

## Short Communication

# A Helical Polyphenylacetylene Having Amino Alcohol Moieties Without Chiral Side Groups as a Chiral Ligand for the Asymmetric Addition of Diethylzinc to Benzaldehyde

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**ABSTRACT** One-handed helical polyphenylacetylenes having achiral amino alcohol moieties, but no chiral side groups, were synthesized by the helix-sense-selective copolymerization of an achiral phenylacetylene having an amino alcohol side group with a phenylacetylene having two hydroxyl groups. Since the resulting helical copolymers were successfully utilized as chiral ligands for the enantioselective alkylation of benzaldehyde with diethylzinc, we can conclude that the main-chain chirality based on the one-handed helical conformation is useful for the chiral catalysis of an asymmetric reaction for the first time. The enantioselectivities of the reaction were controlled by the optical purities of the helical polymer ligands. In addition, the polymer ligands could be easily recovered by precipitation after the reaction. *Chirality* 27:454–458, 2015. © 2015 Wiley Periodicals, Inc.

**KEY WORDS:** chiral polymer ligand; one-handed helical main-chain; poly(substituted acetylene); achiral amino alcohol

Researchers have been inspired by the one-handed helices in natural compounds, which afford biological macromolecules with a variety of sophisticated functions, and have developed artificial one-handed helical macromolecules.<sup>1–11</sup> Although one-handed helical polymers can be expected as chiral catalysts of enantioselective organic reactions, there have been only a few reports about them because the control of the chiral structures of the main-chain chirality are currently in progress. In general, polymer catalysts have the advantage of easy recycling. Therefore, the development of chiral polymer catalysts for asymmetric reactions is important. However, since the chiralities of most one-handed helical polymers were derived from chiral substituents containing asymmetric atoms, such as asymmetric carbons,<sup>12–14</sup> i.e., they contained two kinds of asymmetric structures, therefore, there have been only a few reports about the enantioselective reactions catalyzed by chiral polymers whose chiral structures arise solely from the one-handed helical conformation.<sup>15–18</sup> Thus, it was difficult to estimate the chiral catalysis of the main-chain chirality itself. In other words, there was not enough information to estimate the chiral induction ability of the chiral main chain.

Poly(substituted acetylenes) prepared using a rhodium catalyst, such as [Rh(nbd)Cl]<sub>2</sub> (nbd: norbornadiene), are generally helical polymers,<sup>1</sup> and their main-chain conformation can be *cis-transoidal*<sup>19–21</sup> or *cis-cisoidal*<sup>9,22–24</sup> depending on the chemical structures of the monomers. Some of the authors (Aoki et al.) have developed two synthetic routes for the one-handed helical poly(substituted acetylene)s. One was an asymmetric induced polymerization (AIP) in which chiral-substituted acetylenes were used as a monomer to afford dynamic helical *cis-transoidal* polyacetylenes.<sup>24–27</sup> The other was a helix-sense-

selective polymerization (HSSP) in which achiral acetylene monomers having two hydroxyl groups and a chiral initiator were used to afford static helical *cis-cisoidal* polyacetylenes.<sup>28–31</sup> Although one-handed helical poly(substituted acetylenes) have been widely studied, their application as asymmetric catalysts is still limited.<sup>14</sup> There are no reports regarding asymmetric organic reactions catalyzed by helical polyacetylene whose chiral structures arise solely from the one-handed helical conformation. In addition, although it was reported that some dynamic helical poly(substituted acetylenes) showed interesting controllable enantioselectivities in asymmetric reactions due to their controllable helical sense,<sup>16–18</sup> there are no reports on the ability of static and stable helical poly(substituted acetylenes).

Catalytic enantioselective diethylzinc addition to aldehydes is one of the most important approaches for the synthesis of optically active secondary alcohols as versatile building blocks for biologically and pharmaceutically active compounds.<sup>32,33</sup>

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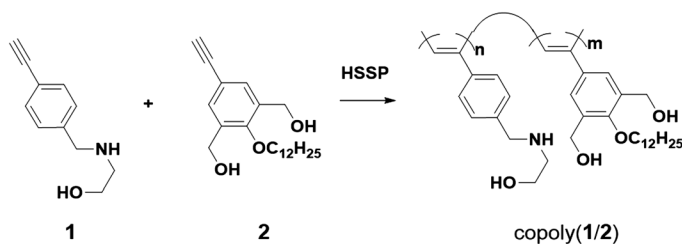
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Chiral amino alcohol was known as one kind of superior chiral catalysts for this purpose. Catalytic asymmetric diethylzinc addition to aldehydes has also been recognized to be a model reaction to evaluate a new catalyst's potential.<sup>34</sup>

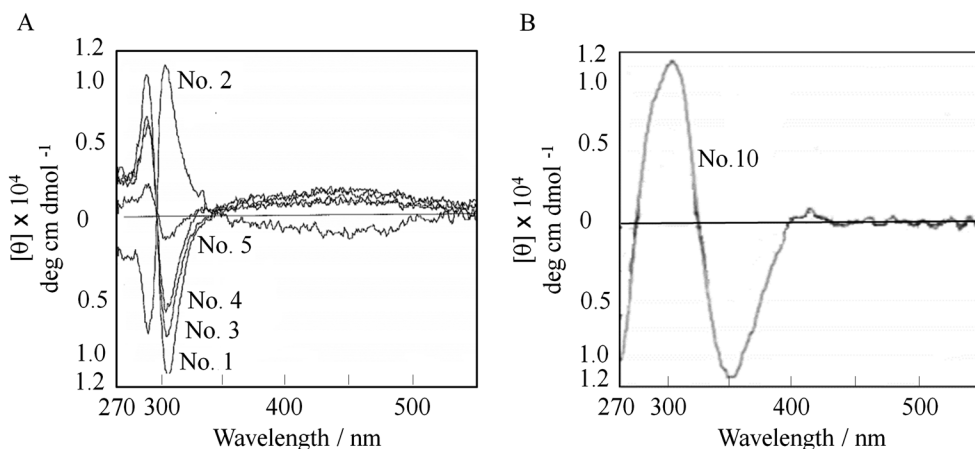
In this communication, to investigate the potential of the one-handed helical conformation of poly(substituted acetylenes) for asymmetric catalysis, we synthesized a novel chiral polymeric ligand for asymmetric catalyst for diethylzinc addition to benzaldehyde, i.e., a one-handed helical copolyacetylene having achiral amino alcohol pendant groups without the coexistence of any chiral moiety (copoly(1/2) in Chart 1). As a reference, a one-handed helical copolymer having chiral groups at the same time was prepared by the AIP of **1** with a chiral phenylacetylene (PSPA) bearing a chiral pinanylsilyl group and used for the reaction (Scheme S1). Achiral phenylacetylene monomer **1** having an amino alcohol residue was synthesized and copolymerized with **2** according to Scheme S1 and Scheme 1 (the detailed procedures are described in the Supporting Information).

The helix-sense-selective copolymerization of the two achiral phenylacetylenes, i.e., **1** having an amino alcohol residue and **2** having two hydroxyl groups, using  $[\text{Rh}(\text{nbd})\text{Cl}]_2(\text{nbd}$ : norbornadiene) as the polymerization initiator in toluene in the presence of (*S*)- or (*R*)-PEA, was carried out in accordance with our previously reported method to afford the chiral copoly(1/2) having achiral amino alcohol residues. The resulting copoly(1/2) showed the same CD absorptions as that of the homopoly(2) having the one-handed helical *cis-cisoidal* main chain prepared by the HSSP in our previous report,<sup>23,28</sup> i.e., strong and weak absorptions at the wavelengths around 307 and 430 nm with the opposite sign (Figure 1A),

indicating its predominant one-handed helical *cis-cisoidal* main-chain conformation. The signs of the CD spectra of the two copolymers prepared using (*S*)- or (*R*)-PEA were opposite (mirror image) (Figure 1A, Nos.1 and 2). This indicated that their helical senses of the corresponding copolymers were controllable in the HSSP. Hence, this copolymer has the potential to catalyze asymmetric reactions with a controllable enantioselectivity. The circular dichroism (CD) intensity of copoly(1/2) decreased with the increasing content of unit **1** in the copolymer (Table 1, Nos.1, 3–5). During the HSSP, under the control of the chiral rhodium initiator, the helical sense of the main chain of the poly(substituted acetylene) was induced, and the intramolecular hydrogen bonds between the hydroxyl groups of unit **2** could stabilize the induced helicity and made the helical conformation tight to be *cis-cisoidal*. Unit **1**, having no hydroxyl group, had no ability to maintain the induced helicity in the corresponding sequence, and therefore, the increased content of unit **1** in the copolymer weakened the chiral induction efficiency and the stability of the induced helicity during the HSSP, resulting in the decreased CD intensity. The AIP of **1** with a chiral phenylacetylene PSPA having a chiral pinanyl group afforded copoly(1/PSPA) having amino alcohol pendant groups (No. 10 in Table 1). The resulting copolymer showed the same CD pattern as the homopoly(PSPA) in our previous report,<sup>26</sup> i.e., two split absorptions at the wavelengths around 370 and 321 nm (Figure 1B) indicating its one-handed helical *cis-transoidal* conformation. All the resulting copolymers showed good solubilities in the common organic solvents, such as tetrahydrofuran (THF) and chloroform, although the homopoly(**1**) was totally insoluble.



**Scheme 1.** Synthesis of a chiral polymeric catalyst (copoly(1/2)) with its chiral structure alone in the one-handed helical backbone by helix-sense-selective copolymerization of achiral monomers(1 and 2)



**Fig. 1.** CD spectra of copoly(1/2) (A) and copoly(1/PSPA) (B) in THF at 25 °C (concentration =  $1 \times 10^{-3}$  M, optical path length = 1 mm) (for the codes, see chart 1 and table 1).

**TABLE 1.** Enantioselective alkylation of benzaldehyde with diethylzinc using one-handed helical polyphenylacetylenes as the chiral ligand<sup>a</sup>

No.	Chiral polymer catalyst			Asymmetric reaction			
	Code	Unit <b>1</b> content (%)	$[\theta]/10^4$ (deg cm/dmol)	Solvent	Yield <sup>f</sup> (%)	%ee <sup>g</sup>	Selectivity
1 <sup>b</sup>	copoly( <b>1/2</b> )	2.0	-1.2 <sup>d</sup>	THF	20.0	28.3	S
2 <sup>c</sup>		4.0	1.1 <sup>d</sup>	THF	19.3	20.4	R
3 <sup>b</sup>		3.4	-0.92 <sup>d</sup>	THF	18.9	13.8	S
4 <sup>b</sup>		10.0	-0.71 <sup>d</sup>	THF	17.5	5.3	S
5 <sup>b</sup>		20.0	-0.20 <sup>d</sup>	THF	13.8	2.7	S
6 <sup>c</sup>		4.0	0 <sup>d</sup>	THF/DMSO (9/1 v/v)	18.3	0.85	R
7	Racemic copoly( <b>1/2</b> )	4.0	0	THF	9.3	0	-
8 <sup>c</sup>	Homopoly( <b>2</b> )	100	1.2	THF	2.2	0	-
9	Monomer <b>2</b>	-	0	THF	5.2	0	-
10	copoly( <b>1/ PSPA</b> )	2.0	1.1 <sup>e</sup>	THF	9.4	16.1	S

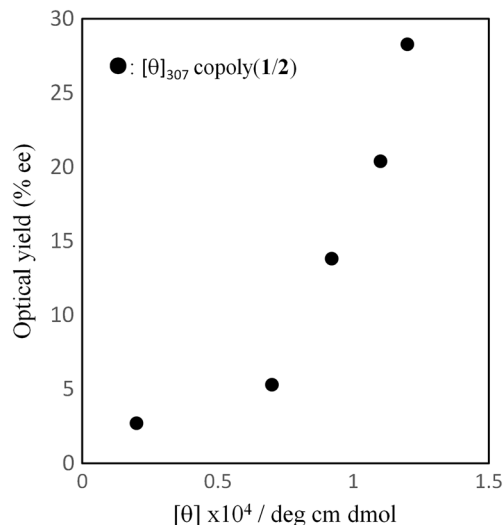
<sup>a</sup>Reactions were carried out for 24 h at 0 °C.<sup>b</sup>Copolymerized by using (*S*)-PEA as the cocatalyst.<sup>c</sup>Copolymerized by using (*R*)-PEA as the cocatalyst.<sup>d</sup> $[\theta]_{307}$ .<sup>e</sup> $[\theta]_{321}$ .<sup>f</sup>by GC.<sup>g</sup>By HPLC on Chiralcel OB.

The one-handed helical copoly(**1/2**)s, whose chirality arose solely from their one-handed helical conformation, were employed as optically active organocatalysts for the enantioselective diethylzinc addition to benzaldehyde in THF at 0 °C, the results of which are summarized in Table 1. For comparison, the result using the one-handed helical copoly(**1/PSPA**) prepared by the copolymerization of achiral **1** with chiral **PSPA** as the organocatalyst is also shown in Table 1.

The one-handed helical polymers without any other chiral moieties, copoly(**1/2**) (Table 1, No. 1) functioned as chiral catalysts because the optically active 1-phenylpropan-1-ol was obtained by the alkylation of benzaldehyde by diethylzinc in their presence as shown in Table 1. This was the direct evidence for the ability of the one-handed helical conformation to promote enantioselective catalysis. To the best of our knowledge, this is the first example of such a finding.

The copoly(**1/2**)s having the opposite CD sign prepared using (*S*)- or (*R*)-PEA showed the opposite enantioselectivity (Nos. 1 and 2 in Table 1), while the racemic copoly(**1/2**) (No. 7) prepared by using racemic PEA did not show any enantioselectivity. These facts indicated that the enantioselectivities can be controlled by the main-chain chirality of the polymeric asymmetric catalyst. Table 1 Nos.1,3-5 and Figure 2 show the relationship between the optical yields of the asymmetric addition and the CD intensities of the main-chain region of the polymers used as the catalysts. The optical yields (% enantiomeric excess [ee]) of the alkylations by copoly(**1/2**) increased with the increasing CD intensities. In other words, the higher one-handedness of the helix sense of the polymeric catalyst could produce higher enantioselectivity. These findings indicate the importance of the main-chain chiral helicity as the chiral source for the asymmetric alkylation of benzaldehyde. The primary importance of the macromolecular helicity regarding the enantioselectivity was also

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**Fig. 2.** Plots of the optical yield of benzaldehyde alkylation versus  $[\theta]$  values of the copolymer catalyst.

unambiguously supported by the following fact. Copoly(**1/2**) dissolved in THF/DMSO (9/1 v/v), in which its one-handed helical conformation was almost lost, showed almost no enantioselectivity (0.85% ee) (No. 6 in Table 1 and Figure S1). (Note: Because the polar DMSO molecules break the intramolecular hydrogen bonds, the resulting polymer showed no CD indicating the chiral structure was not maintained.)

The homopoly(**2**) prepared using (*R*)-PEA (No. 8) and monomer **2** (No. 9) showed no enantioselectivity and much lower yields for the diethylzinc addition to the benzaldehyde. It was found that the amino alcohol residue is necessary, as the ligand and the hydroxyl groups in **2** (monomer) and **2** unit in the polymers did not function as a chiral ligand.

As a reference, the copoly(**1**/PSPA) was also used as a catalyst for the alkylation of benzaldehyde and showed a lower optical yield (16.1% ee) than copoly(**1**/**2**) containing a similar amount of unit **1**, as shown in Table 1, Nos.1 and 10. The higher optical yield using copoly(**1**/**2**) might be caused by the tighter and more rigid chiral helical *cis-cisoid* conformation of copoly(**1**/**2**) making the chiral environment in copoly(**1**/**2**) more stable, and therefore, the chirality could be transferred more efficiently during the alkylation of benzaldehyde resulting in the higher enantioselectivity. The relatively loose and soft chiral helical *cis-transoidal* conformation of copoly(**1**/PSPA) made the chiral environment surrounding the active sites (amino alcohol groups' positions) unstable, which caused the lower optical yield than that using copoly(**1**/**2**). All the polymer catalysts could be easily and effectively recovered by precipitating the reaction mixture in methanol with more than 80% recovery yields.

In summary, novel copolyphenylacetylenes having achiral amino alcohol pendent groups (copoly(**1**/**2**)), whose chiral structures arise solely from the one-handed helical conformation, was successfully prepared by the helix-sense-selective copolymerization of two achiral phenylacetylenes, i.e., **1** having an achiral amino alcohol residue and **2** having two hydroxyl groups, using a chiral catalytic system ([Rh(nbd)Cl]<sub>2</sub>/(S)- or (R)-phenylethylamine). The chiral helical polymers were successfully used as the chiral ligand to catalyze the enantioselective diethylzinc addition to benzaldehyde in higher enantioselectivities than a chiral polymer having its chiral structures both in the main chain and the side groups. Since the sign of the chirality and %ee of the products of the alkylation catalyzed by copoly(**1**/**2**)s was controlled by the sign of the chirality and %ee of the catalyst, a controllable enantioselectivity of this polymeric chiral catalyst was found. In addition, the polymer catalysts could be recovered by precipitation after the reaction. To the best of our knowledge, this is the first example of an asymmetric catalyst for the enantioselective alkylation by one-handed helical polyphenylacetylenes without any other chiral moieties as a chiral ligand for the catalyst.

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article at the publisher's web-site.

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