Chiroptical inversion induced by sandwiching units in chiral polythiourethane†

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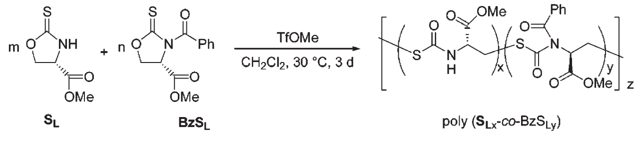
Chiroptical behavior of a hydrogen-bond-regulated chiral polythiourethane segment was inversed by sandwiching sterically demanding segments in copolymers prepared by cationic ring-opening copolymerization of chiral cyclic thiourethanes derived from L-serine.

The control of the chiroptical properties of polymers, which typically correlate well with their high-order structure, is a crucial subject in the designing of chiral polymers with the desired function. A successful example is the helical inversion of chiral polymers (*e.g.*, polysilane,[1,2] polyacetylene,[3–8] and polyisocyanate[9,10]), whose secondary structures depend on low energy interactions. However, it has been difficult to control the chiroptical behavior of polymers with high-order structures stabilized by hydrogen-bonds although their control is essential for the construction of stable but tunable chiral architectures. In contrast to synthetic polymers, drastic changes in the high-order structure stabilized by hydrogen-bonds are often observed in mutated proteins. This suggests that the appropriate sequences in chiral synthetic polymers may control their high-order structures, even if they are stabilized by hydrogen-bonds. Living or controlled polymerization that yields chiral polymers with a variety of functional groups is an effective method to obtain chiral polymers with regulated sequences in order to control their chiroptical properties. We recently reported the chiroptical behavior of chiral polythiourethanes, which are analoguous to γ-peptides,[11] obtained by the living polymerization of cyclic thiourethanes derived from L-serine, depending on the substituents on the nitrogen atoms that would regulate the secondary structures by either hydrogen-bonds or steric controls.[12–14] As compared with the inescapable steric regulation, the regulation by hydrogen-bonds may be reorganizable due to its lability, *i.e.*, if a chiral polythiourethane comprises both hydrogen-bonding and sterically regulating sequences, the properties of the labile hydrogen-bonding sequence may vary along with the steric regulation. Accordingly, various chiral polythiourehanes were prepared from a chiral cyclic thiourethane (**S$_L$**) and its *N*-benzoyl derivative (**BzS$_L$**) (Scheme 1), and the chiroptical behavior of the obtained polymers was investigated. Herein, we describe the chiroptical inversion of the hydrogen-bond-regulated polythiourethane (**S$_L$**) segment by the sterically demanding **BzS$_L$** segment.



Scheme 1 Cationic ring-opening copolymerization of **S$_L$** with **BzS$_L$**.

Cationic ring-opening copolymerization of **S$_L$** with **BzS$_L$** were conducted using methyl trifluoromethanesulfonate (TfOMe) as an initiator under several feed molar ratios at 30 °C in CH$_2$Cl$_2$ to obtain the corresponding copolymers [poly(**S$_L$**-*co*-**BzS$_L$**)], whose compositions were determined by ^{1}H NMR spectrocopy (see ESI, Fig. S1†). Across the border of the feed ratios between **S$_L$**-rich and equimolar, the specific rotation ($[\alpha]_D^{25}$) of the copolymers altered drastically from positive to negative values (Table 1). Therefore, we investigated the copolymerization behavior of **S$_L$** and **BzS$_L$** under a feed molar ratio of 50 : 50. Fig. 1 shows the time–conversion curves of **S$_L$** and **BzS$_L$** (denoted by the red lines). When **S$_L$** was completely consumed, the conversion of **BzS$_L$** was merely 26%. Subsequently, the polymerization rate of **BzS$_L$** increased rapidly. This observation indicates that the obtained copolymer is a gradient copolymer. This did not agree with our initial presumption that the less different rates of the homopolymerizations ($k_{\mathrm{pSL}}/k_{\mathrm{pBzSL}} = 2.7$) might result in the formation of a random copolymer.[6] In contrast, the copolymerization of the isomer **S$_D$** with **BzS$_L$** yielded a random copolymer (the blue lines in Fig. 1). This differing copolymerization behavior may originate from the sterically mismatched and matched pairs of the propagating ends and the next monomers, respectively.[15]

The chiroptical behavior of poly(**S$_L$**-*co*-**BzS$_L$**) was evaluated by CD spectroscopy (see ESI, Fig. 2S†). In addition to $[\alpha]_D^{25}$, the

Table 1 Cationic ring-opening copolymerization of **S$_L$** with **BzS$_L$**^{a}

Run	Feed ratio (molar) **S$_L$** : **BzS$_L$**	Yield^b (%)	$x : y^c$	M_n (M_w/M_n)^d	$[\alpha]_D^{25e}$/°
1	80 : 20	80	87 : 13	6900 (1.19)	85.6
2	60 : 40	90	74 : 26	7100 (1.23)	73.8
3	50 : 50	93	51 : 49	7300 (1.25)	−70.0
4	40 : 60	85	16 : 84	6500 (1.45)	−79.4
5	20 : 80	79	12 : 88	7300 (1.55)	−106.4

^{a} Conditions: total monomer (3.0 mmol) in CH$_2$Cl$_2$ (6.0 mL), [M]/[I] = 32.9, 30 °C, 3 days. ^{b} Insoluble part of ethyl ether. ^{c} Determined by ^{1}H NMR spectra. ^{e} Estimated by SEC (polystyrene standard; eluent: DMF containing 50 mM lithium bromide and 50 mM phosphoric acid). ^{d} Measured by a polarimeter at 25 °C (c = 0.1 g dL^{-1}, CH$_2$Cl$_2$).

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† Electronic supplementary information (ESI) available: Experimental procedures and details. The results of the copolymerizations, and NMR and CD spectra, SEC profiles of block copolymers, and DSC thermograms. See DOI: 10.1039/b600417b

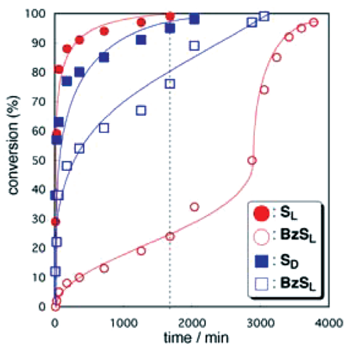

Fig. 1 Time–conversion plots for the copolymerization of $\mathbf{S_L}$ and $\mathbf{S_D}$ with $\mathbf{BzS_L}$ in the presence of TfOMe in CH_2Cl_2 at 30 °C; $[TfOMe]_0$ = 0.015 M, $[\mathbf{S_L}]/[\mathbf{BzS_L}] = [\mathbf{S_D}]/[\mathbf{BzS_L}] = 1.0$, $[\text{total monomers}]_0/[TfOMe]_0$ = 32.9.

Cotton effects attributed to the ester group (228 nm) change drastically from positive to negative across the same border. In the linearly combined presumable Cotton effects, only the poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$) curve differs significantly from that of the obtained copolymer (see ESI, Fig. 3S†). This unexpected chiroptical behavior of poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$) (line (a)) was further emphasized by a comparison with the chiroptical behaviors of the block copolymers [poly($\mathbf{S_{L53}}$-*b*-$\mathbf{BzS_{L47}}$) (line (b) in Fig. 2, M_n = 7400, M_w/M_n = 1.22, $[\alpha]_D^{25} = -43.2°$), and poly($\mathbf{S_{D50}}$-*b*-$\mathbf{BzS_{L50}}$) (line (c), M_n = 7600, M_w/M_n = 1.19, $[\alpha]_D^{25} = -198.5°$)], which agree well with the linearly combined presumable patterns (see ESI, Fig. 4S†). The Cotton effects attributable to the ester group in the CD spectrum were negative in the cases of poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$) and poly($\mathbf{S_{D50}}$-*b*-$\mathbf{BzS_{L50}}$), but were positive only in the case of poly($\mathbf{S_{L53}}$-*b*-$\mathbf{BzS_{L47}}$). This result led to a hypothesis that the ester groups of poly($\mathbf{S_L}$) units in poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$) are forced to acquire an inverse conformation by sandwiching poly($\mathbf{BzS_L}$) units in a smilar manner with the so-called "sergeants and soldiers" type polymers[17–21] first explored for copolymers of chiral and achiral isocyanates.[17–19] Namely, in our study, the $\mathbf{BzS_L}$ units with inescapable steric regulation can be regarded as the sergeants that conform the conformational arrangements of the $\mathbf{S_L}$ units, the soldiers, by overcoming the conformational regulation with hydrogen bonds. However, the CD spectral patterns of poly($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$) with other compositions are similar to those expected from the linearly combined ones. Accordingly, we assumed that the incomplete inversion originates from the gradient sequence in poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$), which results in the presence of poly($\mathbf{S_L}$) segments with a poly($\mathbf{BzS_L}$) segment only to either of the termini (*i.e.*, poly($\mathbf{S_L}$) segments near another terminus without poly($\mathbf{BzS_L}$) segments will be free from constraint by poly($\mathbf{BzS_L}$) segments). We prepared poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$)) ($\mathbf{S_L}$: $\mathbf{BzS_L}$ = 51 : 49) by subsequent polymerization of a mixture of $\mathbf{BzS_L}$ and $\mathbf{S_L}$ after that of $\mathbf{BzS_L}$. Poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_D}$-*co*-$\mathbf{BzS_L}$)) ($\mathbf{S_D}$: $\mathbf{BzS_L}$ = 50 : 50) was also prepared by the identical procedure (see ESI, Fig. 5S†). The elution peaks of SEC revealed clear shifts towards the higher molecular weight region after the prepolymerization keeping unimodal distributions, supporting the successful formation of the block copolymers, and the molecular weights of the obtained block copolymers are almost identical values.

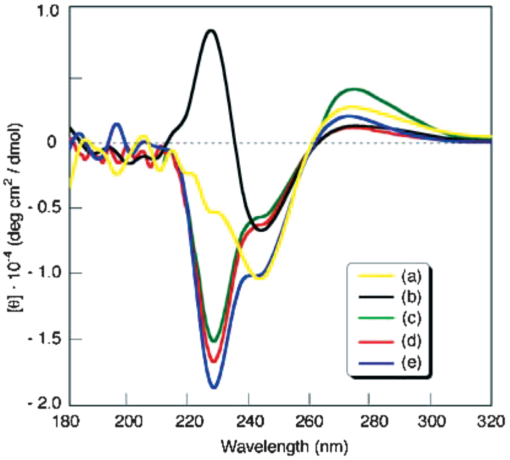

Fig. 2 CD spectra of (a) poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$), (b) poly($\mathbf{S_{L53}}$-*b*-$\mathbf{BzS_{L47}}$), (c) poly($\mathbf{S_{D50}}$-*b*-$\mathbf{BzS_{L50}}$), (d) poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$), and (e) poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_D}$-*co*-$\mathbf{BzS_L}$) in CH_2Cl_2 (c = 0.1 g dL^{-1}).

As expected, poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$)) (line (d)) exhibits a negative Cotton effect attributable to the ester groups in the poly($\mathbf{S_L}$) segments, whereas poly($\mathbf{S_{L53}}$-*b*-$\mathbf{BzS_{L47}}$) (line (b)) and poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$) (line (a)), consisting of identical copolymer compositions, exhibit significantly positive and weakly negative Cotton effects, respectively. Interestingly, the specific rotation and the CD spectral patterns of poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$) (line (d), $[\alpha]_D^{25} = -159.7°$) and poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_D}$-*co*-$\mathbf{BzS_L}$) (line (e), $[\alpha]_D^{25} = -186.5°$) are almost identical. These data indicate that the chiroptical behavior of poly($\mathbf{S_L}$) segments in poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$) is considerably inversed by sandwiching poly($\mathbf{BzS_L}$) segments, which force the inverse conformation from both sides (Fig. 3).

The inversion by sterical constraint had a direct effect on the secondary structure of the copolymers. The ^{13}C NMR spectra of the copolymers in $CDCl_3$ appears to suggest the inverse conformation of the poly($\mathbf{S_L}$) segment as shown in Fig. 4. Although four carbonyl peaks assignable to thiourethane and ester moieties of poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$) was observed at 164.40 and 166.58, 171.16

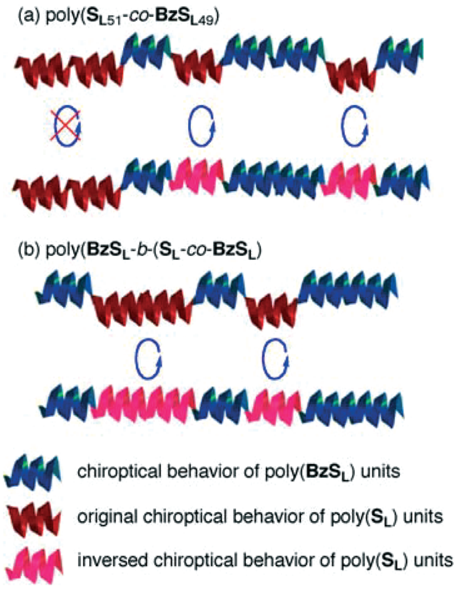

Fig. 3 Plausible mechanism of the chiroptical inversion.

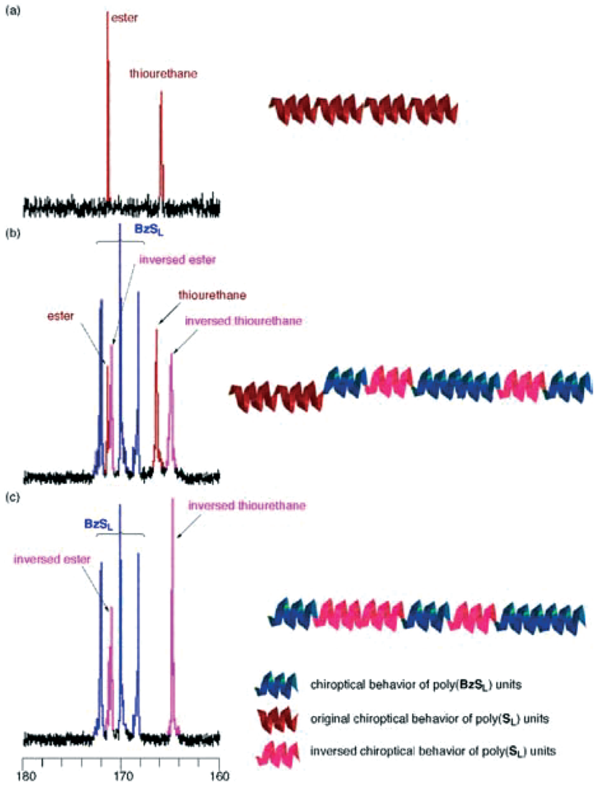

Fig. 4 ^{13}C NMR spectra (CDCl$_3$) of (a) poly($\mathbf{S_L}$), (b) poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$), and (c) poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$)).

and 171.20 ppm, respectively, aside from the peak of the poly($\mathbf{BzS_L}$) moiety, the carbonyl peaks assignable to the thiourethane and ester of poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$)) were shifted completely to a higher magnetic field due to the weaker hydrogen-bonds. Furthermore, the inversed carbonyl peaks of the block copolymer were in good agreement with those of poly($\mathbf{S_L}$) and racemic polymer [poly($\mathbf{S_{DL}}$)] in DMSO solution.[13] The absorptions resulted from NH and carbonyl groups of the ester and thiourethane moieties in copolymers which were also observed by the IR spectrum, in which the absorptions attributable to the NH moiety of copolymers except poly($\mathbf{S_{L51}}$-*co*-$\mathbf{BzS_{L49}}$) and poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$)) appeared to the almost similar region, approximately 3301 cm^{-1}. The absorptions of excluded copolymers were observed at lower field than those of the copolymers, indicating the change of the hydrogen bonding by this inversion. This inversion also affects the thermal behavior of the copolymers. Constraint poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$)) has a melting temperature (T_m) of 27 °C lower than that of native poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_D}$-*co*-$\mathbf{BzS_L}$)), and its heat of fusion is also significantly lower (see ESI, Fig. 6S†). These findings suggest that the slightly lower Cotton effect of constraint poly($\mathbf{BzS_L}$-*b*-($\mathbf{S_L}$-*co*-$\mathbf{BzS_L}$)) originates from the substantial but slightly incomplete inversion.

In conclusion, we inversed the chiroptical behavior of optically active polythiourethane segments by sandwiching segments, which would have originated from the conformational inversion confirmed by the NMR spectroscopic study. We think this phenomenon is similar to the manner in which a white piece in the board game 'Othello' flips to black when sandwiched by black pieces. This can be a new strategy to control the architecture of chiral polymers with a stabilized secondary structure by hydrogen-bonds in the main chain similarly with naturally occurring macromolecules.

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