Non-hydrogen-bonding-based, solvent-dependent helix inversion between pure *P*-helix and pure *M*-helix in poly(quinoxaline-2,3-diyl)s bearing chiral side chains[†]

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Poly(quinoxaline-2,3-diyl)s bearing chiral (R)-2-butoxy side chains adopt pure right- or left-handed screw senses in CHCl₃ and 1,1,2-trichloroethane, respectively.

Efficient control of the screw sense of helical macromolecules has gained much attention during the search for their novel macromolecular functions.¹ Particular attention has been paid to helical polymers with no unracemizable stereogenic centers or axes in the polymer main chain, because they are virtually interconvertible between the two mirror image helical senses. Their nonracemic helical structures are typically induced by chiral groups attached as side chains or as terminal groups. Recent interest has focused on the reversible control of the helical sense of such polymers by external, symmetric stimuli such as heat,² light,³ solvent,^{4,5} and metal ions.⁶ It should be noted that most reported macromolecular right–left (P-M) transitions of the helical sense do not concern the degree of screw-sense induction, although it must be the most important measure for the applicability and controllability of chiral macromolecular systems.

Poly(quinoxaline-2,3-divl)s are a unique class of helical polymers, being prepared via living polymerization of o-diisocyanobenzenes.7 We have succeeded in the screw-sense selective synthesis of the polymers by introducing a chiral terminal group, which is derived from the chiral initiators.⁸ Our recent report has demonstrated that poly(quinoxaline-2,3diyl)s bearing a metal-binding phosphorus group in the middle of the polymer backbone induce enantioselectivity up to 87% ee in the palladium-catalyzed asymmetric hydrosilylation of styrenes.9 In this Communication, we report the synthesis of a series of poly(quinoxaline-2,3-diyl)s bearing chiral side chains devoid of a chiral terminal group. We observed a nonlinear relationship between the calculated s.e. (screw-sense excess) and the number of chiral units in the polymer backbone, which can be rationalized by a linear relationship in terms of free energy. We found a unique solvent-dependent helical-sense induction, leading to formation of pure right-handed helix in chloroform and of pure left-handed helix in 1,1,2-trichloroethane.

A series of random copolymers of achiral 1 and (*S*)- or (*R*)-2, which has (*S*)- or (*R*)-2-butoxymethyl groups as side chains, respectively, was prepared with an achiral organonickel initiator with various ratios of 1 and 2 (Scheme 1, Table 1).¹⁰ In addition to those copolymers consisting of 40 monomer units in total, homopolymers, poly-2, with higher polymerization degrees (n = 100 and 200) were prepared in a similar way. All the polymers obtained in these experiments are highly soluble in common organic solvents such as hexane, toluene, THF, ether and CHCl₃. The averaged molecular weights as well as PDI (M_w/M_n) were almost constant for all the 40 mers consisting of various ratios of 1 and 2, suggesting that the reactivities of 1 and 2 are almost equal under the polymerization conditions.



Scheme 1 Random living copolymerization of achiral monomer 1 and enantiopure chiral monomer (R)- or (S)-2.

Table 1 Properties of homopolymers (poly-1 and poly-(R)-2) and random copolymers poly-1/(R)- 2^a

Polymer					
	1/Ni ^b	$2/Ni^c$	$M_{\rm n}/10^{3d}$	$M_{\rm w}/M_{\rm n}$	$g_{\rm abs}/10^{-3e}$
Poly-1	40	0	6.8	1.08	_
Poly-1/2 (95/5)	38	2	7.5	1.07	0.56
Poly-1/2 (90/10)	36	4	7.7	1.07	1.07
Poly-1/2 (80/20)	32	8	7.7	1.08	1.76
Poly-1/2 (70/30)	28	12	8.2	1.08	2.13
Poly-1/2 (50/50)	20	20	7.9	1.08	2.38
Poly-1/2 (30/70)	12	28	7.9	1.09	2.34
Poly-2	0	40	7.9	1.07	2.36
Poly-2 (100)	0	100	28	1.06	2.32
Poly-2 (200)	0	200	58	1.04	2.46

^{*a*} Data for poly-1/(S)-2 are shown in the supplementary information. ^{*b*} Molar ratio of 1 and the initiator. ^{*c*} Molar ratio of 2 and the initiator. ^{*d*} Polystyrene standard. ^{*e*} Dissymmetry factor ($\Delta \varepsilon / \varepsilon$) per monomer unit at 366 nm.

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Fig. 1 Plots of screw-sense excesses (curve) and energy difference (straight line) in chloroform against mean number of chiral (R)- or (S)-2 units in poly-1, poly1/2, and poly-2.

As a measure of the degree of single-handed screw sense, CD spectra were measured in CHCl₃. All polymers containing (R)-2 showed typical spectra for the *P*-helical poly(quinoxaline-2.3diyl)s with varying intensities, which are represented by dissymmetry factors ($\Delta \varepsilon / \varepsilon$) per monomer unit, *i.e.*, g_{abs} (Table 1).¹¹ The nonlinear relationship between g_{abs} and mean numbers of the chiral units in 40 mers has been converged into a hyperbolic tangent curve, when 100% pure P-helix is assumed to have g_{abs} of 2.39 $\times 10^{-3}$ (the dotted curve in Fig. 1).^{12,13} This assumption leads to the establishment of a linear relationship between the energy difference between P and M helices and the mean numbers of chiral units (Fig. 1, the straight line). From the linear relationship, we conclude that poly(quinoxaline-2,3-diyl)s are in an equilibrium between P- and M-helices, of which the energy difference between the two screw senses is proportional to the number of chiral units in the polymer chain. Moreover, it also leads us to the conclusion that each polymer chain has no jointing of P- and M-helices. It is assumed that each chiral monomer unit gains 0.59 kJ mol⁻¹ for the *P*-helix in CHCl₃.

We observed an intriguing dependence of the CD intensities of poly-(R)-2 (n = 40) on solvent (Fig. 2). In particular, use of 1,1,2trichloroethane (1,1,2-TCE) resulted in a complete switch of its screw sense to M (the red curve in Fig. 2). The CD spectra continuously changed with the change of the 1,1,2-TCE/CHCl₃ ratio. In a 60:40 mixture of 1,1,2-TCE and CHCl₃, no Cotton effect was observed, indicating that the left- and right-handed helical macromolecules coexist almost in a 1:1 ratio. The helix inversion could be repeated several times with no drop of s.e. by changing the solvent through evaporation in vacuo.¹⁴ The plot of ΔG against the content of chiral monomer units also shows their linear relationship, from which the gained energy difference per (R)- or (S)-2 unit in 1,1,2-TCE was determined to be 0.35 kJ mol^{-1} for the M-helix (Fig. 3). Although the magnitude of this value was considerably smaller than that in CHCl₃ (0.59 kJ mol⁻¹), accumulation of 40 monomer units was sufficient to form an



Fig. 2 CD spectra of poly-(R)-**2** in 1,1,2-trichloroethane/CHCl₃ with varied ratios.



Fig. 3 Plots of screw-sense excesses (curve) and energy difference (straight line) in 1,1,2-trichloroethane against mean number of chiral (*R*)- or (*S*)-2 units in poly-1, poly1/2, and poly-2.



Fig. 4 Estimated screw-sense excesses of poly-(*R*)-2 in various solvents. The screw-sense excesses are estimated by comparison of the *g* values obtained in each solvent with the maximum *g* value (2.39×10^{-3}) in CHCl₃.

almost perfect *M*-helix. CD measurements for poly-(*R*)-**2** (40 mer) in various solvents revealed that the *P*-helical conformation was strongly preferred in CHCl₃, CH₂Cl₂, THF, and 1-butanol, while moderate *P*-helix induction was observed in 1,1,1-TCE, 1-chlorobutane, and 1-bromobutane (Fig. 4). In valeronitrile (BuCN), 1,2dichloroethane (1,2-DCE), and 1,3-dichloropropane (1,3-DCP), moderate *M*-helix induction was observed.

Another interesting feature is the dependence of the CD intensity on polymerization degree (Fig. 4). Thus, poly-(R)-2(40 mer) showed ca. 50% s.e. in 1-chlorobutane, suggesting each monomer unit favors the P-helix over the M-helix by just 0.06 kJ mol^{-1} . The corresponding 100 mer (the light blue bar) and 200 mer (the dark blue bar) resulted in the formation of P-helix with 75% and >95% s.e, respectively. This significant increase in the screw-sense excess clearly relies on the long helix persistent length of poly(quinoxaline-2,3-diyl)s. Although a solvent-dependent switch of screw sense has been reported for several chiral polymer systems,⁴ most of them rely on hydrogen bonding at the polymer side chains containing amide groups. As far as we are aware, there is only one precedent for non-hydrogen-bonding-based switch of helical chirality by achiral solvents, in which cis-polyacetylene bearing chiral 2-methylbutoxy groups was measured in CHCl₃ and hexane.^{4d} In that system, however, no s.e. was determined and helix induction in CHCl₃ was much less than that in hexane.

Although the origin of the change of helical chirality in poly-2 is not clear at this moment, the phenomenon is not limited to the polyquinoxalines bearing 2-butoxymethyl side chains. The corresponding polyquinoxaline poly-3 bearing 3-methylpentyl side chains, in which the oxygen atom of the 2-butoxymethyl group is replaced with a methylene group, showed a similar solvent dependent switch of helical chirality. Thus, poly-(S)-3, whose side chains have virtually the same chirality as those in poly-(S)-2, took (M)- or (P)-helical structure in CHCl₃ and 1,1,2-TCE, respectively (Fig. 5). Although the degree of helix sense induction in each solvent has not been determined yet, this result suggests



Fig. 5 CD spectra of poly-(S)-3 in 1,1,2-trichloroethane and CHCl₃.

that the solvent-dependent helix inversion does not rely crucially on the presence of an oxygen atom in the side chain.



It seems to be interesting to discuss the cause of the solvent dependent helical sense inversion. Fig. 6 shows four representative conformers A-D of helical poly(quinoxaline-2,3-diyl) poly-(R)-2 bearing chiral (R)-2-butoxy group, of which only 5 quinoxaline units are shown. The (R)-2-butoxy groups except for those on the central quinoxaline ring are omitted for clarity. The anti orientation of the two (R)-2-butoxy groups should be preferred for the steric reason. Steric repulsion between the (R)-2-butoxy group and the quinoxaline ring in conformers B and C may make these conformations unfavorable, resulting in the preferential formation of conformers A and D. We assume that, for any reason, the conformer A is favorable in chloroform, and conformation D is favored in 1,1,2-TCE, although the cause of the solventdependent conformational change of the chiral groups should be clarified. The observed helix inversion of poly-(S)-3 indicates that the solvent-dependent conformational change of the chiral side chains is not limited to the alkoxy group, but extended to the chiral alkyl group, which lacks an oxygen atom.



Fig. 6 Possible conformations of poly-(*R*)-**2**. Only five quinoxaline units, of which chiral side chains except for those on the central quinoxaline ring are omitted for clarity, are shown.

In summary, we have established that poly(quinoxaline-2,3diyl)s bearing chiral (R)-2-butoxy side chains adopt pure right- and left-handed screw senses in CHCl₃ and 1,1,2-trichloroethane, respectively. The degrees of helix-sense induction were determined by analyses of free energy differences of copolymers consisting of achiral and chiral monomer units with varying ratios. We assume that the helix switch may depend on solventinduced conformational changes of the chiral side chains. Although each chiral group may gain a very small energy for one helix, its accumulation in the helical polymer backbones can cause a large macromolecular conformational change.¹² Studies for establishing the origin of the conformational change are currently being undertaken in this laboratory.

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- 13 See the Supplementary Information.
- 14 When solid poly-(*R*)-**2** was obtained by evaporation of CHCl₃ and dissolved in 1,1,2-TCE at rt, gradual *P*-to-*M* helical inversion was observed in the CD spectra. It takes a few hours to complete.