ACS Macro Letters

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Complementary Induction of Right- and Left-Handed Helical Structures by the Positioning of Chiral Groups on the Monomer Units: Introduction of (−)-Menthol as Side Chains of Poly(quinoxaline-2,3-diyl)s

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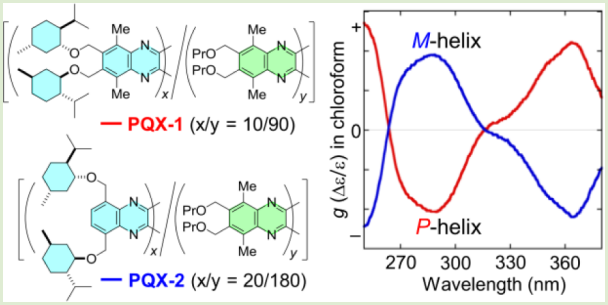
Supporting Information

ABSTRACT: Poly(quinoxaline-2,3-diyl) bearing menthyloxymethyl side chains derived from (−)-menthol at the 6- and 7-positions of the quinoxaline ring showed a single, right-handed helical structure in chloroform. Upon introduction of the same (−)-menthol-derived side chains into the 5- and 8-positions, a single, left-handed helical structure was formed in chloroform. The former poly(quinoxaline-2,3-diyl)s showed solvent-dependent inversion of the helical sense in 1,1,2-trichloroethane to form a left-handed helical structure with high screw sense purity. Copolymers bearing both menthyloxymethyl and *o*-(diphenylphosphino)phenyl groups in their side chains served as highly enantioselective chiral ligands in the palladium-catalyzed hydrosilylation of styrene.



Increasing attention has been focused on the control of the helical structure of synthetic polymers, aiming at applications in chiral technologies.[1−6] In particular, much effort has been devoted to the control of screw sense in helical polymers devoid of chiral stereogenic elements in their main chains since their screw sense can be switched reversibly to another mirror image screw sense by external stimuli such as guest molecules, temperature, solvent, etc.[7−18] The induction of a nonracemic helical main chain structure has been achieved most conveniently by the introduction of a chiral auxiliary into the polymer side chains. Nonracemic helical structures have thus been successfully induced in polyacetylenes,[19−21] polyisocyanates,[22−28] polyisocyanides,[29−35] polyguanidines,[36,37] and polysilanes.[38,39]

We recently established a macromolecular system where nonracemic helical structure is induced by the introduction of chiral 2-butoxymethyl side chains,[40] utilizing poly(quinoxaline-2,3-diyl) as a polymer scaffold.[41−44] By the introduction of (*R*)-2-butoxymethyl groups at the 6- and 7-positions of the quinoxaline ring, a pure right-handed helical structure is formed in various organic solvents, such as $CHCl_3$. The helical structure undergoes solvent-dependent inversion of the helical sense to the left in 1,1,2-trichloroethane (1,1,2-TCE). We confirmed that, in $CHCl_3$ and 1,1,2-TCE, pure right- and left-handed helical structures, respectively, were formed selectively under thermodynamic control. The system was successfully extended to new polymer-based chiral catalysts, showing not only high enantioselectivities but also a switch of chirality for the highly enantioselective production of both enantiomers in various palladium-catalyzed reactions.[45−49]

In the strategy where induction of the helical sense relies on the chiral side chains, the cost and availability of the side chains are important from the viewpoint of practicality. In many cases, including our system, the use of expensive and hardly available chiral auxiliaries has been required. Utilizing an inexpensive chiral auxiliary taken from the natural chiral pool would thus be an attractive possibility. However, the use of naturally occurring chiral substances often presents difficulties in terms of obtaining their unnatural enantiomers, making it difficult to obtain either of the two helical structures.

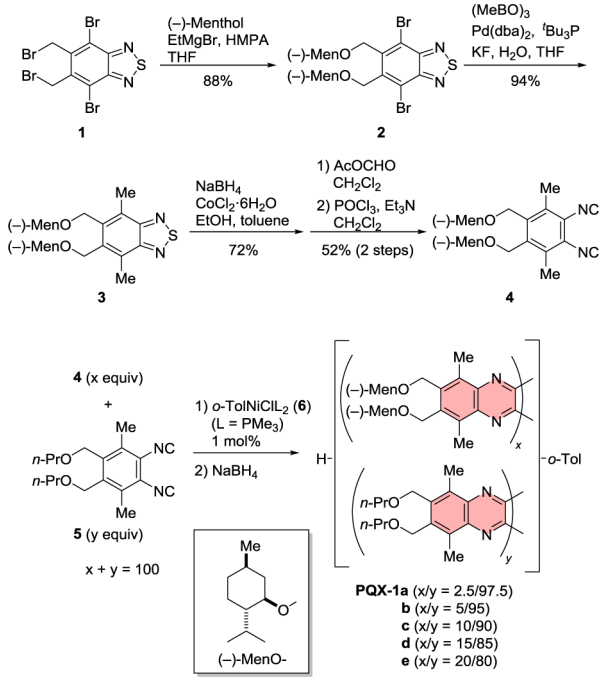
In this paper, we discuss the possibility of the induction of both helical senses from a single natural molecule, i.e., (−)-menthol, in our poly(quinoxaline-2,3-diyl) system. The introduced chiral side chains on the monomer unit can change the induced helical sense completely. Application of the helical sense induction to catalytic asymmetric synthesis is also demonstrated.

Diisocyanobenzene **4** bearing menthyloxymethyl groups, derived from (−)-menthol, was prepared from the versatile building block **1** with (−)-menthol via five steps (Scheme 1). The chiral monomer **4** was copolymerized with achiral monomer **5**, which has propoxymethyl side chains at its 6- and 7-positions, in the presence of organonickel initiator **6**. We

Received: June 24, 2013
Accepted: August 16, 2013
Published: August 20, 2013

   dx.doi.org/10.1021/mz4003326 | *ACS Macro Lett.* 2013, 2, 790−793

Scheme 1. Synthesis of PQX-1



prepared copolymer **PQX-1a-e** with various ratios of **4** and **5**, maintaining a degree of polymerization of 100, by using 1 mol % **6** in the living polymerization. Polymerization of monomer **4** without **5** failed due to low solubility of the resultant homopolymer. Thus, copolymers **PQX-1a-e** showed differences in their circular dichroism (CD) spectra: the intensities of the spectra depended on the ratio of **4** to **5**, but the shapes of the spectra remained unchanged. The g values, i.e., Kuhn's dissymmetry factors, which are proportional to the screw sense excess, were plotted against the number of chiral monomer units in the 100mers (Figure 1). The g value, i.e.,

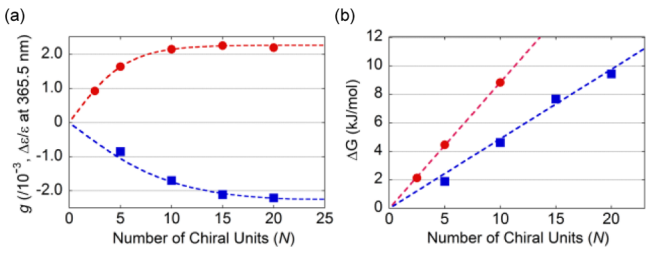


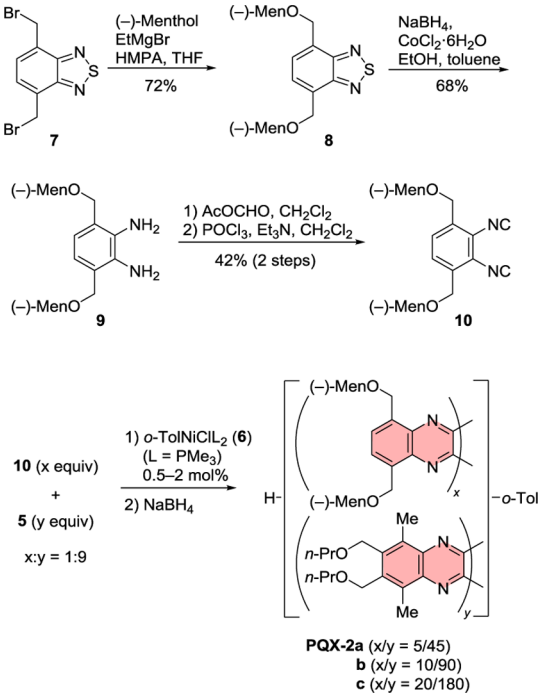
Figure 1. (a) Relationships between number of chiral units N and dissymmetry factor g of **PQX-1** in $CHCl_3$ (red circle) and 1,1,2-TCE (blue square). (b) Relationships between number of chiral units N and helical stabilization energy ΔG in $CHCl_3$ (red circle) and 1,1,2-TCE (blue square).

screw sense excess, reached a maximum upon the inclusion of 15 chiral monomer units. A hyperbolic tangent curve can be fitted to the nonlinear plot of the number of chiral units against the g values in 100mers, assuming that a 100% pure right-handed helix has a g value of 2.27×10^{-3}. This assumption led to the establishment of a linear relationship between the energy difference (ΔG) between the right-handed and left-handed helices and the number of chiral units. From the slope of the linear relationship, each chiral monomer unit is assumed to gain 0.89 kJ/mol for the stabilization of the right-handed helical structure in **PQX-1** in $CHCl_3$. This helix stabilization energy (E_h) is higher than the value (0.59 kJ/mol) reported in our original system using 2-butoxymethyl side chains for the induction of main chain helical chirality.[40]

The copolymers **PQX-1** showed solvent-dependent switching of helical chirality. In 1,1,2-TCE, which we reported to induce helical inversion in a previous system,[40] we again observed the formation of a left-handed helical structure. To induce a pure left-handed helical structure in 1,1,2-TCE, more than 20 chiral monomer units were required, and the E_h in 1,1,2-TCE is assumed to be 0.48 kJ/mol for a left-handed helical structure.

We then turned our attention to the introduction of the same (−)-menthyloxymethyl side chains at the 5- and 8-positions of the quinoxaline ring. Monomer **10** was prepared from di(bromomethyl)thiadiazole **7** via four steps (Scheme 2). In

Scheme 2. Synthesis of PQX-2



the copolymerization of **10** with achiral **5**, we had difficulty with the estimation of the E_h of the copolymers with different **10**/**5** ratios because the shapes of the CD spectra change depending on the ratio.[50] To estimate the E_h of the chiral units derived from **10**, we synthesized copolymers of **10** and **5** in which the degrees of polymerization were varied, while keeping the ratio of **10** to **5** at 1:9. It is interesting to note that the helical sense formed in $CHCl_3$ was found to be "left", in contrast to the formation of the right-handed helical structure with chiral monomer **4** derived from the menthol with same absolute configuration. We assumed the E_h in $CHCl_3$ to be 0.40 kJ/mol for the left-handed helical structure (Figure 2). Interestingly, in contrast to **PQX-1**, **PQX-2** did not undergo helical inversion in 1,1,2-TCE. In 1,1,2-TCE, we observed an even higher stabilization energy (0.68 kJ/mol) for the left-handed helix.

We then prepared high-molecular-weight ternary copolymers **PQXphos-1** from chiral monomer **4**, achiral monomer **5**, and phosphorus-containing monomer **11** for application to chiral ligands for palladium-catalyzed asymmetric hydrosilylation

dx.doi.org/10.1021/mz4003326 | ACS Macro Lett. 2013, 2, 790−793

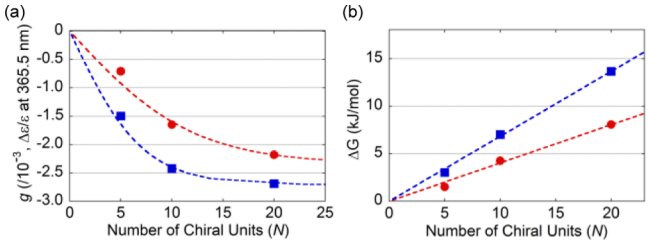
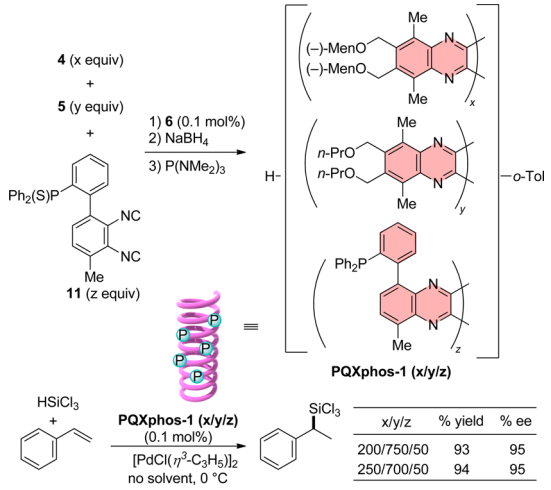


Figure 2. (a) Relationships between number of chiral units N and dissymmetry factor g of **PQX-2** in $CHCl_3$ (red circle) and 1,1,2-TCE (blue square). (b) Relationships between number of chiral units N and helical stabilization energy ΔG in $CHCl_3$ (red circle) and 1,1,2-TCE (blue square).

Scheme 3. Synthesis of Ternary Copolymers PQXphos-1 as Chiral Ligands for Palladium-Catalyzed Hydrosilylation of Styrene



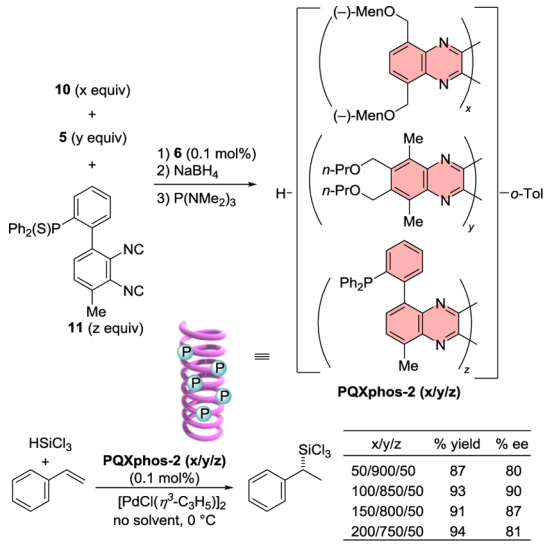
x/y/z	% yield	% ee
200/750/50	93	95
250/700/50	94	95

(Scheme 3).[51] To induce a pure right-handed helical structure, we introduced 20−25% chiral units for the preparation of the 1000mer. Coordination units (5%) were incorporated by using monomer **11** according to our previous optimization.[47] **PQXphos-1** containing 20% and 25% chiral (−)-menthyloxymethyl side chains both afforded an enantioenriched product with 95% ee (*S*) in the palladium-catalyzed hydrosilylation of styrene with trichlorosilane.

We also prepared **PQXphos-2** (1000mer) by copolymerization of **5**, **10**, and **11** (Scheme 4). It was interesting to find that, in spite of the g values reaching a maximum when 15% chiral units were incorporated, the enantioselectivities of the hydrosilylation reached a maximum upon the inclusion of 10% chiral units. Incorporation of a greater percentage of chiral units resulted in lower enantioselectivity. It is likely that the incorporation of a bulky chiral group at the 5- and 8-positions results in disorder of the helical structure by steric repulsion. As a result of the two conflicting effects of an increase in the percentage of chiral monomer units, the highest enantioselectivity was attained when 10% chiral units were incorporated. These results of asymmetric reactions clearly demonstrated the formation of right- and left-handed helical structures with high screw-sense excesses in those systems.

In summary, we have established that the position of the introduction of a chiral side chain to the monomer unit alters the induced screw sense of dynamic helical polymers. On the basis of this finding, even natural chiral auxiliaries, which are

Scheme 4. Synthesis of Ternary Copolymers PQXphos-2 as Chiral Ligands for Palladium-Catalyzed Hydrosilylation of Styrene



x/y/z	% yield	% ee
50/900/50	87	80
100/850/50	93	90
150/800/50	91	87
200/750/50	94	81

often available in only one of the two enantiomeric forms, can be utilized for the selective induction of both right- and left-handed helical structures. In addition, we found that even helical polyquinoxalines whose single-handed screw sense is induced by rigid (−)-menthol undergo solvent-dependent inversion of the helical sense, as observed in the related polymer whose helical chirality was induced by a flexible 2-butoxy group. Our findings may be extended to the synthesis of new polymer-based chiral ligands whose helical sense formation relies on a readily available chiral auxiliary.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details and characterization data of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by CREST, Japan Science and Technology Agency (JST).

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