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Rhodium-Catalyzed Allyl Transfer from Homoallyl Alcohols to Aldehydes via Retro-Allylation Followed by Isomerization into Ketones

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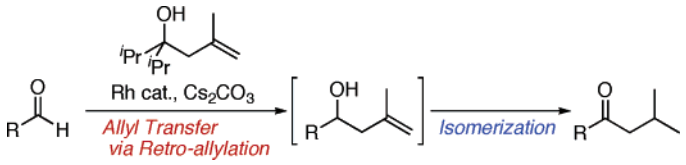
ABSTRACT



Retro-allylation of homoallyl alcohol by rhodium catalysis occurs to generate allylrhodium species. This allylrhodium reacts with aldehydes to give the corresponding secondary alcohols in situ. Isomerization of these alcohols proceeds in the same pots to furnish the corresponding saturated ketones in good yields.

Allylation of carbonyl compounds is among the most important reactions in organic synthesis.[1] Although many allylmetal reagents are used for the allylation, rhodium-mediated carbonyl allylation is quite rare.[2,3]

Recently, we have developed the metal-mediated retro-allylation of homoallyl alcohols as a carbon−carbon bond-cleavage strategy and succeeded in the generation and use of regio- and stereochemically defined allylmetals.[4] In the course of this study, we found that this system could be applied to rhodium catalysis. Herein, we wish to report a new method for the generation of allylrhodium reagents from homoallyl alcohols via retro-allylation[5] and their reaction with carbonyl compounds involving allylation.

Treatment of benzaldehyde (**1a**, 0.5 mmol) with homoallyl alcohol **2a** (1.0 mmol) in the presence of 2.5 mol % of $[RhCl(cod)]_2$, 10 mol % of $P(^tBu)_3$, and 15 mol % of cesium carbonate in refluxing xylene (5.0 mL) for 24 h provided 3-methyl-1-phenyl-1-butanone (**3a**) in 83% yield (Scheme 1). Retro-allylation of homoallyl alcohol by rhodium catalysis would occur to generate σ-methallylrhodium,[6] which is in equilibrium with π-methallylrhodium. Methallylation of **1a** followed by isomerization of the corresponding secondary alcohol would furnish the product (vide infra). This is the first example of transition-metal-catalyzed allyl transfer to carbonyl compounds via retro-allylation.[7]

(1) (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207−2293. (b) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763−2793.

(2) (a) Shi, M.; Lei, G.-X.; Masaki, Y. *Tetrahedron: Asymmetry* **1999**, *10*, 2071−2074. (b) Masuyama, Y.; Kaneko, Y.; Kurusu, Y. *Tetrahedron Lett.* **2004**, *45*, 8969−8971.

(3) Rhodium-catalyzed allylic alkylations: (a) Tsuji, J.; Minami, I.; Shimidzu, I. *Tetrahedron Lett.* **1984**, *25*, 5157−5160. (b) Hayashi, T.; Okada, A.; Suzuka, T.; Kawatsura, M. *Org. Lett.* **2003**, *5*, 1713−1715. (c) Evans, P. A.; Uraguchi, D. *J. Am. Chem. Soc.* **2003**, *125*, 7158−7159. (d) Ashfeld, B. L.; Miller, K. A.; Martin, S. F. *Org. Lett.* **2004**, *6*, 1321−1324. (e) Yasui, N.; Mizutani, K.; Yorimitsu, H.; Oshima, K. *Tetrahedron* **2006**, *62*, 1410−1415.

(4) (a) Fujita, K.; Yorimitsu, H.; Oshima, K. *Chem. Rec.* **2004**, *4*, 110−119. (b) Fujita, K.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2004**, *69*, 3302−3307. (c) Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2005**, *7*, 3577−3579. (d) Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2006**, *128*, 2210−2211.

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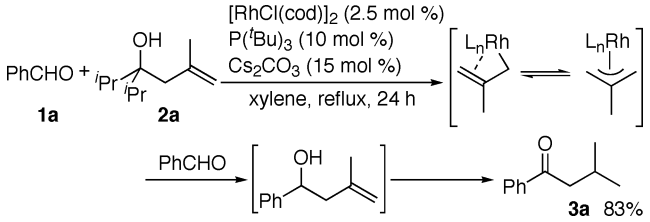
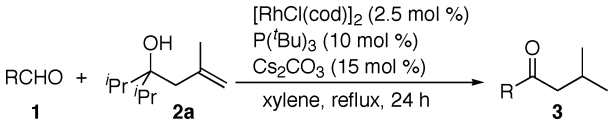
Scheme 1



We performed the sequential methallylation−isomerization reaction of an array of aldehydes (Table 1). The reaction of

Table 1. Sequential Methallylation−Isomerization of Various Aldehydes via Retro-Allylation



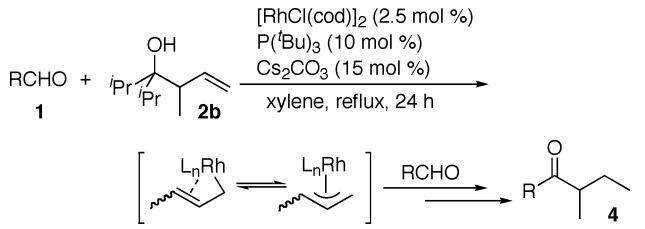
entry	1	3	yield (%)[a]
1	4-MeC_6H_4CHO (**1b**)	**3b**	79 (66)
2	4-$CF_3C_6H_4CHO$ (**1c**)	**3c**	73 (65)
3	4-$MeOC_6H_4CHO$ (**1d**)	**3d**	85 (77)
4	4-ClC_6H_4CHO (**1e**)	**3e**	71 (54)
5	4-$PhCOC_6H_4CHO$ (**1f**)	**3f**	66[b]
6	4-$MeOCOC_6H_4CHO$ (**1g**)	**3g**	91 (68)
7	$CH_3(CH_2)_{10}CHO$ (**1h**)	**3h**	70

[a] Determined by ^1H NMR. Isolated yields are in parentheses. [b] Isolated yield.

4-methylbenzaldehyde (**1b**) proceeded smoothly to give the corresponding saturated ketone **3b** in 79% yield (entry 1). Both electron-deficient and electron-rich aromatic aldehydes underwent the methallylation−isomerization sequence (entries 2 and 3). Substitution of a chlorine atom on the aromatic ring did not prevent the reaction (entry 4). Ketone and ester functionalities were compatible under the reaction conditions (entries 5 and 6). Aliphatic aldehyde as well as aromatic ones participated in the reaction. Dodecanal (**1h**) was converted to the corresponding saturated ketone **3h** in 70% yield (entry 7).

Not only the generation of methallylrhodium but also that of crotylrhodium could be achieved (Table 2). Benzaldehyde (**1a**) was exposed to a solution of homoallyl alcohol **2b** in

Table 2. Sequential Crotylation−Isomerization of Various Aldehydes via Retro-Allylation



entry	1	4	yield (%)[a]
1[b]	PhCHO (**1a**)	**4a**	70
2	4-MeC_6H_4CHO (**1b**)	**4b**	60 (49)
3[c]	4-$CF_3C_6H_4CHO$ (**1c**)	**4c**	50
4	4-$MeOC_6H_4CHO$ (**1d**)	**4d**	52
5	4-ClC_6H_4CHO (**1e**)	**4e**	51
6	4-$PhCOC_6H_4CHO$ (**1f**)	**4f**	48 (48)[d]
7[b]	4-$MeOCOC_6H_4CHO$ (**1g**)	**4g**	64 (59)[e]

[a] Determined by ^1H NMR. Isolated yields are in parentheses. [b] With 5 mol % of Cs_2CO_3. [c] The reaction was carried out in refluxing toluene for 24 h. [d] α-Adduct, 1-(4-benzoylphenyl)-1-pentanone, was obtained in 3% yield. [e] α-Adduct, 1-(4-methoxycarbonylphenyl)-1-pentanone, was obtained in 3% yield.

xylene under the same conditions as those for the methallyl transfer to provide α-substituted ketone **4a** in 70% yield. This regioselectivity strongly suggests that the reaction involves generation of a σ-crotylrhodium reagent via retro-allylation.[8] Namely, the reaction would proceed via a mechanism completely different from the Lewis acid-mediated allyl transfer reactions reported by Nokami and Loh.[9] Other aromatic aldehydes underwent the sequential crotylation−isomerization. 4-Methylbenzaldehyde (**1b**) was converted to the corresponding saturated ketone in 60% yield (entry 2). The transformations of trifluoromethyl-, methoxy-, and chloro-substituted benzaldehydes resulted in good yields (entries 3−5). The reaction of an aldehyde moiety predominated over that of ketone and ester as observed in the methallyl transfer (entries 6 and 7).

Allyl and prenyl transfers were also examined (Scheme 2). The sequential allylation−isomerization of benzaldehyde (**1a**) with homoallyl alcohol **2c** led to low yield. Interestingly, the reaction with **2d** provided the unexpected ketone **6** in 62% yield. The formation of **6** proceeded as follows. The σ-prenylrhodium **A** generated via retro-prenylation was difficult to react with **1a** due to steric repulsion at the γ position. Accordingly, **A** was isomerized to σ-prenylrhodium **C** through π-prenylrhodium **B**. The following β-H elimination occurred from **C** to give rhodium hydride species and

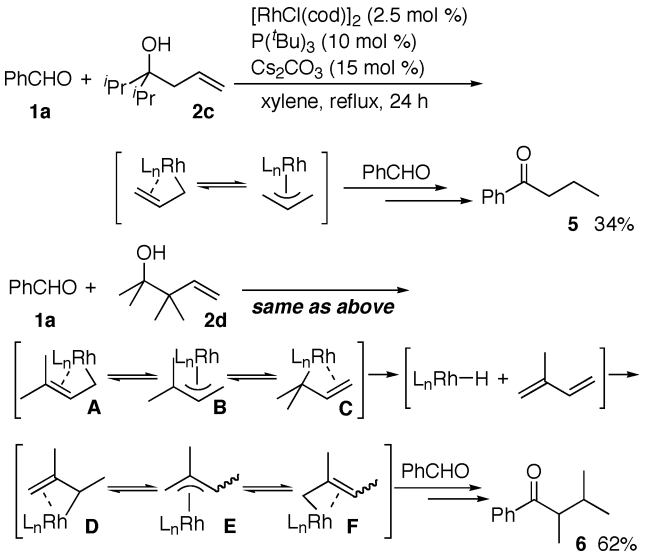
(6) For convenience, throughout the manuscript, crotylation, methallylation, and prenylation are defined as introductions of the 1-methyl-2-propenyl, 2-methyl-2-propenyl, and 1,1-dimethyl-2-propenyl groups, respectively, into a carbonyl group. On the other hand, the crotyl, methallyl, and prenyl groups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

(7) Retro-allylations from lithium, magnesium, and zinc alkoxides were observed. (a) Benkeser, R. A.; Siklosi, M. P.; Mozdzen, E. C. *J. Am. Chem. Soc.* **1978**, *100*, 2134−2139. (b) Gerard, F.; Miginiac, P. *Bull. Chim. Soc. Fr.* **1974**, 2527−2533. (c) Jones, P.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 186−195. Under harsh conditions, retro-allylation took place by the action of tin: (d) Peruzzo, V.; Tagliavini, G. *J. Organomet. Chem.* **1978**, *162*, 37−44. (e) Giesen, V. *Dissertation University Marburg* **1989**. Ruthenium-catalyzed deallylation was reported: (f) Kondo, T.; Kodoi, K.; Nishinaga, E.; Okada, T.; Morisaki, Y.; Watanabe, Y.; Mitsudo, T. *J. Am. Chem. Soc.* **1998**, *120*, 5587−5588.

(8) σ-Crotylrhodium is known to react with aldehydes at the γ position. See ref 2b.

(9) Representative examples: (a) Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S. *J. Am. Chem. Soc.* **1998**, *120*, 6609−6610. (b) Nokami, J.; Anthony, L.; Sumida, S. *Chem.−Eur. J.* **2000**, *6*, 2909−2913. (c) Nokami, J. *J. Synth. Org. Chem. Jpn.* **2003**, *61*, 992−1001. (d) Tan, K.-T.; Chng, S.-S.; Cheng, H.-S.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 2958−2963. (e) Lee, C.-L. K.; Lee, C.-H. A.; Tan, K.-T.; Loh, T.-P. *Org. Lett.* **2004**, *6*, 1281−1283. Also see: (f) Rychnovsky, S. D.; Marumoto, S.; Jaber, J. J. *Org. Lett.* **2001**, *3*, 3815−3818. (g) Crosby, S. R.; Harding, J. R.; King, C. D.; Parker, G. D.; Willis, C. L. *Org. Lett.* **2002**, *4*, 577−580. (h) Samoshin, V. V.; Smoliakova, I. P.; Hank, M. M.; Gross, P. H. *Mendeleev Commun.* **1999**, 219−221. (i) Horiuchi, Y.; Taniguchi, M.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1994**, *35*, 7977−7980.

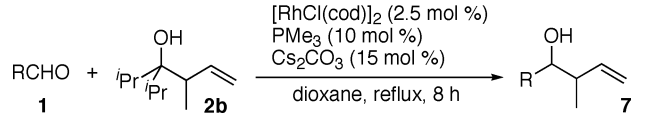
Scheme 2



isoprene. Subsequent hydrorhodation of isoprene followed by the reaction of **1a** with **F**, which is in $\sigma-\pi-\sigma$ equilibrium (**D**−**E**−**F**), furnished **6**.

The change of the reaction conditions could suppress the secondary isomerization (Table 3). Treatment of benzaldehyde (**1a**, 0.5 mmol) with homoallyl alcohol **2b** (1.0 mmol) in the presence of 2.5 mol % of $[RhCl(cod)]_2$, 10 mol % of PMe_3, and 15 mol % of cesium carbonate in refluxing dioxane (5.0 mL) for 8 h provided the corresponding secondary homoallyl alcohol **7a** in 62% yield (*erythro*/*threo* = 49:51) (entry 1).[10] Electron-deficient and electron-rich aromatic aldehydes as well as functionalized ones were converted to the corresponding alcohols in moderate to good yields (entries 2−7). Unfortunately, no stereoselectivity was observed in all cases.

Table 3. Crotylation of Various Aldehydes via Retro-Allylation

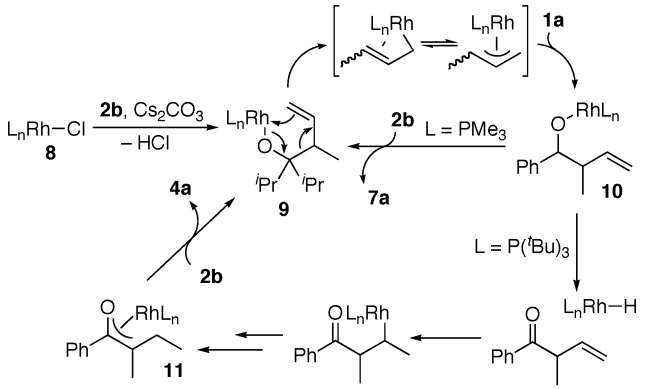


entry	1	7	yield (%)[a]	*erythro*/*threo*
1	PhCHO (**1a**)	**7a**	62 (58)	49:51
2	4-MeC_6H_4CHO (**1b**)	**7b**	54 (49)	54:46
3	4-$CF_3C_6H_4CHO$ (**1c**)	**7c**	60 (44)	56:44
4	4-$MeOC_6H_4CHO$ (**1d**)	**7d**	52 (34)	52:48
5	4-ClC_6H_4CHO (**1e**)	**7e**	59[b]	58:42
6	4-$PhCOC_6H_4CHO$ (**1f**)	**7f**	58[b]	56:44[c]
7[d]	4-$MeOCOC_6H_4CHO$ (**1g**)	**7g**	65 (59)	56:44

[a] Determined by ^1H NMR. Isolated yields are in parentheses. [b] Isolated yields. [c] Tentatively assigned. [d] With 30 mol % of Cs_2CO_3.

We are tempted to assume the detailed mechanism as shown in Scheme 3. Initial ligand exchange between rhodium species **8** and homoallyl alcohol **2b** with the aid of cesium carbonate provides the intermediate **9**. Retro-allylation then occurs to generate σ-crotylrhodium, which is in equilibrium with π-crotylrhodium. Subsequent crotylation of **1a** with the σ-crotylrhodium at the γ position furnishes **10**. With PMe_3 as a phosphine ligand, alkoxide exchange between **10** and **2b** proceeds to produce the secondary homoallyl alcohol **7a** and to regenerate **9**. In contrast, use of $P(^tBu)_3$ isomerizes **10** to oxa-π-allylrhodium **11** through iterative β-H elimination−hydrorhodation.[11] Finally, ligand exchange between **11** and **2b** gives **4a** and **9**. $P(^tBu)_3$-coordinated **10** would undergo the alkoxide exchange between **10** and **2b** less efficiently than PMe_3-coordinated **10**.

Scheme 3



In summary, we have extended the retro-allylation to a rhodium-catalyzed system and found a new route to the generation of allylrhodium. In addition, the allylrhodium was found to have high efficiency in allylation of carbonyl compounds. Further developments of the retro-allylation system in other transformations catalyzed by other transition metals are now in progress.

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Supporting Information Available: Detailed experimental procedures and characterization data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Throughout this manuscript, we have adopted the unambiguous *erythro*/*threo* nomenclature proposed by Noyori: Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1981**, *103*, 2106−2108.

(11) Rh-catalyzed isomerization of unsaturated carbinols: (a) Uma, R.; Crévisy, C.; Grée, R. *Chem. Rev.* **2003**, *103*, 27−52. (b) Saïah, M. K. E.; Pellicciari, R. *Tetrahedron Lett.* **1995**, *36*, 4497−4500. (c) Shintani, R.; Okamoto, K.; Hayashi, T. *J. Am. Chem. Soc.* **2005**, *127*, 2872−2873. (d) Yamabe, H.; Mizuno, A.; Kusama, H.; Iwasawa, N. *J. Am. Chem. Soc.* **2005**, *127*, 3248−3249.