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Chiral Amplification Based on Sergeants and Soldiers Effect in Helically Folded Poly(naphthalenecarboxamide)

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Supporting Information

Chiral amplification is an important phenomenon and is related to the origin of homochirality in nature.[1] Hierarchical chiral amplification from the chirality of small molecules, such as amino acids, to macromolecular chirality, such as the helical sense of the α-helix of peptides, and further from macromolecular chirality to higher-order structures, allows the control of sophisticated reactions and functions in biological systems.[2]

Chiral amplification of polymer is based on the amplification of main-chain helical sense induced by a small chiral bias through cooperativity between the monomer units and has been reported in a variety of artificial helical polymers.[3] In this connection, the term "sergeants and soldiers effect" has been used to describe the chiral amplification observed in copolymers composed of chiral and achiral monomer units.[3a] This effect operates not only in artificial helical polymers but also in supramolecular systems[4] and foldamers,[5] which adopt predominantly folded structures induced by local helical preferences stabilized by noncovalent interactions in many conformational equilibria between folded and random-coil structures.[6]

We previously investigated the sergeants and soldiers effect in copolymers of poly(*p*-benzamide)s with chiral and achiral tri(ethylene glycol) side chains and found that no chiral amplification was observed in an organic solvent.[7] Recently, we have reported that poly(naphthalenecarboxamide) with the same chiral side chain adopts a predominantly right-handed helical structure in solution.[8] In common organic solvents, the CD intensity of the poly(naphthalenecarboxamide) increased with decreasing temperature, as in the case of the poly(*p*-benzamide).[9] On the other hand, the CD intensity in water/methanol = 7/3 (v/v), which was dramatically larger than that in organic solvents, increased with decreasing temperature and then saturated in the range 0−15 °C. No dependence of the concentration of the polymer in the aqueous solvent on the CD spectra can rule out the possibility of chiral aggregation. These results imply that the helical structure is stabilized by an intramolecular self-association driven by a solvophobic effect, and the right-handed helical sense bias of the polyamide is saturated in the range 0−15 °C. This simple modification of the main chain from benzene ring to naphthalene ring appears to introduce a potential intramolecular self-association ability of the aromatic polyamides in aqueous solution. Therefore, we expected that the chiral amplification of poly(naphthalenecarboxamide) would be observed in an aqueous solvent. In this Communication, we report the synthesis of random copolymers of poly(naphthalenecarboxamide) with chiral and achiral tri(ethylene glycol) side chains and the observation of chiral amplification based on the sergeants and soldiers effect by means of measurement of the CD spectra of the random copolymers. Furthermore, it was confirmed that the chiral amplification of similar random copolymers of poly(*p*-benzamide)s with the same chiral and achiral side chains was not observed even in the same aqueous solvent.

Copolymerization of chiral monomer **1** and achiral monomer **2** was carried out in the presence of phenyl 4-methylbenzoate as an initiator and lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS) as a base under several conditions (Table 1).[8,10] The copolymer **3** obtained as the polymerization progressed was followed by GPC, and the chiral monomer unit ratio was estimated from the ^{1}H NMR spectrum after purification of the products by HPLC (Figure 1 and Figure S1). In the copolymerizations at the feed ratio $[\mathbf{1}]_0/[\mathbf{2}]_0 = [C]_0/[A]_0 = 10/90$ (entry 1), the GPC elution curves of the products shifted toward the higher-molecular-weight region, maintaining low polydispersity (Figure 1a). The ratios of the chiral monomer unit to the achiral monomer unit ([C]/[A]) in the products remained almost constant during the polymerization, indicating that random copolymerization proceeded. In the copolymerization at $[C]_0/[A]_0 = 32/68$ (entry 2) and 51/49 (entry 3), however, the chiral monomer unit ratio gradually increased as the polymerization progressed (Figure 1b, c). These results imply that there was a gradient in the segment composition of the copolymer. Chiral homopolymer **4** was also synthesized by the polymerization of chiral monomer **1** under the same conditions (entry 4).

In order to investigate the helical sense bias of **3** and **4**, UV and CD spectra were measured in chloroform, methanol, and water/methanol = 7/3 (v/v) (Figure 2 and Figure S2). These CD spectra exhibited a plus-to-minus pattern, viewed from longer wavelength, at 220−300 nm, indicating that **3** and **4** adopt a predominantly right-handed helical conformation in all the solvents we examined.

To accurately examine the chiral amplification behavior, the Kuhn dissymmetry factor *g*, which is defined as $\Delta\varepsilon/\varepsilon$ (ε: molar absorptivity) at 250 nm, of the random copolymer was plotted against the chiral monomer unit ratio in the polymers (Figure 3). The plot of $|g_{250}|$ value in chloroform and methanol showed a linear relationship with the increasing chiral ratio. This indicates that the cooperativity between the monomer units is weak, as in the case of poly(*p*-benzamide) with the same side chain, in organic solvents. On the other hand, the CD spectra in

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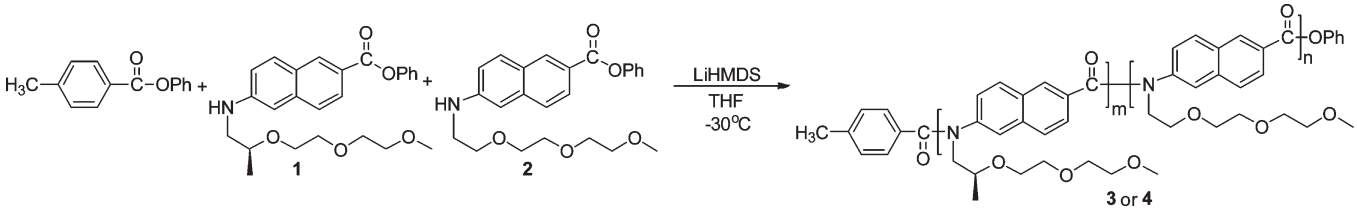
Table 1. Copolymerization of 1 and 2 and Homopolymerization of 1[a]



entry	$[C]_0/[A]_0$[b]	$[M]_0$[c]	time (h)	polymer[d]	M_n[e]	M_w/M_n[e]	chiral ratio (%)[f]
1	10/90	0.29	175	**3a**	5250	1.08	10
2	32/68	0.33	20	**3b**	6980	1.12	21
3	51/49	0.27	27.5	**3c**	5450	1.12	39
4	100/0	0.50	8.5	**4**	7140	1.14	100

[a] Polymerization was carried out in the presence of an initiator and LiHMDS as a base in THF at −30 °C. [b] Feed ratio of chiral monomer ($[C]_0$) to achiral monomer ($[A]_0$). [c] Concentration of the monomers (M). [d] Purified by HPLC. [e] Estimated by GPC based on polystyrene standards (eluent: THF). [f] Estimated by ^{1}H NMR.

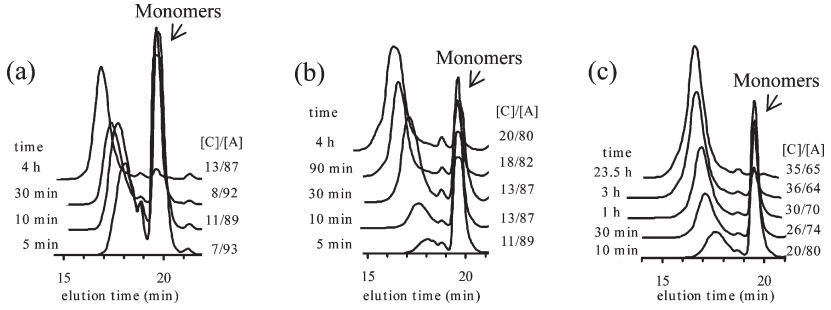


Figure 1. GPC profiles during the polymerizations ((a) Table 1, entry 1; (b) entry 2, (c) entry 3, [C]/[A] = the ratio of the chiral monomer unit to achiral monomer unit in the copolymer, estimated by ^{1}H NMR).

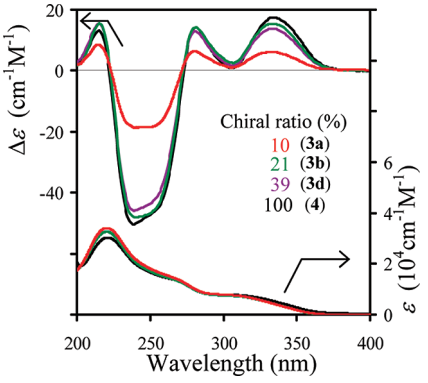


Figure 2. UV spectra of **3** and **4** at room temperature and CD spectra of **3** and **4** at 25 °C in water/methanol = 7/3 (v/v).

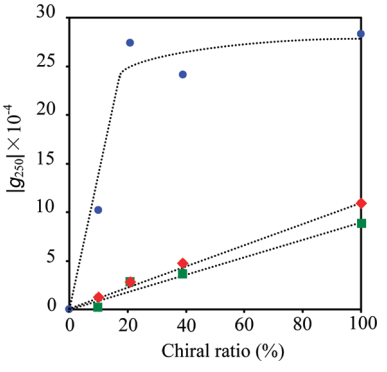
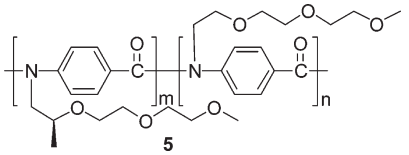


Figure 3. Plot of Kuhn dissymmetry factor ($g = \Delta\varepsilon/\varepsilon$) at 250 nm of **3** and **4** in chloroform (red diamond), methanol (green square), and water/methanol = 7/3 (v/v) (blue circle) against chiral unit ratio. The dotted lines are shown simply to guide the eye.

water/methanol = 7/3 (v/v) were clearly different from those in the organic solvents, as we expected. As shown in Figure 3, the $|g_{250}|$ value of **3b** was 0.002 74, which is ca. 100-fold greater than that in the organic solvents, and almost the same as that of homopolymer **4** ($|g_{250}|$ = 0.002 83). Even the $|g_{250}|$ value of **3a**, in which only 21% of the chiral unit is present in the copolymer, was ca. 10-fold greater than that in the organic solvents. Curiously, the $|g_{250}|$ value of **3c** was 0.002 41, which is lower than that of **3b**. The reason for this is unclear at this point, although it is presumably related to the fact that **3c** showed a slight tendency to form a gradient copolymer. However, the overall relationship between $|g_{250}|$ value and the chiral unit ratio showed distinct nonlinearity in the CD spectra in water/methanol = 7/3 (v/v). These results clearly demonstrate that strong cooperativity between the monomer units composing the helical structure would

arise from the intramolecular self-association of the main chain of the poly(naphthalenecarboxide), driven by the solvophobic effect in the aqueous solvent system, as we expected.

In order to elucidate whether the chiral amplification of **3** is based on the solvophobic effect of the naphthalene ring in the backbone of the polymer, similar UV and CD studies of several random copolymers of poly(*p*-benzamide), **5**, synthesized as reported in our previous paper,[7] were conducted in the same aqueous solvent (water/methanol = 7/3 (v/v)) (Figure S3). As a result, the $|g_{250}|$ value linearly changed in proportion to the chiral unit ratio of **5**. This linear relationship indicates that there is almost no cooperativity between the monomer units along the copolymer **5**, as in the case of the sergeants and soldiers experiments with poly(*p*-benzamide)s and poly(naphthalenecarboxamide) in common organic solvents. This result strongly suggests that the chiral amplification of the poly(naphthalenecarboxamide) in the aqueous solvent can be attributed to enhancement of the cooperativity between the monomer units by means of the solvophobic effect of the more hydrophobic naphthalene ring in the backbone.



5

It should be noted that we have found two kinds of solvents in which poly(naphthalenecarboxamide) adopts helical conformation: one does not induce chiral amplification, while the other induces chiral amplification. In general, foldamers adopt random-coil or helical conformation, depending on the solvent.[6b,d] On the other hand, poly(naphthalenecarboxamide) in solution can switch on and off cooperativity between the monomer units composing the helical structure according to the nature of the solvent without completely collapse of the helical structure. This folding mutation of the polyamide by solvent effect is clearly different from the case of the ordinary foldamers. A possible explanation is that, compared to foldamers, the polyamide can readily adopt a helical conformation with three monomer units per turn on the basis of the high preference of cis conformation of the amide linkage and the syn arrangement of the three consecutive aromatic units connected by two amide linkages.

In conclusion, we have synthesized random copolymers of naphthalenecarboxamides with chiral and achiral side chains and demonstrated the occurrence of chiral amplification based on the sergeants and soldiers effect. As for the synthesis, copolymerization at $[C]_0/[A]_0$ = 10/90 proceeded randomly, while the polymerization at $[C]_0/[A]_0$ = 32/68 and 51/49 gave a copolymer with a slight composition gradient. The $|g_{250}|$ values of the poly(naphthalenecarboxamide)s in water/methanol = 7/3 (v/v) showed a distinctive nonlinear increment as the chiral unit ratio was increased, in contrast to the poly(naphthalenecarboxamide)s in organic solvents and poly(*p*-benzamide)s even in the same aqueous solvent. The simple modification of the main chain from benzene ring to naphthalene ring appears to change the potential intramolecular self-association ability of these polyamides sufficiently to allow the induction of switchable cooperativity between the monomer units according to the nature of the solvent, without complete collapse of helical conformation. Further studies of helically folded poly(naphthalenecarboxamide)s are under way.

■ ASSOCIATED CONTENT

Supporting Information. Text describing the polymerization procedure and figures showing the NMR, UV, and CD spectra of **3** and **4** as well as the UV and CD spectra of **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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