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Immobilization of Heterobimetallic Multifunctional Asymmetric Catalyst

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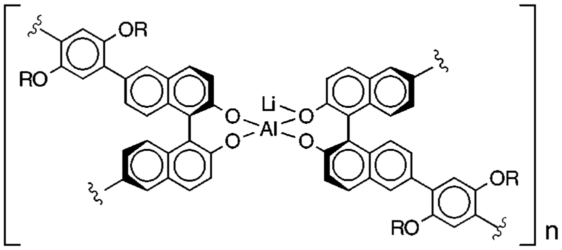
ABSTRACT



Immobilization of an asymmetric AlLibis(binaphthoxide) catalyst (ALB) is described. The immobilized ALBs (poly-ALBs) are readily prepared from polymeric BINOL derivatives and $LiAlH_4$. The combined use of 9 mol % of BuLi with ca. 10 mol % (as a monomeric catalyst) of 6,6′-aryl-tethered poly-ALB gave the Michael adducts with up to 93% ee. After completion of the reaction, the insoluble catalyst was recovered in air and is reusable.

Heterobimetallic multifunctional catalysts[1] have been recognized as new type of catalysts, which realize highly efficient asymmetric reactions. For example, the AlLibis(binaphthoxide) complex (ALB),[2] which consists of aluminum, lithium, and two molecules of BINOLs, enabled excellent enantioselective Michael reactions of malonates with enones in up to 99% ee (Figure 1).

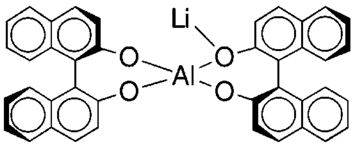


Figure 1. AlLibis(binaphthoxide) complex (ALB).

Immobilization of the heterobimetallic catalysts is fascinating for the development of an environmentally benign process in which the insoluble catalyst is reusable after filtration from the reaction mixture. The preparation of immobilized catalysts has been traditionally studied by introducing of chiral ligands to a sterically disordered polymer backbone (e.g., polystyrene). In such a system, the chiral ligands are randomly oriented along the polymer chain, making it very difficult to systematically modify the heterobimetallic catalysts on a polymer. We envisioned the use of chiral conjugated and sterically regular polymeric BINOL derivatives[3] for the efficient construction of immobilized heterobimetallic multifunctional catalysts. These polymers would have the ability to prepare polymeric catalysts where the catalytic centers are highly organized along the polymer chain. Herein, we report the first immobilization of a heterobimetallic multifunctional asymmetric catalyst using

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(1) Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1236−1256.
(2) Arai, T.; Sasai, H.; Aoe, K.; Okamura, K.; Date, T.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 104−106.
(3) (a) Hu, Q.-S.; Zheng, X.-F.; Pu, L. *J. Org. Chem.* **1996**, *61*, 5200−5201. (b) Hu, Q.-S.; Huang, W.-S.; Vitharana, D.; Zheng, X.-F.; Pu, L. *J. Am. Chem. Soc.* **1997**, *119*, 12454−12464. For reviews, see: (c) Pu, L. *Chem. Rev.* **1998**, *98*, 2405−2494. (d) Pu, L. *Chem. Eur. J.* **1999**, *5*, 2227−2232.

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conjugated polymeric BINOL derivatives. The immobilized ALB was readily recovered by simple filtration and was reusable.

In the creation of practically useful immobilized heterobimetallic multifunctional catalysts, $LiAlH_4$ was reacted with polymeric BINOL (**1a**),[3a] which was directly conjugated at the 6,6′-position of the BINOLs (Figure 2, top). When $LiAlH_4$ powder was added to a THF solution of **1a**, spontaneous formation of an insoluble complex was observed, with associated hydrogen gas generation.

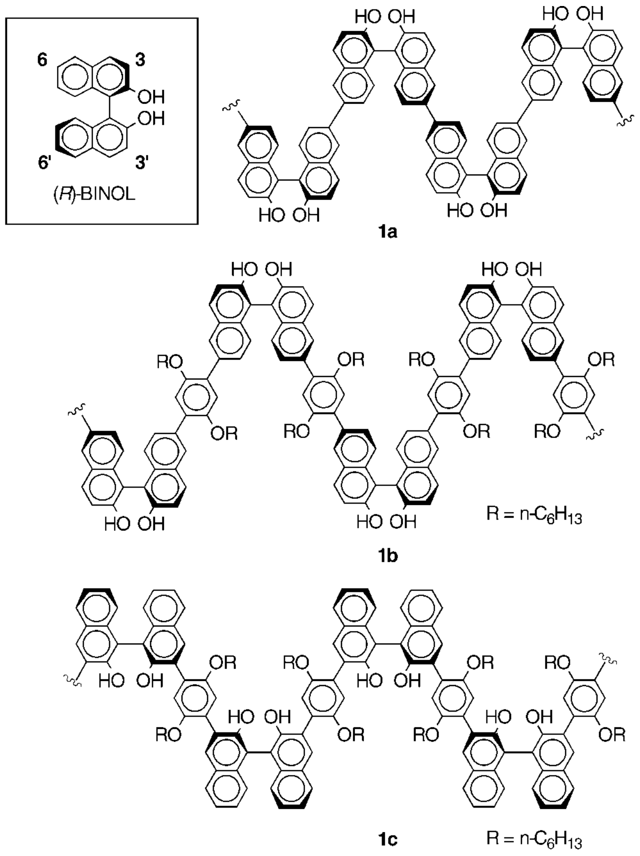
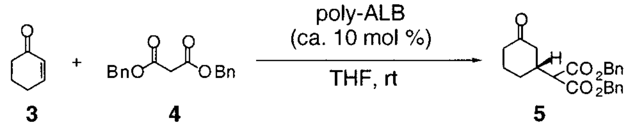


Figure 2. Polymeric BINOL derivatives.

$$\text{Polymeric BINOL derivatives } \mathbf{1a\text{-}c} \xrightarrow{LiAlH_4} \text{Poly-ALB complexes } \mathbf{2a\text{-}c}$$

The resulting insoluble polymeric ALB catalyst (poly-ALB) **2a** was revealed to have moderate catalytic activity in the asymmetric Michael reaction of 2-cyclohexenone (**3**) with dibenzyl malonate (**4**) and produced the target Michael adduct (**5**) in 32% yield with 55% ee (Table 1, entry 1). The reaction of a 6,6′-aryl-tethered polymeric BINOL derivative (**1b**)[3b] with $LiAlH_4$ was also found to form an insoluble complex (**2b**) smoothly.[4,5] The insoluble catalyst **2b** improved the enantiomeric excess of **5** to give values up to 85% ee. This significant improvement may be attributed to the flexibility of **2b**, which should reduce the constraint on the catalyst formation. The separation of the catalytic sites on the polymer chain would also allow easy access of substrates to the catalytic sites. These preliminary results prompted us to conduct further studies using the second-generation ALB (ALB-II).[6]

Table 1. Asymmetric Michael Reaction Catalyzed by Poly-ALB



3 + **4** → **5**

entry	catalyst	time (h)	yield (%)	ee (%)
1	**2a**	73	32	55
2	**2a-II**[a]	26	85	58
3	**2b**	49	69	85
4	**2b-II**[a]	48	78	93
5	**2c**	49	26	56
6	**2c-II**[a]	52	66	11

[a] The second generation of poly-ALB: 0.9 molar equiv of BuLi was added to ca. 10 mol % of the parent poly-ALBs.

We have shown that addition of an equivalent quantity of a basic reagent to the ALB catalyst dramatically enhances the catalytic activity without reducing the enantiomeric excesses of the Michael adducts. The combined use of 9 mol % of BuLi with ca. 10 mol % (as a monomeric catalyst) of poly-ALB **2b** (poly-ALB-II (**2b-II**)) showed enhancement of the catalytic activity and produced the adduct in 78% yield with up to 93% ee (Table 1, entry 4).[7] To represent other types of poly-ALBs, the polymeric BINOL derivative (**1c**),[3b] conjugated at the 3,3′-position on BINOLs, was also examined. Compared to the 6,6′-tethered polymers (**1a**, **1b**) **1c** did not produce the insoluble complex upon reaction with $LiAlH_4$. In addition, the solution phase reactions using **2c** resulted in poor catalytic activity and was limited to a low level of asymmetric induction. Starting from the 3,3′-tethered BINOL derivative, catalyst formation would be sterically disfavored. As a result, the immobilized second-generation catalyst of poly-ALB **2b** (poly-ALB-II (**2b-II**)) was revealed to be the most promising for further studies. After 48 h the

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(4) **Preparation of poly-ALB catalyst (2b):** To a stirred solution of (*R*)-6,6′-aryl-tethered binaphthol derivative **1b** (57.4 mg, 0.1 mmol as a monomer) in THF (1 mL) was added a powder of $LiAlH_4$ (1.9 mg, 0.05 mmol) at 0 °C. After being stirred for 12 h at room temperature, the resulting suspension was directly used as a poly-ALB catalyst.

(5) The influence of the ratio of $LiAlH_4$ and **1b** on the Michael reaction of **3** with **4** after 24 h at room temperature is as follows: 1:1 (67% yield, 32% ee), 1:2 (49%, 87% ee), 1:3 (19% yield, 89% ee).

(6) (a) Arai, T.; Yamada, Y. M. A.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *Chem. Eur. J.* **1996**, *2*, 1368−1372. (b) Arai, T.; Sasai, H.; Yamaguchi, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 441−442.

(7) **Preparation of poly-ALB-II catalyst (2b-II):** To a suspension of poly-ALB catalyst (**2b**) (0.05 mmol as a monomeric catalyst) in THF was added a solution of BuLi (28 μL, 0.045 mmol) in hexane at 0 °C. After being stirred for 1 h at room temperature, the resulting suspension was directly used as a poly-ALB-II catalyst.

reaction was quenched by addition of 1 N HCl. The chiral polymeric BINOL derivative (**1b**) was recovered from the evaporated mixture by precipitation with methanol. Moreover, it is noteworthy that the immobilized poly-ALB-II (**2b-II**) is directly recovered and reusable.

As shown in Table 2, the catalyst was quantitatively recovered by simple filtration, and the catalyst exhibited activity even after being used five times.[8] In general, an aluminum Lewis acid catalyst was difficult to reuse because of the highly moisture-sensitive character. In the case of poly-ALB-II (**2b-II**) catalyzed reactions, although the catalytic activity was gradually reduced after being reused several times, the addition of basic reagents restored the catalytic activity (Table 2, entry 6). These results showed that the immobilized aluminum catalyst in this study resisted deactivation by moisture.

Table 2. Reuse of Immobilized Poly-ALB-II (**2b-II**)

$$\mathbf{3} + \mathbf{4} \xrightarrow[\text{THF, rt, 48 h}]{\text{poly-ALB-II (}\mathbf{2b\text{-}II}\text{) (ca. 10 mol \%)}} \mathbf{5}$$

run	yield (%)	ee (%)	recovery of catalyst
1	78	93	quant.
2	66	89	98%
3	68	88	97%
4	56	76	95%
5	51	73	95%
6[a]	83	85	93%

[a] 5 mol % of BuLi was added to the poly-ALB-II (**2b-II**) recovered from run 5.

In conclusion, the insoluble AlLibis(binaphthoxide) complex (ALB) was constructed by reaction of chiral polymeric BINOL derivatives with $LiAlH_4$. The immobilized poly-ALB catalyst produced the Michael adducts in excellent ee, and the insoluble catalyst was readily recovered and was reusable. This is the first example of the immobilization of a heterobimetallic multifunctional catalyst.[9] The observation that the aluminum-based chiral catalyst can be recovered in air with retention of most of its catalytic activity and enantioselectivity is very remarkable. This demonstrates that the polybinaphthyl structure not only allows easy separation of the catalysts from the reaction medium but can also lead to more stable catalysts. The applications of polymeric BINOLs to the preparation of other heterogeneous catalysts are in progress.

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(8) **Experimental procedure for 2b-II catalyzed asymmetric Michael reactions:** To a stirred suspension of poly-(*R*)-ALB-II (**2b-II**) (0.05 mmol as a monomeric catalyst) in THF were added cyclohexenone (**3**) (48 μL, 0.5 mmol) and dibenzyl malonate (**4**) (125 μL, 0.5 mmol) at room temperature. After being stirred for 48 h at the same temperature, the reaction mixture was filtered to separate immobilized catalyst from the reaction mixture. The organic extracts were concentrated to give an oily residue. Purification by flash chromatography (SiO_2, 25% acetone/hexane) gave the Michael adduct **5** (165 mg, 87%) in 93% ee. After the residue was dried under reduced pressure, poly-(*R*)-ALB-II (**2b-II**) (60 mg, quant.) was recovered and reused to the next reaction.

(9) Recently reported immobilized catalysts for asymmetric Michael reactions: (a) Kim, Y. S.; Matsunaga, S.; Das, J.; Sekine, A.; Ohshima, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 6506−6507. (b) Matsunaga, S.; Ohshima, T.; Shibasaki, M. *Tetrahedron Lett.* **2000**, *41*, 8473−8478.