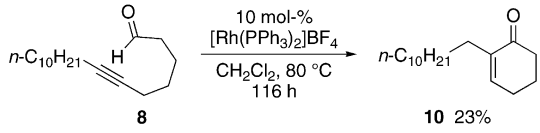
A series of 5-alkynals was subjected to the above optimal reaction conditions as shown in Table 6. The reaction of 6-alkyl-5-alkynal **1k** afforded the corresponding cyclohexenone **4k** in good yield at room temp. (Entry 1), but the reaction of 6-aryl-5-alkynal **1l** required elevated temperature (80 °C) and the product yield was lower than that of **1k** (Entry 2). Not only linear 5-alkynal **1k**, but also branched 5-alkynal **1h**, bearing a substituent at the 4-position, also furnished the corresponding cyclohexenone **4h**, although a lower yield was observed (Entry 3). The cyclizations of the coordinating propargylic ethers **1a** and **1c** preferentially furnished *endo*/*trans* hydroacylation products, similarly to the cyclizations of 4-alkynals possessing propargylic ether moieties (Entries 4 and 5).[6c]

The reaction of 6-alkynal **8** in the presence of 10 mol-% $[Rh(PPh_3)_2]BF_4$ was also investigated at room temp., but it was extremely sluggish. Although tandem *exo*/*cis* hydroacylation-isomerization product **10** was obtained in 23% yield at elevated temperature (80 °C),[7] no *endo*/*trans* hydroacylation product was obtained (Scheme 11).

Table 6. Rh^{I+}/PPh_3-catalyzed isomerizations of 5-alkynals to cyclohexenones.[a]

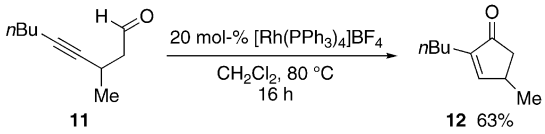


[a] Reactions were conducted with $[Rh(PPh_3)_2]BF_4$ (0.050 mmol), **1** (0.50 mmol), and CH_2Cl_2 (2.0 mL) at room temp. [b] Isolated yield. [c] At 80 °C. [d] Catalyst: 20 mol-%.



Scheme 11. Rh^{I+}/PPh_3-catalyzed reaction of a 6-alkynal.

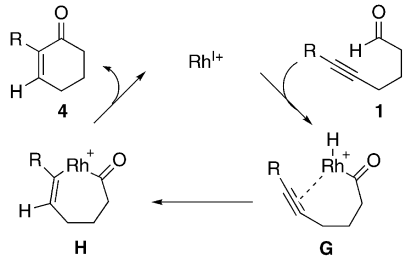
Next, the cationic rhodium(I)/PPh_3 catalyst system was applied to the transformation of 4-alkynal **11**. In this case, employment of 4 equiv. of PPh_3 relative to rhodium and elevated temperature (80 °C) are effective, and the corresponding *endo*/*trans* hydroacylation product **12** was obtained in 63% yield (Scheme 12).



Scheme 12. Rh^{I+}/PPh_3-catalyzed reaction of 4-alkynal.

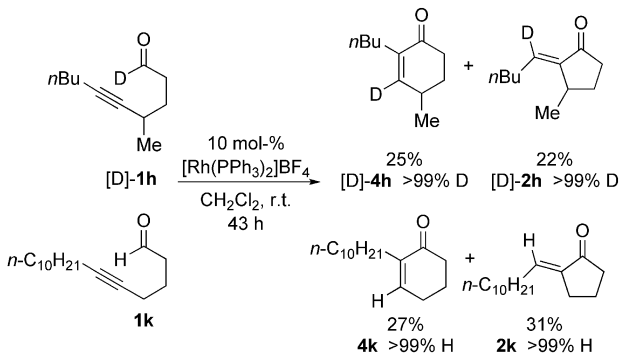
Scheme 13 depicts a possible mechanism for the intramolecular *endo*/*trans* hydroacylation of 5-alkynals **1**.[20] We propose that the rhodium(I) catalyst oxidatively inserts into the aldehyde C–H bond, affording the rhodium acyl hydride

G. *endo*/*trans* addition of the rhodium hydride to the metal-bound alkyne then provides seven-membered rhodium metallacycle **H**. Reductive elimination furnishes cyclohexenones **4** and regenerates the rhodium(I) catalyst.



Scheme 13. Possible mechanism for *trans* hydroacylation of 5-alkynals to give cyclohexenones.

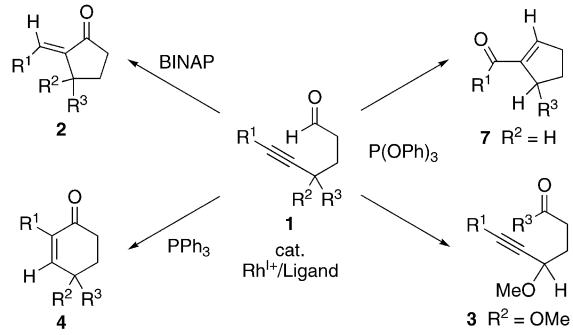
Consistently with the proposed reaction pathway, a crossover experiment with the 1:1 mixture of deuterium-labeled 5-alkynal [D]-**1h** and 5-alkynal **1k** furnished deuterated cyclized products ([D]-**4h** and [D]-**2h**) and nondeuterated cyclized products (**4k** and **2k**) exclusively. Stereospecific incorporation of the deuterium into the β positions of both cyclohexenone [D]-**4h** and α-alkylidenecyclopentanone [D]-**2h** was also observed (Scheme 14).[20]



Scheme 14. Crossover deuterium-labeling experiment.

Conclusions

In conclusion, we have determined the effects of ligands and substituents in the cationic rhodium(I) complex-catalyzed transformations of 5-alkynals as summarized in Scheme 15. A catalytic isomerization of 4-alkyl-4-methoxy-5-alkynals to γ-alkynyl ketones proceeded in the presence of $[Rh(P(OPh)_3)_2]BF_4$ as a catalyst. $Cu(OTf)_2$ and $AgBF_4$ are also effective catalysts for this isomerization. In the case of 5-alkynals having no 4-methoxy substituent, an intramolecular addition of aldehyde to alkyne proceeded in the presence of $[Rh(P(OPh)_3)_2]BF_4$ as a catalyst to give cyclopent-1-enyl ketones. The substituents at the 4-positions of 5-alkynals play important roles in the selection of two isomerization pathways. The first catalytic *endo*/*trans* hydroacylation of acyclic 5-alkynals leading to monocyclic cyclohexenones was also developed in the presence of $[Rh(PPh_3)_2]BF_4$ as a catalyst. Crossover deuterium-labeling studies indicated that these isomerization reactions proceed intramolecularly.



Scheme 15. Effect of ligands and substituents in cationic rhodium(I) complex-catalyzed transformations of 5-alkynals.

Experimental Section

General Methods: ^{1}H NMR spectra were recorded on a 300 MHz instrument (JEOL AL 300). ^{13}C NMR spectra were obtained with complete proton decoupling at 75 MHz (JEOL AL 300). HRMS data were obtained on a JEOL JMS-700 instrument. Infrared spectra were obtained on a JASCO A-302. Anhydrous CH_2Cl_2 (No. 27,099-7) and anhydrous $(CH_2Cl)_2$ (No. 28,450–5) were obtained from Aldrich and used as received. Solvents for the synthesis of substrates were dried with molecular sieves (4 Å) prior to use. All other reagents were obtained from commercial sources and used as received. All reactions were carried out under argon or nitrogen in oven-dried glassware with magnetic stirring.

Starting Materials: Alkynals **1h**, **1j**, **1k**, **1l**, **1m, 8**, [D]-**1h**, and **11** were synthesized by literature procedures.[7]

Alkynal 1a: *n*BuLi (1.58 M in *n*-hexane, 23 mL, 36 mmol) was added at 0 °C to a solution of hex-1-yne (5.2 mL, 46 mmol) in THF (120 mL), and the resulting solution was stirred at 0 °C for 0.5 h. 1,1-Dimethoxybutan-3-one was added at 0 °C, and the system was stirred at room temp. for 0.5 h. MeI (9.4 mL, 0.15 mol) and DMSO (90 mL) were added, and the resulting mixture was stirred at 80 °C for 1 h. The reaction mixture was then diluted with water and extracted with Et_2O. The organic layer was washed with water and brine, dried with Na_2SO_4, and concentrated. Water (35 mL) and AcOH (100 mL) were added to the residue, and the resulting mixture was stirred at 80 °C for 0.5 h. The reaction mixture was diluted with water and extracted with Et_2O. The organic layer was washed with saturated aqueous Na_2CO_3, dried with Na_2SO_4, and concentrated, which afforded crude 3-methoxy-3-methylnon-4-ynal (5.1 g).

A lithium diisopropylamide solution consisting of *n*BuLi (1.58 M in *n*-hexane, 34 mL, 54 mmol) and diisopropylamine (8.0 mL, 57 mmol) in THF (65 mL) was added to a cooled (–10 °C) and stirred suspension of (methoxymethyl)triphenylphosphonium chloride (19.4 g, 56.6 mmol) in THF (61 mL). A solution of crude 3-methoxy-3-methylnon-4-ynal (5.1 g) in THF (55 mL) was added to the deep red solution, which was kept at –10 °C for 1 h and then diluted with saturated aqueous $NaHCO_3$. After extraction with Et_2O, the combined organic layers were dried with Na_2SO_4, filtered, and concentrated. A solution of the residue in THF (375 mL) was treated at room temp. with aqueous HCl (10%, 75 mL) for 24 h. Saturated aqueous $NaHCO_3$ was added slowly to neutralize

HCl and then extracted with Et_2O. The combined organic extracts were then washed with brine, dried with Na_2SO_4, concentrated, and purified on a silica gel column chromatography (hexane/EtOAc, 15:1), which furnished **1a** (5.2 g, 26 mmol, 48% yield) as a pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 9.78 (t, J = 1.5 Hz, 1 H), 3.30 (s, 3 H), 2.75–2.50 (m, 2 H), 2.21 (t, J = 6.9 Hz, 2 H), 2.10–1.88 (m, 2 H), 1.58–1.30 (m, 4 H), 1.39 (s, 3 H), 0.92 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.4, 86.7, 79.9, 72.8, 51.2, 39.6, 34.5, 30.7, 25.8, 21.9, 18.2, 13.5 ppm. IR (neat): $\tilde{\nu}$ = 3350, 2900, 1720, 1080 cm^{-1}. HRMS: (EI) calcd. for $C_{12}H_{20}O_2$: 196.1463; found: 196.1426 $[M]^+$.

Alkynal 1b: The title compound was prepared from phenylacetylene by the procedure for **1a**. Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 9.83 (t, J = 1.5 Hz, 1 H), 7.45–7.37 (m, 2 H), 7.48–7.28 (m, 3 H), 3.40 (s, 3 H), 2.82–2.59 (m, 2 H), 2.12 (dt, J = 7.5, 1.5 Hz, 2 H), 1.52 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.3, 131.7, 128.5, 128.3, 122.4, 89.1, 86.2, 73.2, 51.6, 39.5, 34.4, 25.6 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1720, 1440, 1370, 1260, 1180, 880, 760, 690 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{16}O_2$: 216.1150; found: 216.1160 $[M]^+$.

Alkynal 1c: The title compound was prepared from 5-chloropent-1-yne by the procedure for **1a**. Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 9.78 (t, J = 1.8 Hz, 1 H), 3.65 (t, J = 6.6 Hz, 2 H), 3.30 (s, 3 H), 2.72–2.49 (m, 2 H), 2.42 (t, J = 6.6 Hz, 2 H), 2.09–1.90 (m, 4 H), 1.69 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.1, 84.6, 81.2, 72.8, 51.4, 43.6, 39.5, 34.5, 31.3, 25.8, 16.1 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1720, 1430, 1370, 1270, 1180, 1150, 1080 cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{14}ClO_2$: 201.0682; found: 201.0678 $[M - CH_3]^+$.

Alkynal 1d: The title compound was prepared from (trimethylsilyl)-acetylene by the procedure for **1a**. Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 9.79 (m, 1 H), 3.32 (s, 3 H), 2.75–2.50 (m, 2 H), 2.01 (dt, J = 1.8, 7.8 Hz, 2 H), 1.40 (s, 3 H), 0.19 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.0, 105.4, 90.6, 72.9, 51.4, 39.4, 34.2, 25.5, –0.03 ppm. IR (neat): $\tilde{\nu}$ = 3350, 2950, 1720, 1250, 1080, 840, 760 cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{17}O_2Si$: 197.0998; found: 197.0953 $[M - CH_3]^+$.

Alkynal 1f: A solution of 2-(2-bromoethyl)-1,3-dioxolane (12.5 g, 69 mmol) in THF (20 mL) was added to a stirred suspension of magnesium (3.0 g, 69 mmol) in THF (80 mL) and the reaction mixture was stirred at room temp. for 30 min. The solution was cooled to 0 °C, CuBr powder (9.3 g, 65 mmol) was added, and the resulting mixture was stirred at 5–15 °C for 20 min. After cooling to –70 °C, a solution of isobutyryl chloride (5.8 mL, 55 mmol) in THF (100 mL) was added over 15 min, and the reaction mixture was stirred at –70 °C for an additional 1 h. The reaction mixture was warmed to room temp. and stirred at room temp. for 18 h. The mixture was poured into an ice-cold solution of aqueous HCl (2 M, 200 mL) and was extracted with Et_2O (3× 100 mL). The combined organic layers were dried with Na_2SO_4, concentrated, and purified on a silica gel column (hexane/EtOAc, 5:1) to give 1-(1,3-dioxolan-2-yl)-4-methylpentan-3-one (3.0 g, 17.6 mmol, 32% yield) as a pale yellow oil.

*n*BuLi (1.58 M in *n*-hexane, 8.4 mL, 13 mmol) was added at 0 °C to a solution of hex-1-yne (2.0 mL, 16.5 mmol) in THF (45 mL), and the resulting solution was stirred at 0 °C for 0.5 h. A solution of 1-(1,3-dioxolan-2-yl)-4-methylpentan-3-one (1.9 g, 11 mmol) in THF (10 mL) was added at 0 °C, and the mixture was stirred at room temp. for 0.5 h. MeI (3.4 mL, 55 mmol) and DMSO (34 mL) were added, and the resulting mixture was stirred at 80 °C for 1 h. The reaction mixture was then diluted with water and extracted with Et_2O. The organic layer was washed with water and brine, dried with Na_2SO_4, and concentrated. Water (5 mL) and AcOH (15 mL) were added to the residue, and the resulting mixture was stirred at 60 °C for 1 h. The reaction mixture was diluted with water and extracted with Et_2O. The organic layer was washed with saturated aqueous Na_2CO_3, dried with Na_2SO_4, and concentrated, which afforded **1f** (1.1 g, 4.9 mmol, 94% yield) as a pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 9.79 (t, J = 1.5 Hz, 1 H), 3.27 (s, 3 H), 2.70–2.48 (m, 2 H), 2.24 (t, J = 6.9 Hz, 2 H), 2.10–1.83 (m, 3 H), 1.58–1.33 (m, 4 H), 1.01 (d, J = 6.9 Hz, 3 H), 0.92 (t, J = 7.2 Hz, 3 H), 0.92 (d, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.7, 88.4, 79.5, 51.2, 39.2, 33.9, 30.9, 27.2, 22.0, 18.3, 18.0, 16.6, 13.7 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1690, 1070 cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{15}O_2$: 167.1071; found: 167.1030 $[M - C_4H_9]^+$.

Alkynal 1e: The title compound was prepared from 1-(1,3-dioxolan-2-yl)hexan-3-one[21] by the procedure for **1f**. 1-(1,3-Dioxolan-2-yl)-hexan-3-one was prepared from 2-(2-bromoethyl)-1,3-dioxolane and butyryl chloride by the procedure for **1f**. Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 9.78 (t, J = 1.8 Hz, 1 H), 3.28 (s, 3 H), 2.71–2.45 (m, 2 H), 2.22 (t, J = 6.9 Hz, 2 H), 1.96 (t, J = 7.2 Hz, 2 H), 1.72–1.30 (m, 8 H), 0.93 (t, J = 7.2 Hz, 3 H), 0.92 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.6, 87.7, 79.5, 75.9, 51.1, 40.5, 39.4, 31.3, 30.8, 21.9, 18.3, 17.3, 14.3, 13.6 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2900, 1700, 1420, 1280, 1080 cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{15}O_2$: 167.1071; found: 167.1030 $[M - C_4H_9]^+$.

Alkynal (–)-1b: (*R*)-BINAP (49.8 mg, 0.080 mmol) and $[Rh(cod)_2]$-BF_4 (32.5 mg, 0.080 mmol) were dissolved in CH_2Cl_2 (2.0 mL) and the mixture was stirred at room temp. for 5 min. H_2 was introduced into the resulting solution through a Schlenk tube. After stirring at room temp. for 1 h, the resulting solution was concentrated to dryness. Alkynal **1b** (173.0 mg, 0.800 mmol) was added to the residue by using CH_2Cl_2 (3.5 mL). The mixture was stirred at room temp. for 2 h. The resulting solution was concentrated and purified on a silica gel column (hexane/EtOAc, 20:1) to give (–)-**1b** (57.7 mg, 0.267 mmol, 33% yield, 18% *ee*) as a colorless oil. $[\alpha]_D^{25}$ = –0.84 (*c* = 1.615 in Et_2O, 18% *ee*). GC: Chiraldex B-DM column, 150 °C isothermal, retention times: 28.9 min (minor isomer) and 30.0 min (major isomer).

Aldehyde 5: The Grignard reagent prepared from bromobenzene (7.41 g, 47.2 mmol) and Mg (1.30 g, 52.0 mmol) in THF (15 mL) was added dropwise at room temp. to a solution of 1,1-dimethoxybutan-3-one (4.00 g, 30.3 mmol) in THF (30 mL), and the resulting mixture was stirred at room temp. for 1 h. MeI (9.4 mL, 152 mmol) and DMSO (91 mL) were added, and the resulting mixture was stirred at 80 °C for 1 h. The reaction was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated. Water (30 mL) and AcOH (88 mL) were added to the residue, and the resulting mixture was stirred at 80 °C for 0.5 h. The reaction mixture was diluted with water and extracted with Et_2O. The organic layer was washed with saturated aqueous Na_2CO_3, dried with Na_2SO_4, and concentrated, which afforded the crude aldehyde (4.6 g).

A lithium diisopropylamide solution consisting of *n*BuLi (1.58 M in hexane, 30.9 mL, 48.8 mmol) and diisopropylamine (7.3 mL, 51 mmol) in THF (56 mL) was added to a cooled (–10 °C) suspension of (methoxymethyl)triphenylphosphonium chloride (17.6 g, 51.4 mmol) in THF (56 mL). A solution of the crude aldehyde (4.6 g) in THF (56 mL) was added to the deep red solution. The resulting solution was kept at –10 °C for 1 h and then diluted with saturated aqueous $NaHCO_3$. After extraction with Et_2O, the or-

ganic layer was dried with Na_2SO_4 and concentrated to afford the crude enol ether. A solution of the crude enol ether in THF (206 mL) was treated with aqueous HCl (10%, 47 mL) at room temp. for 3 h. Saturated aqueous $NaHCO_3$ was added slowly to neutralize the acid, and the system was extracted with Et_2O. The organic layer was washed with brine, dried with Na_2SO_4, concentrated, and purified on a silica gel column (hexane/EtOAc, 10:1), which furnished **5** (0.93 g, 4.7 mmol, 16% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.67 (t, J = 1.8 Hz, 1 H), 7.49–7.25 (m, 5 H), 3.11 (s, 3 H), 2.48–2.29 (m, 2 H), 2.16–1.99 (m, 2 H), 1.55 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.0, 128.6, 127.5, 126.2, 125.8, 65.8, 55.3, 50.4, 23.8, 15.2 ppm. IR (neat): $\tilde{\nu}$ = 3424, 2978, 2934, 1720, 1660, 1494, 1446, 1122, 1073, 765, 701, 472 cm^{-1}. HRMS (EI): calcd. for $C_9H_{11}O$: 135.0810; found: 135.0796 [M – CH_2CH_2CHO]$^+$.

Alkynal [D]-1g: The title compound was prepared from 4-methoxydodec-5-ynal (**1g**)[21] by following the procedure for the synthesis of 1-deuterio-4-methyldec-5-ynal ([D]-**1h**).[7] Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.01 (tt, J = 6.0, 1.8 Hz, 1 H), 3.37 (s, 3 H), 2.61 (t, J = 6.6 Hz, 2 H), 2.22 (dt, J = 7.2, 1.8 Hz, 2 H), 2.03 (q, J = 7.2 Hz, 2 H), 1.57–1.44 (m, 2 H), 1.44–1.21 (m, 6 H), 0.89 (t, J = 6.9 Hz, 3 H) ppm. ^{2}H NMR ($CHCl_3$, 61 MHz): δ = 9.81 (s) ppm.

Alkynal [D]-1a: The title compound was prepared from 4-methoxy-4-methyldec-5-ynal (**1a**) by following the procedure for the synthesis of 1-deuterio-4-methyldec-5-ynal ([D]-**1h**).[7] Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.30 (s, 3 H), 2.75–2.50 (m, 2 H), 2.21 (t, J = 6.9 Hz, 2 H), 2.10–1.88 (m, 2 H), 1.58–1.41 (m, 4 H), 1.39 (s, 3 H), 0.92 (t, J = 7.2 Hz, 3 H) ppm. ^{2}H NMR ($CHCl_3$, 61 MHz): δ = 9.81 (s) ppm.

Alkynal 1i: The title compound was prepared from oct-1-yne and hept-2-enal by following the procedure for the synthesis of 4-methyldec-5-ynal (**1h**).[7] Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.81 (t, J = 1.8 Hz, 1 H), 2.72–2.49 (m, 2 H), 2.39–2.26 (m, 1 H), 2.15 (dt, J = 7.2, 1.8 Hz, 2 H), 1.88–1.74 (m, 1 H), 1.71–1.58 (m, 1 H), 1.54–1.29 (m, 14 H), 0.90 (t, J = 7.2 Hz, 3 H), 0.89 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.5, 82.6, 82.3 42.1, 35.2, 31.31, 31.29, 29.6, 29.0, 28.5, 27.7, 22.6, 22.5, 18.7, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 2900, 2860, 2720, 1720, 1440, 1380 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{28}O$: 236.2140; found: 236.2124 [M]$^+$.

Representative Procedure for Isomerization of Alkynals: (Using Rh catalyst: Table 2, Entry 1): $(PhO)_3P$ (31.0 mg, 0.10 mmol) and $[Rh(cod)_2]BF_4$ (20.3 mg, 0.050 mmol) were dissolved in CH_2Cl_2 (2.0 mL) and the mixture was stirred at room temp. for 0.5 h. H_2 was introduced into the resulting solution through a Schlenk tube. After stirring at room temp. for 1 h, the resulting solution was concentrated to dryness. Alkynal **1a** (98.1 mg, 0.500 mmol) was added to the residue in CH_2Cl_2 (2.0 mL). The mixture was stirred at room temp. for 16 h. The resulting solution was concentrated and purified by silica gel preparative TLC (hexane/EtOAc, 5:1) to give **3a** (75.5 mg, 0.385 mmol, 77% yield) as a colorless oil.

Representative Procedure for Isomerization of Alkynals with Cu Catalyst (see Table 2, Entry 3): $Cu(OTf)_2$ (18.1 mg, 0.050 mmol) was dissolved in CH_3CN (1.0 mL) and the mixture was stirred at room temp. for 5 min. Alkynal **1a** (98.1 mg, 0.500 mmol) was added to the mixture in CH_3CN (1.0 mL) and the system was stirred at room temp. for 15 h. The resulting solution was concentrated and purified by silica gel preparative TLC (hexane/EtOAc, 5:1) to give **3a** (68.1 mg, 0.347 mmol, 69% yield) as a colorless oil.

Representative Procedure for Isomerization of Alkynals with Ag Catalyst (see Table 2, Entry 5): $AgBF_4$ (5.84 mg, 0.030 mmol) was dissolved in CH_2Cl_2 (1.0 mL) and the mixture was stirred at room temp. for 5 min. Alkynal **1a** (58.9 mg, 0.300 mmol) was added to the mixture in CH_2Cl_2 (1.0 mL) and stirred at room temp. for 14 h. The resulting solution was concentrated and purified by silica gel preparative TLC (hexane/EtOAc, 5:1) to give **3a** (37.6 mg, 0.192 mmol, 64% yield) as a colorless oil.

Ketone 3a: Yield 77% (76 mg). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.98 (tt, J = 1.8, 6.3 Hz, 1 H), 3.36 (s, 3 H), 2.61 (t, J = 7.2 Hz, 2 H), 2.22 (dt, J = 1.8, 6.9 Hz, 2 H), 2.16 (s, 3 H), 2.00–1.90 (m, 2 H), 1.56–1.30 (m, 4 H), 0.92 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 208.2, 86.8, 77.9, 70.1, 56.1, 39.0, 30.6, 29.9, 29.6, 21.8, 18.2, 13.4 ppm. IR (neat): $\tilde{\nu}$ = 2920, 1700, 1340, 1100 cm^{-1}. HRMS (EI): calcd. for $C_8H_{13}O$: 125.0966; found: 125.0926 [M – CH_2CH_2COMe]$^+$.

Ketone 3b: Yield 71% (71 mg). Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.47–7.41 (m, 2 H), 7.34–7.29 (m, 3 H), 4.24 (t, J = 6.0 Hz, 1 H), 3.45 (s, 3 H), 2.70 (t, J = 7.5 Hz, 2 H), 2.18 (s, 3 H), 2.12–2.04 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 208.2, 131.6, 128.4, 128.2, 122.4, 87.1, 86.2, 70.4, 56.5, 38.9, 30.0, 29.4 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1700, 1340, 1160, 1100, 960, 760, 700 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{16}O_2$: 216.1150; found: 216.1072 [M]$^+$.

Ketone 3c: Yield 74% (80 mg). Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.99 (tt, J = 1.8 and 6.1 Hz, 1 H), 3.66 (t, J = 6.2 Hz, 2 H), 3.37 (s, 3 H), 2.61 (t, J = 7.2 Hz, 2 H), 2.44 (dt, J = 1.8, 7.0 Hz, 2 H), 2.17 (s, 3 H), 2.05–1.85 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 208.2, 84.7, 79.2, 70.1, 56.3, 43.6, 39.0, 31.2, 30.0, 29.5, 16.1 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1700, 1340, 1100 cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{17}ClO_2$: 216.0917; found: 216.0860 [M]$^+$.

Ketone 3d: Yield 24% (25 mg). Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.98 (t, J = 6.3 Hz, 1 H), 3.37 (s, 3 H), 2.61 (t, J = 6.3 Hz, 2 H), 2.15 (s, 3 H), 1.96 (q, J = 6.3 Hz, 2 H), 0.17 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 208.1, 103.6, 91.1, 70.4, 56.4, 38.9, 30.0, 29.2, 0.1 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1700, 1340, 1240, 1090, 840, 760 cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{17}O_2Si$: 197.0998; found: 197.0939 [M – CH_3]$^+$.

Ketone 3e: Yield 43% (48 mg). Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.98 (tt, J = 1.8 and 6.3 Hz, 1 H), 3.36 (s, 3 H), 2.58 (t, J = 7.5 Hz, 2 H), 2.40 (t, J = 7.2 Hz, 2 H), 2.22 (dt, J = 1.8, 6.9 Hz, 2 H), 1.95 (q, J = 7.5 Hz, 2 H), 1.61 (sextet, J = 7.2 Hz, 2 H), 1.53–1.32 (m, 4 H), 0.91 (t, J = 7.2 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 210.5, 86.9, 78.0, 70.3, 56.1, 44.8, 38.0, 30.7, 29.6, 21.8, 18.3, 17.2, 13.7, 13.5 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1700, 1320, 1100 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{24}O_2$: 224.1776; found: 224.1721 [M]$^+$.

Ketone 3f: Yield 57% (64 mg). Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.98 (tt, J = 1.8, 6.0 Hz, 1 H), 3.37 (s, 3 H), 2.69–2.51 (m, 3 H), 2.23 (dt, J = 1.8, 6.9 Hz, 2 H), 2.00–1.89 (m, 2 H), 1.54–1.33 (m, 4 H), 1.10 (d, J = 7.2 Hz, 6 H), 0.91 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 214.2, 78.1, 70.4, 56.2, 40.9, 35.7, 30.7, 29.7, 21.9, 18.32, 18.25, 18.2, 13.6 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1700, 1440, 1320, 1180, 1100, 1020, 960 cm^{-1}. HRMS (EI): calcd. for $C_{14}H_{24}O_2$: 224.1776; found: 224.1755 [M]$^+$.

Cyclopentanone 2a (Scheme 3): Yield 77% (76 mg). BINAP was used as a ligand. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.78 (t, J = 7.2 Hz, 1 H), 3.17 (s, 3 H), 2.56–1.95 (m, 5 H), 1.90–1.75 (m, 1 H), 1.50 (s, 3 H), 1.55–1.20 (m, 4 H), 0.93 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 205.1, 142.6, 138.2, 81.8, 50.3, 35.9, 31.1, 30.8, 27.2, 25.6, 22.5, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 2900,

1720, 1640, 1500, 1440, 1220, 1180, 1080, 1040, 820, 720 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{20}O_2$: 196.1463; found: 196.1458 $[M]^+$.

Ketone (+)-3b: Yield 51% (24 mg). $[\alpha]_D^{25}$ = +1.44 (*c* = 1.615 in Et_2O, 5% *ee*). HPLC: CHIRALCEL OD-H, hexane/*i*PrOH (99:1), 1.0 mL min^{-1}, retention times: 11.5 min (major isomer) and 12.9 min (minor isomer).

Isomerization of 5-Alkynal [D]-1g (Scheme 6): The reaction of deuterium labeled 5-alkynal [D]-**1g** was conducted according to the procedure for **1a**. The ratios of X = H/Y = H were determined by ^1H NMR integration of 9.78 ppm/4.00 ppm.

Ketone [D]-3a: Yield 72% (18 mg). Colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 3.36 (s, 3 H), 2.61 (t, *J* = 7.2 Hz, 2 H), 2.22 (t, *J* = 6.6 Hz, 2 H), 2.16 (s, 3 H), 1.94 (t, *J* = 7.2 Hz, 2 H), 1.30–1.59 (m, 4 H), 0.91 (t, *J* = 6.6 Hz, 3 H) ppm. ^2H NMR ($CHCl_3$, 61 MHz): δ = 3.96 (s) ppm.

Ketone 7h: Yield 62% (52 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.69–6.63 (m, 1 H), 3.11–2.97 (m, 1 H), 2.72–2.50 (m, 3 H), 2.50–2.32 (m, 1 H), 2.21–2.04 (m, 1 H), 1.67–1.46 (m, 3 H), 1.41–1.23 (m, 2 H), 1.07 (d, *J* = 6.9 Hz, 3 H), 0.91 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 199.4, 150.0, 142.5, 38.9, 38.2, 31.9, 31.7, 26.9, 22.4, 19.6, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 2890, 1660, 1440, 1360 cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{18}O$: 166.1358; found: 166.1393 $[M]^+$.

Ketone 7i: Yield 71% (84 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.70–6.64 (m, 1 H), 3.03–2.90 (m, 1 H), 2.69–2.31 (m, 3 H), 2.11–1.95 (m, 1 H), 1.73–1.53 (m, 4 H), 1.42–1.15 (m, 12 H), 0.88 (t, *J* = 6.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 199.6, 149.0, 142.9, 43.5, 39.3, 33.1, 32.1, 31.7, 29.7, 29.0, 28.9, 24.7, 22.9, 22.5, 14.12, 14.05 ppm. IR (neat): $\tilde{\nu}$ = 2880, 1660, 1455, 1375 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{28}O$: 236.2140; found: 236.2119 $[M]^+$.

Ketone 7j: Yield 47% (46 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 400 MHz): δ = 6.68–6.59 (m, 1 H), 2.77–2.67 (m, 2 H), 2.63 (t, *J* = 7.6 Hz, 2 H), 2.49–2.35 (m, 1 H), 2.20–2.09 (m, 2 H), 1.65–1.54 (m, 2 H), 1.38–1.20 (m, 6 H), 1.05 (d, *J* = 6.8 Hz, 3 H), 0.88 (t, *J* = 6.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 199.5, 144.7, 142.0, 42.0, 38.9, 38.8, 31.8, 31.7, 29.1, 24.7, 22.6, 21.5, 14.1 ppm. IR (neat): $\tilde{\nu}$ = 2940, 1660, 1425, 1375 cm^{-1}. HRMS (EI): calcd. for $C_{13}H_{22}O$: 194.1671; found: 194.1643 $[M]^+$.

Ketone 7k: Yield 43% (51 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.77–6.67 (m, 1 H), 2.64 (t, *J* = 7.5 Hz, 2 H), 2.60–2.49 (m, 4 H), 1.92 (quint, *J* = 7.5 Hz, 2 H), 1.67–1.53 (m, 2 H), 1.38–1.16 (m, 14 H), 0.88 (t, *J* = 6.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 199.5, 145.7, 143.0, 39.0, 33.8, 31.8, 30.6, 29.52, 29.46, 29.42, 29.37, 29.3, 24.7, 22.7, 22.6, 14.1 ppm. IR (neat): $\tilde{\nu}$ = 2870, 1660, 1440, 1360 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{28}O$: 236.2140; found: 236.2093 $[M]^+$.

Ketone 9: Yield 19% (24 mg). Colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.94–6.84 (m, 1 H), 2.61 (t, *J* = 7.2 Hz, 2 H), 2.30–2.17 (m, 4 H), 1.71–1.50 (m, 6 H), 1.39–1.12 (m, 14 H), 0.88 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.9, 139.4, 139.2, 37.0, 31.7, 29.6, 29.49, 29.45, 29.3, 26.0, 24.9, 23.1, 22.7, 22.0, 21.6, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 2870, 1660, 1440, 1180 cm^{-1}. HRMS (EI) calcd. for $C_{17}H_{30}O$: 250.2297; found: 250.2250 $[M]^+$.

Ketone [D]-7h: Yield 46% (19 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 3.12–2.97 (m, 1 H), 2.69–2.51 (m, 3 H), 2.49–2.35 (m, 1 H), 2.20–2.04 (m, 1 H), 1.66–1.47 (m, 3 H), 1.33 (sextet, *J* = 7.2 Hz, 2 H), 1.07 (d, *J* = 6.6 Hz, 3 H), 0.91 (t, *J* = 7.2 Hz, 3 H) ppm. ^2H NMR ($CHCl_3$, 61 MHz): δ = 6.70 (s) ppm.

Representative Procedure for Isomerization of Alkynals (Table 6, Entry 1): Under Ar, PPh_3 (26.2 mg, 0.10 mmol) and $[Rh(cod)_2]BF_4$ (20.3 mg, 0.050 mmol) were dissolved in CH_2Cl_2 (2.0 mL) and the mixture was stirred at room temp. for 0.5 h. H_2 was introduced into the resulting solution through a Schlenk tube. After stirring at room temp. for 1 h, the resulting solution was concentrated to dryness. A CH_2Cl_2 (2.0 mL) solution of **1k** (118.2 mg, 0.500 mmol) was added to the residue. The mixture was stirred at room temp. for 93 h. The resulting solution was concentrated and purified by silica gel preparative TLC (hexane/EtOAc, 20:1) to give **4k** (63.4 mg, 0.268 mmol, 54% yield) as a colorless oil and **2k** (35.7 mg, 0.151 mmol, 30% yield) as a colorless oil.

Cyclohexenone 4a: Yield 30% (29 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.48 (s, 1 H), 3.28 (s, 3 H), 2.64 (ddd, *J* = 11.4, 6.9, 4.8 Hz, 1 H), 2.47–2.33 (m, 1 H), 2.33–2.07 (m, 3 H), 1.95–1.82 (m, 1 H), 1.45–1.23 (m, 4 H), 1.38 (s, 3 H), 0.90 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 198.7, 148.0, 140.1, 73.1, 50.3, 35.1, 32.6, 30.4, 28.9, 24.0, 22.4, 13.9 ppm. IR (neat): $\tilde{\nu}$ = 2850, 1660, 1420, 1350, 1050 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{20}O_2$: 196.1463; found: 196.1425 $[M]^+$.

Cyclohexenone 4c: Yield 46% (45 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.58 (s, 1 H), 3.52 (t, *J* = 6.6 Hz, 2 H), 3.29 (s, 3 H), 2.65 (ddd, *J* = 16.8, 6.6, 4.8 Hz, 1 H), 2.49–2.18 (m, 4 H), 2.00–1.80 (m, 3 H), 1.39 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 198.4, 149.4, 138.3, 73.0, 50.3, 44.4, 35.0, 32.7, 31.0, 26.9, 23.8 ppm. IR (neat): $\tilde{\nu}$ = 2870, 1660, 1420, 1360, 1260, 1180, 1050, 860, 720 cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{17}ClO_2$: 216.0917; found: 216.0869 $[M]^+$.

Cyclohexenone [D]-4h: Yield 25% (21 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 2.62–2.24 (m, 3 H), 2.24–1.97 (m, 3 H), 1.70–1.50 (m, 1 H), 1.46–1.19 (m, 4 H), 1.13 (d, *J* = 7.2 Hz, 3 H), 0.90 (t, *J* = 6.9 Hz, 3 H) ppm.

Cyclohexenone [D]-2h: Yield 22% (18 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 3.15–2.98 (m, 1 H), 2.50–2.11 (m, 4 H), 2.19–1.93 (m, 1 H), 1.78–1.62 (m, 1 H), 1.51–1.28 (m, 4 H), 1.15 (d, *J* = 7.1 Hz, 3 H), 0.91 (t, *J* = 7.1 Hz, 3 H) ppm.

Supporting Information (see also the footnote on the first page of this article): Compound characterization data of all known compounds (**6**, **7l**, **7m**, **4k**, **2k**, **4l**, **2l**, **4h**, **2h**, **10**, and **12**) and ^1H NMR spectra of all new compounds (**1a**, **1b**, **1c**, **1d**, **1e**, **1f**, **1i**, **2a**, **3a**, **3b**, **3c**, **3d**, **3e**, **3f**, **4a**, **4c**, **5**, **7h**, **7i**, **7j**, and **7k**).

Acknowledgments

This work was partly supported by the Fujisawa Foundation, Kyowa Hakko Kogyo Co., Ltd., Japan, and a Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Culture, Sports, Science and Technology, Japan (No. 19028015, Chemistry of Concerto Catalysis).

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Received: June 15, 2007
Published Online: August 31, 2007

