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Double-Chelation-Assisted Rh-Catalyzed Intermolecular Hydroacylation

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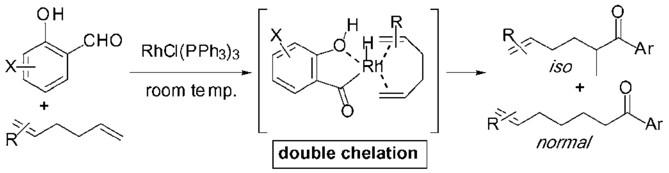
ABSTRACT

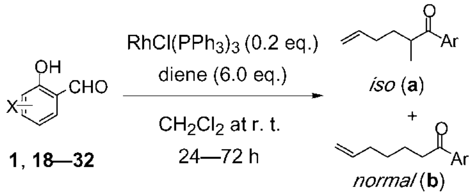


Rh-Catalyzed intermolecular hydroacylation between salicylaldehydes and 1,5-hexadienes proceeded under remarkably mild reaction conditions to afford a mixture of *iso*- and *normal*-hydroacylated products in good yields. The experiments using deuterated salicylaldehyde-*d* revealed that “double chelation” of salicylaldehyde and 1,5-hexadiene to Rh-complex played vital roles in the catalytic cycle of intermolecular hydroacylation.

Rhodium complexes have widely been used as catalysts such as in hydrogenation, isomerization, and hydroformylation.[1] Among them, Rh-catalyzed C−C bond formation via C−H activation intrigues many organic and organometallic chemists.[2] We have reported that an Rh-complex catalyzed an intramolecular hydroacylation of 4-pentenals, i.e., cyclization of 4-pentenals into cyclopentanones, albeit an intermolecular hydroacylation could not proceed due to the competitive decarbonylation.[3,4] Recently, the Jun[5] and Miura groups[6] independently reported novel Rh-catalyzed intermolecular hydroacylation based on the chelation of salicylaldehyde or imine bearing 2-amino-3-picoline, albeit these reactions require rigorous conditions.[7] Here we describe for the first time that double chelation of both aldehyde and olefin to an Rh-complex promotes intermolecular hydroacylation under remarkably mild reaction conditions.

The hydroacylation between salicylaldehyde **1** (X = H) and some alkynes stimulated us to scrutinize hydroacylation between **1** and olefins using $RhCl(PPh_3)_3$ (Scheme 1).

Scheme 1



1, **18—32**

Fortunately, the hydroacylation of **1** with 1-hexene proceeded to afford a hydroacylated product, even though the isolated yield was merely 4% after 3 days.[8] Next, we adopted 1,5- and 1,4-dienes as an olefin because in the case of Rh-

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(3) (a) Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972**, *13*, 1287. (b) Taura, Y.; Tanaka, M.; Wu, W.-M.; Funakoshi, K.; Sakai, K. *Tetrahedron* **1991**, *47*, 4879. (c) Tanaka, M.; Imai, M.; Fujio, M.; Sakamoto, E.; Takahashi, M.; Eto-Kato, Y.; Wu, X.-M.; Funakoshi, K.; Sakai, K.; Suemune, H. *J. Org. Chem.* **2000**, *65*, 5806. (d) Tanaka, M.; Takahashi, M.; Sakamoto, E.; Imai, M.; Matsui, A.; Fujio, M.; Funakoshi, K.; Sakai, K.; Suemune, H. *Tetrahedron* **2001**, *57*, 1197 and 1205.

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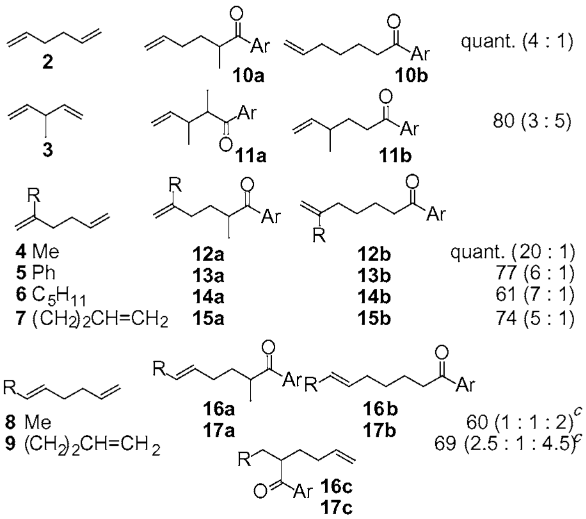
catalyzed hydroformylation, some dienes were rapidly reacted.[1c,9] The results are summarized in Table 1. The hydroacylation of **1** with 1,5-hexadiene **2** (6.0 equiv) in the presence of $RhCl(PPh_3)_3$ (0.2 equiv) proceeded at room temperature to give the hydroacylated product **10**; even the use of 10 mol % Rh-complex or 1.5 equiv of **2** caused the reaction to proceed in quantitative yield. The ^1H NMR spectrum of **10** showed the methine signal at δ 3.54 (sestet, $J = 6.9$ Hz) and methylene signals at δ 3.07 (t, $J = 7.3$ Hz), as well as the methyl signal at δ 1.22 (d, $J = 6.9$ Hz), suggesting that the product was a mixture of *iso*-**10a** and *normal*-**10b** in a ratio of 4 to 1. The hydroacylation of 3-methyl-1,4-pentadiene **3** afforded the products **11a**,**b** in 80% yield; preferentially the terminal site was acylated in a ratio of 5 to 3. The hydroacylation of 1,6-heptadiene gave only a low yield of product (4%).[10] The reaction of 2-substituted 1,5-hexadienes **4**−**6** afforded the products **12**−**14**, which were reacted at the less substituted olefin site, and *iso*-products **12a**−**14a** were obtained in preference to *normal*-**12b**−**14b**. The internal *exo*-olefin in triene **7** did not react, but the terminal olefin reacted to give **15a**,**b** in 74%. The hydroacylation of 2,5-dimethylhexa-1,5-diene did not proceed at all. In the case of 1,5-heptadiene **8**, which was a 1,5-hexadiene bearing a methyl group at the terminus, the reaction proceeded to give hydroacylated products **16a**−**c** in 60% total yields but did not afford the product acylated at the C6-position of **8**. In the case of triene **9**, the internal disubstituted olefin was more reactive than the terminal olefin to give hydroacylated **17a**−**c** in 69% total yields. These results suggest that the 1,4- or 1,5-diene structure, which chelates to the Rh metal, is necessary for the hydroacylation.

Table 1. Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde **1** and Dienes **2**−**9**



entry	olefin[a]	products[b]	% yield (ratio)
1	**2**	**10a** **10b**	quant. (4 : 1)
2	**3**	**11a** **11b**	80 (3 : 5)
3	**4** Me	**12a** **12b**	quant. (20 : 1)
4	**5** Ph	**13a** **13b**	77 (6 : 1)
5	**6** C_5H_{11}	**14a** **14b**	61 (7 : 1)
6	**7** $(CH_2)_2CH{=}CH_2$	**15a** **15b**	74 (5 : 1)
7	**8** Me	**16a** **16b** **16c**	60 (1 : 1 : 2)[c]
8	**9** $(CH_2)_2CH{=}CH_2$	**17a** **17b** **17c**	69 (2.5 : 1 : 4.5)[c]

[a] Cyclohexene, 1,5-cyclooctadiene, 5-hexen-2-one, 1,3-hexadiene, 1,3-cyclohexadiene, or 2,5-dimethylhexa-1,5-diene was also examined, but the reaction did not proceed at all. [b] Reaction was usually completed in 24 h. In the cases that the hydroacylation did not proceed completely, the reaction was terminated after 72 h. [c] NaOAc (0.2 equiv) was added as an additive.

Next, we examined the effect of aldehydes by treatment with $RhCl(PPh_3)_3$ (0.2 equiv) and **2** (6.0 equiv) at room temperature. The hydroacylation of benzaldehydes bearing no 2-hydroxy function such as 3-hydroxy- and 4-hydroxy-benzaldehydes did not proceed or proceeded in very low yields, but that of various 2-hydroxybenzaldehydes proceeded to give the products as a mixture of *iso* (**a**) and *normal* (**b**). The results are summarized in Table 2. The hydroacylation was tolerant of various functional groups in the aromatic ring. However, another hydroxy group at the C3-, C4-, or C5-position of 2-hydroxybenzaldehyde was practically ineffective; this may be attributed to the fact that the hydroxy group may coordinate to the Rh metal. Alkyl substituents and naphthalene skeletons were also somewhat disadvantageous, but the steric and electronic effects of the substituents are not clear.

To obtain mechanistic information, we examined the reaction using deuterated salicylaldehyde **1**-*d*. The reaction of **1**-*d* (1.0 equiv) and **2** (6.0 equiv) by $RhCl(PPh_3)_3$ (0.2 equiv) afforded products **10a**,**b** in which no deuterium was detected. Therefore, the reaction was performed using 0.9 equiv of diene **2**; in this case, the isolated **10a**-*d* showed the methyl signal at δ 1.22 (m, 2.4H; ca. 60% deuterium content) and **10b**-*d* showed methylene signals at δ 1.74−1.79 (m,

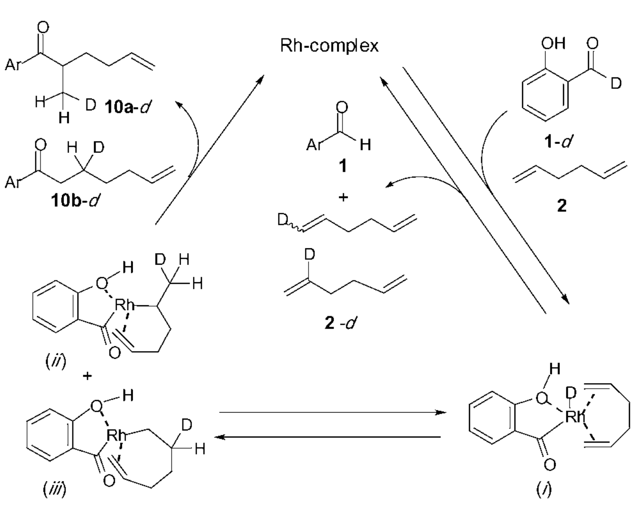


Figure 1. Plausible mechanisms for hydroacylation of **1**-*d*.

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(8) See Supporting Information.

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(10) Distance between the two olefins is too long for the chelation.

Table 2. Hydroacylation between 2-Hydroxybenzaldehydes **18**−**32** and 1,5-Hexadiene **2**

entry	aldehyde[a]	products: % yield (ratio of **a**:**b**)
1	2,5-dihydroxybenzaldehyde **18**	**33**: 90 (3:1)
2	2-hydroxy-5-methoxybenzaldehyde **19**	**34**: quantitative (3:1)
3	2-hydroxy-5-methylbenzaldehyde **20**	**35**: 42 (3:1)
4	5-bromo-2-hydroxybenzaldehyde **21**	**36**: quantitative (5:1)
5	5-chloro-2-hydroxybenzaldehyde **22**	**37**: quantitative (4:1)
6	2-hydroxy-5-nitrobenzaldehyde **23**	**38**: 73 (2:1)
7	2-hydroxy-5-trifluoromethoxybenzaldehyde **24**	**39**: 73 (3:1)
8	2,3-dihydroxybenzaldehyde **25**	**40**: 58 (3:1)
9	2-hydroxy-3-methoxybenzaldehyde **26**	**41**: quantitative (3.5:1)
10	2-hydroxy-3-methylbenzaldehyde **27**	**42**: 71 (4.5:1)
11	2,4-dihydroxybenzaldehyde **28**	**43**: 75 (4:1)
12	2-hydroxy-4-methoxybenzaldehyde **29**	**44**: quantitative (2:1)
13	2-hydroxy-1-naphthaldehyde **30**	**45**: 56 (2:1)
14	1-hydroxy-2-naphthaldehyde **31**	**46**: 82 (2:1)
15	2-hydroxy-5-methylbenzene-1,3-dicarbaldehyde **32**	**47**: 64 (3:1)[b]

[a] Benzaldehyde, *o*-phthalaldehyde, 2-vinylaldehyde, or *o*-anisaldehyde was also tested, but the hydroacylation did not proceed. The reaction of 3-hydroxybenzaldehyde afforded a hydroacylated product in merely 3% yield. [b] Bishydroacylated products were also formed in 21% as a regiomeric mixture.

1.3H; ca. 70% deuterium content) in the ^{1}H NMR spectra, and also MS spectra supported the existence of deuterium in **10a**,**b**-*d*.[8] These results mean that rapid interconversion processes exist, and the diene **2** rapidly coordinates to the Rh metal and dissociates from the Rh metal. On the basis of these experiments, we present a tentative catalytic cycle as outlined in Figure 1. Intermediates *i*−*iii*, in which both the diene and salicylaldehyde bind to the Rh-complex by chelation, play vital roles in the intermolecular hydroacylation.[11]

Concentration of the reaction and addition of $AgClO_4$, AgOTf, CsF, Na_2CO_3, or NaOAc affect the ratio of *iso*- and *normal*-products **10** and also accelerate the rate of hydroacylation. In $CHCl_3$, $ClCH_2CH_2Cl$, or EtOH as a solvent, the reaction proceeded smoothly, but the use of MeCN or $MeNO_2$ was not effective.[12,13] Neutral Rh complexes such as $\{Rh[P(PhMe)_3]\ _2\}Cl$ and [Rh(dppf)]Cl and cationic Rh complexes such as $[Rh(PPh_3)_2]ClO_4$ and $[Rh(dppe)]ClO_4$ prepared in situ could be also used as a catalyst.[8,14]

We have achieved Rh-catalyzed intermolecular hydroacylation under very mild reaction conditions based on the "double-chelation" concept.[15] The application of the double chelation to other metals and reactions is currently underway.[16]

Acknowledgment. Dedicated to Prof. K. Sakai in memory of the discovery of Rh-catalyzed hydroacylation 30 years ago. This work was partly supported by a Grant-in-Aid for Scientific Research (C) from Japan Society for the Promotion of Science.

Supporting Information Available: Synthetic scheme of 1,5-dienes and **1**-*d*, reaction conditions, experimental procedures, and spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] As an intermediate, μ^2-ligand- or η^6-Ph-bi-Rh-complex or heptacoordinated Rh may exist in chelations of both salicylaldehyde and diene. See: Nagashima, H.; Tatebe, K.; Ishibashi, T.; Nakaoka, A.; Sakakibara, J.; Itoh, K. *Organometallics* **1995**, *14*, 2868. See also ref 1b.

[12] Hydroacylation between **1** and **2** using $RhCl(PPh_3)_3$ (0.2 equiv), NaOAc (0.2 equiv), and $AgClO_4$ (0.2 equiv) in the solvent of 5% EtOH in CH_2Cl_2 was completed in 15 min, and **10a**,**b** were obtained in 90%.

[13] Additives of bases and alcohols may affect the phenolic hydroxy group and change the chelation effects, and those of Ag salts may affect the property of the Rh complex.

[14] Ratio of regioisomers was very sensitive to the reaction conditions.

[15] Double chelation of aldehyde and diene derived from Rh-complex $[Rh(diene)Cl]_2$ was observed by Jun. See ref 5a and: Jun, C.-H. *J. Organomet. Chem*. **1990**, *390*, 361. Also, for chelations of imine bearing picoline and allyl alcohol, see: Jun, C.-H.; Han, J.-S.; Kang, J.-B.; Kim, S. *J. Organomet. Chem*. **1994**, *474*, 183.

[16] (a) Chelation-assisted hydroesterificatin by ruthenium: Ko, S.; Na, Y.; Chang, S. *J. Am. Chem. Soc.* **2002**, *124*, 750. (b) For chelation-assisted hydrosilylation by $RhCl(PPh_3)_3$, see ref 11.