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Asymmetric Hydroformylation with Highly Crosslinked Polystyrene-Supported (*R,S*)-BINAPHOS–Rh(I) Complexes: The Effect of Immobilization Position

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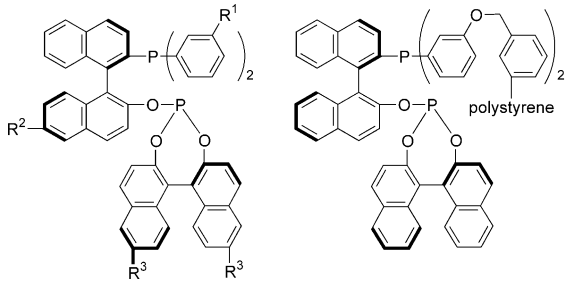
Abstract—A new class of polymer-supported (*R,S*)-BINAPHOS **1e** in which the parent BINAPHOS has two alkoxy-substituents at the 3-positions of the phenyls, has been synthesised. Using its Rh(I) complex, asymmetric hydroformylation of olefins proceeded with higher enantioselectivity in some cases compared to the conventional polymer-supported **1c**.

Asymmetric hydroformylation of olefins serves as a direct route to optically active aldehydes which are valuable precursors for various pharmaceuticals and agrochemicals.[1] Previously, we developed a chiral phosphinephosphite ligand (*R,S*)-BINAPHOS (**1a**) and demonstrated its Rh(I) complex as the first example of a truly efficient catalyst for asymmetric hydroformylation of various olefins.[2] Recently, Leitner[3] and we[4] found that introduction of a substituent on each of the two phenyls at their 3-positions (e.g., methoxy-substituted **1b**) significantly improved the catalytic activity and regio- and enantio-selectivities of asymmetric hydroformylation.

Immobilization of homogeneous chiral catalysts onto insoluble support is one of the current trends in organic synthesis due to the easy separation and recycling of the catalyst.[5] In 1998, we immobilized Rh(I)-(*R,S*)-BINAPHOS onto a highly crosslinked polystyrene support at the 6-position of one of the naphthalenes (**1c**), without reducing the excellent performance of the catalyst.[6] One of the unique features of this immobilization is the extremely high content of divinylbenzene (over 50 mol%) to prepare polystyrene, whose pore size and surface area were precisely studied by Gagné, recently.[7]

Here, we report the synthesis of a new class of polymer-supported (*R,S*)-BINAPHOS **1e** in which the parent BINAPHOS has two alkoxy-substituents at the 3-positions of the phenyls, as was so for the homogeneous ligand **1b** (Fig. 1). Using a Rh(I) complex of **1e**, asymmetric hydroformylation of styrene, vinyl acetate, and (*Z*)-2-butene were examined.

Synthesis of **1e** was accomplished in several steps starting from the methoxy-substituted phosphine oxide **2**[4]



1a: R^1~R^3 = H [=(*R,S*)-BINAPHOS]
b: R^1 = OCH_3, R^2, R^3 = H
c: R^1 = R^3 = H, R^2 = polystyrene
d: R^1 = H, R^2 = R^3 = polystyrene

1e

Figure 1. Chiral phosphinephoshite ligand (*R,S*)-BINAPHOS (**1a**) and its derivatives.

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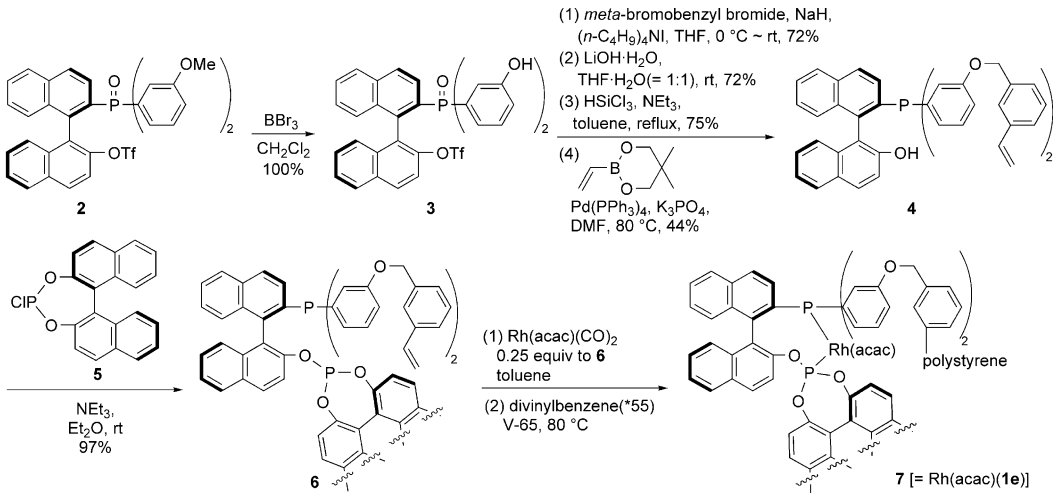
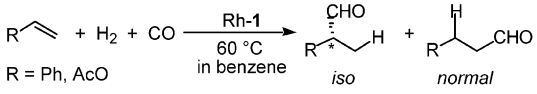


Scheme 1. Synthesis of a new polystyrene-supported Rh(I)–(*R,S*)-BINAPHOS complex **7** [= Rh(acac)(**1e**)].

(Scheme 1). After cleavage of the methoxy ethers, the two hydroxyl groups of **3** were alkylated with *meta*-bromobenzyl bromide followed by hydrolysis of the triflate and reduction of the phosphine oxide. Two vinyl groups were introduced via Suzuki–Miyaura coupling. The phosphine part **4** thus obtained was coupled with chlorophosphite **5** to afford divinyl-(*R,S*)-BINAPHOS **6**.

For the preparation of polystyrene-supported Rh complex from **6**, two approaches are available: (i) copolymerization of ligand **6** with styrene/divinylbenzene first and then Rh-complex formation with the resulting polymeric ligand, and (ii) Rh-complex formation with ligand **6** first and then copolymerization of the resulting Rh-**6** complex with styrene/divinylbenzene. In this work, the latter method, complexation-then-polymerization, was employed due to the following reason. Previously, we compared the two methods with two BINAPHOS derivatives **1c** and **1d**.[8] No difference in catalytic performance was observed between the two methods with ligand **1c** which is immobilized at a single point. On the other hand, three-point attached **1d** showed significant loss of %ee when the polymerization-then-complexation method was employed. The difference between **1c** and **1d** was attributed to the flexibility of the ligand conformation. Apparently, the multipoint-attached **1d** has less flexibility, and by the polymerization-then-complexation method, the fixed ligand conformation was not always suitable for the Rh-coordination. In the complexation-then-polymerization method, however, Rh atom seems to have behaved as a template to order the ligand conformation which fits to the Rh-coordination. Considering its multipoint-attachment nature, ligand **6** was first mixed with $Rh(acac)(CO)_2$ in toluene to form complex Rh(acac)(**6**) and then copolymerized with divinylbenzene (55% content, the rest is ethylstyrene) initiated by V-65 (= azobis(2,4-dimethylvaleronitrile)) to form **7** [= Rh(acac)(**1e**)].

The polymer supported catalyst **7** was subjected to asymmetric hydroformylation of styrene under hydrogen and carbon monoxide (total pressure of 20 atm, H_2/CO = 1/1) at 60 °C [Eq. (1)]. The reaction was carried out in benzene and the polymer-supported catalyst **7** was scattered in the solution by stirring. The result is compared with the ones having homogeneous parent ligand **1a**, methoxy-substituted **1b**, and the previous polymer-supported **1c** (Table 1). With **1e**, the corresponding aldehydes were obtained with 85% *iso*-selectivity and in 92% ee (entry 1). The values are comparable to the data with homogeneous **1a** (entry 2), slightly higher than supported **1c** (entry 3), and a little lower than that with methoxy-substituted homogeneous **1b** (entry 4). On the other hand, the use of **1e** diminished the % ee in hydroformylation of vinyl acetate (compare entry 4 with 5 and 6).



(1)

Unlike most of the asymmetric hydrogenation, hydroformylation with Rh-**1a** does not require the use of polar solvents. Taking advantage of this point, we

Table 1. Asymmetric hydroformylation of styrene and vinylacetate catalyzed by Rh(I)–(*R,S*)-BINAPHOS complexes

Entry	Olefin R =	Ligand	S/C	Conv (%)	*i*/*n*	% ee of *iso*-
1[a]	Ph	**1e**	2000	>99	85/15	92
2[a,d]		**1a**	2000	>99	89/11	92
3[a,e]		**1b**	2000	>99	93/7	95
3[a,d]		**1c**	2000	>99	85/15	90
4[b]	AcO	**1e**	500	87	84/16	86
5[c,d]		**1a**	500	98	84/16	92
6[c,d]		**1c**	500	67	87/13	92

[a] H_2/CO = 10 atm/10 atm, 12 ~ 13 h.
[b] H_2/CO = 40 atm/40 atm, 25 h.
[c] H_2/CO = 50 atm/50 atm, 42 h.
[d] Ref 6.
[e] Ref 4.

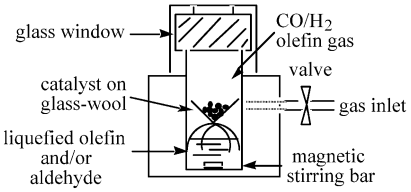


Figure 2. Vapor-phase asymmetric hydroformylation apparatus.

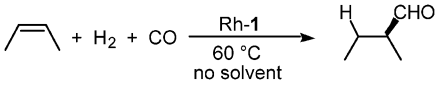
Table 2. Asymmetric hydroformylation of (*Z*)-2-butene catalyzed by Rh(I)–(*R,S*)-BINAPHOS complexes in several systems[c,d]

Entry	System	Ligand	TOF (h^{-1})	ee (%)
1[a]	Dispersion (**A**)	**1e**	14	82
2[b]		**1c**	24	80
3	Homogeneous	**1b**	7.6	90
4		**1a**	23	82
5[a]	Fixed bed (**B**)	**1e**	18	81
6[b]		**1c**	27	80

[a]$H_2/CO = 1/1$; 40 atm, 3 h.
[b]$H_2/CO = 1/1$; 32 atm, 4 h.
[c]$H_2/CO = 1/1$; 32 atm, 9 h.
[d]$H_2/CO = 1/1$; 32 atm, 8 h.

reported the vapor–solid two-phase asymmetric hydroformylation.[8] Using a fixed bed, substrates with high vapor pressure were successfully converted to the corresponding aldehydes with high % ee's (Fig. 2).

Asymmetric hydroformylation of (*Z*)-2-butene was also examined with the new ligand **1e** both with the dispersion in benzene solution (A) and with the fixed bed system (B) (Table 2). As shown, the enantioselectivities with **1e** (entries 1 and 5) were higher that that with **1c** (entries 2 and 6), but the difference is almost negligible compared to the significant improvement with **1b** (entry 3) from **1a** (entry 4). With **1e**, the turnover frequencies were slightly lower than those with **1c**.



(2)

In conclusion, we have demonstrated that immobilization of Rh-(*R,S*)-BINAPHOS is also possible at the phosphine phenyls. Although the active Rh-center in **1e** is located closer to the polymer backbone compared to **1c**, the loss in catalytic activity was less significant and enantioselectivities were improved in some cases. However, the effect of 3-alkoxy-substituent in **1e** was not always as remarkable as homogeneous ligand **1b**.

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