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Optically active dendronized polymers as a new type of macromolecular chiral catalysts for asymmetric catalysis

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Abstract—Optically active ephedrine-bearing dendronized polymers were synthesized by using the Suzuki coupling polymerization. These novel polymers are soluble in common organic solvents such as THF, toluene and chloroform. Their application as a new type of macromolecular chiral catalysts for asymmetric catalysis was studied. The combination features of more catalytic sites, higher solubility and nanoscopic dimensions of optically active dendronized polymers make them more efficient than the corresponding linear polymeric and dendritic chiral catalysts. This study provides a new direction for the design and synthesis of macromolecular chiral catalysts. © 2002 Elsevier Science Ltd. All rights reserved.

The development of highly efficient macromolecular chiral catalysts for asymmetric catalysis is of great interest to both academia and industry. Easy recovery and reuse, simplified reaction work-up and potential to conduct reactions in a flow reactor or flow membrane reactor for the continuous production are among the attractive features of using macromolecular chiral catalysts.[1,2] To date, two types of macromolecular chiral catalysts have been developed: linear polymeric chiral catalysts and dendritic chiral catalysts. Although linear polymeric chiral catalysts with the enantioselectivity parallel to that of monomeric chiral catalysts have been developed,[3,4] their efficiency for asymmetric catalysis has been limited due to the nature of one catalytic site per repeat unit. Dendritic catalysts with chirality derived from the periphery of the dendrimer can have many catalytic sites around the dendrimer.[5] They could potentially be more efficient than linear polymeric catalysts. However, periphery-modified dendritic chiral catalysts have found limited success in asymmetric catalysis.[6] Most of the periphery-modified dendritic catalysts developed to date showed lower enantioselectivity than their corresponding monomeric catalysts. It is speculated that the lower enantioselectivity results from the highly condensed packing in the periphery of the dendrimers which causes the chiral environment very different from that of monomeric catalysts. Lower generation dendrimers that are less densely packed in the periphery have thus been used for the asymmetric catalysis and showed that they can mostly maintain the enantioselectivity of monomeric chiral catalysts. However, because the size difference between lower generation dendrimers and small molecules such as the reaction products is relatively small, it is more difficult to recover the dendritic catalysts from the reaction mixture by filtration or precipitation. It is thus fundamentally interesting and practically very useful to develop new types of macromolecular chiral catalysts that will combine both the advantages of dendritic and linear polymeric chiral catalysts.

In our laboratory, we are interested in synthesizing optically active dendronized polymers for asymmetric catalysis as well as for materials application. Dendronized polymers are macromolecules with dendritic side chains attached to polymeric cores.[7–10] Optically active dendronized polymers containing less densely packed, lower generation dendritic wedges with monomeric chiral units in their peripheries have great potential to compete with linear polymers and dendrimers for asymmetric catalysis. They could overcome the densely packing problem existing in the dendrimer-based chiral catalysts without sacrificing the advantage of easy recovery by either filtration or precipitation. They also possess multiple catalytic sites per repeat unit with higher solubility. These optically active dendronized polymers represent a new type of macromolecular chiral catalysts. Herein we report the synthesis of (1*R*,2*S*)-ephedrine-bearing dendronized polymers **1** and **2** as the first optically active dendronized polymers for asymmetric catalysis.

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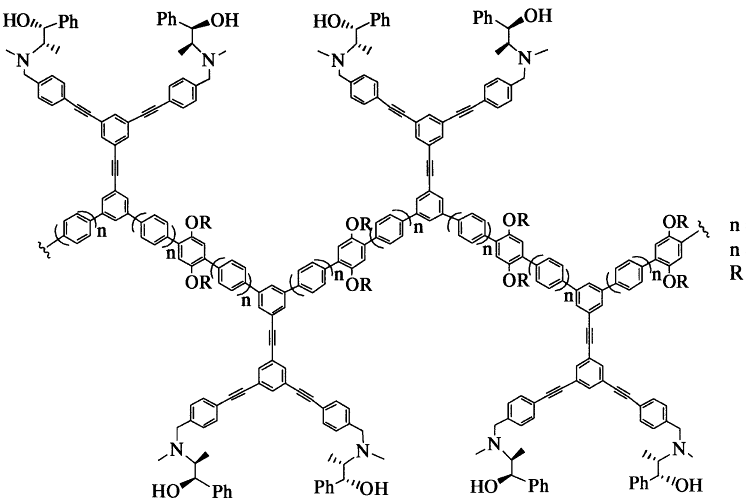
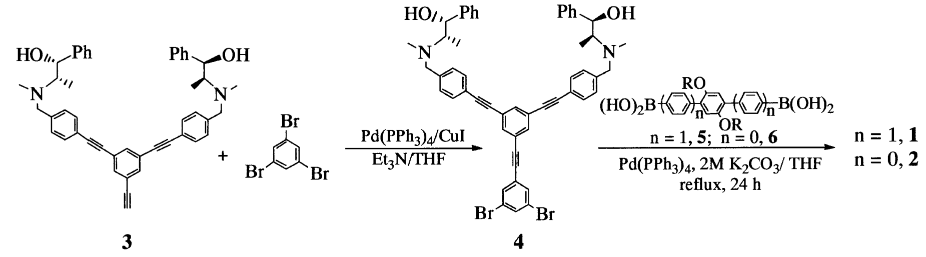


n = 1, **1**
n = 0, **2**
R = n-C_6H_{13}

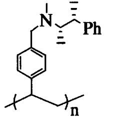
We have chosen (1*R*,2*S*)-ephedrine-bearing dendronized polymers with poly(phenylene) backbones as the first examples of optically active dendronized polymers for asymmetric catalysis because of the well-established chemistry of optically active ephedrine-bearing linear polymers and dendrimers,[6a–b,11,12] and the stiffness and easy elaboration of poly(phenylene) backbones.

We have carried out the synthesis of optically active dendronized polymers **1** and **2** by the Suzuki coupling polymerization of optically active dendronized monomer **4** with diboronic acid **5**[12] and **6**,[13] respectively (Scheme 1).[7a] Dendronized monomer **4** was prepared in 80% yield by $Pd(PPh_3)_4$/CuI-catalyzed coupling reaction of **3** with 1,3,5-tribromobenzene (2.5 equiv.).[6a]

Both **1** and **2** were obtained in high yields and are soluble in common organic solvents such as THF, toluene, and dichloromethane. Gel permeation chromatography (GPC) analysis (polystyrene standards) shows the molecular weight of **1** is $M_w = 141\,100$, $M_n = 50\,400$ (PDI = 2.80). The specific optical rotation of **1** is $[\alpha]_D = -43.1$ (*c* 0.42, CH_2Cl_2). The molecular weight of **2** is $M_w = 20\,600$, $M_n = 12\,700$, PDI = 1.62. Its specific optical rotation is $[\alpha]_D = -36.2$ (*c* 0.42, CH_2Cl_2). Both **1** and **2** gave well-resolved ^1H NMR spectra which are consistent with the expected structures.



Scheme 1. Synthesis of optically active dendronized polymers **1** and **2**.



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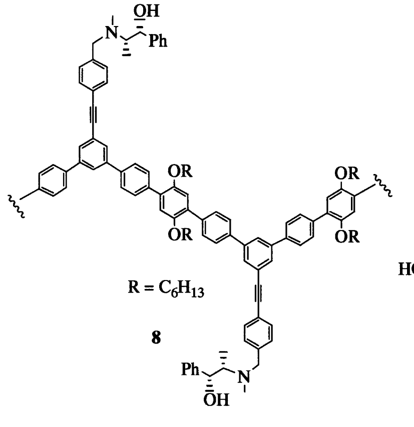

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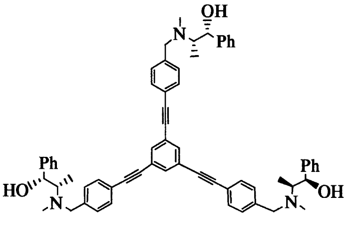

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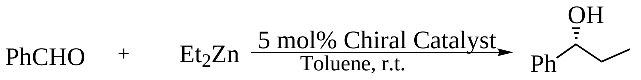

Scheme 2. The catalytic asymmetric addition of Et_2Zn to benzaldehyde.

We have used **1** and **2** as macromolecular chiral catalysts for the asymmetric addition of diethylzinc to benzaldehyde (Scheme 2)[14] and have compared the catalytic properties of these dendronized polymers with their corresponding linear polymeric and dendritic chiral catalysts. We find that **1** and **2** are more efficient than their corresponding linear polymeric and dendritic chiral catalysts. In the presence of 5 mol% of **1** or **2** (based on the polymer repeat unit) in toluene, diethylzinc adds to benzaldehyde to afford the addition product (*R*)-1-phenyl-1-propanol in 75% e.e. and 73% e.e., respectively.[15] The enantioselectivity of **1** and **2** is as good as that of polymers **7** (76% e.e.) and **8** (74% e.e.), and dendrimer **9** (78% e.e.) for the same reaction.[6a,11c,12] 99% conversion of benzaldehyde is observed after 12 h for both **1** and **2**. However, 24 h are needed to achieve the same conversion when **8** was used to catalyze the reaction.[12] Compared to **9** which was recovered by flash chromatography after the reaction,[6a] **1** and **2** can be easily recovered by filtration and reused. The recovered **1** shows the same reactivity and enantioselectivity (99% conversion of benzaldehyde after 12 h, 76% e.e.). Although **1** only shows 76% enantioselectivity for the asymmetric addition of Et_2Zn to benzaldehyde due to the nature of ephedrine chiral units, it can be anticipated that highly enantioselective dendronized polymers can be developed when highly enantioselective monomeric chiral units are used for the construction of dendronized polymers.

In summary, the first optically active ephedrine-bearing dendronized polymers as a new type of macromolecular chiral catalysts for asymmetric catalysis have been designed and synthesized. The combination features of more catalytic sites, higher solubility and nanoscopic dimensions of optically active dendronized polymers make them more efficient than their corresponding linear polymeric and dendritic chiral catalysts. This study provides a new direction for the design and synthesis of highly efficient macromolecular chiral catalysts.

Acknowledgements

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15. The e.e.s were measured by using HPLC (Chiralcel OD column). The configuration of 1-phenyl-1-propanol was assigned based on specific optical rotation and HPLC results.