Bis(oxazolinyl)phenylrhodium(III) Aqua Complex: Efficiency in Enantioselective Addition of Methallyltributyltin to Aldehydes under Aerobic Conditions

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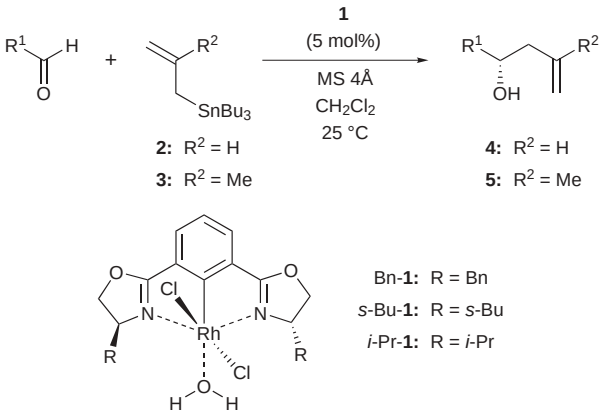
Abstract: A simple and general protocol is described for the enantioselective addition of methallyltributyltin to aldehydes catalyzed by chiral (Phebox)$RhCl_2(H_2O)$ complexes **1** [Phebox = 2,6-bis(oxazolinyl)phenyl]. The reaction can be performed even under aerobic conditions to afford the corresponding optically active homoallylic alcohols in good yields with high enantioselectivities (90–99% ee).

Key words: aerobic conditions, allylation, asymmetric catalysis, rhodium, pincer complex

Ever since Shaw reported the transition metal complexes bearing P–C–P type pincer ligands in 1976,[2a] a variety of pincer-based complexes have been extensively studied in terms of not only structural characterization and bonding properties but also active catalysts in organic synthesis.[2] It is well known that the characteristic features of these pincer complexes are high degrees of both air- and thermal stability.

Previously, we have reported chiral rhodium(III) aqua complexes **1**[3] bearing Phebox as an N-C-N pincer ligand [Phebox = bis(oxazolinyl)phenyl]. We also found that these aqua complexes **1** acted as novel transition-metal Lewis acid catalysts for the enantioselective addition of allyltributyltin to aldehydes[3b,c] in the presence of dry 4 Å molecular sieves (MS 4A) under standard conditions such as in anhyd CH_2Cl_2 under an argon atmosphere.[4] Although the enantioselectivities of the obtained allylated products were moderate (43–80% ee), these catalysts **1** proved to be air-stable, water-tolerant, and recoverable chiral transition-metal complexes. Since we expect that this catalytic system will see wide application for the above characteristic features, we have been conducting studies to facilitate the operation employed in such reactions as much as possible. Most of the asymmetric reactions using Lewis acid catalysts are performed under strictly anhyd conditions to prevent the decomposition of the moisture-sensitive catalysts.[5] However, we found that the present Phebox-Rh(III) complexes **1** catalyze the reaction, even in CH_2Cl_2 without distillation and under aerobic conditions, to afford the methallyl addition products with excellent enantioselectivities. Here we report the simple procedure for the Rh-catalyzed enantioselective methallyl addition to aldehydes, without the need for anhyd conditions (Scheme 1).



Scheme 1

The non-dehydrated procedure for the reaction of benzaldehyde and allyltributyltin **2** was examined using 5 mol% of *i*-Pr-Phebox-derived complex *i*-Pr-**1** in non-distilled CH_2Cl_2 in the presence of commercial, non-dried MS 4A under aerobic conditions at 25 °C. The first, and obvious, point to notice is that the reaction by this procedure gives the allylated product **4** without loss of both the chemical yield and enantioselectivity (Table 1, entries 1 vs 2). This method is not necessitated by special techniques and apparatus, therefore, anyone can perform the reaction easily. We next examined the methallylation reaction under the same conditions. Although the reactivity of the methallyltributyltin **3** was relatively lower than that of the parent allyltributyltin **2**, extension of the reaction time from 7 hours to 12 hours led to satisfactory yield. Compared with the allylation reaction catalyzed by **1**, enantioselectivity of the methallylated product **5a** increased remarkably to 93% ee (entry 3). The best substituent on the Phebox ligand in terms of the enantioselectivity in the methallyl addition reaction proved to be the *i*-Pr group (entries 3–5).

Table 2 summarizes the results obtained for the methallylation reaction of a variety of aldehydes with 5 mol% of *i*-Pr-**1** in CH_2Cl_2 solution at 25 °C under aerobic conditions.[6] All reactions resulted in high yields (90–97%) with both aromatic and aliphatic aldehydes for 12 h, except in the case of *p*-chlorobenzaldehyde. Reactivity of the *p*-chlorobenzaldehyde was lower than those of the other aldehydes, however, the chemical yield of **5b**

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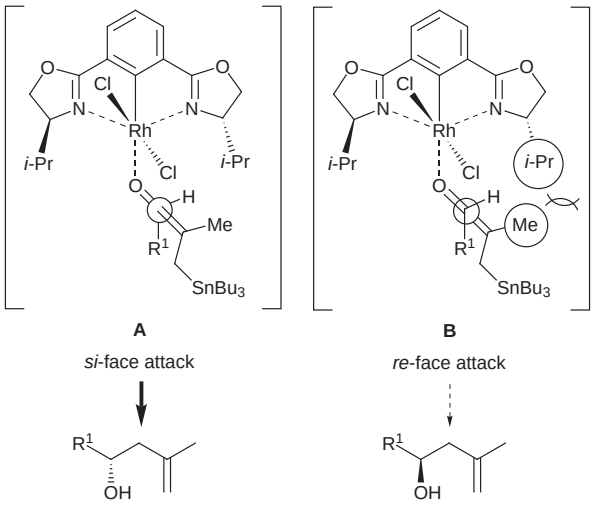
Table 1 Enantioselective Addition of Allyl- and Methallyltributyltins (**2**,**3**) to Benzaldehyde Catalyzed by (Phebox)$RhCl_2(H_2O)$ Complexes **1**[a]

Entry	Complex	Allyltin/ product	Time	Yield (%)	ee (%)[b]
1[c]	*i*-Pr-**1**	**2/4**	7 h	88	51
2	*i*-Pr-**1**	**2/4**	7 h	85	50
3	*i*-Pr-**1**	**3/5a**	12 h	95	93
4	*s*-Bu-**1**	**3/5a**	12 h	94	92
5	Bn-**1**	**3/5a**	12 h	99	91

[a] All reactions were carried out using 0.25 mmol of benzaldehyde, 0.375 mmol (1.5 equiv) of allyltins (**2** or **3**), and 0.0125 mmol (5 mol%) of **1** in the presence of MS 4 Å (125 mg) in CH_2Cl_2 (1 mL) at 25 °C.
[b] Determined by chiral HPLC analysis (Daicel CHIRALCEL OD-H).
[c] Previous result under dehydrated conditions.

reached to 82% by prolongation of the reaction time to 24 h (entry 2). The enantioselectivities in all reactions were achieved over 90% ee for such standard aldehydes. Especially, the ee of the (*E*)-cinnamaldehyde-derived product **5f** recorded a value of 99% (entry 6). In all of the cases, methallyltributyltin **3** attacks the *si* face of the aldehyde's C=O planes,[7] it is the same π-face selectivity as in the case of allyltributyltin **2**.[3b,c]

The reason why the methallylated products **5** show much higher enantioselectivities than the allylated ones is explained by the antiperiplanar transition states (Scheme 2, **A** and **B**), which have been proposed previously.[3b,c] When the allyltins **2** and **3** approach the carbonyl *re*-face through the antiperiplanar **B**, which gives the opposite enantiomer, the steric repulsion occurs between one *i*-Pr group on the oxazoline rings and the substituent at the β-position of allyltins (H for **2**, and Me for **3**). The steric bulkiness of Me group is expected to be more important than that of H, therefore, enantioselectivities of the methallylated products might increase remarkably.



Scheme 2

Table 2 Enantioselective Addition of Methallyltributyltin **3** to Various Aldehydes Catalyzed by (*i*-Pr-Phebox)$RhCl_2(H_2O)$ Complex *i*-Pr-**1**[a]

Entry	Aldehyde	Product	Yield (%)	ee (%)[b]	Config.[c]
1	PhCHO	**5a**	95	93	(–)-*S*
2[d]	4-ClC_6H_4CHO	**5b**	82	90	(–)-*S*
3	4-$MeOC_6H_4CHO$	**5c**	97	94	(–)-*S*
4	2-furyl-CHO	**5d**	95	92	(–)-*S*
5	$PhCH_2CH_2CHO$	**5e**	92	91	(+)-*R*
6	(*E*)-PhCH=CHCHO	**5f**	90	99	(–)-*S*
7	(*E*)-*n*-PrCH=CHCHO	**5g**	95	94[e]	(–)-*S*

[a] All reactions were carried out using 0.25 mmol of aldehyde, 0.325 mmol (1.5 equiv) of methallyltributyltin **3** and 0.0125 mmol (5 mol%) of chiral catalyst *i*-Pr-**1** in 1 mL of CH_2Cl_2 in the presence of 4 Å molecular sieves (125 mg) at 25 °C for 12 h.
[b] Determined by chiral HPLC analysis.
[c] Assignment by comparison of the sign of optically rotation with reported value.
[d] 24 h.
[e] Determined after converting to the benzoate.

The main features of the present catalytic system are as follows: 1) there is no need to use anhyd solvent and dry MS 4 Å, and inert atmospheres; 2) the procedure is straightforward because the reaction can be performed by simply mixing substrates and the catalyst *i*-Pr-**1** at room temperature (low reaction temperatures are not required); 3) chiral Lewis acid *i*-Pr-**1** can be easily recovered[9] in high yield by column chromatography; 4) various optically active homoallylic alcohols can be provided with high enantioselectivity (up to 99% ee), and the absolute stereochemistry of the methallylated products can also be predicted. Hence, this simple procedure should be broadly applicable in asymmetric organic synthesis.[10]

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(4) In the presence of MS 4 Å, this catalytic reaction was slightly accelerated but the enantioselectivity was not changed, see ref.[3b]

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(6) **General Procedure for the Catalytic Enantioselective Addition of Methallyltributyltin 3 to Aldehydes Catalyzed by *i*-Pr-1.** To a suspension of MS 4A (125 mg) in CH_2Cl_2 (1 mL) were added (*i*-Pr-Phebox)$RhCl_2(H_2O)$ complex *i*-Pr-**1** (6.1 mg, 0.0125 mmol, 5 mol%), aldehyde (0.25 mmol) and methallyltributyltin (0.375 mmol, 1.5 equiv) at 25 °C. After stirring the reaction mixture for 12 h at that temperature, the reaction mixture was concentrated under reduced pressure. The residue was dissolved 5 mL of Et_2O, and this solution was treated with a mixture of 1 N HCl (5 mL) and solid KF (ca. 0.5 g) at r.t. for 30 min. The resultant precipitate was filtered off, the filtrate was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by silica gel chromatography (hexane–Et_2O = 3:1, then EtOAc as eluent for recovering *i*-Pr-**1**) gave homoallylic alcohol, the enantioselectivity was determined by chiral HPLC analysis. **5a:** Daicel CHIRALCEL OD-H, UV Detector 254 nm, hexane–*i*-PrOH = 20:1, flow rate 0.5 mL/min. t_R = 13.1 min (*S*), 14.6 min (*R*); **5b:** Daicel CHIRALCEL OJ, UV Detector 254 nm, hexane–*i*-PrOH = 30:1, flow rate 0.5 mL/min. t_R = 16.9 min (*S*), 19.1 min (*R*); **5c:** Daicel CHIRALCEL OD-H, UV Detector 230 nm, hexane–*i*-PrOH = 30:1, flow rate 0.5 mL/min. t_R = 20.9 min (*R*), 22.9 min (*S*); **5d:** Daicel CHIRALCEL OD-H, UV Detector 230 nm, hexane–*i*-PrOH = 40:1, flow rate 0.5 mL/min. t_R = 18.1 min (*S*), 19.1 min (*R*); **5e:** Daicel CHIRALCEL OD-H, UV Detector 254 nm, hexane–*i*-PrOH = 20:1, flow rate 0.5 mL/min. t_R = 13.5 min (*S*), 19.2 min (*R*); **5f:** Daicel CHIRALCEL OD-H, UV Detector 254 nm, hexane–*i*-PrOH = 20:1, flow rate 1.0 mL/min. t_R = 10.9 min (*R*), 20.8 min (*S*); **5g:** The %ee was determined after converting to the benzoate ester. Daicel CHIRALPAK AD, UV Detector 254 nm, hexane–*i*-PrOH = 200:1, flow rate 0.5 mL/min. t_R = 9.4 min (*R*), 11.2 min (*S*).

(7) **5a:** $[\alpha]_D^{23}$ –48.7 (*c* 0.63, Et_2O); lit.[8a] $[\alpha]_D^{20}$ –19.70° (*c* 9.90, Et_2O) for 40% ee (*S*); **5b:** $[\alpha]_D^{22}$ –44.5 (*c* 0.77, benzene); lit.[8b] $[\alpha]_D^{21}$ –40.4° (*c* 3.15, benzene) for 88% ee (*S*); **5c:** $[\alpha]_D^{23}$ –67.9 (*c* 0.99, $CHCl_3$); **5d:** $[\alpha]_D^{21}$ –49.2° (*c* 0.61, $CHCl_3$); **5e:** $[\alpha]_D^{22}$ +15.8° (*c* 0.85, $CHCl_3$); lit.[8b] $[\alpha]_D^{23}$ +16.6 (*c* 2.66, $CHCl_3$) for 67% ee (*R*); **5f:** $[\alpha]_D^{22}$ –19.4 (*c* 0.26, benzene); lit.[8c] $[\alpha]_D$ +19.0 (*c* 1.44, benzene) for 84% ee (*R*); **5g:** $[\alpha]_D^{20}$ –3.30 (c 0.79, benzene); lit.[8c] $[\alpha]_D$ +4.04 (*c* 1.93, benzene) for 77% ee (*R*).

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