Double Chelation Assisted Rh-Catalyzed Intermolecular Hydroacylation

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Supporting Information

Preparation of Substrates

Table 1 Rh-Catalyzed intermolecular hydroacylation.

Entry	Rh(PPh ₃) ₃ Cl (Equivalent)	1,5-Hexadiene (Equivalent)	Solvent	Conc.	Reaction Time (h)	Products 10	
						Yield (%)	Ratio of a : b
1	0.2	6	CH ₂ Cl ₂	0.4	24	quant.	4 : 1
2	1.0	6	CH ₂ Cl ₂	0.4	13	quant.	8 : 1
3	0.2	6	CH ₂ Cl ₂	0.1	36	quant.	2 : 1
4	0.2	6	CH ₂ Cl ₂	2	2	quant.	4 : 1
5	0.2	1.5	CH ₂ Cl ₂	1	72	95	4 : 1
6	0.2	6	MeCN	0.4	72	2	4 : 1
7	0.2	6	toluene	0.4	72	12	7 : 1
8	0.2	6	MeNO ₂	0.4	72	6	6 : 1
9	0.2	6	CHCl ₃	0.4	72	77	5 : 1
10	0.2	6	EtOH	0.4	72	77	1 : 1
11	0.2	6	ClCH ₂ CH ₂ Cl	0.4	72	50	4 : 1
12 ^a	0.1	2	CH ₂ Cl ₂ ^b	0.1	18	quant.	2 : 1

a) Na₂CO₃ (0.1 eq.) was added as an additive; b) 5% EtOH in CH₂Cl₂ was used as a solvent.

Table 2 Effect of Rh-complexes and Additives on Intermolecular Hydroacylation Reaction.

Entry	Rh-complex ^a (0.2 eq.)	Additive	Reaction Time (h)	Products 10	
				Yield (%)	Ratio of a : b
1	Rh(PPh ₃) ₃ Cl	—	20	quant.	4 : 1
2	Rh(PPh ₃) ₃ Cl	AgClO ₄ (0.05 eq.)	2	90	2 : 3
3	Rh(PPh ₃) ₃ Cl	AgClO ₄ + NaOAc ^{b,c}	15 min	90	1 : 1
4	Rh(PPh ₃) ₃ Cl	AgOTf (0.20 eq.)	4	quant.	4 : 1
5	Rh(PPh ₃) ₃ Cl	CsF (0.20 eq.)	5	quant.	6 : 1
6	Rh(PPh ₃) ₃ Cl	Na ₂ CO ₃ (0.50 eq.)	13	quant.	3 : 1
7	Rh(PPh ₃) ₃ Cl	NaOAc (0.2eq.) ^c	4	quant.	5 : 1
8 ^d	[Rh(PPh ₃) ₂]Cl	—	72	60	4 : 1
9 ^d	[Rh(dppe)]Cl ^f	—	72	9	1 : 4
10 ^d	[Rh(dppf)]Cl ^f	—	72	44	7 : 1
11 ^d	[Rh(tri- <i>o</i> -tolylphosphine) ₂]Cl	—	72	quant.	12 : 1
12 ^e	[Rh(PPh ₃) ₂]ClO ₄	—	72	57	4 : 1
13 ^e	[Rh(dppe)]ClO ₄	—	72	30	1.3 : 1

a) The reaction was carried out using salicylaldehyde (1 eq.) and 1,5-hexadiene (6 eq.) at room temperature in CH₂Cl₂ under an Ar atmosphere.

b) AgClO₄ (0.2 eq.) and NaOAc (0.2 eq.) were added.

c) 5% EtOH in CH₂Cl₂ was used as a solvent.

d) In the entries 8—11, Rh-complex was prepared in situ from [RhCl(cyclooctene)]₂ and ligands.

e) In the entries 12 and 13, Rh-complex was prepared in situ from [Rh(NBD)(ligands)_n]ClO₄ by hydrogenation.

f) dppe: 1,2-bis(diphenylphosphino)ethane; dppf: 1,1'-bis(diphenylphosphino)ferrocene;

Table 3

Rh-Catalyzed Intermolecular Hydroacylation of Deuterated Aldehyde

Entry	Aldehyde	1,5-Hexadiene (eq.)	Time (h)	Products		
				Yield % (Ratio)	¹ H NMR Spectra	
1	R-CHO	6	20	quant. (4 : 1)	1.22 (d, <i>J</i> = 6.9 Hz, 3H)	1.74-1.79 (m, 2H)
2	R-CDO	6	48	37 (5 : 1)	1.22 (d, <i>J</i> = 6.9 Hz, 3H)	1.74-1.79 (m, 2H)
3	R-CDO	0.9	48	20 (4 : 1)	1.22 (m, <i>J</i> = 6.9 Hz, 2.4H)	1.74-1.79 (m, 1.3H)

Experimental Section.

General Methods. ^1H NMR spectra were determined at 270 MHz, 400MHz, or 500 MHz. Infrared spectra were recorded on a JASCO A-100 or a NICOLET AVATAR-320 spectrometer (neat). FABMS and FAB(+)HRMS spectra were taken on a JEOL JMS 610H or JEOL SX102 spectrometer. The other general procedures were followed as described in the previous papers (ref. 3c and d in the text).

A Typical Procedure for the Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde and Diene. A solution of salicylaldehyde (1.00 mmol), diene (6.00 mmol), and $\text{Rh}(\text{PPh}_3)_3\text{Cl}$ (184 mg, 0.20 mmol) in CH_2Cl_2 (2.5 mL) was stirred at room temperature under an Ar atmosphere. After being stirred for 24—72 h, the solution was evaporated, diluted with ether, and the precipitate was filtered off. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel (EtOAc in hexane) to give the hydroacylated products as a mixture of *iso*- and *normal*-isomers.

1-(2-Hydroxyphenyl)heptan-1-one.¹⁾ $\text{Rh}(\text{PPh}_3)_3\text{Cl}$ -Catalyzed hydroacylation between salicylaldehyde **1** and 1-hexene at room temperature afforded a hydroacylated product in 4% yield as a colorless oil: IR (neat) 2925, 1635 cm^{-1} ; ^1H NMR (CDCl_3) δ 12.40 (s, 1H), 7.76 (br d, $J = 9\text{ Hz}$, 1H), 7.47 (br t, $J = 9\text{ Hz}$, 1H), 6.99 (br d, $J = 9\text{ Hz}$, 1H), 6.89 (br t, $J = 9\text{ Hz}$, 1H), 2.99 (t, $J = 7.3\text{ Hz}$, 2H), 1.75 (m, 2H), 1.25—1.50 (m, 6H), 0.90 (t, $J = 6.9\text{ Hz}$, 3H); FAB(+)HRMS calcd for $\text{C}_{13}\text{H}_{19}\text{O}_2$ (M^++H) 207.1385, found 207.1380.

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 1,5-Hexadiene (2). A solution of salicylaldehyde **1** (122 mg, 1.00 mmol), 1,5-hexadiene **2** (493 mg, 6.00 mmol), and $\text{Rh}(\text{PPh}_3)_3\text{Cl}$ (184 mg, 0.2 mmol) in CH_2Cl_2 (2.5 mL) was stirred at room temperature under an Ar atmosphere. After being stirred for 24 h, the solution was evaporated, diluted with ether, and the resulting precipitate was filtered off. The filtrate was concentrated, and the residue was purified by column chromatography on silica gel. The fraction eluted with 10% EtOAc in hexane afforded the hydroacylated products **10a** and **10b** (204 mg, quant.) as a mixture of isomers in the ratio of 4 to 1. Each compounds **10a** and **10b** could be separated by preparative TLC. **1-(2-Hydroxyphenyl)-2-**

methylhex-5-en-1-one (10a). A colorless oil; IR (neat) 3075, 2975, 2935, 1637, 1612 cm^{-1} ; ^1H NMR (CDCl_3) δ 12.57 (s, 1H), 7.79 (br d, $J = 9$ Hz, 1H), 7.49 (br t, $J = 9$ Hz, 1H), 6.99 (br d, $J = 9$ Hz, 1H), 6.90 (br t, $J = 9$ Hz, 1H), 5.85 (m, 1H), 4.96—5.09 (m, 2H), 3.54 (sextet, $J = 6.9$ Hz, 1H), 2.14 (m, 2H), 1.95 (m, 1H), 1.60 (m, 1H), 1.22 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (68 MHz, CDCl_3) δ 210.6, 163.2, 137.8, 136.3, 129.8, 118.8, 118.7, 118.7, 115.4, 39.2, 32.7, 31.4, 17.5; FAB(+)HRMS calcd for $\text{C}_{13}\text{H}_{17}\text{O}_2$ (M^++H) 205.1228, found 205.1203. **1-(2-Hydroxyphenyl)-hept-6-en-1-one (10b).** A colorless oil; IR (neat) 3076, 2934, 1640, 1615 cm^{-1} ; ^1H NMR (CDCl_3) δ 12.38 (s, 1H), 7.77 (br d, $J = 9$ Hz, 1H), 7.47 (br t, $J = 9$ Hz, 1H), 6.99 (br d, $J = 9$ Hz, 1H), 6.89 (br t, $J = 9$ Hz, 1H), 5.81 (m, 1H), 4.95—5.07 (m, 2H), 3.07 (t, $J = 7.3$ Hz, 2H), 2.11 (m, 2H), 1.79 (quintet, $J = 7.4$ Hz, 2H), 1.51 (m, 2H); ^{13}C NMR (68 MHz, CDCl_3) δ 206.7, 162.5, 138.3, 136.2, 129.9, 119.3, 118.8, 118.6, 114.8, 38.1, 33.5, 28.5, 23.9; FABMS m/z 205 (M^++H), 204 (M^+).

Rh(PPh_3) $_3$ Cl-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 3-Methyl-1,4-pentadiene (3). Rh(PPh_3) $_3$ Cl-Catalyzed hydroacylation between salicylaldehyde **1** and 3-methyl-1,4-pentadiene **3** at room temperature afforded **11a** and **11b** in 80% yield as a mixture of isomers in the ratio of 3 to 5. IR (neat) 3078, 2968, 1639, 1615 cm^{-1} ; ^1H NMR (CDCl_3) δ 12.57 (s, 0.38H), 12.39 (s, 0.62H), 7.77 (m, 1H), 7.45 (br t, $J = 9$ Hz, 1H), 6.99 (m, 1H), 6.89 (br t, $J = 9$ Hz, 1H), 5.70 (m, 1H), 6.92—5.10 (m, 2H), 3.50 (quintet, $J = 6.9$ Hz, 0.38H), 2.98 (m, 1.24H), 2.66 (sextet, $J = 6.9$ Hz, 0.38H), 2.23 (m, 0.62H), 1.60—1.86 (m, 1.14H), 1.18 (d, $J = 6.9$ Hz, 1.14H), 1.07 (d, $J = 6.6$ Hz, 1.86H), 1.03 (d, $J = 6.9$ Hz, 1.14H); The major isomer **11b** could be isolated by preparative TLC. **11b:** A colorless oil: IR (neat) 3075, 2970, 1640, 1610 cm^{-1} ; ^1H NMR (CDCl_3) δ 12.38 (s, 1H), 7.77 (br d, $J = 9$ Hz, 1H), 7.45 (br t, $J = 9$ Hz, 1H), 6.99 (br d, $J = 9$ Hz, 1H), 6.89 (br t, $J = 9$ Hz, 1H), 5.70 (m, 1H), 6.92—5.10 (m, 2H), 2.98 (m, 2H), 2.23 (m, 1H), 1.60—1.86 (m, 2H), 1.07 (d, $J = 6.6$ Hz, 3H); FAB(+)HRMS calcd for $\text{C}_{13}\text{H}_{17}\text{O}_2$ (M^++H) 205.1228, found 205.1228.

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 1,6-Heptadiene. Rh(PPh_3) $_3$ Cl-Catalyzed hydroacylation between salicylaldehyde **1** and 1,6-heptadiene in refluxing CH_2Cl_2 afforded the hydroacylated product in 4% yield as a mixture of regioisomers, and with some contaminations. A colorless oil: IR (neat) 3075, 2850, 1635, 1610, 1580 cm^{-1} ; ^1H NMR

(CDCl₃) δ 12.38—12.68 (m, 1H), 7.78 (br d, J = 9 Hz, 1H), 7.46 (br t, J = 9 Hz, 1H), 7.00 (br d, J = 9 Hz, 1H), 6.89 (br t, J = 9 Hz, 1H), 5.80 (m, 1H), 4.90—5.10 (m, 2H), 3.00 (t, J = 7.3 Hz, 0.9H), 0.85—3.60 (other H); FAB(+)HRMS calcd for C₁₄H₁₉O₂ (M⁺+H) 219.1385, found 219.1361.

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 2-Methyl-1,5-hexadiene (4). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between salicylaldehyde **1** and 2-methyl-1,5-hexadiene **4** at room temperature afforded a mixture of **12a** and **12b** (quant.) in the ratio of 20 to 1. A colorless oil: IR (neat) 3075, 1640, 1610, 1580 cm⁻¹; ¹H NMR (CDCl₃) δ 12.58 (s, 0.95H), 12.39 (s, 0.05H), 7.79 (br d, J = 9 Hz, 1H), 7.47 (br t, J = 9 Hz, 1H), 6.99 (br d, J = 9 Hz, 1H), 6.90 (br t, J = 9 Hz, 1H), 4.72 (br s, 1H), 4.65 (br s, 1H), 3.53 (m, 0.95H), 3.00 (t, J = 7.3 Hz, 0.1H), 1.95—2.20 (m, 3.05H), 1.71 (s, 3H), 1.55—1.75 (m, 1.05H), 1.24 (d, J = 6.9 Hz, 2.85H); FAB(+)HRMS calcd for C₁₄H₁₉O₂ (M⁺+H) 219.1385, found 219.1409.

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 2-Phenyl-1,5-hexadiene (5). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between salicylaldehyde **1** and 2-phenyl-1,5-hexadiene **5** at room temperature afforded a mixture of **13a** and **13b** (77%) in the ratio of 6 to 1. A colorless oil: IR (neat) 3073, 2938, 1637 cm⁻¹; ¹H NMR (CDCl₃) δ 12.54 (s, 0.86H), 12.36 (s, 0.14H), 6.75—7.73 (m, 9H), 5.30 (br s, 0.86H), 5.28 (br s, 0.14H), 5.08 (br s, 0.14H), 5.05 (br s, 0.86H), 3.50 (sestet, J = 6.9 Hz, 0.86H), 2.97 (t, J = 7.3 Hz, 0.28H), 2.58 (br t, J = 7.5 Hz, 2H), 2.03 (sestet, J = 6.9 Hz, 0.86H), 1.78 (quintet, J = 7.3 Hz, 0.28H), 1.50—1.65 (m, 1.14H), 1.22 (d, J = 6.9 Hz, 2.58H).

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 2-Pentyl-1,5-hexadiene (6). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between salicylaldehyde **1** and 2-pentyl-1,5-hexadiene **6** at room temperature afforded **14a** and **14b** (61%) as a mixture of isomers in the ratio of 7 to 1. A colorless oil: IR (neat) 3075, 2930, 1638 cm⁻¹; ¹H NMR (CDCl₃) δ 12.59 (s, 0.87H), 12.39 (s, 0.13H), 7.77 (br d, J = 9 Hz, 1H), 7.48 (br t, J = 9 Hz, 1H), 6.98 (br d, J = 9 Hz, 1H), 6.89 (br t, J = 9 Hz, 1H), 4.73 (s, 1H), 4.69 (s, 1H), 3.53 (sestet, J = 6.9 Hz, 0.87H), 3.00 (t, J = 7.3 Hz, 0.26H), 1.25—2.10 (m, 12.26H), 1.23 (d, J = 6.9 Hz, 2.61H), 0.88 (t, J = 7.3 Hz, 3); FABMS m/z 275 (M⁺+H).

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 5-Methylenenona-1,8-diene (7). The Rh(PPh₃)₃Cl-catalyzed hydroacylation between salicylaldehyde **1** and 5-methylenenona-1,8-diene **7** at room temperature afforded **15a** and **15b** (74%) as a mixture of isomers in the ratio of 5 to 1. A colorless oil: IR (neat) 3077, 2975, 2934, 1638, 11615 cm⁻¹; ¹H NMR (CDCl₃) δ 12.57 (s, 0.83H), 12.38 (s, 0.17H), 7.77 (br d, *J* = 9 Hz, 1H), 7.48 (br t, *J* = 9 Hz, 1H), 6.98 (br d, *J* = 9 Hz, 1H), 6.89 (br t, *J* = 9 Hz, 1H), 5.81 (m, 1H), 4.92—5.05 (m, 2H), 4.75 (br s, 1H), 4.73 (br s, 1H), 3.52 (sestet, *J* = 6.9 Hz, 0.83H), 3.01 (t, *J* = 7.3 Hz, 0.34H), 1.94—2.20 (m, 6.83H), 1.49—1.78 (m, 1.51H), 1.24 (d, *J* = 6.9 Hz, 2.49H); FAB(+)HRMS calcd for C₁₇H₂₃O₂ (M⁺+H) 259.1698, found 259.1657.

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 1,5-Heptadiene (8). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between salicylaldehyde **1** and 1,5-heptadiene **8** at room temperature afforded **16a,b,c** in 60% yield as a mixture of regioisomers (a : b : c = 1 : 1 : 2). A colorless oil: IR (neat) 2938, 1634, 1582 cm⁻¹; EI-HRMS calcd for C₁₄H₂₈O₂ (M⁺) 218.1307, found 218.1283. Each compound **16a,b,c** could be separated by preparative TLC. **16a**: A colorless oil; ¹H NMR (CDCl₃) δ 12.58 (s, 1H), 7.78 (br d, *J* = 9 Hz, 1H), 7.47 (br t, *J* = 9 Hz, 1H), 6.99 (br d, *J* = 9 Hz, 1H), 6.89 (br t, *J* = 9 Hz, 1H), 5.31—5.53 (m, 2H), 3.53 (sestet, *J* = 6.9 Hz, 1H), 2.09 (q, *J* = 7.1 Hz, 2H), 1.92 (m, 1H), 1.56 (br s, 3H), 1.54 (m, 1H), 1.24 (d, *J* = 6.9 Hz, 3H). **16b**: A colorless oil; ¹H NMR (CDCl₃) δ 12.39 (s, 1H), 7.76 (br d, *J* = 9 Hz, 1H), 7.46 (br t, *J* = 9 Hz, 1H), 6.98 (br d, *J* = 9 Hz, 1H), 6.89 (br t, *J* = 9 Hz, 1H), 5.30—5.55 (m, 2H), 2.95—3.02 (m, 2H), 2.00—2.15 (m, 2H), 1.15—1.80 (m, 7H). **16c**: A colorless oil; ¹H NMR (CDCl₃) δ 12.67 (s, 1H), 7.79 (br d, *J* = 9 Hz, 1H), 7.47 (br t, *J* = 9 Hz, 1H), 7.00 (br d, *J* = 9 Hz, 1H), 6.90 (br t, *J* = 9 Hz, 1H), 5.76 (m, 1H), 4.91—5.10 (m, 2H), 3.43 (m, 1H), 1.20—2.15 (m, 6H), 0.91 (t, *J* = 7.2 Hz, 3H).

Rh-Catalyzed Intermolecular Hydroacylation between Salicylaldehyde (1) and 1,5,9-Decatriene (9). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between salicylaldehyde **1** and 1,5,9-decatriene **9** at room temperature afforded **17a,b,c** in 69% yield as a mixture of regioisomers (a : b : c = 2.5 : 1 : 4.5). Each compound **17a,b,c** could be separated by preparative TLC. **1-(2-Hydroxyphenyl)-2-methyldeca-5,9-dien-1-one (17a)**. A colorless oil: IR (neat) 3445 (br), 3075, 2933, 1635 cm⁻¹; ¹H

NMR (CDCl₃) δ 12.58, 12.57 (s, total 1H), 7.78 (br d, J = 9 Hz, 1H), 7.46 (br t, J = 9 Hz, 1H), 6.99 (br d, J = 9 Hz, 1H), 6.90 (br t, J = 9 Hz, 1H), 5.76 (m, 1H), 5.32—5.43 (m, 2H), 4.92—5.02 (m, 2H), 3.54 (sextet, J = 6.9 Hz, 1H), 2.00—2.12 (m, 6H), 1.91 (m, 1H), 1.50 (m, 1H), 1.23 (d, J = 6.9 Hz, 3H); FAB(+)HRMS calcd for C₁₇H₂₃O₂ (M⁺+H) 259.1698, found 259.1714. **1-(2-Hydroxyphenyl)undeca-6,10-dien-1-one (17b)**. A colorless oil: IR (neat) 3075, 2928, 1641, 1615 cm⁻¹; ¹H NMR (CDCl₃) δ 12.39, 12.37 (s, total 1H), 7.76 (br d, J = 9 Hz, 1H), 7.48 (br t, J = 9 Hz, 1H), 6.98 (br d, J = 9 Hz, 1H), 6.87 (br t, J = 9 Hz, 1H), 5.80 (m, 1H), 5.35—5.60 (m, 1.3H), 4.90—5.11 (m, 3.7H), 2.98 (m, 2H), 2.05—2.14 (m, 6H), 1.36—1.80 (m, 4H); FAB(+)HRMS calcd for C₁₇H₂₃O₂ (M⁺+H) 259.1698, found 259.1743. **2-(3-Butenyl)-1-(2-hydroxyphenyl)hept-6-en-1-one (17c)**. A colorless oil: IR (neat) 3077, 2930, 1635, 1611 cm⁻¹; ¹H NMR (CDCl₃) δ 12.66 (s, 1H), 7.78 (br d, J = 9 Hz, 1H), 7.48 (br t, J = 9 Hz, 1H), 7.00 (br d, J = 9 Hz, 1H), 6.90 (br t, J = 9 Hz, 1H), 5.75 (m, 2H), 4.91—5.02 (m, 4H), 3.49 (m, 1H), 1.34—2.14 (m, 10H); FAB(+)HRMS calcd for C₁₇H₂₃O₂ (M⁺+H) 259.1698, found 259.1669.

Rh-Catalyzed Intermolecular Hydroacylation between 2,5-Dihydroxybenzaldehyde (18) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2,5-dihydroxybenzaldehyde **18** and 1,5-hexadiene **2** at room temperature afforded **33a** and **33b** (90%) as a mixture of isomers in the ratio of 3 to 1. A colorless oil: IR (neat) 3396 (br), 3077, 2935, 1642, 1620 cm⁻¹; ¹H NMR (CDCl₃) δ 12.12 (s, 0.75H), 11.94 (s, 0.25H), 7.22 (dd, J = 3.0, 5.6 Hz, 1H), 7.02 (m, 1H), 6.89 (dd, J = 5.6, 9.0, 1H), 5.81 (m, 1H), 4.95—5.07 (m, 2H), 4.73 (br s, 1H), 3.45 (sextet, J = 6.9 Hz, 0.75H), 2.94 (t, J = 7.3 Hz, 0.50H), 2.05—2.18 (m, 2H), 1.94 (m, 0.75H), 1.72—1.80 (m, 0.50H), 1.43—1.62 (m, 1.25H), 1.22 (d, J = 6.9 Hz, 2.25H); FAB(+)HRMS calcd for C₁₃H₁₇O₃ (M⁺+H) 221.1178, found 221.1192.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-5-methoxy-benzaldehyde (19) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2-hydroxy-5-methoxybenzaldehyde **19** and 1,5-hexadiene **2** at room temperature afforded **34a** and **34b** (quant.) as a mixture of isomers in the ratio of 3 to 1. A colorless oil: IR (neat) 3070, 2925, 1630, 1605 cm⁻¹; ¹H NMR (CDCl₃) δ 12.15 (s, 0.75H), 11.97 (s, 0.25H), 7.22 (br s, 1H), 7.12 (br d, J = 9 Hz, 1H), 6.94 (br d, J = 9 Hz, 1H), 5.79 (m, 1H), 4.97—5.05 (m, 2H), 4.97—5.05 (m, 2H), 3.80 (s, 3H), 3.48 (sextet, J = 6.9 Hz, 0.75H), 2.97 (t, J = 7.3 Hz, 0.50H), 2.10 (m, 2H), 1.95 (m, 0.75H), 1.75 (quintet, J = 7.3 Hz, 0.50H),

1.45—1.65 (m, 1.25H), 1.23 (d, J = 6.9 Hz, 2.25H); FAB(+)HRMS calcd for $C_{14}H_{19}O_3$ ($M^+ + H$) 235.1334, found 235.1371.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-5-methylbenzaldehyde (20) and 1,5-Hexadiene (2). Rh(PPh_3)₃Cl-Catalyzed hydroacylation between 2-hydroxy-5-methylbenzaldehyde **20** and 1,5-hexadiene **2** at room temperature afforded **35a** and **35b** (42%) as a mixture of isomers in the ratio of 3 to 1. A colorless oil: IR (neat) 3400 (br), 3080, 1665, 1645, 1600 cm^{-1} ; 1H NMR ($CDCl_3$) δ 12.40 (s, 0.75H), 12.21 (s, 0.25H), 7.55 (br s, 1H), 7.30 (br d, J = 9 Hz, 1H), 6.89 (br d, J = 9 Hz, 1H), 5.84 (m, 1H), 4.96—5.05 (m, 2H), 3.53 (sextet, J = 6.9 Hz, 0.75 H), 2.98 (t, J = 7.4 Hz, 0.50H), 2.33 (s, 3H), 2.02—2.15 (m, 2H), 1.90—2.00 (m, 1.0H), 1.76 (quintet, J = 7.4 Hz, 0.50H), 1.40—1.62 (m, 1.25H), 1.22 (d, J = 6.9 Hz, 2.25H); FAB(+)HRMS calcd for $C_{14}H_{19}O_2$ ($M^+ + H$) 219.1385, found 219.1380.

Rh-Catalyzed Intermolecular Hydroacylation between 5-Bromo-2-hydroxybenzaldehyde (21) and 1,5-Hexadiene (2). Rh(PPh_3)₃Cl-Catalyzed hydroacylation between 5-bromo-2-hydroxybenzaldehyde **21** and 1,5-hexadiene **2** at room temperature afforded **36a** and **36b** (quant.) as a mixture of isomers in the ratio of 5 to 1. A colorless oil: IR (neat) 3069, 2967, 1644, 1609 cm^{-1} ; 1H NMR ($CDCl_3$) δ 12.46 (s, 0.83H), 12.28 (s, 0.17H), 7.85 (br s, 1H), 7.53 (br d, J = 9 Hz, 1H), 6.90 (br d, J = 9 Hz, 1H), 5.78 (m, 1H), 4.98—5.08 (m, 2H), 3.45 (sextet, J = 6.9 Hz, 0.83H), 2.97 (t, J = 7.3 Hz, 0.34H), 2.11 (m, 2H), 1.50—2.00 (m, 2.34H), 1.23 (d, J = 6.9 Hz, 2.49H); FAB(+)HRMS calcd for $C_{13}H_{16}BrO_2$ ($M^+ + H$) 283.0334, found 283.0316.

Rh-Catalyzed Intermolecular Hydroacylation between 5-Chloro-2-hydroxybenzaldehyde (22) and 1,5-Hexadiene (2). Rh(PPh_3)₃Cl-Catalyzed hydroacylation between 5-chloro-2-hydroxybenzaldehyde **22** and 1,5-hexadiene **2** at room temperature afforded **37a** and **37b** (quant.) as a mixture of isomers in the ratio of 4 to 1. A colorless oil: IR (neat) 3080, 2950, 1650, 1625 cm^{-1} ; 1H NMR ($CDCl_3$) δ 12.44 (s, 0.8H), 12.26 (s, 0.2H), 7.72 (br s, 1H), 4.40 (br d, J = 9 Hz, 1H), 6.94 (br d, J = 9 Hz, 1H), 5.79 (m, 1H), 4.97—5.08 (m, 2H), 3.45 (sextet, J = 6.9 Hz, 0.8H), 2.97 (t, J = 7.3 Hz, 0.4H),

2.12 (m, 2H), 1.95 (m, 0.8H), 1.76 (quintet, $J = 7.3$ Hz, 0.4H), 1.45—1.65 (m, 1.2H), 1.23 (d, $J = 6.9$ Hz, 2.4H); FAB(+)HRMS calcd for $C_{13}H_{16}Cl_1O_2$ ($M^+ + H$) 239.0839, found 239.0862.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-5-nitrobenzaldehyde (23) and 1,5-Hexadiene (2). Rh(PPh_3)₃Cl-Catalyzed hydroacylation between 2-hydroxy-5-nitrobenzaldehyde **23** and 1,5-hexadiene **2** at room temperature afforded **38a** and **38b** (73%) as a mixture of isomers in the ratio of 2 to 1. A colorless oil: IR (neat) 3075, 2925, 1640 cm^{-1} ; 1H NMR ($CDCl_3$) δ 13.18 (s, 0.67H), 13.00 (s, 0.33H), 8.74 (br s, 1H), 8.35 (br d, $J = 9$ Hz, 1H), 7.10 (br d, $J = 9$ Hz, 1H), 5.81 (m, 1H), 4.98—5.10 (m, 2H), 3.60 (sextet, $J = 6.9$ Hz, 0.67H), 3.10 (t, $J = 7.1$ Hz, 0.67H), 2.10—2.18 (m, 2H), 2.01 (m, 0.67H), 1.81 (m, 0.33H), 1.51—1.69 (m, 1.99H), 1.28 (d, $J = 6.9$ Hz, 2.01H); FAB(+)HRMS calcd for $C_{13}H_{16}N_1O_4$ ($M^+ + H$) 250.1079, found 250.1093.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-5-trifluoromethoxybenzaldehyde (24) and 1,5-Hexadiene (2). Rh(PPh_3)₃Cl-Catalyzed hydroacylation between 2-hydroxy-5-trifluoromethylbenzaldehyde **24** and 1,5-hexadiene **2** at room temperature afforded **39a** and **39b** (73%) as a mixture of isomers in the ratio of 3 to 1. A colorless oil: IR (neat) 3080, 1640 (br), 1590, 1480 cm^{-1} ; 1H NMR ($CDCl_3$) δ 12.48 (s, 0.75H), 12.30 (s, 0.25H), 7.60 (br s, 1H), 7.40 (br d, $J = 9$ Hz, 1H), 7.01 (br d, $J = 9$ Hz, 1H), 5.80 (m, 1H), 4.96—5.08 (m, 2H), 3.45 (sextet, $J = 6.9$ Hz, 0.75H), 2.98 (t, $J = 7.3$ Hz, 0.50H), 2.10 (m, 2H), 1.51—2.00 (m, 2.50H), 1.24 (d, $J = 6.9$ Hz, 2.25H); FAB(+)HRMS calcd for $C_{14}H_{16}F_3O_3$ ($M^+ + H$) 289.1051, found 289.1057.

Rh-Catalyzed Intermolecular Hydroacylation between 2,3-Dihydroxybenzaldehyde (25) and 1,5-Hexadiene (2). Rh(PPh_3)₃Cl-Catalyzed hydroacylation between 2,3-dihydroxybenzaldehyde **25** and 1,5-hexadiene **2** at room temperature afforded **40a** and **40b** (58%) as a mixture of isomers in the ratio of 3 to 1. A colorless oil: IR (neat) 3477 (br), 3070, 2976, 1636 cm^{-1} ; 1H NMR ($CDCl_3$) δ 12.50—12.90 (br, 1H), 7.31 (br d, $J = 9$ Hz, 1H), 7.12 (br d, $J = 9$ Hz, 1H), 6.81 (br t, $J = 9$ Hz, 1H), 5.90 (br s, 1H), 5.75 (m, 1H), 4.95—5.06 (m, 2H), 3.42 (sextet, $J = 6.9$ Hz, 0.75 H), 2.99 (t, $J = 7.3$ Hz, 0.50H), 2.10 (m, 2H), 1.95 (m, 0.75H), 1.75 (quintet, $J = 7.3$ Hz, 0.50H), 1.40—1.60 (m, 1.25H), 1.23 (d, $J = 6.9$ Hz, 2.25H); FAB(+)HRMS calcd for $C_{13}H_{17}O_3$ ($M^+ + H$) 221.1178, found 221.1167.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-3-methoxybenzaldehyde (26) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2-hydroxy-3-methoxybenzaldehyde **26** and 1,5-hexadiene **2** at room temperature afforded **41a** and **41b** (quant.) as a mixture of isomers in the ratio of 3.5 to 1. A colorless oil: IR (neat) 3100, 1640, 1600 cm^{−1}; ¹H NMR (CDCl₃) δ 12.91 (s, 0.78H), 12.71 (s, 0.22H), 7.38 (br d, *J* = 9 Hz, 1H), 7.06 (br d, *J* = 9 Hz, 1H), 6.85 (br t, *J* = 9 Hz, 1H), 5.80 (m, 1H), 4.96—5.03 (m, 2H), 3.91 (s, 3H), 3.54 (sestet, *J* = 6.9 Hz, 0.78H), 3.00 (t, *J* = 7.4 Hz, 0.44H), 2.10 (m, 2H), 1.49—2.05 (m, 2.44H), 1.23 (d, *J* = 6.9 Hz, 2.34H); FAB(+)HRMS calcd for C₁₄H₁₉O₃ (M⁺+H) 235.1334, found 235.1313.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-3-methylbenzaldehyde (27) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2-hydroxy-3-methylbenzaldehyde **27** and 1,5-hexadiene **2** at room temperature afforded **42a** and **42b** (71%) as a mixture of isomers in the ratio of 4.5 to 1. A colorless oil: IR (neat) 3077, 1633 cm^{−1}; ¹H NMR (CDCl₃) δ 12.89 (s, 0.82H), 12.69 (s, 0.18H), 7.63 (br d, *J* = 9 Hz, 1H), 7.33 (br d, *J* = 9 Hz, 1H), 6.80 (br t, *J* = 9 Hz, 1H), 5.79 (m, 1H), 4.96—5.03 (m, 2H), 3.56 (sestet, *J* = 6.9 Hz, 0.82H), 2.99 (t, *J* = 7.4 Hz, 0.36H), 2.26 (s, 3H), 1.49—2.13 (m, 4.36H), 1.22 (d, *J* = 6.9 Hz, 2.46H); FAB(+)HRMS calcd for C₁₄H₁₉O₂ (M⁺+H) 219.1385, found 219.1362.

Rh-Catalyzed Intermolecular Hydroacylation between 2,4-Dihydroxybenzaldehyde (28) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2,4-dihydroxybenzaldehyde **28** and 1,5-hexadiene **2** at room temperature afforded **43a** and **43b** (75%) as a mixture of isomers in the ratio of 4 to 1. A colorless oil: IR (neat) 3335 (br), 3070, 2974, 1632 cm^{−1}; ¹H NMR (CDCl₃) δ 13.16 (s, 0.8H), 12.91 (s, 0.2H), 7.68 (br d, *J* = 9 Hz, 1H), 6.90 (br, 1H), 6.39—6.44 (m, 2H), 5.79 (m, 1H), 4.94—5.05 (m, 2H), 3.44 (sestet, *J* = 6.9 Hz, 0.8H), 2.90 (t, *J* = 7.3 Hz, 0.4H), 2.09 (m, 2H), 1.92 (m, 0.8H), 1.75 (quintet, *J* = 7.3 Hz, 0.4H), 1.40—1.65 (m, 1.2H), 1.21 (d, *J* = 6.9 Hz, 2.4H); FAB(+)HRMS calcd for C₁₃H₁₇O₃ (M⁺+H) 221.1178, found 221.1174.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-4-methoxybenzaldehyde (29) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2-hydroxy-4-methoxybenzaldehyde **29** and 1,5-hexadiene **2** at room temperature afforded **44a** and **44b** (quant.) as a mixture of isomers in the ratio of 2 to 1. A colorless oil: IR (neat) 3077, 2973, 2936, 1630 cm⁻¹; ¹H NMR (CDCl₃) δ 13.10 (s, 0.67H), 12.88 (s, 0.33H), 7.68 (m, 1H), 6.42—6.46 (m, 2H), 5.80 (m, 1H), 4.94—5.07 (m, 2H), 3.84 (s, 3H), 3.44 (sextet, *J* = 6.9 Hz, 0.67H), 2.90 (t, *J* = 7.2 Hz, 0.66 H), 1.96—2.15 (m, 2H), 1.90 (m, 0.67H), 1.74 (quintet, *J* = 7.1 Hz, 0.66H), 1.43—1.61 (m, 1.33H), 1.21 (d, *J* = 6.9 Hz, 2.01H); FAB(+)HRMS calcd for C₁₄H₁₉O₃ (M⁺+H) 235.1334, found 235.1319.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-1-naphthaldehyde (30) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2-hydroxy-1-naphthaldehyde **30** and 1,5-hexadiene **2** at room temperature afforded **45a** and **45b** (56%) as a mixture of isomers in the ratio of 2 to 1. A colorless oil: IR (neat) 3350 (br), 3075, 1670, 1620 cm⁻¹; ¹H NMR (CDCl₃) δ 12.98 (s, 0.33H), 12.00 (s, 0.67H), 7.77—8.06 (m, 3H), 7.56 (m, 1H), 7.41 (m, 1H), 7.16 (br d, *J* = 9 Hz, 1H), 5.75 (m, 1H), 4.74—5.05 (m, 2H), 3.72 (sextet, *J* = 6.9 Hz, 0.67H), 3.18 (t, *J* = 7.3 Hz, 0.66H), 1.35 (d, *J* = 6.9 Hz, 2.01H), 1.44—2.20 (m, 4.66H); FABMS *m/z* 255.0 (M⁺+H), 254.0 (M⁺).

Rh-Catalyzed Intermolecular Hydroacylation between 1-Hydroxy-2-naphthaldehyde (31) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 1-hydroxy-2-naphthaldehyde **31** and 1,5-hexadiene **2** at room temperature afforded **46a** and **46b** (82%) as a mixture of isomers in the ratio of 2 to 1. A colorless oil: IR (neat) 3061, 1625 cm⁻¹; ¹H NMR (CDCl₃) δ 14.39 (s, 0.7H), 14.14 (s, 0.3H), 8.49—8.44 (m, 1H), 7.78—7.50 (m, 4H), 7.29—7.25 (m, 1H), 5.91—5.74 (m, 1H), 5.0—4.95 (m, 2H), 3.64—3.57 (m, 0.7H), 3.07 (t, *J* = 7.3 Hz, 0.6H), 2.18—1.51 (m, 4.6H), 1.28 (d, *J* = 6.9 Hz, 2.1H); FAB(+)HRMS calcd for C₁₇H₁₉O₂ (M⁺+H) 255.1385, found 255.1362.

Rh-Catalyzed Intermolecular Hydroacylation between 2-Hydroxy-5-methylbenzene-1,3-dicarbaldehyde (32) and 1,5-Hexadiene (2). Rh(PPh₃)₃Cl-Catalyzed hydroacylation between 2-hydroxy-5-methylbenzene-1,3-dicarbaldehyde **32** and 1,5-hexadiene **2** at room temperature afforded **47a** and **47b** (64%) as a mixture of isomers in the ratio of 3 to 1, accompanied with bis-hydroacylated

products in 21% yield. **Monohydroacylated products (47a) and (47b).** A colorless oil: IR (neat) 3075, 3020, 2977, 2935, 1687, 1640 cm^{-1} ; ^1H NMR (CDCl_3) δ 12.94 (s, 0.75H), 12.78 (s, 0.25H), 10.45 (s, 1H), 7.82 (m, 2H), 5.79 (m, 1H), 4.97—5.08 (m, 2H), 3.55 (sextet, $J = 6.9$ Hz, 0.75H), 3.03 (t, $J = 7.3$ Hz, 0.50H), 2.36 (s, 3H), 2.02—2.15 (m, 2H), 1.96 (m, 0.75), 1.78 (quintet, $J = 7.3$ Hz, 0.50H), 1.51—1.65 (m, 1.25H), 1.25 (d, $J = 6.9$ Hz, 2.25H); FAB(+)HRMS calcd for $\text{C}_{15}\text{H}_{19}\text{O}_3$ (M^++H) 247.1334, found 247.1327.

Bishydroacylated products. A colorless oil: IR (neat) 3075, 3019, 2933, 1673, 1638, 1216 cm^{-1} ; ^1H NMR (CDCl_3) δ 13.30, 13.29, 13.26, 12.94 (s, total 1H), 7.69—7.83 (m, 2H), 5.81 (m, 2H), 4.94—5.07 (m, 4H), 3.60 (m, 1.3H), 3.05 (t, $J = 7.3$ Hz, 1.4H), 2.36, 2.34 (s, total 3H), 2.05—2.15 (m, 4H), 1.43—2.05 (m, 5.4H), 1.19—1.26 (m, 3.9H); FAB(+)HRMS calcd for $\text{C}_{21}\text{H}_{29}\text{O}_3$ (M^++H) 329.2117, found 329.2132.

Ref.

- 1) M. Robert, B. Jean Marie, *Chim. Anal. (Paris)*, **50** (9), 464-82 (1968).

DT-110

MS-2-A

DEPT135

COM

MS-2-A

MS-2-B

DEPT135

COM

MS-2-B

KT1-8

DDT-90

- 111-MIX

MI-604

MI-522

C:\WINNMR98\DATA\YAKKA\Imai\hydroacylation-1.5-hepta.als
Hydroacylation-1.5-hepta

MI-419-A

MI-419-A'

MI-419-C'

MI-419-B'

K1-84-2.h1

Pulse Sequence: s2pu1
DATE Nov 2 2002
SOLVENT cdcl3
OBSERVE H1
FREQUENCY 399.861 MHz
SPECTRAL WIDTH 6134.0 Hz
ACQUISITION TIME 2.671 sec
RELAXATION DELAY 2.329 sec
PULSE WIDTH 6.0 usec
TEMPERATURE 29.0 deg. C.
NO. REPEATITIONS 4
DOUBLE PRECISION ACQUISITION
DATA PROCESSING
RESOLUTION ENHANCEMENT -0.0 Hz
F1 SIZE 65536
TOTAL ACQUISITION TIME 1 minutes

DDT173

MI-613

MS-144

MI-421

MI-612

MS-113

NO-7

MS-14

MI-537-B

MI-537-A

Bis hydroacylated
products

5.0

10a-d

MS-143-A,h1
exp8 s2pul

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solvent	CDC13	dn	H1
file	exp	dpr	35
ACQUISITION		dof	0
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tn	H1	dmm	c
at	4.371	dmf	200
np	87424	dseq	
sw	10000.0	dres	1.0
fb	5600	homo	n
bs	4	temp	30.0
as	4	PROCESSING	
tpwr	60	wfille	
pw	4.1	proc	1p
dl	3.630	fn	65536
tof	653.5	match	f
nt	16		
ct	16	werr	
alock	n	wexp	
gain	32	wbs	
FLAGS		wit	wfc
ll	n		
ln	n		
dp	y		
hs	nm		
DISPLAY			
sp	150.2		
wp	7147.4		
vs	201		
ac	0		
wc	250		
hzmm	28.59		
ls	1246.83		
rfl	1861.9		
rfl	0		
th	7		
lms	140.000		
nm	cdc ph		

13 12 11 10 9 8 7 6 5 4 3 2 1 ppm

CC(=O)c1ccccc1C(=O)C(C)CC=C

round

SAMPLE		DEC. & VT	
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solvent	CDCl3	dn	H1
file	exp	dpr	35
ACQUISITION			
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tn	H1	dof	nmn
at	4.371	dmf	c
np	87424	dreq	200
sw	10000.0	dres	1.0
fb	5600	homo	n
bs	4	temp	30.0
ss	4	PROCESSING	
tpwr	60	wfile	ip
pw	4.1	proc	65536
dl	3.629	fn	f
tof	607.2	math	
nt	32	weir	
ct	32	weap	
alook	n	whs	wft
gain	46	wnt	
FLAGS			
ll	n		
ln	n		
dp	y		
hs	nm		
DISPLAY			
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wp	7147.4		
vs	549		
sc	0		
wm	250		
hzmm	28.59		
is	1696.10		
rfl	1907.4		
rfd	0		
ch	7		
ins	100.000		
nm	cde	ph