Multicomponent Asymmetric Catalysis

Metal-Bridged Polymers as Insoluble Multicomponent Asymmetric Catalysts with High Enantiocontrol: An Approach for the Immobilization of Catalysts without Using any Support**

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Immobilization, as a methodology to effectively recover and reuse asymmetric catalysts, has attracted the interest of many research groups resulting in a large number of catalysts being subjected to investigation.[1] Multicomponent asymmetric catalysts,[2,3] composed of plural ligands, metals, and functional moieties, have proved to be challenging systems in this regard (Figure 1). Multicomponent asymmetric catalysts function like enzymes in facilitating a wide range of regio- and stereoselective reactions that make use of the synergistic cooperation between the active sites; it is important to maintain the structural motif during immobilization if high reactivities are to be realized. The conventional approach, which involves the random introduction of ligand and functional units onto a sterically irregular polymer backbone, resulted in less effective catalysts. Multidentate ligands with attached sites for metals at the opposite sides in the molecular skeleton readily form insoluble metal-bridged polymers (Figure 2). If chiral metal-bridged regions on the generated polymer function as asymmetric catalysts, a simple and efficient approach for the immobilization of multicomponent asymmetric catalysts without the need for a polymer support would be realized. While metal–organic coordination networks, including metal-bridged polymers, have been utilized for catalytic asymmetric reactions, the enantioselectivity of the products obtained has been very low.[4]

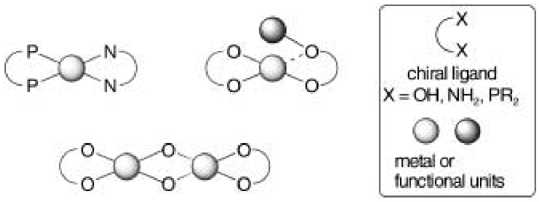

Figure 1. Schematic representation of multicomponent asymmetric catalysts.

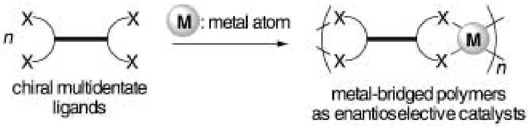

Figure 2. A concept of metal-bridged polymers as enantioselective catalysts.

Herein, the synthesis of insoluble multicomponent asymmetric catalysts by the self-assembly of multidentate ligands containing binol (binol = 1,1′-bi-2-naphthol)[5] with metal ions such as Al^{3+} or Ti^{4+} is described. To obtain the metal-bridged polymers, (*R*,*R*)-6,6′-bis(binol) derivatives (**2a–c**) and (*R*,*R*)-6,6′-bi(binol) (**2d**) were synthesized[6] by linking the binol units at 6-position (Figure 3).[7]

We have reported the ready preparation of Al–Li–bis(binaphthoxide) complex (ALB) as a multicomponent asymmetric catalyst by the reaction of $LiAlH_4$ with two molar equivalents of binol (Figure 4).[2b] ALB was revealed to have

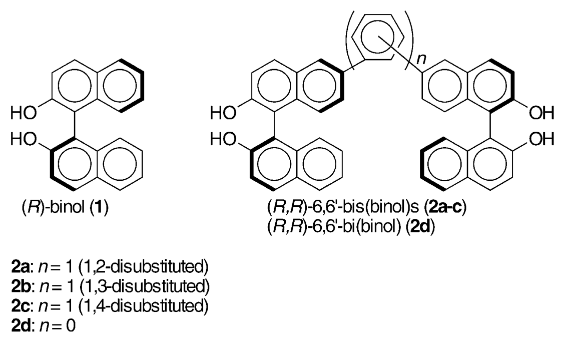

Figure 3. (*R*,*R*)-6,6′-bis(binol) derivatives (**2a–c**) and (*R*,*R*)-6,6′-bi(binol) (**2d**).

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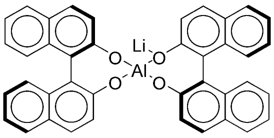
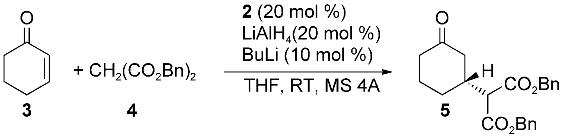


Figure 4. Al-Li-bis(binaphthoxide) complex (ALB).

high enantioselectivity in the asymmetric Michael reaction (e.g., 2-cyclohexenone (**3**) with dibenzyl malonate (**4**)). The catalyst activity of ALB can be increased by the addition of about one equivalent of a basic reagent such as BuLi to form ALB II catalyst while maintaining high enantiocontrol.[2c] Ligands **2a–d** were examined in the first attempt at creating a chiral metal-bridged polymer that could function as ALB II-type catalyst in the enantioselective Michael reaction of **3** with **4**. The addition of $LiAlH_4$ (1 equivalent) to a homogeneous solution of **2** (1 equivalent) in THF at 0 °C spontaneously gave a white precipitate. After the reaction mixture was stirred for 0.5 h, BuLi (0.5 equivalents) was added to the obtained white solid. ALB II (20 mol%) was used as the heterogeneous catalyst in the enantioselective Michael reaction. The results with ligands **2a–d** are summarized in Table 1.

Table 1: Enantioselective Michael reaction catalyzed by Al-bridged polymer.



Entry	**2a–d**	*t* [h]	Yield [%][a]	*ee* [%][b]
1	**2a**	48	94	6
2	**2b**	48	69	17
3	**2c**	48	89	88
4	**2d**	48	86	96
5	ALB[c]	72	88	99
6	ALB II[c]	12	Quant	97

[a] Isolated yield. [b] Determined by HPLC (Daicel Chiralpak AS). [c] 10 mol% of catalyst was used. See reference [2c].

Heterogeneous catalysts derived from **2a** and **2b** afforded the Michael adduct **5** with *ee* values of 6% and 17%, respectively (entries 1 and 2). The low *ee* values are attributable to the bent shape of the ligands that facilitate the formation of unsuitable aggregates.[2d] In contrast, heterogeneous catalysts derived from **2c** and **2d**, in which each pair of the phenolic hydroxy groups is situated at the opposite sides in the multidentate ligands, gave the Michael adduct **5** with high enantioselectivity. As we have previously reported that polystyrene-supported ALB derived from randomly introduced binol derivatives on polystyrene resin afforded **5** with no enatiomeric excess,[8] there is obviously an advantage in the present method that uses a metal-bridged polymer for immobilizing ALB. The ability of the insoluble polymer to act as an asymmetric catalyst was confirmed by the following experiments: The heterogeneous catalyst derived from **2d** and $LiAlH_4$ was allowed to settle and the clear supernatant solution removed with a syringe under argon. The supernatant solution exhibited no catalyst activity in the Michael reaction, whereas the precipitate afforded **5** with *ee* value of 91%. In addition two reactions were carried out with **3** and **4** under optimized conditions. One reaction was quenched after 8 h during which **5** was obtained in 22% yield with an *ee* value of 94%. The supernatant solution of the other reaction was separated from the heterogeneous catalyst and stirred further for 40 h. This reaction afforded **5** in 19% yield with an *ee* value of 90%. In addition ligand **2d** was not observed in the supernatant solution. These results confirm the absence of catalyst activity in the solution phase. The heterogeneous catalyst as Al-bridged polymer, derived from **2d** and $LiAlH_4$, was characterized by elemental analysis and by a comparison of its IR spectrum with that of the ALB complex. Characteristic absorptions for Al-bridged polymer are similar to ALB complex.[9]

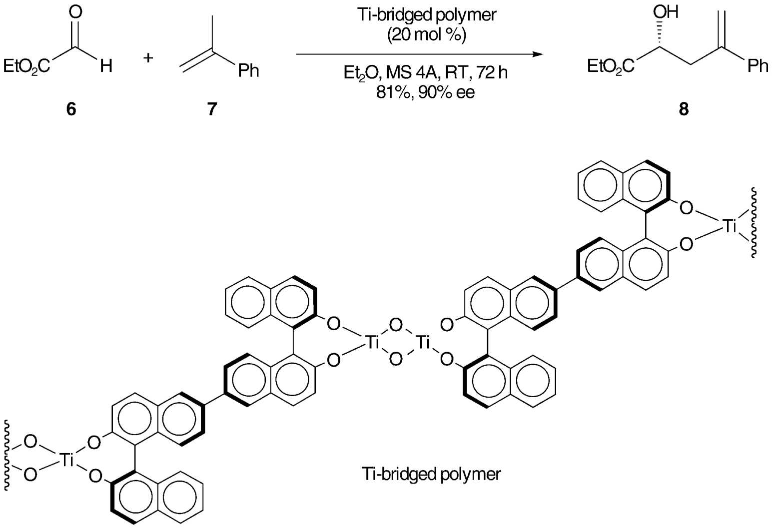
Having been encouraged by the success with Al-bridged polymer as an insoluble asymmetric catalyst, we examined the reuse of the catalyst in asymmetric Michael reaction (Table 2). The reuse experiments were performed by removal of the clear supernatant solution containing the product with a syringe under argon followed by the addition of substrates. The metal-bridged polymer maintained its activity even after being reused three times, albeit with a slight decrease in enantioselectivity (yield: 74%, *ee* value of 85%).

Table 2: Reuse of Al-bridged polymer in enantioselective Michael reaction of **3** with **4**.[a]

Cycle	*t* [h]	Yield [%][b]	*ee* [%][c]
1	72	88	96
2	98	86	87
3	98	74	85
4	98	60	77
5	98	59	77

[a] Al-bridged polymer generated from **2d** (1 mol equiv), $LiAlH_4$ (1 mol equiv) and BuLi (0.5 mol equiv) in the presence of MS 4A was used. [b] Isolated yield. [c] Determined by HPLC (Daicel Chiralpak AS).

The generality of the concept of chiral metal-bridged polymer catalysis was also demonstrated through asymmetric carbonyl–ene reaction by using a Ti–binol complex.[2i] A solution of $Ti(O\text{-}i\text{Pr})_4$ (2 equivalents) in toluene and H_2O (four molar equivalents) were added to a solution of **2d** in CH_2Cl_2. The solution was stirred at room temperature for 24 h to afford the precipitate. After removal of the solvents at 80 °C under reduced pressure, the residue was dried in vacuo at 80 °C for 19 h. The resulting red solid was characterized by elemental analysis and by comparison of its IR spectrum with hitherto known titanium complex,[2i] and found to be a titanium-bridged polymer. The characteristic absorptions for titanium-bridged polymer are similar to the parent titanium complex.[10] As shown in Scheme 1, the titanium-bridged polymer catalyzed the reaction of aldehyde **6** and olefin **7** to give the product **8** in 81% yield with an *ee* value of 90%. In contrast to the Al-bridged polymer, Ti-bridged polymer could be recovered in air. After being reused four times the Ti-



Scheme 1. Asymmetric carbonyl–ene reaction catalyzed by Ti-bridged polymer.

Table 3: Reuse of Ti-bridged polymer in enantioselective carbonyl–ene reaction of **6** with **7**.

Cycle	*t* [h]	Yield [%][a]	*ee* [%][b]
1	98	88	88
2	98	72	92
3	98	71	89
4	147	88	88
5	147	66	88

[a] Yield of isolated product. [b] Determined by HPLC (Daicel Chiralpak AS).

bridged polymer exhibited consistent catalytic selectivity affording **8** with an *ee* value of 88% (Table 3).

The results presented herein is the first example of a chiral metal-bridged polymer, formed by a metal-mediated self-assembly of chiral multidentate ligands, that functions as an asymmetric catalyst with high enantioselectivity. This novel method offers the possibility of immobilization of multi-component asymmetric catalysts without using any support.[8,11] The design of other types of chiral multidentate ligands is currently being pursued.

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[10] Ti-bridged polymer: Elemental analysis calcd (%) for polymeric $C_{47}H_{30}O_6Ti_2$ (containing one molecule of toluene per active site): C 71.78, H 3.84; found: C 71.96, H 4.15. IR: Ti-binol complex 1585, 1499, 1458, 1333, 1234, 1113, 1078, 974, 935, 814, 746 cm^{-1},

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