

Double-Chelation-Assisted Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehydes and 1,4-Penta- or 1,5-Hexadienes

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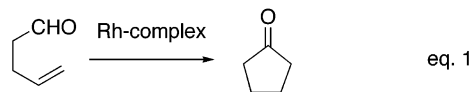
Intermolecular hydroacylation between salicylaldehydes **1**, **26–40** and 1,4-penta- or 1,5-hexadienes **4–13** by Rh-catalyst proceeded under mild reaction conditions to give a mixture of *iso*- and *normal*-hydroacylated products **14–25**, **41–55**, and **57–60**. In the hydroacylation reaction, chelation of both salicylaldehyde and diene to the Rh-complex plays a crucial role. The ratio of *iso*- and *normal*-hydroacylated products could be regulated by the addition of salicylic acid or amines. The effects of various Rh-complexes, solvents, and additives were examined, and the plausible mechanisms of the catalytic cycle were proposed on the basis of the deuterium-labeling salicylaldehyde experiments.

Introduction

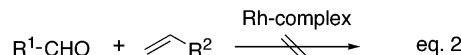
Carbon–carbon bond-forming reactions via C–H bond activation have extensively been the focus of study in the fields of organic and organometallic chemistry.¹ Rhodium complexes have widely been used as catalysts, as in hydrogenation, decarbonylation, and isomerization, and also for C–C bond formation.² Among them, Rh-catalyzed intramolecular hydroacylation of 4-pentenals, i.e., cyclization of 4-pentenals into cyclopentanones via C–H activation, was discovered by Sakai in 1972, albeit at that time the reaction required a stoichiometric amount of RhCl(PPh₃)₃ (Wilkinson complex) (Scheme 1, eq 1).³ After the discovery, the Rh-promoted intramolecular hydroacylation was developed into catalytic reactions and also asymmetric reactions.^{3,4} However, the competitive decarbonylation reaction prevented us and the other groups from developing the hydroacylation into an intermolecu-

SCHEME 1

i) intramolecular hydroacylation



ii) intermolecular hydroacylation



lar version (eq 2). Exclusively Rh-catalyzed hydroformylation^{2d} and the exceptional intermolecular hydroacylation of ethylene were reported by several groups.⁵ Recently, the Jun group reported that novel Rh-catalyzed intermolecular hydroacylation reactions occurred in the case where 2-amino-3-picoline was added as a cocatalyst.^{6,7} Also, the Miura group reported that Rh-catalyzed intermolecular hydroacylation of alkynes or allenes occurred in the case where salicylaldehyde was used as an aldehyde and an Rh-complex having a phosphinoferrocene ligand was used as the Rh-complex, albeit the reaction between salicylaldehyde and olefins could not proceed.⁸ In both Rh-catalyzed hydroacylations, the chelation of

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salicylaldehyde or an imine bearing 2-amino-3-picoline to the Rh-complex suppresses the decarbonylation side reaction. However, both reactions require rigorous conditions, and the hydroacylation does not occur at room temperature. Here we describe for the first time that “double-chelation” of both aldehyde and olefin to the Rh-complex promotes intermolecular hydroacylation, and the reactions between salicylaldehyde derivatives and 1,4-penta- or 1,5-hexadienes proceed under remarkably mild reaction conditions to give a mixture of *iso*- and *normal*-hydroacylated products in good yields.⁹

Results and Discussion

Rh-Catalyzed Hydroacylation between Salicylaldehyde and Olefins. Miura's Rh-catalyzed intermolecular hydroacylation between salicylaldehyde **1** and some alkynes stimulated us to scrutinize the hydroacylation reaction between **1** and olefins by using RhCl(PPh₃)₃. Fortunately, the hydroacylation between salicylaldehyde **1** and 1-hexene **2** in the presence of RhCl(PPh₃)₃ (0.2 equiv) yielded a hydroacylated product **14b**, even though the reaction required long reaction time (72 h) and the yield of **14b** was very poor (4%, entry 1). The hydroacylation reaction did not proceed at all when benzaldehyde was used instead of **1**. Therefore, the chelation of the phenolic hydroxyl function plays a vital role in the Rh-catalyzed intermolecular hydroacylation. The isolation of **14b** prompted us to study the further hydroacylation of salicylaldehyde with various olefins. Unfortunately, the hydroacylation between salicylaldehyde and olefins such as 2-octene, styrene, and cyclohexene did not proceed at all, but that between **1** and allyl alcohol **3** proceeded to produce a mixture of **15a** and **15b** in the ratio 1:9 in 14% yield (entry 2). Refluxing in dichloroethane was detrimental to the hydroacylation because isomerization of olefin in allyl alcohol occurred. Next, we examined 1,4-penta- and 1,5-hexadienes as olefins because in the case of Rh-catalyzed hydroformylation some dienes were rapidly reacted.¹⁰ The results are summarized in Table 1.

The hydroacylation of **1** with 1,5-hexadiene **4** (6.0 equiv) by RhCl(PPh₃)₃ (0.2 equiv) proceeded at room temperature to afford the hydroacylated product **16**. Even the use of 10 mol% Rh-complex or 1.5 equiv of **4** promoted the reaction to proceed in excellent yields (entries 3–6). The ¹H NMR spectrum of **16** showed the methine signal at δ 3.54 (sextet, J = 6.9 Hz) and methylene signal 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*-**16a** and *normal*-**16b** in a 4:1 ratio. Increasing the equivalent of the Rh-complex promotes the hydroacylation and seems to improve the ratio of *iso*- and *normal*-products. The hydroacylation of 3-methyl-1,4-pentadiene **5** afforded the products **17a,b** in 91% yield (entry 7); preferentially the terminal site

was acylated in a ratio of 5:3 and that of 1,4-pentadien-3-ol **6** exclusively gave the *normal*-product **18b** in 93% yield (entry 8). The hydroacylation of 1,4-pentadienes proceeded faster than that of 1,5-hexadiene, but 1,4-pentadiene, having a terminal substituent at the olefin (1,4-hexadiene), was less reactive (9% yield). The hydroacylation of 1,6-heptadiene gave only a low yield of product (4%), suggesting that the distance between the two olefins is too long for the chelation to the Rh-complex. The reaction of 2-substituted 1,5-hexadienes **7–10** afforded *iso*-products **19a–22a**, which were reacted at the less-substituted olefin, in preference to *normal*-**19b–22b** (entries 9–12). The internal *exo*-olefin in the triene **10** did not react at all, but the terminal olefin site reacted to give **22a,b** in 74% yield. The hydroacylation of 2,5-dimethylhexa-1,5-diene did not proceed. In the case of 1,5-heptadiene **11**, which is a 1,5-hexadiene bearing a methyl group at the terminus, the reaction gave hydroacylated products **23a–c** in 60% total yields but no acylated product at the C6-position of **11** (entry 13). In the case of triene **12**, the internal disubstituted olefin was more reactive than the terminal monosubstituted olefin, and the hydroacylation afforded **24a–c** in 35% total yields (entry 14). Addition of a base, such as NaOAc and K₂CO₃, may deprotonate the phenolic hydroxyl group and accelerate the reaction, and thus the yield of products **24** was increased to 69% (entry 15). In the case of 4-vinylcyclohexene **13**, which is a 1,5-hexadiene with one olefin existing in the ring, the hydroacylation gave a mixture of **25a–c** in 17% yield (entry 16). The low yield may be attributed to the hindrance of the vinyl function and the lesser flexibility of the diene structure. 1,5-Cyclooctadiene, 1,3-hexadiene, and 1,3-cyclohexadiene were not suitable for the Rh-catalyzed hydroacylation. Thus, these results suggest that the 1,4-penta- or 1,5-hexadiene structure, which chelates to the Rh-complex, is crucial for the intermolecular hydroacylation.¹¹

Effect of Substituent in Salicylaldehyde on the Rh-Catalyzed Hydroacylation. Next, we examined the effect of aldehydes by treatment with RhCl(PPh₃)₃ (0.2 equiv) and **4** (6.0 equiv) at room temperature. The results are summarized in Table 2. The hydroacylation of benzaldehydes bearing no 2-hydroxyl function, such as benzaldehyde, *o*-phthalaldehyde, 2-vinylbenzaldehyde, *o*-anisaldehyde, 3-hydroxybenzaldehyde, or 4-hydroxybenzaldehyde, did not proceed or proceeded in very low yields, but that of various 2-hydroxybenzaldehydes proceeded to give the products **41–55** as a mixture of *iso* (**a**) and *normal* (**b**), with preferentially *iso*-compound (**a**) as a major product. The Rh-catalyzed hydroacylation was tolerant of various functional groups such as hydroxy, methoxy, halogeno, and the nitro function in the aromatic ring. However, another hydroxyl group at the C3-, C4-, or C5-position of 2-hydroxybenzaldehyde was practically ineffective; this may be attributed to the fact that the hydroxyl group may coordinate to the Rh-complex or the poor solubility of some dihydroxybenzaldehydes in CH₂-Cl₂ (entries 1, 8, and 11). Alkyl substituents and naphthalene skeletons were also somewhat disadvantageous, but the steric and electronic effects of the substituents are not clear. In the case of 1,3-dicarbonyl **40**,

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TABLE 1.

entry	olefin (6 eq.) ^a	RhCl(PPh ₃) ₃ (Eq.)	reaction time (h)	results	
				products	yield % (ratio of products)
1		0.2	72		4
2		0.2	72		14 (1 : 9)
3		0.1	48		quant. (3 : 1)
4		0.2 ^b	24		quant. (4 : 1)
5		0.5	24		quant. (7 : 1)
6		1.0	14		quant. (8 : 1)
7		0.2	2		91 (3 : 5)
8		0.2	1		93
9		0.2	24		quant. (20 : 1)
10		0.2	72		77 (6 : 1)
11		0.2	72		61 (7 : 1)
12		0.2	72		74 (5 : 1)
13		0.2 ^c	72		60 (1 : 1 : 2)
14		0.2	72		35 (2 : 1 : 3)
15		0.2 ^c	72		69 (2.5 : 1 : 4.5)
16		0.2	72		17 (1.5 : 3 : 1)

^a Cyclohexene, 2-octene, styrene, 1,5-cyclooctadiene, 5-hexen-2-one, 1,3-hexadiene, 1,3-cyclohexadiene, and 2,5-dimethylhexa-1,5-diene were also examined, but the reaction did not proceed at all. ^b The hydroacylation proceeded even using 3.0 equiv of 1,5-hexadiene (quant), and 1.5 equiv of 1,5-hexadiene (95%). ^c NaOAc (0.2 equiv) was used as an additive.

monohydroacylated products **55a** and **55b** were obtained in 64% yield, accompanied by bishydroacylated products in 21% yield (entry 15).

Instead of salicylaldehyde, 2-hydroxybenzyl alcohol **56** could be used for the hydroacylation.¹² That is to say, the reaction of 2-hydroxybenzyl alcohol **56** and 1,5-hexadiene **4** (6.0 equiv) by RhCl(PPh₃)₃ at room temperature afforded the hydroacylated products **16a,b** in 45% yields.

In this process, at first the Rh-complex and 1,5-hexadiene were worked as an oxidizer, and the 2-hydroxybenzyl alcohol **56** was converted into the salicylaldehyde **1**, and then the produced **1** and 1,5-hexadiene **4** reacted to give **16a,b**.

The hydroacylation of 1,4-pentadienes with 5-halogeno-2-hydroxybenzaldehydes was also examined because the hydroacylation of 1,5-hexadiene **4** with 5-halogeno-2-hydroxybenzaldehydes reacted faster than with salicylaldehyde. However, the hydroacylation of 1,4-pentadiene **5** or **6** with 5-halogeno-2-hydroxybenzaldehyde **29** or **30**

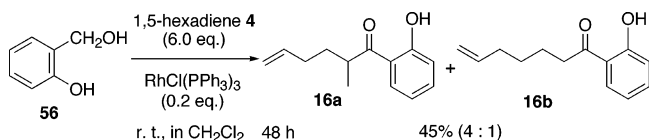
(12) Jun, C.-H.; Huh, C.-W.; Na, S.-J. *Angew. Chem., Int. Ed.* **1998**, 37, 145 and references therein.

TABLE 2.

entry	aldehyde ^{a)}	reaction time (h)	products		yield % (ratio)
1	X =	72			41: 90 (3 : 1)
2	27: OMe	24			42: quant. (3 : 1)
3	28: Me	72			43: 42 (3 : 1)
4	29: Br	48			44: quant. (5 : 1)
5	30: Cl	4			45: quant. (4 : 1)
6	31: NO ₂	24			46: 73 (2 : 1)
7	32: OCF ₃	72			47: 73 (3 : 1)
8	X =	72 ^{c)}			48: 58 (3 : 1)
9	33: OH	24			49: quant. (3.5 : 1)
10	34: OMe	72			50: 71 (4.5 : 1)
	35: Me				
11	X =	72 ^{c)}			51: 75 (4 : 1)
12	36: OH	24			52: quant. (2 : 1)
	37: OMe				
13		24			53: 56 (2 : 1)
	38		53a	53b	
14		24			54: 82 (2 : 1)
	39		54a	54b	
15		72			55: 64 (3 : 1) ^{b)}
	40		55a	55b	

^{a)} Benzaldehyde, *o*-phthalaldehyde, 2-vinylbenzaldehyde, and *o*-anisaldehyde were also examined, but the reaction did not proceed. Reaction of 3-hydroxybenzaldehyde afforded a hydroacylated product in merely 3% yield. ^{b)} Bishydroacylated products were formed in 21% yield as a regioisomeric mixture. ^{c)} The use of 0.1 equiv of Rh-complex afforded almost the same yield of products.

SCHEME 2



reacted slower than with salicylaldehyde, and the yield of product decreased, as shown in Table 3. The hydroacylation of **5** preferentially gave the *normal*-products (**b**) (entries 1 and 2), and that of 1,4-pentadien-3-ol **6** exclusively afforded the *normal*-products (**b**) but no *iso*-products (**a**) (entries 3 and 4). The hydroxyl group in **6** may affect the reaction to give the *normal*-product (**b**) exclusively, but the reason is not clear.¹³

Effect of Solvents, Additives, and Rh-Complexes. We examined the effect of solvents, additives, and Rh-

complexes on the hydroacylation. The results are summarized in Tables 4 and 5. In CH₂Cl₂, CHCl₃, EtOH, and ClCH₂CH₂Cl as solvent or even without a solvent (neat), the reaction proceeded smoothly, but the use of CH₃CN, DMF, toluene, THF, or CH₃NO₂ was not effective. Especially, the solvent of 5% EtOH in CH₂Cl₂ was superior to that of CH₂Cl₂ only. Concentration of the reaction affects the ratio of *iso*- and *normal*-products **16** and accelerates the rate of hydroacylation.

Addition of a base such as Na₂CO₃, NaOAc, and CsF accelerates the rate of hydroacylation, presumably as a result of the deprotonation of phenolic hydrogen (entries 1–3), whereas the addition of AgOTf or AgClO₄ also accelerates the reaction rate because the Rh-complex probably become a cationic species (entries 4 and 5). Above all, the hydroacylation between **1** and **4** by using RhCl(PPh₃)₃ (0.2 equiv), NaOAc (0.2 equiv), and AgClO₄ (0.2 equiv) in the solvent of 5% EtOH in CH₂Cl₂ was completed in 15 min at room temperature and in 30 min

(13) Jun, C.-H.; Han, J.-S.; Kang, J.-B.; Kim, S.-I. *J. Organomet. Chem.* **1994**, 474, 183.

TABLE 3.

<div style="display: flex; justify-content: space-around; align-items: center;"> <div> 29: Br; 30: Cl </div> <div> 5 or 6 (6.0 eq.) </div> <div> $\xrightarrow[\text{in CH}_2\text{Cl}_2 \text{ at r. t.}]{\text{RhCl(PPh}_3)_3 \text{ (0.2 eq.)}}$ </div> <div> <i>iso (a)</i> </div> <div> <i>normal (b)</i> </div> </div>					
entry	aldehyde	1,4-diene	reaction time (h)	products	
1	X = 29: Br	 5	24	 57a, 58a	57: 75 (1 : 2) 58: 79 (2 : 5)
2	X = 30: Cl				
3	X = 29: Br	 6	72	 59b, 60b	59b: 53 60b: 59
4	X = 30: Cl				

TABLE 4. Effect of Solvent on Rh-catalyzed Intermolecular Hydroacylation.

entry	RhCl(PPh ₃) ₃ (equiv)	1,5-hexadiene (equiv)	solvent	reaction time (h)	products 16 yield % (ratio a:b)
1	0.2	6	CH ₂ Cl ₂	24	quant (4:1)
2	0.2	6	neat	24	90 (5:1)
3	0.2	6	CH ₃ CN	72	39 (3:1)
4	0.2	6	DMF	72	16 (7:1)
5	0.2	6	toluene	72	12 (7:1)
6	0.2	6	THF	72	8 (7:1)
7	0.2	6	CH ₃ NO ₂	72	6 (6:1)
8	0.2	6	CHCl ₃	72	77 (5:1)
9	0.2	6	EtOH	72	77 (1:1)
10	0.2	6	ClCH ₂ CH ₂ Cl	72	50 (4:1)
11 ^a	0.1	2	CH ₂ Cl ₂ ^b	18	quant (2:1)

^a Na₂CO₃ (0.10 equiv) was used as an additive. ^b 5% EtOH in CH₂Cl₂ was used as a solvent.

TABLE 5. Effect of Rh-Complex and Additive on Intermolecular Hydroacylation

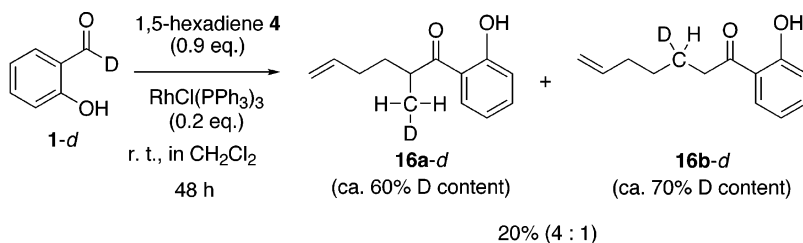
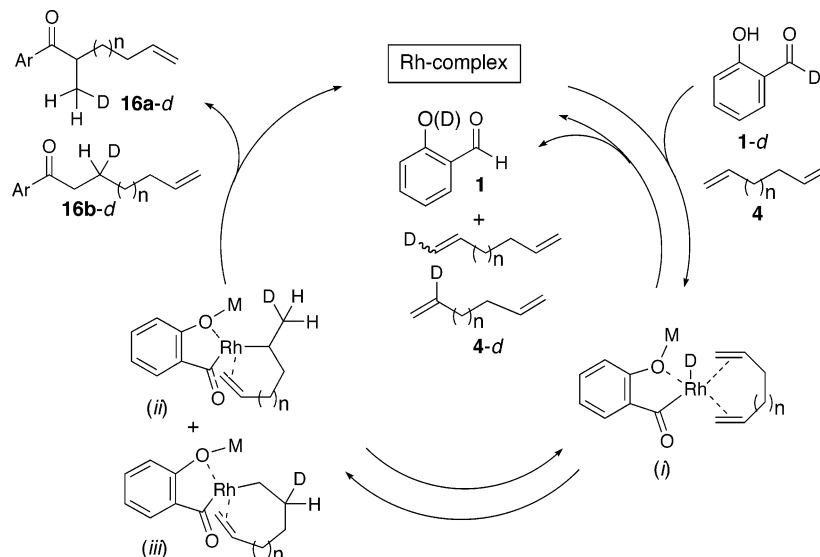
entry	Rh-complex ^a (0.2 equiv)	additive	reaction time (h)	products 16 yield % (ratio a:b)
1	RhCl(PPh ₃) ₃	Na ₂ CO ₃ (0.50 equiv)	13	quant (3:1)
2	RhCl(PPh ₃) ₃	NaOAc (0.20 equiv) ^b	4	quant (5:1)
3	RhCl(PPh ₃) ₃	CsF (0.20 equiv)	5	quant (6:1)
4	RhCl(PPh ₃) ₃	AgOTf (0.20 equiv)	4	quant (4:1)
5	RhCl(PPh ₃) ₃	AgClO ₄ (0.05 equiv)	2	90 (2:3)
6	RhCl(PPh ₃) ₃	AgClO ₄ + NaOAc ^{b,c}	15 min	93 (1:1)
7	RhCl(PPh ₃) ₃	salicylic acid (0.20 equiv)	72	quant (10:1)
8	RhCl(PPh ₃) ₃	salicylic acid (1.0 equiv)	72	74 (20:1)
9	[RhCl(C ₈ H ₁₄) ₂]		72	25 (3:1)
10 ^d	[RhCl(C ₈ H ₁₄) ₂] + PPh ₃ × 2		72	60 (4:1)
11	[RhCl(C ₈ H ₁₄) ₂] + dppe ^f		72	9 (1:4)
12	[RhCl(C ₈ H ₁₄) ₂] + dppe	AgClO ₄ + NaOAc ^{b,c}	72	48 (2:1)
13	[RhCl(C ₈ H ₁₄) ₂] + dppb		72	20 (3:2)
14	[RhCl(C ₈ H ₁₄) ₂] + dppf		72	44 (7:1)
15	[RhCl(C ₈ H ₁₄) ₂] + (o-MePh) ₃ P × 2		72	quant (12:1)
16	[RhCl(C ₈ H ₁₄) ₂] + (o-MePh) ₃ P × 2	AgClO ₄ + NaOAc ^{b,c}	8	quant (12:1)
17	[RhCl(C ₈ H ₁₄) ₂] + (i-PrO) ₃ P × 2		72	22 (1:1)
18	[RhCl(C ₈ H ₁₄) ₂] + (PhO) ₃ P × 2		72	20 (5:3)
19	[RhCl(C ₈ H ₁₄) ₂] + Et ₃ N × 2		72	46 (1:7)
20	[RhCl(C ₈ H ₁₄) ₂] + (i-Pr) ₂ NH × 2		72	63 (1:8)
21 ^e	[Rh(PPh ₃) ₂]ClO ₄		72	57 (4:1)
22	[Rh(dppe)]ClO ₄		72	30 (4:3)

^a The reaction was carried out using salicylaldehyde (1.0 equiv) and 1,5-hexadiene (6.0 equiv) at room temperature in CH₂Cl₂ under an Ar atmosphere. ^b 5% EtOH in CH₂Cl₂ was used as a solvent. ^c AgClO₄ (0.20 equiv) and NaOAc (0.20 equiv) were added. ^d In entries 10–18, Rh(phosphine)₂Cl was prepared in situ from [Rh(norbornadiene)(ligands)_n]ClO₄ by hydrogenation. ^e dppe = 1,2-bis(diphenylphosphino)ethane; dppb = 1,2-bis(diphenylphosphino)butane; dppf = 1,1'-bis(diphenylphosphino)ferrocene; C₈H₁₄ = cyclooctene.

at 0 °C, and the products **16a,b** were obtained in a 1:1 ratio in 93% yield (entry 6). Interestingly, the addition of salicylic acid changed the ratio of *iso*- and *normal*-

products **16** (entries 7 and 8). When 1.0 equiv of salicylic acid was added, the *iso*-product **16a** was preferentially obtained in a 20:1 ratio. As the Rh-complex, neutral Rh-

SCHEME 3

SCHEME 4. Plausible Catalytic Cycle of Hydroacylation^a

^a M = H, Na, or K; $n = 0$ or 1.

complexes such as $\text{Rh}(\text{PPh}_3)_2\text{Cl}$, $\text{Rh}(\text{dppb})\text{Cl}$, and $\text{Rh}(\text{dppf})\text{Cl}$, prepared in situ from $[\text{RhCl}(\text{cyclooctene})]_2$ and phosphine ligands, and cationic Rh-complexes such as $[\text{Rh}(\text{PPh}_3)_2]\text{ClO}_4$ and $[\text{Rh}(\text{dppe})]\text{ClO}_4$, prepared in situ from $[\text{Rh}(\text{norbornadiene})(\text{ligands})_n]\text{ClO}_4$ by hydrogenation,^{3c} catalyzed the hydroacylation to give a mixture of products **16a,b** (entries 9–14, 21, and 22). The use of neutral $\text{Rh}[(o\text{-MePh})_3\text{P}]_2\text{Cl}$ dominantly afforded the *iso*-hydroacylated product **16a** in a 12:1 ratio (entries 15 and 16). Replacement of phosphine ligands with phosphite ligands could also work, but the catalytic activity seemed to be low (entries 17 and 18). It is noteworthy that the use of $[\text{RhCl}(\text{cyclooctene})]_2$ and amines as a catalyst changed the ratio of hydroacylated products and afforded the *normal*-hydroacylated **16b** preferentially as a major product (entries 19 and 20).

Plausible Mechanisms of Rh-Catalyzed Hydroacylation. We examined the hydroacylation using deuterated salicylaldehyde **1-d**. At first, the reaction between **1-d** (1.0 equiv) and 1,5-hexadiene **4** (6.0 equiv) by $\text{RhCl}(\text{PPh}_3)_3$ (0.2 equiv) was performed, but no deuterium was detected in the isolated products **16a,b** by the ^1H NMR and MS spectra. Thus, the reaction was performed using 0.9 equiv of 1,5-hexadiene **4**; in this case, the deuterium was introduced into the products, i.e., the methyl signal at δ 1.22 (m, 2.4H; ca. 60% deuterium content) in **16a-d** and methylene signals at δ 1.74–1.79 (m, 1.3H; ca. 70% deuterium content) in **16b-d** by the ^1H NMR spectra, and the molecular ion peak m/z 205 ($\text{M} + \text{H}$)⁺ in the MS

spectrum also supported the existence of deuterium in **16a,b-d** (Scheme 3).

These results may be attributed to the fact that rapid interconversion processes exist, and the 1,5-hexadiene **4** and salicylaldehyde **1-d** rapidly coordinate to the Rh-complex and dissociate from the Rh-complex. As a result, nondeuterated salicylaldehyde **1** is yielded in the cycle, and it reacts with **4** faster than the deuterated **1-d** reacts. The deuterium might be transferred into the 1,5-hexadiene, and also may partly be exchanged for the phenolic hydrogen atom.¹⁴ On the basis of these experiments, we present a plausible catalytic cycle, which can explain the accelerated hydroacylation, as outlined in Scheme 4. Intermediates i–iii, in which both the diene and salicylaldehyde bind to the Rh-complex by “double-chelation”, play vital roles in the intermolecular hydroacylation. The addition of a base, such as NaOAc, Na_2CO_3 , and CsF, may deprotonate the phenolic hydroxyl function and change the chelation effects, and that of an Ag salt such as AgOTf and AgClO_4 may affect the property of the Rh-complex. The proposed catalytic cycle is a plausible explanation, but all chelations of salicylaldehyde, 1,5-hexadiene, and bisphosphine ligand may afford a hepta-coordinated Rh-complex.¹⁵ Thus, the real intermediates may be μ^2 -ligand-Rh-complexes or η^6 -Ph-bi-Rh-complexes,¹⁶ and the “double-

(14) A solution of **1-d** (100% deuterium content) and $\text{RhCl}(\text{PPh}_3)_3$ in CDCl_3 was stirred at room temperature for 4 h, and the ^1H NMR spectrum of the solution showed an aldehyde ($-\text{CHO}$) proton peak at δ 9.90 (ca. 0.3H), meaning ca. 70% deuterium content.

(15) Nagashima, H.; Tatebe, K.; Ishibashi, T.; Nakaoka, A.; Sakakibara, J.; Itoh, K. *Organometallics* **1995**, *14*, 2868.

chelation" in those dimeric intermediates may affect the Rh-catalyzed hydroacylation.¹⁷

Conclusion

We have achieved the Rh-catalyzed intermolecular hydroacylation between salicylaldehydes and 1,4-penta- or 1,5-hexadienes. The reaction proceeded under very mild conditions to give a mixture of *iso*- and *normal*-hydroacylated products. By the selection of additives and Rh-complexes, we could regioselectively prepare *iso*- or *normal*-hydroacylated products. The Rh-catalyzed intermolecular hydroacylation might proceed via double-chelated intermediates, and the "double chelation" of aldehyde and diene to the Rh-complex might accelerate the reaction. The application of the "double chelation" concept to other reactions is currently underway.

Experimental Section

General Procedure for RhCl(PPh₃)₃-Catalyzed Hydroacylation between Salicylaldehydes and Dienes. A solution of 2-hydroxybenzaldehyde (1.00 mmol), diene (6.00 mmol), and RhCl(PPh₃)₃ (184 mg, 0.20 mmol) in CH₂Cl₂ (2.5 mL) was stirred at room temperature under an Ar atmosphere. After being stirred for 1–72 h, the solution was evaporated and diluted with ether, and the precipitated Rh-complex was filtered off. The filtrate was concentrated in vacuo, and the residue was purified by column chromatography on silica gel (EtOAc in hexane) to give the hydroacylated products.

4-Hydroxy-1-(2-hydroxyphenyl)hex-5-en-1-one (18b). A solution of salicylaldehyde **1** (122 mg, 1.00 mmol), 1,4-pentadien-3-ol **6** (504 mg, 6.00 mmol), and RhCl(PPh₃)₃ (184 mg, 0.20 mmol) in CH₂Cl₂ (2.5 mL) was stirred at room temperature under an Ar atmosphere. After being stirred for 1 h, the solution was evaporated, and the residue was diluted with Et₂O. The precipitate was filtered off, and the filtrate was evaporated to give an oily residue, which was purified by

column chromatography on silica gel. The fraction eluted with 15% EtOAc in hexane afforded **18b** (192 mg, 93%) as a colorless oil. IR (neat) 3396 (br), 2929, 1639 cm⁻¹; ¹H NMR (CDCl₃) δ 12.28 (s, 1H), 7.80 (br d, *J* = 9 Hz, 1H), 7.46 (br t, *J* = 9 Hz, 1H), 6.97 (br d, *J* = 9 Hz, 1H), 6.89 (br t, *J* = 9 Hz, 1H), 5.95 (m, 1H), 5.28 (d, *J* = 17.2 Hz, 1H), 5.15 (d, *J* = 10.5 Hz, 1H), 4.24 (m, 1H), 3.14 (t, *J* = 7.3 Hz, 2H), 1.90–2.11 (m, 3H); FAB(+)HRMS calcd for C₁₂H₁₅O₃ (M⁺ + H) 207.1021, found 207.0978.

Rh-Catalyzed Intermolecular Hydroacylation between 5-Bromo-2-hydroxybenzaldehyde (29) and 3-Methyl-1,4-pentadiene (5). The RhCl(PPh₃)₃-catalyzed hydroacylation between 5-bromo-2-hydroxybenzaldehyde **29** and 3-methyl-1,4-pentadiene **5** at room temperature afforded **57a,b** (75%) as a mixture of isomers in the ratio of 1 (*iso*) to 2 (*normal*). A colorless oil: IR (neat) 3069, 2967, 1644, 1609 cm⁻¹; ¹H NMR (CDCl₃) δ 12.5 (s, 0.33H), 12.3 (s, 0.67H), 7.84 (m, 1H), 7.51 (br d, *J* = 9 Hz, 1H), 6.88 (br d, *J* = 9 Hz, 1H), 5.70 (m, 1H), 4.94–5.05 (m, 2H), 3.39 (quintet, *J* = 7.0 Hz, 0.33H), 2.94 (br t, *J* = 7.0 Hz, 1.34H), 2.65 (sextet, *J* = 7.0 Hz, 0.33H), 2.22 (septet, *J* = 7.0 Hz, 0.67H), 1.60–1.86 (m, 1.34H), 1.18 (d, *J* = 7.0 Hz, 0.99H), 1.07 (d, *J* = 7.0 Hz, 2.01H), 1.04 (d, *J* = 7.0 Hz, 0.99H); FAB(+)HRMS calcd for C₁₃H₁₆BrO₂ (M⁺ + H) 283.0334, found 283.0316.

General Procedure for the Hydroacylation between Salicylaldehyde and 1,5-Hexadiene by Rh-Complexes. A mixture of [RhCl(cyclooctene)]₂ (49 mg, 0.10 mmol) and bisphosphine (0.20 mmol) in CH₂Cl₂ (3 mL) was stirred at room temperature for 1 h. Then, a solution of salicylaldehyde **1** (122 mg, 1.0 mmol) and 1,5-hexadiene **4** (493 mg, 6.0 mmol) in CH₂Cl₂ (1 mL) was added dropwise to the stirred solution. After being stirred at room temperature for 1–72 h, the solution was concentrated in vacuo to leave the residue, which was dissolved in ether, and the precipitated Rh-complex was filtered off. Removal of the solvent afforded the residue, which was purified by column chromatography on silica gel to give the hydroacylated products.

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Supporting Information Available: Preparation of dienes **8–10** and **1-d**, experimental procedure for **15**, **25** and **58–60**, and copies of the ¹H NMR spectra of all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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