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Monolayer-Protected Au Cluster (MPC)-Supported Ti–BINOLate Complex

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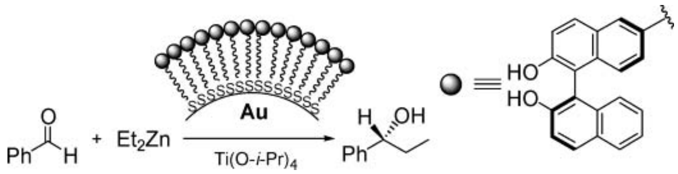
ABSTRACT



Disulfides bearing (*R*)-1,1′-bi-2-naphthol ((*R*)-BINOL) moieties at each terminal position have been successfully introduced on the surface of Au cluster. Ti–BINOLate complex generated from the obtained monolayer-protected Au cluster (MPC) promoted catalytic asymmetric alkylation of benzaldehyde with Et_2Zn to afford the adduct in up to 98% yield with 86% ee. After completion of the reaction, the BINOL-functionalized MPC was easily recovered.

Monolayer-protected metal clusters (MPCs)[1] of nanometer-size have attracted much attention due to their diverse applications in diagnostic,[2] electronic,[3] and photonic devices.[4] In particular, since the design and synthesis of structurally well-defined Au clusters are relatively simple and easy, a large number of functionalized Au clusters have been reported.[5] However, chemical transformation and/or chiral recognition on the surface of MPC has remained a challenge in fine chemical technology.[6]

In many cases, polymer-supported catalysts[7] have exhibited lower catalyst activity than that of the parent homogeneous catalysts. A possible reason for the low activity of polymer-supported catalysts could be the limited access to the catalytic sites, most of which are present deep inside the polymer backbone. When the MPC is prepared with thiols and/or disulfides containing a chiral ligand moiety, the ligands are readily exposed on the surface of metal clusters. Therefore, the catalysts generated from MPC-supported ligands are expected to show high catalyst activity, which would be comparable to the parent homogeneous catalysts, due to the easy access to active sites on the surface of MPC.[8] Herein, we report the first synthesis of MPCs bearing chiral 1,1′-bi-2-naphthol (BINOL) moieties on the Au surface (Scheme 1) and their application to asymmetric reactions.[9]

Toward the development of new asymmetric catalysts installed on Au cluster, disulfides bearing (*R*)-1,1′-bi-2-naphthol ((*R*)-BINOL) moieties at terminal positions were

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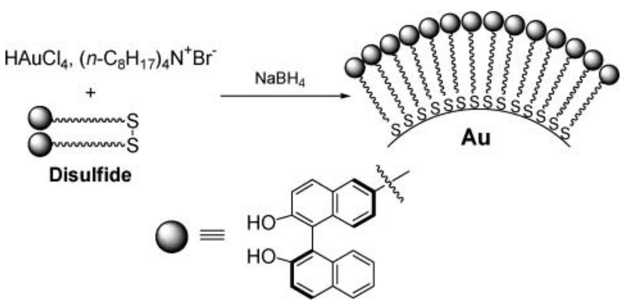
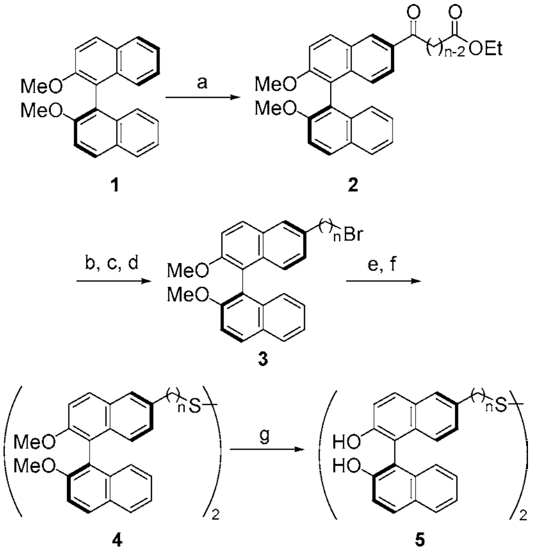
Scheme 1. Introduction of Disulfide Having Two BINOL Units.



selected because BINOL has tremendous applications in enantioselective catalysis.[10] The syntheses of BINOL-terminated disulfides are outlined in Scheme 2. Alkyl chains with varying chain lengths were smoothly introduced at the 6-position of the known 2,2′-dimethoxy-1,1′-binaphthalene (**1**) by Friedel−Crafts acylation reaction[11] to afford compound **2**. After reduction of ketone and ester moieties in **2**, the bromination of the alcohol with PPh_3-CBr_4 gave the corresponding bromide **3**. The bromide **3** was reacted with thiourea to yield the mixture of the disulfide **4** and corresponding thiol. To obtain disulfide **4** as a sole product, the mixture was subsequently treated with iodine in aqueous NaOH. Finally, removal of Me groups on the BINOL moiety was performed with BBr_3 to afford the desired BINOL-terminated disulfide **5**. Preparation of disulfides **5** with various lengths of alkyl chains as spacers ($n = 4$, 5, and 6) has been achieved in 31∼34% overall yield in seven steps starting from (*R*)-**1**.

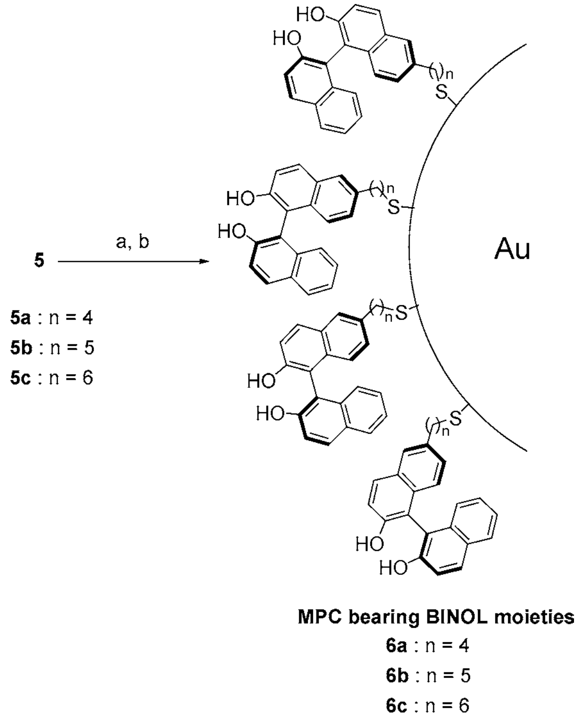
Scheme 2[a]



[a] Reagents and conditions: (a) $AlCl_3$, $EtO_2C(CH_2)_{n-2}COCl$, CH_2Cl_2; (b) TFA, Et_3SiH, CH_2Cl_2; (c) LAH, THF; (d) PPh_3, CBr_4, THF; (e) $(NH_2)_2C{=}S$, DMSO; (f) I_2, aq NaOH; (g) BBr_3, CH_2Cl_2.

With a range of disulfide **5** in hand, BINOL-functionalized MPCs were subsequently synthesized. To a toluene solution of $AuCl_4^-(n\text{-}C_8H_{17})_4N^+$ generated in situ by the treatment of aqueous solution of $HAuCl_4$ with tetraoctylammonium bromide[12] was added the disulfide **5** consisting of two (*R*)-BINOL moieties. Subsequently, the reaction mixture was treated with $NaBH_4$ to obtain the BINOL-functionalized MPCs **6a**, **6b**, and **6c** ($n = 4$, 5, and 6, respectively) quantitatively (Scheme 3). The amount of disulfide **5** immobilized onto MPC **6** was determined by elemental analysis.[13]

Scheme 3. Preparation of MPCs Bearing BINOL Moieties[a]



[a] (a) $HAuCl_4{\cdot}4H_2O$ (2 equiv), $(n\text{-}C_8H_{17})_4N^+Br^-$ (4 equiv); (b) aq $NaBH_4$ (20 equiv).

To demonstrate the catalytic activity of BINOL-functionalized MPC **6**, the catalytic asymmetric alkylation[14] of benzaldehyde (**7**) with Et_2Zn was examined (Table 1).[15]

In all cases, addition of Ti(O-*i*-Pr)$_4$ to MPC **6** resulted in heterogeneous Ti−BINOLate complexes.[16] The alkylation

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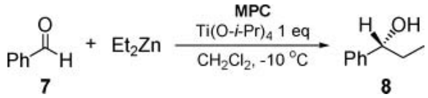
(9) In a remarkable report on similar efforts, Mrksich and co-workers applied the Au cluster bearing dihydroquinidine ligands to the catalytic asymmetric dihydroxylation of styrene: Li, H.; Luk, Y.-Y.; Mrksich, M. *Langmuir* **1999**, *15*, 4957.

Table 1. Catalytic Asymmetric Alkylation Using MPCs



entry	MPC (mol %)[a]	n[b]	Et_2Zn (equiv)	time (h)	yield[c] (%)	ee (%)
1	**6a** (10)	4	2	7	92	80
2	**6b** (10)	5	2	7	98[d]	86
3	**6c** (10)	6	2	7	>95	72
4	**6b** (5)	5	2	7	>95	80
5	**6b** (10)	5	1	16	31	73
6	**6b** (10)	5	3	3	>95	84
7	BINOL (10)		2	7	>95	90

[a] As a monomeric ligand. [b] Lengths of alkyl chains as spacers. [c] Determined by ^1H NMR. [d] Isolated yield.

of **7** with 2 equiv of Et_2Zn in the presence of 1 equiv of $Ti(O\text{-}i\text{-}Pr)_4$ was promoted by 10 mol % **6a** to give the adduct (*R*)-**8** in 92% yield with 80% ee. The use of **6b** improved the enantioselectivity of (*R*)-**8** to 86% ee (entry 2). The amount of **6b** could also be reduced to 5 mol % (entry 4). Among several chain lengths we examined, **6b** induced the best enantiomeric excess on (*R*)-**8** (entries 1−3). Interestingly, the reaction using 3 equiv of Et_2Zn proceeded smoothly keeping the high enantiomeric excess of (*R*)-**8**, while the reaction using 1 equiv of Et_2Zn resulted in reduced enantiomeric excess (entries 5 and 6). The activity of heterogeneous MPC catalyst was close to the soluble parent Ti−BINOLate complex.[17] The high catalyst activity of MPC-supported BINOL catalysts would reflect the naked character of BINOL moieties on the surface of MPC.

The size of **6b** was analyzed by transmission electron microscopy (TEM) and dynamic light scattering (DLS).[18] The TEM image, depicted in Figure 1, confirmed the formation of MPC with a diameter less than 5 nm for the Au core. The distribution of **6b** by DLS exhibited the existence of swollen BINOLate MPC with the following sizes: 85% of 7.6 nm diameter with ca. 15% of 9.0 nm diameter. The size obtained by DLS is significantly larger than that analyzed by TEM. This can be expected because DLS is more sensitive to larger species than smaller ones in a MPC-disperse aggregate sample.

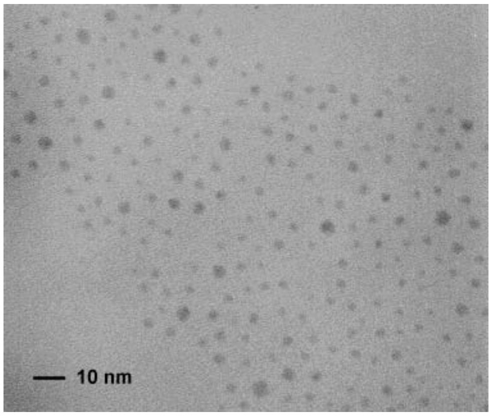


Figure 1. TEM image of **6b**.

As a preliminary result of reuse of **6b**, after termination of the reaction using 1 N HCl, **6b** was easily recovered by precipitation from EtOH and the use of recovered **6b** with $Ti(O\text{-}i\text{-}Pr)_4$ resulted in the adduct in 92% yield with 68% ee. Moreover, after immersing **6b** in 1 N HCl for 3 days, the recovered **6b** still promoted the alkylation reaction to give (*R*)-**8** in 75% yield with 62% ee. During the examination of reuse of the catalysts, no flaked BINOL derivative was observed in the reaction mixture by ^1H NMR and HPLC analysis. These results suggest that the newly prepared BINOL-functionalized MPC is stable and reusable.

In conclusion, BINOL-functionalized MPCs were synthesized and applied in the catalytic asymmetric alkylation of benzaldehyde by forming the Ti−BINOLate complex on the MPC. The MPC used as the ligand was readily recovered from the reaction mixture and showed stability under acidic conditions.

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(13) Elemental analysis of MPCs and the loading of BINOL units on the Au cluster are summarized as follows. **6a**: C, 40.63; H, 5.42; S, 2.84; Au, 45.96; 1.30 mmol/g. **6b**: C, 40.71; H, 4.52; S, 3.11; Au, 46.68; 1.28 mmol/g. **6c**: C, 40.25; H, 4.75; S, 3.61; Au, 46.13; 1.26 mmol/g.

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(15) **Typical Procedure.** A suspension of MPC and $Ti(O\text{-}i\text{-}Pr)_4$ (0.25 mmol) in 0.5 mL of CH_2Cl_2 was stirred at room temperature for 30 min. To the suspension was added **7** (0.25 mmol), and the apparatus was cooled to −10 °C. After stirring for 30 min at this temperature, diethylzinc solution (1.0 M) was added dropwise to the stirred mixture and the entire mixture was stirred for the indicated reaction time. After the addition of 1 N HCl, the crude mixture was extracted with Et_2O and purified by column chromatography on silica gel to give (*R*)-**8**. Optical purity was determined by HPLC analysis using a chiral stationary phase column (DAICEL CHIRALCEL OD-H) with hexane and *i*-PrOH as the eluent.

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(17) We have previously reported that polystyrene-supported Ti−BINOLate complex, which has a spacer at the 6-position of the BINOL moiety, promoted the reaction to afford **8** in 61% yield with 83% ee. The present method is obviously advantageous over our earlier method: Jayaprakash, D.; Sasai, H. *Tetrahedron: Asymmetry* **2001**, *12*, 2589.

(18) Distribution of **6b** was analyzed using dynamic light scattering (DLS) by NIKKISO Co., Ltd.

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Supporting Information Available: Experimental procedures and characterization of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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