J|A|C|S COMMUNICATIONS

Published on Web 05/20/2010

High-Molecular-Weight Polyquinoxaline-Based Helically Chiral Phosphine (PQXphos) as Chirality-Switchable, Reusable, and Highly Enantioselective Monodentate Ligand in Catalytic Asymmetric Hydrosilylation of Styrenes

Takeshi Yamamoto,[†] Tetsuya Yamada,[†] Yuuya Nagata,[†] and Michinori Suginome*[,†,‡]

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, and CREST, Japan Science and Technology Agency (JST), Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

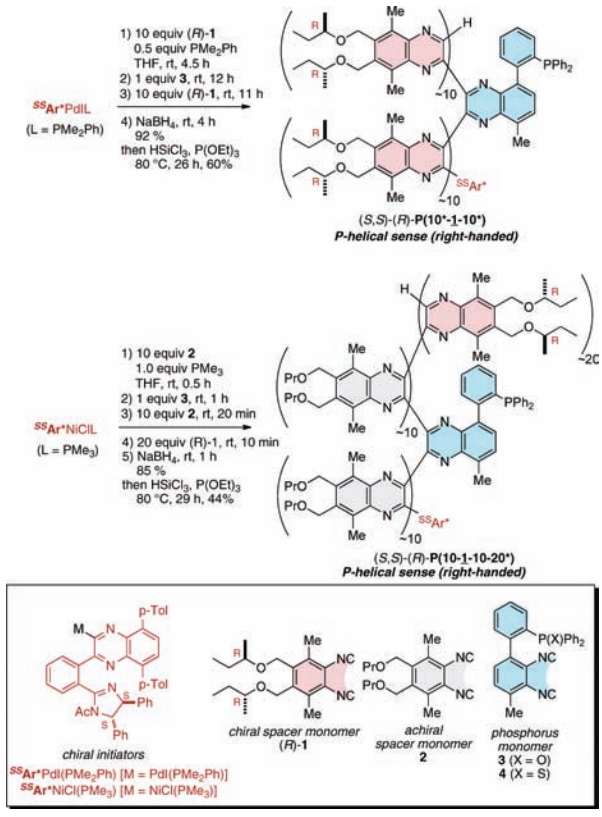
Received March 23, 2010; E-mail: suginome@sbchem.kyoto-u.ac.jp

Increasing attention has focused on polymer-based chiral catalysts in catalytic asymmetric synthesis.[1,2] They typically feature easy separation from the reaction mixture and the possibility of reuse of the catalyst. Most chiral polymer catalysts are designed to immobilize small chiral units such as BINOL (1,1′-binaphthol) and BINAP (2,2′-bis(diphenylphosphino)-1,1′-binaphthyl), which are chosen from the well-established chiral ligand library. In this conventional molecular design, the polymer scaffolds must be "transparent" to avoid any unfavorable perturbation to the chiral reaction sites.

There is a highly contrasting molecular design for polymer-based chiral catalysts, in which chiral induction relies solely on the chiral main chain structure of the polymers.[3] This class of chiral polymer ligand system may be attractive in that the created chiral reaction environment is unique for the polymer system, the catalysts are easily separable and reusable, and fine-tuning or even a dramatic change of the chiral reaction environment would be possible because of the large conformational change of the polymer secondary structures. However, lack of rigidity, homogeneity, and robustness of the chiral polymer scaffold hampered realization of the effective asymmetric catalyst system, although some attempts have already been made using optically active helical polymers, such as the poly(trityl methacrylate) system.[4−8] DNA has been successfully used as a chiral scaffold for highly enantioselective chiral catalysts, in which a catalytically active group is incorporated via noncovalent interactions.[9] However, the restricted availability of enantiomeric, i.e., unnatural, DNA may make application of this particular natural scaffold to asymmetric synthesis difficult.

Quite recently, we have established that single-handed helical poly(quinoxaline-2,3-diyl)[10−12] can serve as a highly effective scaffold to which a diarylphosphino pendant is attached covalently as the metal-binding site.[13] We prepared and used short polyquinoxaline-based phosphine (PQXphos) (ca. 20mers), which carried just one phosphine-bearing unit in the middle of each polymer molecule, whose chiral helical structure was induced solely by a chiral group located at the terminus of the polymer. We achieved 87% ee in palladium-catalyzed asymmetric hydrosilylation of styrenes. In this paper, we report that high-molecular-weight (ca. 1000mer) variants of PQXphos bearing chiral side chains exhibited remarkable profiles for use as chiral polymer ligands in asymmetric synthesis. They showed not only much higher enantioselectivity in asymmetric hydrosilylation of styrenes and formation of insoluble polymer complex but also a solvent-dependent switch of helical chirality, which enables selective production of either enantiomer from a single chiral catalyst at will.

Scheme 1. Synthesis of Oligomer-Based PQXphos (*P*)-**P(10*-1-10*)** and (*S*,*S*)-(*R*)-**P(10-1-10-20*)**

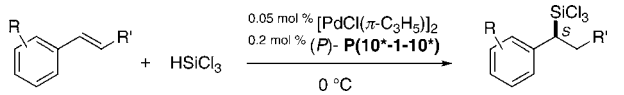


We initiated our study from the synthesis of 20mer-based PQXphos that carries chiral (*R*)-2-butoxymethyl groups instead of achiral propoxymethyl groups in the original PQXphos (Scheme 1).[14] The new PQXphos was prepared by living block copolymerization, in which enantiopure 1,2-diisocyanobenzene ((*R*)-**1**, 10 equiv), phosphorus monomer **3** (1 equiv), and (*R*)-**1** (10 equiv) were successively added to chiral organopalladium initiator ^{S,S}Ar*PdI(PMe$_2$Ph).[12] The obtained PQXphos showed remarkable enantioselectivity in the hydrosilylation of styrenes (Table 1).[15] In comparison with the previously reported PQXphos,[13] which bears achiral side chains and shows 85% ee for unsubstituted styrene, the modified PQXphos exhibited much higher enantioselectivity (entry 1). The high enantioselectivities hold generally for the substituted styrene derivatives including 1-phenylpropene (entry 8) as an internal alkene (entries 2−8).

To check the role of the chiral spacer unit in creating the chiral reaction environment, a modified PQXphos whose phosphine-bearing unit is separated from the chiral spacer block by 10 achiral

[†] Kyoto University.
[‡] JST.

Table 1. Palladium-Catalyzed Asymmetric Hydrosilylation of Styrenes in the Presence of Oligomers-Based PQXphos[a]



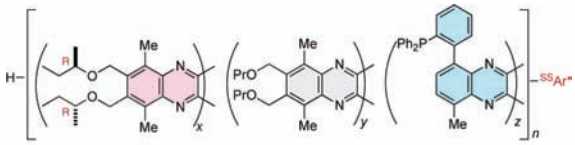
entry	ligand	R	R′	% yield[b]	% ee[c]
1	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	H	H	91	96 (*S*)
2	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	2-Me	H	94	95 (*S*)
3	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	3-Me	H	93	91 (*S*)
4	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	4-Me	H	96	95 (*S*)
5	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	4-MeO	H	96	91 (*S*)
6	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	4-*t*-Bu	H	92	84 (*S*)
7	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	4-F	H	94	92 (*S*)
8	(*S*,*S*)-(*R*)-**P(10*-1-10*)**	H	Me	93	96 (*S*)
9	(*S*,*S*)-(*R*)-**P(10-1-10-20*)**	H	H	93	95 (*S*)

[a] A styrene derivative (1.0 mmol) and trichlorosilane (2.0 mmol) were stirred at 0 °C in the presence of $[PdCl(\pi\text{-allyl})]_2$ (0.50 μmol) with a polymer ligand (2.0 μmol P). [b] Isolated yield (bulb-to-bulb distillation). [c] Determined by chiral HPLC after conversion to the corresponding α-phenylethyl alcohol by $H_2O_2/KHCO_3/KF$ oxidation.

spacer units was prepared by organonickel-initiated living polymerization (Scheme 1).[16] The helical structure of the resultant PQXphos (*S*,*S*)-(*R*)-**P(10-1-10-20*)** is induced by both the terminal chiral group and a block of 20 chiral monomer units, which is located at the other terminus of the polymer and separated from the phosphine-bearing unit by the block of achiral spacer units. Hydrosilylation of styrene with the modified PQXphos under the optimized reaction conditions afforded 95% ee, indicating that the chiral groups on the chiral spacer units do not take part in the local chiral reaction sites directly but play a crucial role to induce a highly pure single-handed helical structure (Table 1, entry 9). As mentioned in the previous work,[13] the helical structure of the polymer main chain may induce axial chirality at the aryl-quinoxaline axis effectively, resulting in creation of chiral reaction sites for highly efficient enantio-discrimination.

Having achieved a significant improvement in enantioselectivity, we moved to utilization of a high-molecular-weight random copolymer (Table 2). We expected that a random copolymer would be more easily accessible than a block copolymer and that a higher polymer would allow us to recycle and reuse the polymer ligand more conveniently than the lower polymers. Mixtures of chiral

Table 2. Palladium-catalyzed Hydrosilylation of Styrene with High-Molecular-Weight PQXphos with Varied Unit Ratios[a]

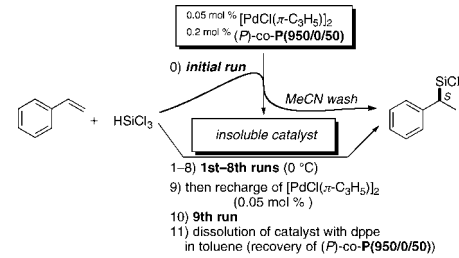


(*S*,*S*)-(*R*)-**P(x*/y/z)**

	(*S*,*S*)-(*R*)-**P(x*/y/z)**				
entry	*x*	*y*	*z*	% yield[b]	% ee[c]
1	0	950	50	98	24 (*S*)
2	50	900	50	98	70 (*S*)
3	100	850	50	96	84 (*S*)
4	200	750	50	96	91 (*S*)
5	450	500	50	98	94 (*S*)
6	950	0	50	94	97 (*S*)
7	1900	0	100	98	97 (*S*)
8	900	0	100	97	94 (*S*)

[a] A styrene derivative (2.0 mmol) and trichlorosilane (3.0 mmol) were stirred at 0 °C in the presence of $[PdCl(\pi\text{-allyl})]_2$ (1.0 μmol) with a polymer ligand (4.0 μmol P). [b] Isolated yield (bulb-to-bulb distillation). [c] Determined after oxidation.

Table 3. Pd-Catalyzed Hydrosilylation of Styrene with Reused (*S*,*S*)-(*R*)-**P(950*/0/50)**[a]



run	time/h	%yield[b]	%ee[c]	run	time/h	%yield[b]	%ee[c]
init	12	94	96	5	37	98	97
1	24	95	97	6	50	97	98
2	24	96	98	7	64	99	98
3	24	97	97	8	70	97	98
4	32	97	97	9	12	98	96

[a] See footnote a in Table 2 for the reaction conditions. Product was isolated by washing the reaction flask with acetonitrile three times followed by bulb-to-bulb distillation. [b] Isolated yield. [c] Determined after oxidation.

monomer (*R*)-**1** (*x* equiv to Ni), achiral monomer **2** (*y* equiv), and phosphorus-containing monomer **4** (*z* equiv), in which the phosphorus atom is protected by a sulfur atom, were copolymerized with various ratios in the presence of the chiral initiator. The use of a sulfur-protected monomer **4** allowed use of HMPT reduction (110 °C) instead of $HSiCl_3$ reduction after polymerization, allowing us to avoid the tedious and problematic filtration step. All of the high-molecular-weight polymers (*S*,*S*)-(*R*)-**P(x*/y/z)** were found to be soluble in common organic solvents such as toluene, THF, and chloroform. Enantioselectivities of the hydrosilylation of styrene nonlinearly increased with an increase in the ratio $(x/(x + y))$ of the chiral monomer unit derived from (*R*)-**1** (Table 2, entries 1−6). For instance, (*S*,*S*)-(*R*)-**P(0*/950/50)**, which has only the chiral terminal group as a source of screw-sense induction, afforded only 24% ee in hydrosilylation of styrene (entry 1). In contrast, (*S*,*S*)-(*R*)-**P(950*/0/50)**, in which all the spacer units have chiral side chains, showed remarkably high enantioselectivity (entry 6). The content of the chiral spacer unit and enantioselectivity have a positive nonlinear relationship, which may be rationalized by the screw-sense excess (s.e.) of the polymer estimated from the *g* values (Kuhn dissymmetry ratio).[17,18] Higher PQXphos (*S*,*S*)-(*R*)-**P(1900*/0/100)** (entry 7) and phosphine-rich (*S*,*S*)-(*R*)-**P(900*/0/100)** (entry 8) also afforded comparable enantioselectivities.

We found that (*S*,*S*)-(*R*)-**P(950*/0/50)** and $[PdCl(\pi\text{-allyl})]_2$ formed insoluble polymer complexes during the hydrosilylation reaction (Table 3).[19] The polymer complex was swollen by organic materials, which could be extracted with an organic solvent, leaving the insoluble polymer complex in the reaction vessel. The polymer complex was not soluble in common organic solvents such as toluene, THF, chloroform, DMSO, methanol, and acetonitrile. We separately found that the insoluble polymer complex could be obtained by mixing (*S*,*S*)-(*R*)-**P(950*/0/50)** with $Pd_2(dba)_3$. The insoluble polymer complex was repeatedly reused as the chiral catalyst for the hydrosilylation reaction (runs 1−8, Table 3). The polymer complex constantly showed high enantioselectivities until the eighth run, although the reaction gradually became sluggish, probably because of a little leaching of the palladium metal in each run.[20] Even so, the eight-time reuse and the easy recovery of the catalyst activity could be important practically.[2] Addition of $[PdCl(\pi\text{-allyl})]_2$ to the insoluble catalyst after the eighth run successfully activated it to the level of the initial cycle, while keeping the enantioselectivity high (run 9). It should be remarked

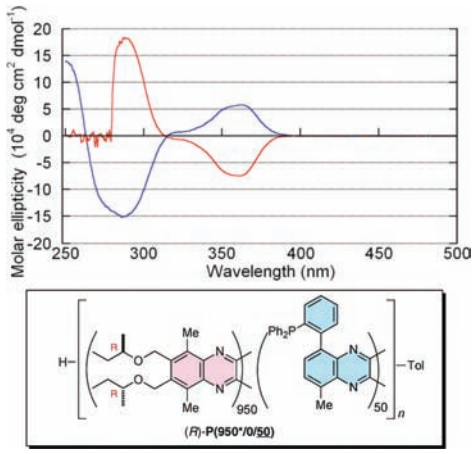


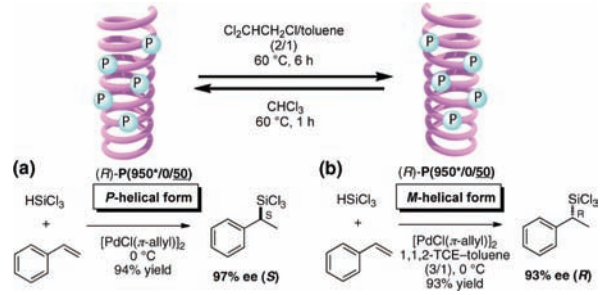
Figure 1. CD spectra of (*R*)-**P(950*/0/50)** in chloroform (blue line) and in a 1,1,2-trichloroethane/toluene (2/1) mixture (red line).

that the insoluble polymer complex became soluble when 1,2-bis(diphenylphosphino)ethane (dppe) was added with toluene. The stronger coordination of dppe to palladium may cause dissociation of the polymer ligand from palladium, leading to the recovery of (*S*,*S*)-(*R*)-**P(950*/0/50)**.

We recently observed a solvent-dependent switch of the helical sense in poly(quinoxaline-2,3-diyl)s prepared from chiral diisocyanide (*R*)-**1**.[14] In comparison with some known macromolecular systems for helix inversion,[21−25] the helix inversion we observed was unique in that both the *P*- and *M*-helices thus formed were determined to have nearly 100% pure helical sense excesses. We became interested in checking if the present PQXphos, which carries a bulky phosphorus pendant group in addition to the aprotic chiral side chains, also underwent reversible change of the helical chirality. We prepared (*R*)-**P(950*/0/50)** through random copolymerization of (*R*)-**1** and **4** with use of achiral organonickel initiator *o*-TolNiCl(PMe$_3$)$_2$ (Figure 1).[16] Although lacking the terminal chiral group, copolymer (*R*)-**P(950*/0/50)** showed exactly the same circular dichroism (CD) spectrum as (*S*,*S*)-(*R*)-**P(950*/0/50)** in $CHCl_3$, indicating that an almost pure *P*-helical structure was formed. The polymer obtained from its $CHCl_3$ or toluene solution showed excellent enantioinduction (97% ee) for the (*S*)-product in asymmetric hydrosilylation of styrene (Scheme 2). When the same polymer was dissolved in a mixture of 1,1,2-trichloroethane/toluene (2/1), gradual inversion of the helical sense was observed by CD measurement (Figure 1). The inversion of the helical sense proceeded smoothly at 60 °C, completing after 6 h to produce the almost pure *M*-helical polymer (Scheme 2). Using the *M*-helical polymer, catalytic hydrosilylation of styrene was carried out in 1,1,2-trichloroethane/toluene, affording 93% ee for the (*R*)-enantiomer. To use the *M*-helical polymer in asymmetric hydrosilylation, use of 1,1,2-trichloroethane with toluene as a solvent was found essential for obtaining high enantioselectivity. Use of an insoluble polymer complex obtained from the *M*-helical polymer with $Pd_2(dba)_3$ without solvent resulted in a significant decrease in ee to 70% (*R*) under otherwise the same reaction conditions.

In this paper, we have demonstrated the unique properties of polymer-based chiral catalysts that cannot be achieved by small-molecule-based, ordinary chiral catalysts. In addition to the easy reuse of the chiral catalyst by virtue of the cross-linking by the formation of a polymer complex, reversible conformational change

Scheme 2. Asymmetric Hydrosilylation Using Chirality-Switchable (*R*)-**P(950*/0/50)** Adopting (a) *P*-Helical Form or (b) *M*-Helical Form



of the polymer backbone could be applied to switch the enantioinduction in asymmetric catalysis. These new observations may prompt exploration of new systems for polymer-based catalysts and of new functions of helical polymers. Further optimization of the catalyst system, extension to other catalyses including asymmetric C−C bond formation, and mechanistic studies on the solvent-dependent inversion of the helical sense are now being pursued in this laboratory.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from MEXT.

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

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JA102428Q