Chiral Catalysts

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Helical Poly(quinoxaline-2,3-diyl)s Bearing Metal-Binding Sites as Polymer-Based Chiral Ligands for Asymmetric Catalysis**

*Takeshi Yamamoto and Michinori Suginome**

In memory of Yoshihiko Ito

A helix is one of the simplest and best-organized chiral structural motifs, being widely found not only in molecules, but in natural and artificial materials. Naturally occurring helical macromolecules, such as DNA, RNA, and polypeptides, adopt one of the two helical senses (right or left) and play vital biological roles, which depend on their three-dimensional chiral structure. Helical synthetic polymers have also gained increasing interest on the basis of recent progress in asymmetric polymer synthesis, which has enabled the selective construction of unnatural macromolecular architectures with nonracemic helical structures.[1] Efficient induction of the main chain helical sense to polymers, such as poly(methacrylate)s,[2] poly(isocyanate)s,[3] poly(isocyanide)s,[4] poly(acetylene)s,[5] and polyguanidines,[6], has been achieved. In the unnatural macromolecular world, even achiral monomers, which have no stereogenic centers, can form helical structures in which either a left- or right-handed helical sense is prevalent.

One of the important functions of chiral biopolymers is to undertake biocatalyses, in which highly enantioselective reactions take place on the chiral architecture. It seems likely that unnatural polymer scaffolds can be tailored exhibit the same properties by virtue of the freedom of molecular design, which allows the possibility of using either a left- or right-handed helix and the introduction of metallic elements that usually are not contained in natural biosystems (Figure 1).[7] The use of chiral helical polymers as scaffolds for chiral reaction environments was first realized with poly(methylmethacrylate)-based chiral polymers,[8,9] followed by the use of other helical polymers as chiral catalysts.[10] However, the degree of asymmetric induction and catalyst efficiency in these systems were still moderate in comparison with existing low-molecular-weight chiral catalysts and polymer catalysts into which low-molecular-weight chiral catalysts are embedded.[11] It is highly desirable to find new polymer systems that enable higher selectivity and catalyst efficiency for the development of practical chiral polymer catalysts.

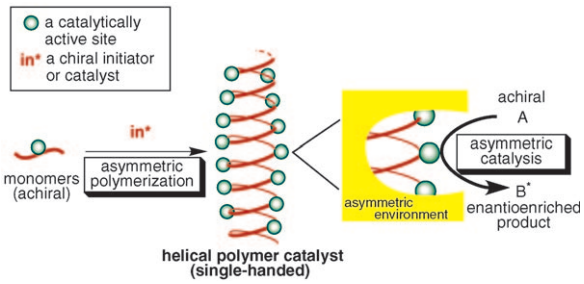

Figure 1. A system for catalytic asymmetric synthesis using optically active, single-handed helical polymers as a chiral catalyst.

The conditions for synthetic helical polymers to serve as practical chiral catalysts in asymmetric synthesis include: a) very high purity for a one-handed screw sense; b) a highly stable helical structure, even in solution, with no racemization or denaturation; c) modifiable side chains onto which catalytically active sites can be introduced without affecting the helical structure. Most nonracemic helical polymers are unable to fulfill all of these requirements, leading to the paucity of highly effective polymer catalysts for asymmetric synthesis.

Poly(quinoxaline-2,3-diyl)s are a unique class of helical polymers prepared by living polymerization of *o*-diisocyanobenzenes.[12] They feature an exceptionally robust helical structure, which shows no change even at 80 °C in solution for several days.[13] The most striking feature of these polymers is the high screw-sense excess, which relies on the chiral terminal group derived from the chiral initiator for the asymmetric living polymerization.[14] With these unique characteristics, we have studied the application of the polyquinoxaline scaffold to new chiral polymer catalysts. Herein, we report the asymmetric synthesis of new quinoxaline polymers with a coordinating group on a side chain, and their use as chiral ligands for transition-metal catalysts. The new monodentate polymer-based ligands are used in palladium-catalyzed asymmetric hydrosilylation of styrenes, affording a remarkable level of asymmetric induction.

For the synthesis of phosphine-substituted polymers, we prepared the *o*-diisocyanobenzene **1**, bearing a diphenylphosphine oxide group, as the monomer for the living polymerization (Scheme 1). To obtain good solubility and to simplify the structural analysis of the polymer, we copolymerized **1** with "spacer monomer" **2**, which has no coordinating group and thus served as the framework of the helical structure. The

[*] T. Yamamoto, Prof. Dr. M. Suginome
Department of Synthetic Chemistry and Biological Chemistry
Graduate School of Engineering, Kyoto University
Katsura, Nishikyo-ku, Kyoto 615-8510 (Japan)
Fax: (+81) 75-383-2722
E-mail: suginome@sbchem.kyoto-u.ac.jp
Homepage: http://www.sbchem.kyoto-u.ac.jp/suginome-lab/

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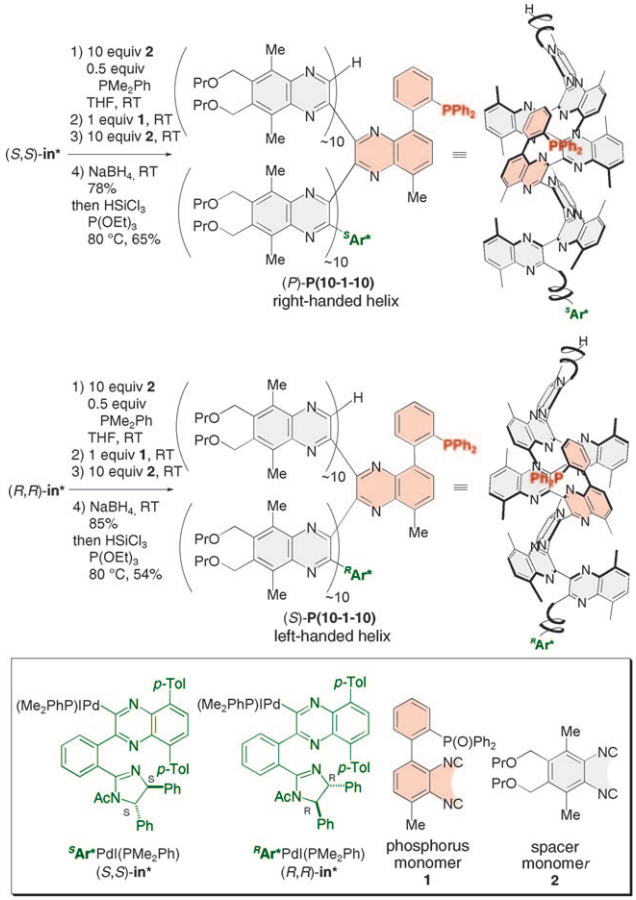
polymer ligand we employed was prepared as follows: Using a chiral organopalladium initiator (*S*,*S*)-**in*** or (*R*,*R*)-**in*** (Scheme 1) with 0.5 equivalents of dimethylphenylphosphine,[15] 10 equivalents of the spacer monomer **2** was



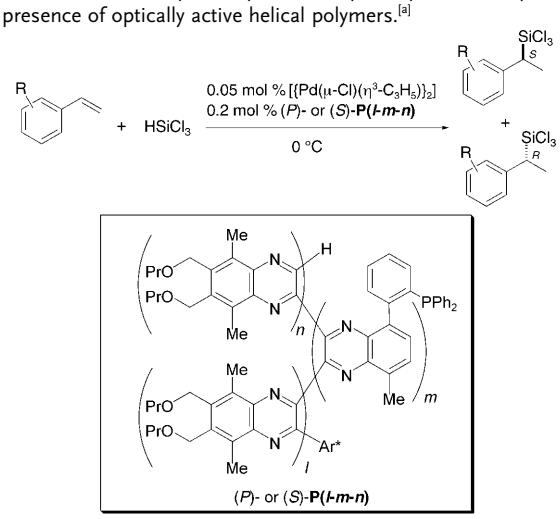
Scheme 1. Synthesis and structure model (right) of optically active *P* and *S* isomers of helical poly(quinoxaline-2,3-diyl) **P(10-1-10)**, bearing a phosphine unit.

polymerized at room temperature. To this living oligomer, which possesses an active palladium site at the terminus, 1.0 equivalents of **1** was added, and the mixture was allowed to react for several hours, until complete consumption of **1** had occurred. The resulting living co-oligomer was treated once more with 10 equivalents of **2**, and then quenched with $NaBH_4$, giving copolymer **PO(10-1-10)**. The phosphine oxide moiety was converted into the diphenylphosphino group by reduction with trichlorosilane.[16] No drop in the screw-sense excess of the polymer backbone was appreciable during the reduction step, which required 24 h at 80 °C. The resultant polymer **P(10-1-10)** was highly soluble in organic solvents, such as THF, toluene, and CH_2Cl_2, and clearly identified by ^1H, ^{13}C, and ^{31}P NMR spectroscopy, gel-permeation chromatography (GPC) analysis, and circular dichroism (CD) spectroscopy, which revealed a screw-sense excess of $>90\%$ on the basis of our previous reports.[14d] Right- and left-handed helical polymers (*P*)-**P(10-1-10)** and (*M*)-**P(10-1-10)** were produced selectively using initiators (*S*,*S*)-**in*** and (*R*,*R*)-**in***, respectively.

Using this copolymer as a chiral ligand, asymmetric hydrosilylation of styrene was examined.[17] The catalyst was prepared by mixing **P(10-1-10)** with $[\{Pd(\mu\text{-}Cl)(\eta^3\text{-}C_3H_5)\}_2]$ in toluene at room temperature. The palladium catalyst prepared from the homopolymer of **2**, which had no phosphine group, had no catalytic activity at all (Table 1, entry 1). In contrast, the catalyst prepared with phosphine polymers (*P*)- and (*M*)-**P(10-1-10)** exhibited remarkable catalytic activity, giving α-trichlorosilylethylbenzene in high yields (Table 1, entries 2 and 3). The hydrosilylation was complete within 24 h with 0.1 mol% palladium loading. Remarkably, the enantiomeric excess of the resultant hydrosilylation products reached 85% *ee* (enantiomeric ratio of 8:92) for both of the enantiomeric helical polymer ligands. The right-handed polymer ligand, (*P*)-**P(10-1-10)**, gave an enantioenriched hydrosilylation product with the *S* configuration and the left-handed ligand, (*M*)-**P(10-1-10)**, gave the *R* product selectively.

Other styrene derivatives were also subjected to the enantioselective hydrosilylation using (*P*)-**P(10-1-10)**. Both *o*-

Table 1: Palladium-catalyzed asymmetric hydrosilylation of styrenes in the presence of optically active helical polymers.[a]



Entry	R	Ligand	Yield [%][b]	*ee* [%][c]
1	H	(*P*)-poly-2	0	–
2	H	(*P*)-P(10-1-10)	97	85 (*S*)
3	H	(*M*)-P(10-1-10)	98	85 (*R*)
4	2-Me	(*P*)-P(10-1-10)	95	86 (*S*)
5	3-Me	(*P*)-P(10-1-10)	94	79 (*S*)
6	4-Me	(*P*)-P(10-1-10)	98	87 (*S*)
7	4-*t*Bu	(*P*)-P(10-1-10)	98	74 (*S*)
8	4-MeO	(*P*)-P(10-1-10)	96	84 (*S*)
9	4-F	(*P*)-P(10-1-10)	97	84 (*S*)
10	H	(*P*)-P(30-1-10)	88	84 (*S*)
11	H	(*P*)-P(10-1-30)	89	84 (*S*)
12	H	(*P*)-P(10-1-0)	94	5 (*S*)
13	H	(*P*)-P(10-2-10)	86	80 (*S*)
14	H	(*P*)-P(10-3-10)	92	76 (*S*)
15	H	(*P*)-P(10-5-10)	91	70 (*S*)

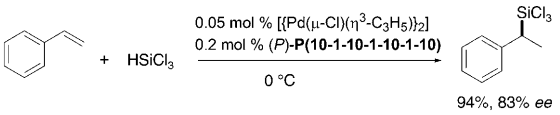
[a] A styrene derivative (1.0 mmol) and trichlorosilane (2.0 mmol) were stirred at 0 °C in the presence of $[\{Pd(\mu\text{-}Cl)(\eta^3\text{-}C_3H_5)\}_2]$ (0.50 μmol, 0.05 mol%) with a polymer ligand (2.0 μmol, 0.2 mol%). [b] Yield of product isolated by bulb-to-bulb distillation. [c] Determined by chiral HPLC after conversion into the corresponding α-phenylethyl alcohol by $H_2O_2/KHCO_3/KF$ oxidation.

and *p*-methylstyrenes afforded the corresponding hydrosilylation products with high enantioselectivity, whereas *m*-methylstyrene resulted in a small drop in enantiomeric excess (Table 1, entries 4–6). Interestingly, substitution by a bulky group at the *p*-position also lowered the enantioselectivity (Table 1, entry 7). Substitution by heteroatomic functional groups at the *para* position did not affect the enantioselectivity (Table 1, entries 8 and 9).

To gain insight into the polymer structure for optimization of enantioselectivity, copolymers (*P*)-**P(*l*-*m*-*n*)** with different monomer composition were prepared under identical reaction conditions to the synthesis of **P(10-1-10)**. Use of the polymer (*P*)-**P(30-1-10)**, in which the phosphine moiety and the terminal chiral group were separated by more spacer units than in (*P*)-**P(10-1-10)**, also led to high enantioselectivity, suggesting that the terminal chiral group has no direct effect on the chiral reaction environment around the palladium atom (Table 1, entry 10). An increase in the number of spacer units on the other side of the phosphorus unit ((*P*)-**P(10-1-30)**) led to the same high enantioselectivity (Table 1, entry 11). However, a polymer with no spacer units on one of the two sides of the phosphine-containing unit,(*P*)-**P(10-1-0)**, failed to give enantioenriched products (Table 1, entry 12). Further examination was undertaken of the influence of the phosphine units in the polymer chain through the synthesis of polymers (*P*)-**P(10-*m*-10)** ($m = 2$, 3, and 5). An increase in the number of contiguous phosphine units resulted in a decrease in the enantioselectivity (Table 1, entries 13–15).

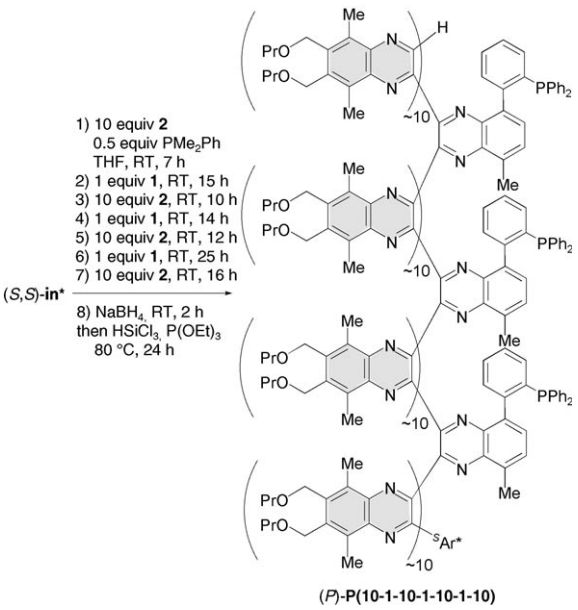
Taking into account the structural requirements for the polymer ligands, we attempted the synthesis of higher polymers with multiple phosphino groups in the polymer chain. The synthesis was achieved by block polymerization, in which batches of **2** (10 equivalents) followed by **1** (1.0 equivalents) were added repeatedly to the reaction mixture and given time (7–25 h) to react prior to subsequent monomer addition (Scheme 2). A heptablock copolymer (*P*)-**P(10-1-10-1-10-1-10)**, in which three phosphine units in the polymer chain were separated by blocks of approximately 10 spacer units, was isolated and used in the catalytic hydrosilylation reaction.

Hydrosilylation proceeded under identical reaction conditions, allowing isolation of the hydrosilylation product with 83% *ee*, with almost no drop in enantioselectivity in comparison with **P(10-1-10)** [Eq. (1)].



(1)

In summary, we have established that helical chirality of fully synthetic polymers can induce enantioselectivities that are comparable to those obtained by low-molecular-weight catalyst systems. Our results have shown the possibility of using poly(quinoxaline-2,3-diyl)s as a scaffold for practical chiral polymer ligands. Further improvement of enantioselectivity, catalyst activity, and catalyst recovery by modification of the polymer structure is currently being undertaken in this laboratory.



Scheme 2. Synthesis of heptablock copolymer (*P*)-**P(10-1-10-1-10-1-10)** by living asymmetric copolymerization of **1** and **2** using chiral initiator (*S*,*S*)-**in***.

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