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LETTERS

Synthesis of optically active polymers with chiral units attached to rigid backbones and their application for asymmetric catalysis

Qiao-Sheng Hu,* Chaode Sun and Colleen E. Monaghan

Department of Chemistry, The City University of New York-College of Staten Island, Staten Island, NY 10314, USA

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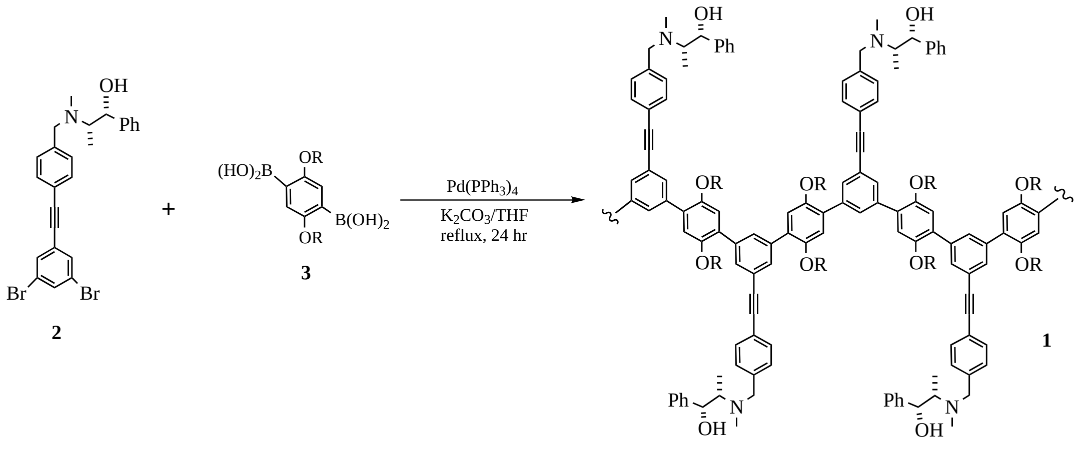
Abstract—Optically active ephedrine-bearing poly(phenylene)s have been synthesized by using the Suzuki coupling polymerization. Their application as polymeric chiral catalysts for asymmetric addition of diethylzinc to aldehydes has been studied and good enantioselectivity was observed. The strategy to synthesize these optically active polymers is potentially useful in the design and synthesis of other polymeric chiral catalysts for asymmetric catalysis. © 2001 Elsevier Science Ltd. All rights reserved.

The development of polymeric chiral catalysts for asymmetric catalysis has attracted extensive attention in recent years.[1] Due to the large size and solubility differences between the small organic molecules and polymers, polymeric chiral catalysts could be easily recovered from the reaction mixture by either filtration or precipitation, and be reused. Using polymeric chiral catalysts can also simplify the purification process and make it possible to conduct reactions in a flow reactor or flow membrane reactors for continuous production. Traditionally, polymeric chiral catalysts were synthesized by attaching a good monomeric chiral catalyst to sterically irregular polymer backbones such as polystyrenes.[2] Although significant enantioselectivity and reactivity drops are often observed due to the microenvironment change after the monomeric catalyst is attached to the irregular polymer backbone, this side-chain attachment strategy has the advantage of easy preparation. Recently, Pu and co-workers developed a new approach to optically active polymers with main chain chirality by incorporating chiral units into rigid polymer backbones.[3] This strategy can mostly preserve the high enantioselectivity of the monomeric chiral catalysts. However, it is sometimes very difficult or impossible to incorporate a monomeric chiral catalyst into the main chain of a polymer.

In our laboratory, we are interested in the development of new strategies, which will combine the advantages of the side-chain attachment strategy and main-chain



Scheme 1. Synthesis of optically active polymer **1**.

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* Corresponding author. Fax: 1-718-982-3910; e-mail: qiaohu@postbox.csi.cuny.edu

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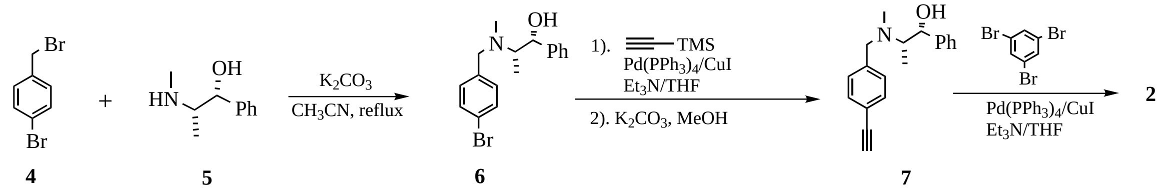
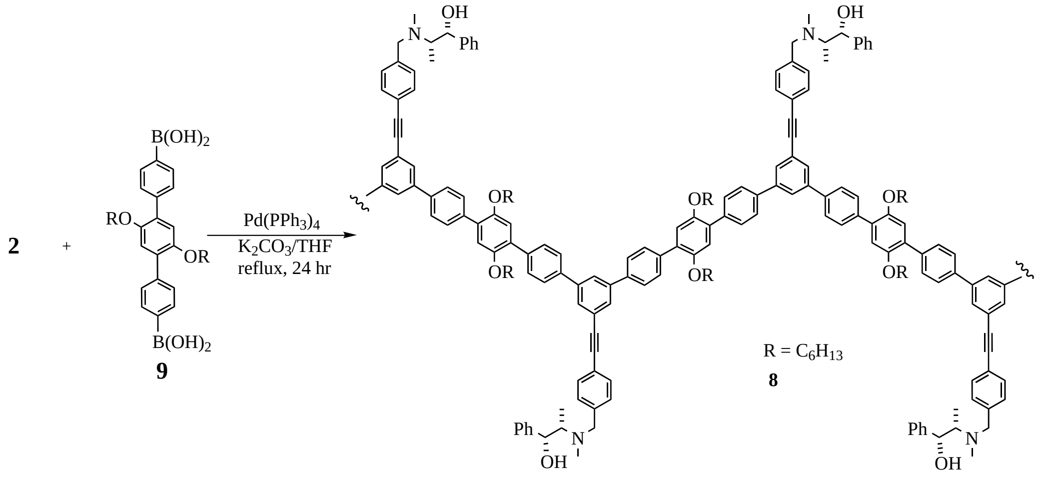
incorporation strategy, for the synthesis of novel optically active polymers. We have constructed optically active polymers with chiral units attached to rigid backbones through the Suzuki coupling polymerization of readily accessible chiral unit-bearing monomers with rigid linkers. In this letter, we report the synthesis of two optically active ephedrine-bearing poly(phenylene)s and their application as polymeric chiral catalysts for asymmetric diethylzinc addition to aldehydes.

We have synthesized (1*R*,2*S*)-ephedrine-bearing poly(phenylene) **1** by reaction of dibromide **2** with a diboronic acid **3**[4] in the presence of a catalytic amount of $Pd(PPh_3)_4$ (Scheme 1).[4,5] (1*R*,2*S*)-Ephedrine was chosen as the chiral unit because (1*R*,2*S*)-ephedrine-containing monomers and polymers have been well studied.[6] The preparation of **2** is shown in Scheme 2. In the presence of potassium carbonate, 4-bromobenzyl bromide (**4**) reacted smoothly with (1*R*,2*S*)-ephedrine (**5**) in acetonitrile to give **6**. $Pd(PPh_3)_4$/CuI-catalyzed cross-coupling of **6** with trimethylsilylacetylene followed by deprotection with K_2CO_3/MeOH yielded **7**.[7,8] Reaction of **7** with 1,3,5-tribromobenzene (2 equiv.) generated **2** in 80% yield. The excess 1,3,5-tribromobenzene can be easily removed by flash chromatography. Pd(0)-catalyzed Suzuki coupling polymerization of **2** and **3** yielded polymer **1** in 95% yield. **1** is soluble in common organic solvents such as methylene chloride, THF and chloroform. Gel permeation chromatography (GPC) analysis (polystyrene standards) shows its molecular weight is $M_w=7,200$, $M_n=4,900$ (PDI = 1.44). The specific optical rotation of **1** is $[\alpha]_D=-28.2$ ($c=0.43$, CH_2Cl_2). The well-resolved ^1H NMR spectrum indicates a well-defined structure.

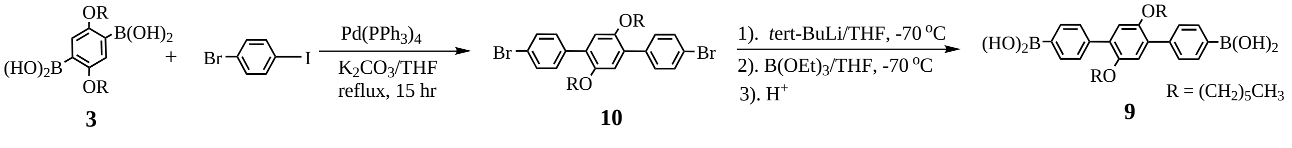
We have also carried out the synthesis of polymer **8** that has a longer linker between the adjacent chiral units by polymerization of **2** with diboronic acid **9** (Scheme 3). Diboronic acid **9** was obtained by a two-step procedure: the Suzuki coupling reaction of **3** with 1-bromo-4-iodobenzene generated **10** which was converted to **9** by reaction with *tert*-butyllithium at −70°C followed by treatment with triethyl borate and hydrolysis (Scheme 4). Polymer **8** was obtained in 95% yield and is also soluble in CH_2Cl_2, THF and chloroform. GPC analysis of **8** shows its molecular weight is $M_w=92\,900$, $M_n=35\,100$ (PDI = 2.65). The specific optical rotation of **8** is $[\alpha]_D=-76.6$ (*c* 0.42, THF). **8** Also gives well-resolved ^1H NMR spectrum, which is consistent with the polymer structures.[9]



Scheme 2. Synthesis of dibromide **2**.

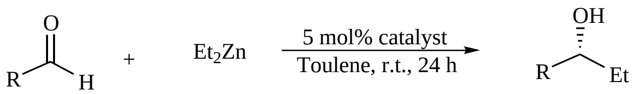


Scheme 3. Synthesis of optically active polymer **8**.



Scheme 4. Preparation of diboronic acid **9**.

Table 1. Asymmetric addition of diethylzinc to aldehydes catalyzed by polymers **1** and **8**[a]



Entry	Aldehydes	Polymer	Yield (%)	e.e. (%)[b]
1	Benzaldehyde	**1**	94	76
2	Anisoaldehyde	**1**	100	75
3	Benzaldehyde	**8**	83	74
4	Anisoaldehyde	**8**	95	74
5[c]	Benzaldehyde	**8**	82	76

[a] The reactions were carried out in toluene by using a 5 mol% polymeric catalyst (based on the polymer repeat unit) at rt for 24 h.

[b] The e.e.s were measured by using HPLC (Chiralcel OD column, hexane/isopropanol = 95:5; flow rate = 1 ml/min). The configuration of the product was assigned based on the specific optical rotation and the retention time of HPLC.

[c] Recovered polymer was used.

We have used **1** and **8** as polymeric chiral catalysts for the asymmetric addition of Et_2Zn to aldehydes (Table 1).[10] When **1** was used to catalyze the reaction of benzaldehyde with diethylzinc at room temperature, chiral 1-phenylpropanol was obtained in 76% e.e. When polymer **8** was used for the same reaction under same conditions, 1-phenylpropanol was obtained in 74% e.e. Similar enantioselectivity was also observed for the diethylzinc addition to anisoaldehyde. The enantioselectivity of these polymers is comparable to the results reported by Soai[6b] and Fréchet,[6e] but lower than that of the monomeric ephedrine derivative **6** (83% e.e for benzaldehyde). The fact that **1** and **8** exhibit the same enantioselectivity indicates that the chiral environment of the catalytically active sites of these two polymers are the same. The polymer catalysts can be easily recovered by precipitation from MeOH. The recovered polymer catalyst showed the same reactivity and enantioselectivity as the original polymer catalyst (entry 5).

In summary, optically active ephedrine-bearing poly(phenylene)s based on polymerization of readily accessible chiral unit-bearing monomers with rigid linkers have been synthesized and their application for asymmetric diethylzinc addition to aldehydes has been studied. The strategy to synthesize these optically active ephedrine-bearing poly(phenylene)s are potentially useful in the design and synthesis of other polymeric chiral catalysts for asymmetric synthesis.

Acknowledgements

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9. Synthesis and characterization of polymer **8**: To a mixture of dibromide **2** (540 mg, 1.05 mmol) and diboronic acid **9** (571 mg, 1.10 mmol) in 2 M K_2CO_3/THF was added $Pd(PPh_3)_4$ (30 mg) under N_2. The mixture was refluxed for 24 h and bromobenzene was added to cap the end. After another 6 h refluxing, the reaction mixture was cooled to room temperature and extracted with CH_2Cl_2. After washing with brine, the solvent was evaporated by using a rota-evaporator. The residue was redissolved in CH_2Cl_2 and precipitated from MeOH. The solid was collected by filtration. The dissolvation–precipitation–filtration sequence was repeated twice again. After drying under vacuum, polymer **8** was obtained in 95% yield (778 mg). GPC (polystyrenes standards): $M_w = 92\ 900$, $M_n = 35\ 100$ (PDI = 2.65). $[\alpha]_D = -76.3$ ($c = 0.42$, THF). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.90 (s, 1H), 7.83 (s, 2H), 7.76 (br. s, 8H), 7.51 (d, $J = 8.4$ Hz, 2H), 7.24–7.33 (m, 5H), 7.22 (d, $J = 8.4$ Hz, 2H), 7.09 (s, 2H), 8.70 (s, 1H), 3.99 (t,

$J = 6.6$ Hz, 4H), 3.62 (s, 2H), 3.21 (s, 1H), 2.93 (m, 1H), 2.21 (s, 3H), 1.72–1.77 (m, 4H), 1.42 (m, 4H), 1.29 (br, s, 8H), 1.01 (d, $J = 8.4$ Hz, 3H), 0.87 (t, $J = 6.0$ Hz, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 150.41, 142.53, 141.74, 140.16, 138.89, 137.89, 135.60, 131.63, 130.34, 130.04, 128.62, 128.04, 127.05, 126.76, 126.19, 124.30, 121.68, 116.15, 89.60, 89.23, 73.91, 69.67, 63.54, 58.85, 38.68, 31.47, 29.32, 25.78, 22.61, 14.03, 9.85. UV–vis λ_{max} (CH_2Cl_2) 229, 293, 337 nm. Anal. calcd for $C_{55}H_{59}NO_3$: C, 84.51; H, 7.55; N, 1.79. Found: C, 83.36; H, 7.49; N 1.79.

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