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Chiroptical Properties of Graft Copolymers Containing Chiral Poly(*n*-hexyl isocyanate) as a Side Chain

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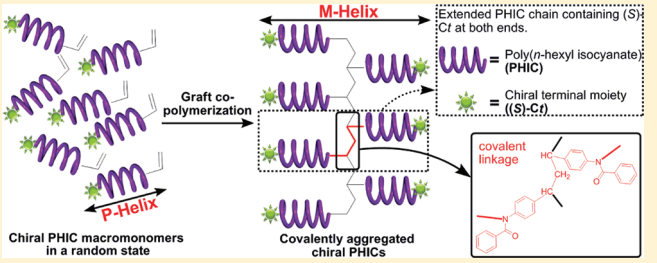
ABSTRACT: Chiral poly(*n*-hexyl isocyanate) (PHIC) macromonomers were synthesized by living anionic polymerization of *n*-hexyl isocyanate (HIC) using the functional initiator sodium *N*-(4-vinylphenyl)benzamide (Na−4VPBA) in tetrahydrofuran (THF) at −98 °C. Polymerization was terminated by (*S*)-2-acetoxypropionyl chloride using pyridine as a catalyst. Initiator efficiency and aggregation behavior during polymerization were also studied. Chiral PHIC macromonomers with varying molecular weight (MW) were synthesized with a narrow molecular weight distribution (MWD). Graft copolymerization of the chiral PHIC macromonomers was performed in toluene at 80 °C under vacuum using free radical polymerization with a 2,2′-azobis(2-methylpropionitrile) (AIBN) initiator. Several experiments were performed to determine the optimum polymerization time for macromonomers and graft copolymers. Formation of the graft copolymer was confirmed using SEC−MALLS, ^{1}H NMR, and circular dichroism (CD). CD spectra showed that graft copolymers adopted a conformation with opposite helical sense and a lower CD intensity as compared with chiral PHIC macromonomers.



INTRODUCTION

Macromolecular and supramolecular helical structures perform sophisticated functions in nature, including recognition, replication, and catalytic activity. Inspired by these discrete helical biopolymers, chemists have constructed various artificial helical polymers and self-assembled supramolecules with controlled helicity from small molecule precursors.[1,2] The amplification of chirality in various helical polymers such as poly(phenylacetylene)s, polyisocyanides, and polysilanes have been studied experimentally and theoretically.[3,4] The transfer of chiral information through noncovalent interactions to helical polymers by a so-called memory effect is also well established.[5,6]

Among all synthetic helical polymers, polyisocyanate is one of the most studied materials in helicity induction, due to its dynamic right-handed (P) and left-handed (M) helical conformations and its ability to induce optical activity.[7,8] The groups of Green,[9] Okamoto,[10] Zentel,[11] and others[12] have conducted a number of noteworthy studies on helicity induction in polyisocyanates. Isocyanate polymers with a single helical screw sense can be obtained by using chiral initiators,[13] monomers,[14] or solvents,[15] which has led to the discovery of several interesting phenomena such as the sergeants-and-soldiers principle[9,16] and the majority rule.[17]

During polymerization poly(*n*-hexyl isocyanate) (PHIC) undergoes rapid trimerization unless an additive is used.[18] The polymerization of *n*-hexyl isocyanate (HIC) has been successfully performed using sodium benzanilide (Na−BA) and sodium benzhydroxide (Na−BH) as initiators; these molecules act as initiators, and they also chain-end protection.[19] Additionally, the Na−BA initiation system gives living PHIC with a long enough lifetime to efficiently perform the termination reaction. Our group has reported helicity induction in PHIC using a Na−BA initiation system and pyridine catalyzed chiral termination. Helicity induction via introduction of a terminal chiral moiety is due to the covalent chiral domino (CCD) effect, in which a chiral moiety is attached to the α-end of the polymeric chain.[20] The terminal chiral moiety of PHIC can induce helicity in up to ∼36 monomer units (i.e., ∼5.0 kDa) through the CCD effect. The chiral initiator can induce helicity in poly(aryl isocyanate) up to ∼12 monomer unit.[10] Helicity induction through the domino effect is also achieved in peptides using covalent and noncovalent interactions[21] and has great biological importance. Several key physiological functions in nature are controlled by stereochemical information transmission through a remote chiral moiety. Such signal transmission is carried out by G-protein coupled receptors (GPCRs), which effect conformational changes in the adjacent proteins and transmit stereochemical information on the nanometer scale through the domino effect.[22]

At lower temperature, polyisocyanates undergo a noncovalently aggregated state, which is observable via a sudden rise in CD intensity.[23,24] This state was first observed by Bur et al. in nonpolar solvents.[25] Later, Green et al. observed polyisocyanates in a pregelled state during the cooling process; a "pre-gel" is a

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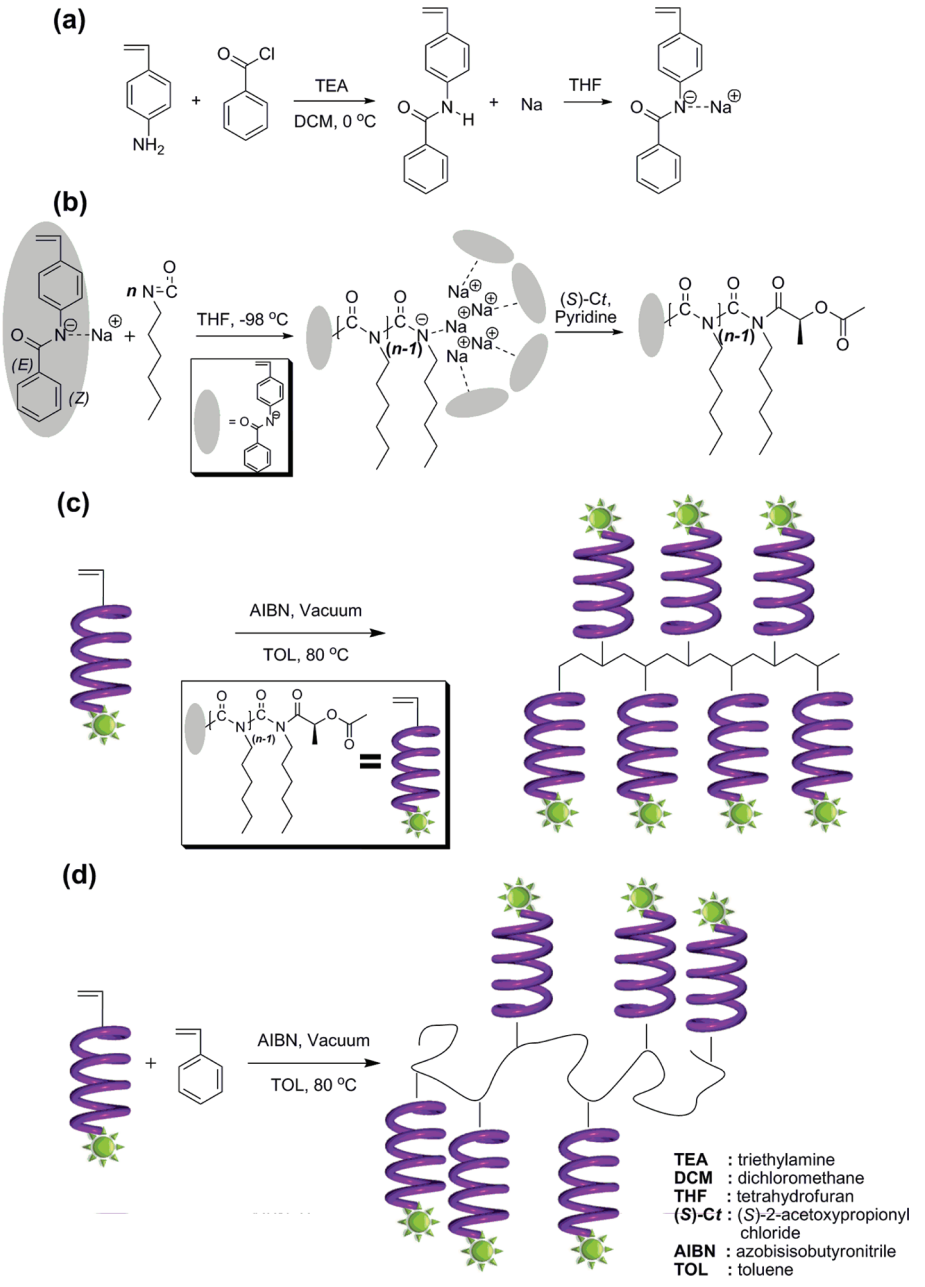
Scheme 1. (a) Synthesis of Initiator Sodium *N*-(4-Vinylphenyl)benzamide, (b) Synthesis of Chiral Macromonomer of Poly(*n*-hexyl isocyanate) (PHIC), (c) Synthesis of Graft Copolymer of PHIC Macromonomer by Free Radical Polymerization, and (d) Synthesis of Random Graft Copolymers of PHIC Macromonomer with Styrene by Free Radical Polymerization



noncovalently aggregated polymer state that forms before precipitation.[26] Aggregated biomacromolecules (peptides) cause some neurodegenerative disorders like Alzheimer's, Parkinson's, and Huntington's diseases.[27]

Graft copolymers containing side chain PHIC are an example of a covalently aggregated state. PHIC macromonomers have been prepared by several groups for synthesis of such graft copolymers, using different synthetic routes. Novak et al. have synthesized PHIC macromonomers with acrylate ends using living coordination polymerization.[28] Se et al. also synthesized acrylate-terminated PHIC but reported poor copolymerizability with methyl methacrylate (MMA).[29] Kikuchi et al. synthesized styryl- or acrylate-terminated PHIC, which showed equivalent reactivity to styryl-terminated PHIC with styrene; these researchers described poor copolymerizability of acrylate-terminated PHIC with MMA due to steric hindrance around double bonds.[30,31] Moreover, in dimensional property analysis of the rod brushes they observed that the main chain stiffness of the rod brush is higher than that of brush consisting of flexible side chains.[32]

In the present work, we examined the chiroptical properties of the covalently aggregated chiral PHIC. For these purposes, chiral graft copolymers containing poly(*N*-(4-vinylphenyl)benzamide as a backbone and chiral PHIC as a side-chain have been synthesized

using a "graft-through" technique. The chiral PHIC macromonomer was synthesized using a functional initiator and chiral terminator through living anionic polymerization. This is the first report so far on the synthesis of PHIC macromonomer using living anionic polymerization. During graft copolymerization, PHIC macromonomers are converted from a discrete random state to a covalently aggregated state. We use the phrase "covalently aggregated chiral PHIC" interchangeably with "graft copolymer of chiral PHIC". Because of the diversity of results in existing reports, the present work will be highly useful in understanding changes in helical sense and the range of transmission of stereochemical information in aggregated states of polymer.

EXPERIMENTAL SECTION

Materials. *n*-Hexyl isocyanate (Aldrich, 97%), pyridine (Aldrich, 99.5%), and (*S*)-2-acetoxypropionyl chloride (Aldrich, $[\alpha]^{20}_{D} = -31°$, 98%) were dried over CaH_2 and vacuum distilled. Tetrahydrofuran (THF, Fisher Scientific, GR grade) was distilled under N_2 after refluxing with sodium for 5 h and distilled again under vacuum from sodium naphthalenide (Na−Naph) solution. Sodium (Aldrich, 99%), calcium hydride (Junsei, 95%), naphthalene (Aldrich, 99%), 2,2′-azobis-(isobutyronitrile) (AIBN, TCI, 98%), 4-vinylaniline (Aldrich, 97%), benzoyl chloride (Aldrich, 99%), triethylamine (TEA, Aldrich, 99%), and dichloromethane (DCM, Aldrich, 99%) were used without further purification.

Initiator. *N*-(4-Vinylphenyl)benzamide (4VPBA) was synthesized in one step as shown in Scheme 1a. A one-neck flask equipped with a dropping funnel and nitrogen gas was charged with 4-vinylaniline (4.50 g, 37.8 mmol) and TEA (6.00 g, 59.3 mmol) in DCM. The stirred mixture was maintained at 0 °C for 1 h, and benzoyl chloride (6.00 g, 42.7 mmol) in DCM was then added dropwise to the solution and stirred in an ice bath for 30 min. The reaction mixture was stirred at 0 °C for 3 h. After completion of the reaction, the remaining salt was removed by filtration, the remaining acidic filtrate was neutralized with sodium bicarbonate, and the product was extracted with chloroform. The synthesized 4VPBA was purified by recrystallization from ethanol three times and dried *in vacuo*. Sodium *N*-(4-vinylphenyl)benzamide (Na−4VPBA) in THF (50 mL) was prepared at room temperature via the reaction of 4VPBA (2.12 g, 9.50 mmol) with elemental sodium (0.180 g, 7.80 mmol), in a 1.2:1.0 ratio. When the color of the reaction mixture turned a light yellow it was frozen in liquid nitrogen and connected to a high vacuum line (10^{-6} Torr) for degassing. After complete degassing, the obtained initiator was stored at −30 °C in glass ampules with break-seals. An appropriate concentration of Na−4VPBA was diluted prior to use. **4VPBA**. ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 6.71 (q, 1H, CH_2=C*H*−), 5.68 (dd, 1H, C*H*$_2$=CH−), 5.20 (dd, 1H, C*H*$_2$=CH−), 7.88 (m, 1H, −N*H*). 7.30−7.80 (8H, two aromatic rings). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 113.18 (*C*H$_2$=CH−), 136.12 (CH$_2$=*C*H−), 165.64 (*C*=O), 120.13, 126.93, 128.81, 131.88, 134.02, 134.94, 136.12, 137.50 (8C, −*C*−H of aromatic ring). IR (KBr, cm^{-1}): 3340 (−NH), 3081, 3054, 1600−1700 (C=O), 1600−1400 (C=C of aromatic ring), 840, 710. Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27; O, 7.17. Found: C, 80.71; H, 5.89; N, 6.25; O, 7.18.

Living Anionic Polymerization of HIC and Chiral Termination. Chiral PHIC macromonomers were synthesized as shown in Scheme 1b. The unidirectional initiator Na−4VPBA was used to synthesize chiral PHIC macromonomer under high vacuum (10^{-6} Torr) in a glass apparatus following a standard procedure.[33] In a typical polymerization procedure, a solution of Na−4VPBA initiator (0.190 g, 0.860 mmol) in 7.30 mL of THF was transferred to the reaction flask through the break-seal and the solution temperature was then equilibrated to −98 °C. The polymerization was performed by dissolution of the monomer HIC (0.790 g, 6.23 mmol) in 15.40 mL of THF and addition to the initiator solution. The polymerization reaction was terminated after 60 min by adding an excess of (*S*)-2-acetoxypropionyl chloride (*S*-type of the chiral terminator, (*S*)-C*t*), followed in quick succession with pyridine, to the grown polymer chain. The polymer was precipitated into methanol, filtered, and dried in *vacuo*. The polymer was obtained with a yield of 99%. The d*n*/d*c* value of the PHIC macromonomer (CH-2) was obtained to be 0.0908 mL/g. The molecular weight and molecular weight distribution of the polymer were obtained to be 5.00 kDa and 1.10, respectively. Several polymerization reactions were conducted to check the efficiency of the initiators; in those cases polymerization reactions were terminated using acidified methanol. Dissolution in THF and reprecipitation in methanol was repeated to obtain highly pure polymers. The polymers were further dissolved in benzene and freeze-dried for characterization. The solvent-soluble components were analyzed by weighing the residue after evaporation of solvent, and ^{1}HNMR was used to check whether any unreacted monomers or trimers remained. PHIC macromonomer: ^{1}H NMR ($CDCl_3$, 300 MHz)), δ (ppm): 0.9 (3H, C*H*$_3$), 1.0−2.0 (8H, (C*H*$_2$)$_4$), 3.7 (2H, N−C*H*$_2$-), 5.20 (dd, 1H, C*H*$_2$=CH−), 5.68 (dd, 1H, C*H*$_2$=CH−), 6.71 (q, 1H, CH$_2$=C*H*−). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 14.5 (*C*H$_3$), 22.5 (*C*H$_2$), 26.2 (*C*H$_2$), 28.5 (*C*H$_2$), 31.5 (*C*H$_2$), 48.6 (N−*C*H$_2$−), 156.8 (*C*=O). IR (KBr, cm^{-1}): 2959, 2932, 2860 (CH$_2$), 1700 (C=O), 1349/1297 (disubstituted amide), 1227, 1175, 1092, 785, 728 (CH$_2$).

Synthesis of the Graft Copolymer. The purified and freeze-dried chiral PHIC (CH-1) macromonomer (0.40 g, 93.0 μmol) was further dried under vacuum at 10^{-6} Torr. Polymerization of the macromonomer was performed in 0.93 mL toluene using AIBN (1.53 mg, 11.3 μmol) as an initiator at 80 °C as shown in Scheme 1c. The mixture of the macromonomer, solvent, and initiator was placed in glass ampules, degassed three times using freeze−thaw cycles, sealed under high vacuum (10^{-6} Torr) and placed in a thermostatted bath. After completion of the reaction, the reaction mixture was precipitated in methanol, filtered and dried under vacuum. Unreacted macromonomer from the product was completely removed by three rounds of fractional precipitation using THF and methanol. The graft copolymer was freeze-dried with benzene. The chiral graft copolymer was obtained with a yield of 86%. The d*n*/d*c* value of the graft copolymer was observed to be 0.0887 mL/g. The CG-1's molecular weight and molecular weight distribution was found to be 31.0 kDa and 1.43, respectively. PHIC graft copolymer: ^{1}H NMR ($CDCl_3$, 300 MHz)), δ (ppm): 0.9 (3H, C*H*$_3$), 1.0−2.0 (8H, (C*H*$_2$)$_4$), 3.7 (2H, N−C*H*$_2$-). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 14.5 (*C*H$_3$), 22.5 (*C*H$_2$), 26.2 (*C*H$_2$), 28.5 (*C*H$_2$), 31.5 (*C*H$_2$), 48.6 (N-*C*H$_2$-), 156.8 (*C*=O). IR (KBr, cm^{-1}): 2958, 2931, 2860 (CH$_2$), 1702 (C=O), 1350/1298 (disubstituted amide), 1228, 1172, 1093, 784, 729 (CH$_2$).

Characterization. The ^{1}H and ^{13}C NMR spectra were measured using a JEOL JNMLA300WB, using $CDCl_3$ as the solvent. Chemical shifts were referenced to tetramethylsilane (TMS) at 0 ppm. Molecular weights were determined from the response of a multiangle laser light scattering detector system (MALLS), SEC−LS, (OPTI LAB-DSP interferometric refractometry 478−009−690 and DAWN EOS laser photometer 113-E, Wyatt Technology) with four columns (HR 0.5, HR 1, HR 3, and HR 4, Waters Styragel columns run in series with column pore sizes 50, 100, 500, and 1000 Å, respectively). THF with triethylamine (for the prevention of adsorption of hydrophilic polymer onto the column) was used as the mobile phase at a flow rate of 1.0 mL/min. The d*n*/d*c* value for the polymer in THF at 40 °C was measured with an LED (Optilab DSP) source. After d*n*/d*c* was measured for five different concentrations of each polymer sample, SEC−LS data were gained with refractive index detection at 40 °C. FTIR spectra were run with Perkin-Elmer System 2000 using KBr pellets. Circular dichroism (CD) and ultraviolet (UV) spectra were measured on a JASCO-J-720 spectropolarimeter using a

Table 1. Synthesis of Chiral Macromonomers of Poly(*n*-hexyl isocyanate) with and without Chiral Termination at −98 °C in Tetrahydrofuran

	amount of reagent (mmol)					$M_n \times 10^{-3}$			
run	Na−4VPBA	HIC	pyridine	(*S*)-C*t*	time (min)	calcd[d]	obsd[e]	MWD M_w/M_n[e]	yield (%)
H-1[a]	0.09	4.42	-	-	30	6.09	28.1	1.10	89(11)[f]
H-2[a]	0.43	5.10	-	-	60	1.51	7.60	1.08	100
H-3[a]	0.24	4.59	-	-	60	2.43	11.6	1.10	99
H-4[a]	0.10	4.48	-	-	60	5.60	27.2	1.09	100
H-5[a]	0.11	4.59	-	-	80	5.41	24.1	1.10	92(8)[g]
CH-1[b]	1.03	5.86	3.56	2.98	60/20[c]	1.06	4.30	1.07	98
CH-2[b]	0.86	6.23	2.97	2.46	60/20[c]	1.25	5.00	1.10	99
CH-3[b]	0.87	7.06	3.45	2.78	60/20[c]	1.37	5.50	1.08	99
CH-4[b]	0.88	8.04	2.75	2.59	60/20[c]	1.49	6.00	1.06	100
CH-5[b]	1.66	12.6	3.35	2.86	60/20[c]	1.27	5.10	1.08	100

[a] Polymerization without chiral termination. [b] Polymerization with chiral termination. [c] Polymerization time is 60 min and termination reaction time is 20 min. [d] M_n = {[HIC]/[Na−4VPBA] × molecular weight of HIC} + molecular weight of Na−4VPBA + molecular weight of (*S*)-C*t*. [e] Molecular weight (M_n) and Molecular weight distribution (MWD) were measured by size exclusion chromatography multiangle laser light scattering (SEC−MALLS) in THF/Et_3N at 40 °C. [f] The unreacted monomer amounts are presented in parentheses. [g] The yield of trimer is presented in parentheses. Na−4VPBA: sodium *N*-(4-vinylphenyl)benzamide. (*S*)-C*t*: (*S*)-type chiral terminator ((*S*)-2-acetoxypropionyl chloride). HIC: *n*-hexyl isocyanate.

cell path length of 0.1 cm. Specific ellipticity values are expressed in molar ellipticity [Θ]. All CD spectra were smoothed using a Savitzky-Golay filter with OriginPro-8.1 software. All CD samples were prepared in concentration of 1 mg/mL. Elemental analysis was carried out using an EA 1110 analyzer (CE instrument, Italy).

RESULTS AND DISCUSSION

Role of Na−4VPBA as an Initiator. 4VPBA was successfully synthesized in one pot with 4-vinylaniline and benzoyl chloride in the presence of triethylamine, as shown in Scheme 1a. Reaction of 4VPBA with sodium metal in THF gave a dark yellow solution of Na−4VPBA. Even at room temperature, Na−4VPBA did not attack the vinyl group of other initiator molecules. Na−4VPBA has structural similarity to Na−BA, and it also exhibited weak reactivity similar to Na−BA, due to efficient charge delocalization by the phenyl rings and the carbonyl group.[19a] To study the initiation and aggregation behavior of Na−4VPBA, several polymerizations was performed at different time intervals as shown in Table 1. The optimum polymerization time with 100% yield was determined to be 60 min. If polymerization was terminated before 60 min (H-1) a significant amount of unreacted monomer remained in the traces of filtered solution. If the polymerization time exceeded 60 min (H-5) the polymer chain showed signs of degradation after complete consumption of all monomer; as a result, trimers of HIC are evident in found in the traces of filtered solution. The efficiency of Na−4VPBA initiator (efficiency of initiator = (calculated MW/observed MW) × 100) was found to be between 19 and 21% in each polymerization (H-1 to H-5).

The anion content in Na−4VPBA was estimated by reaction of Na−4VPBA with CH_3COCl following a standard procedure and was found to be quantitatively with at least 95% yield of the *N*-acetyl-*N*-(4-vinylphenyl)benzamide.[19a] Despite of having ∼95% reactive anion, only ∼20% of the initiator molecules initiated polymerization. Therefore, like Na−BA, as per our expectation, Na−4VPBA initiator also had a dual function;[19a] the remaining ∼80% of initiator molecules protected the living chain-end by preventing the backbiting reaction. This dual function for initiators can be attributed to the tendency of Na−4VPBA to form a cluster through charge interactions.

Synthesis of Chiral Macromonomers. HIC was introduced into the reactor containing Na−4VPBA; on addition, the color of Na−4VPBA changed from dark yellow to pale yellow, indicating the formation of the amide anion of HIC. The growing polymer chain has very low reactivity even with acid chloride, so pyridine was used as a catalyst to ensure complete termination. Table 1 (CH-1 to CH-4) shows the result of living anionic polymerization of HIC with Na−4VPBA initiator in THF at −98 °C. The PHIC macromonomers were obtained with quantitative yields of ∼99% in each case. The obtained chiral PHIC macromonomers varied in molecular weight (MW) in the range of 4.3−6.0 kDa, with a narrow molecular weight distribution (MWD), lower than 1.10, as determined by SEC−MALLS. As shown in Figure 1a, the ^{1}H NMR spectrum of CH-2 clearly indicates attributable to the vinyl benzyl group of the initiator, acetyl group of terminator, and hydrogen of aliphatic HIC chain. Moreover, no -NH peak was evident, which clearly indicates that the introduction of the chiral moiety to the N-terminus proceeded to completion. By relative study of peak intensity of the functional initiator, chiral terminator and monomer; the number of monomeric unit in the polymeric chain was observed to be ∼37. SEC−MALLS showed that CH-2 had a MW of 5.0 kDa and DP ∼36, which was in well accordance with the observed MW by ^{1}H NMR. This suggests that the present initiator was efficient enough to perform living polymerization of HIC and afforded well-defined chiral PHIC macromonomers with quantitative double-bond and chiral functionality. The reactive vinyl group of the Na−4VPBA initiation system did not give any side reactions during polymerization.

Graft Copolymerization of Chiral PHIC. The purified macromonomer was polymerized using free radical polymerization, which led to covalent aggregation of the chiral PHIC as shown in Scheme 1c. Table 2 shows the results of free radical polymerization of the chiral PHIC macromonomer in toluene using AIBN as an initiator at 80 °C. The PHIC macromonomers of different MW (M_n = 4.30−11.6 kDa) were polymerized to establish the

optimum conditions. After 6 h, a unimodal curve of SEC for the graft copolymer was observed with a very small peak for unreacted macromonomer, which was removed from the product mixture by fractional precipitation using THF and methanol to give completely pure graft copolymer, as shown in Figure 2. The degree of polymerization (DP) of PHIC macromonomer was approximately ~8.0 in almost all cases, as shown in Table 2. Figure 1b shows the ^{1}H NMR spectra of the graft copolymer; the inset figure shows the disappearance of the vinyl group peaks of the macromonomer after graft copolymerization. Moreover, a clear shift in the SEC curve was observed for the graft copolymers, as shown in Figure 2. The ^{1}H NMR and SEC data clearly show the formation of graft copolymer from PHIC macromonomer.

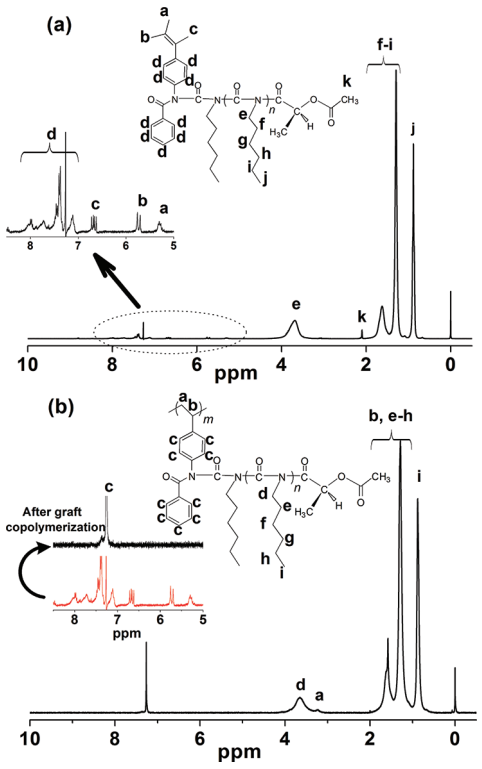


Figure 1. (a) ^{1}H NMR of chiral macromonomer of poly(*n*-hexyl isocyanate) (CH-2) (b) ^{1}H NMR of graft copolymer (CG-4) showing disappearance vinyl group peaks of the chiral macromonomer.

Chiroptical Properties of Chiral PHIC Macromonomers and Their Graft Copolymers. CD spectra of chiral PHIC macromonomers with varying MW in the range 4.3−6.0 kDa are shown in Figure 3a. The chiral PHIC macromonomer showed a positive Cotton effect at 255 nm due to a characteristic n−π^* transition of the polyisocyanate backbone and had a conformation with a P-helical sense. The CD intensity of chiral PHIC macromonomer increased as the MW increased from 4.3 kDa to 5.0 kDa, and decreased gradually for 5.5 kDa and 6.0 kDa. Therefore, helicity can be induced by the covalent domino effect in the chiral PHIC macromonomer by (*S*)-C*t* in a domain (MW) up to 5.0 kDa, i.e. up to a DP of ~36. These data are consistent in the context of domains (MW) influenced by terminal chiral moiety for previously reports of chirally terminated PHIC.[20]

Figure 3b shows the CD spectra of chiral PHIC macromonomers of different MW and their graft copolymers. Surprisingly, the chiral graft copolymers adopted a conformation with M-helical sense, which is opposite to the P-helical sense of chiral PHIC macromonomers; moreover, the graft copolymers had lower CD intensity as compared with the chiral PHIC macromonomer. In other words, the PHIC adopted a helical conformation with opposite sense at the covalently aggregated states. The intriguing results convinced us to look carefully at the packing pattern of PHIC chains in the graft copolymers.

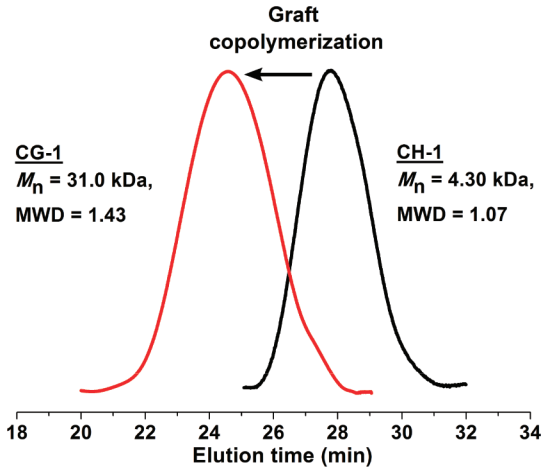


Figure 2. SEC curve of chiral PHIC macromonomer (CH-1) and graft copolymer (CG-1).

Table 2. Synthesis of Chiral Graft Copolymers at 80 °C in Toluene

	amount of reagents (μmol)			M_n/MWD[c]		
run[a]	AIBN	macromonomer[b]	styrene	macromonomer	graft copolymer	DP[d]
CG-1	9.3	93.0	-	(CH-1) 4.30 kDa/1.07	31.0 kDa/1.43	7.2
CG-2	9.0	90.4	-	(CH-2) 5.00 kDa/1.06	46.4 kDa/1.64	9.2
CG-3	9.6	95.4	-	(CH-3) 5.50 kDa/1.10	46.0 kDa/1.45	8.4
CG-4	9.2	93.2	-	(CH-4) 6.00 kDa/1.08	44.0 kDa/1.70	7.5
RG-5	10.2	40.1	80	(CH-5) 5.10 kDa/1.08	42.6 kDa/1.44	-
RG-6	10.5	40.4	200	(CH-5) 5.10 kDa/1.08	43.4 kDa/1.43	-
RG-7	10.9	39.5	400	(CH-5) 5.10 kDa/1.08	37.8 kDa/1.51	-

[a] All Polymerizations were conducted at 80 °C for 6 h. [b] Poly(*n*-hexyl isocyanate) macromonomer synthesized using Na−4VPBA initiator and (*S*)-C*t* terminator. [c] Molecular weight (M_n) and Molecular weight distribution (MWD) were measured by size exclusion chromatography multiangle laser light scattering (SEC−MALLS) in THF/Et_3N at 40 °C. [d] Degree of polymerization.

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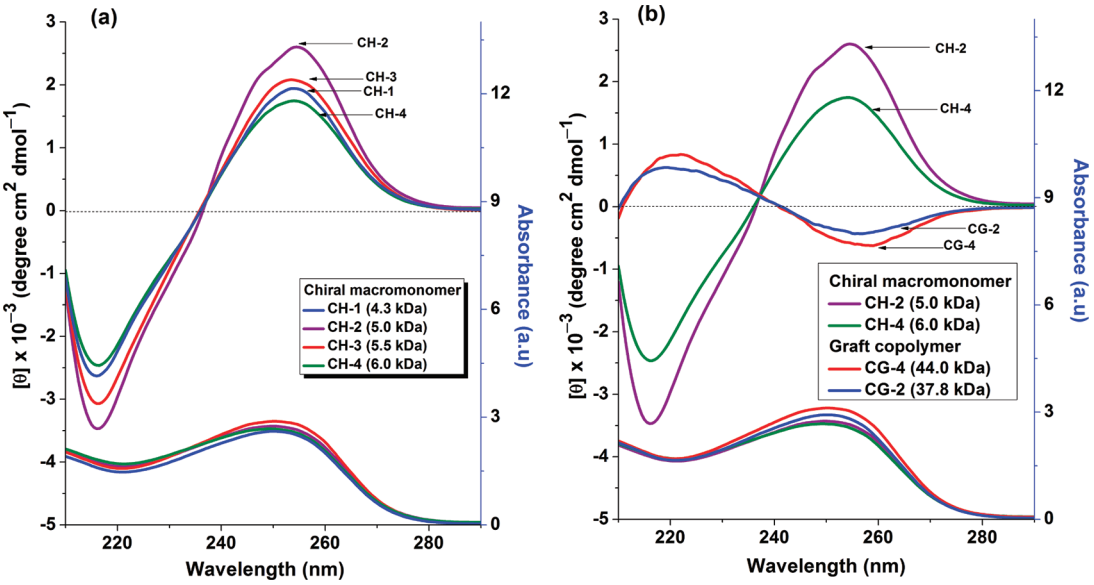
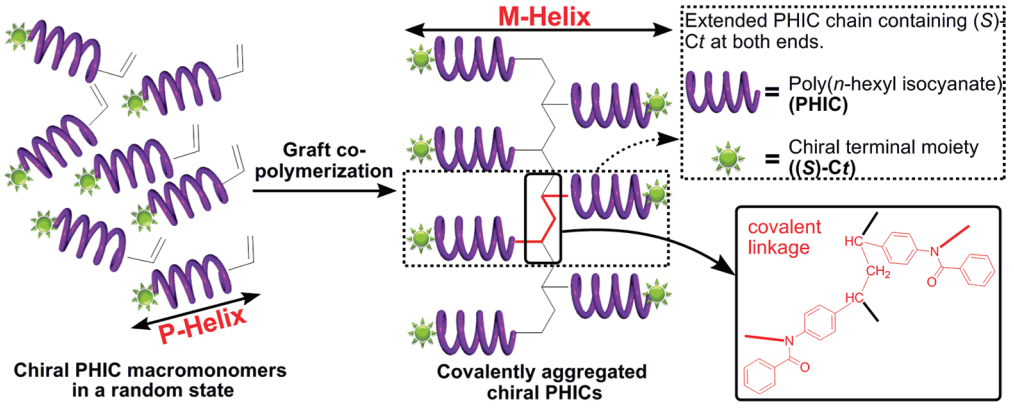


Figure 3. (a) CD (upper) and UV (lower) spectra of chiral macromonomers of poly(*n*-hexyl isocyanate) with varying molecular weight, and (b) CD (upper) and UV (lower) spectra of chiral macromonomers of poly(*n*-hexyl isocyanate) and the graft copolymers synthesized from them (spectra a and b were measured in hexane at 1 mg/mL, with a cell path length of 0.1 cm at 25 °C).

Scheme 2. Representation of the Possible Aggregated States of the Chiral Poly(*n*-hexyl isocyanate) Macromonomers



During graft copolymerization, chiral PHIC macromonomers are converted from a random state to a covalently aggregated state, as shown in Scheme 2. As previously mentioned, noncovalently aggregated polyisocyanates show a sudden rise in CD intensity.[23−26] This can be explained in the context of the packing of helical chains in the pregel in two different ways.[7] Polyisocyanate chains align in close parallel packing in the aggregates, and adopt an energetically favorable conformation with reduced helix reversals that allows for longer helical segments and enhanced cooperativity.[26] In addition, high CD intensity can occur due to the formation of a helical superstructure of polyisocyanate chains in the aggregates, in which the amide chromophores are in an additional chiral environment. This kind of chiral arrangement of helical polymers in aggregates has been reported in DNA samples.[34]

The above-discussed chiroptical property was observed in the noncovalently aggregated state of chiral polyisocyanates. In those cases, helicity was induced by a cooperative effect. The present system differed from all previous systems in two ways: (a) here, helicity was induced in the chiral PHIC macromonomer by the covalent chiral domino effect[20] and (b) the aggregation was due to covalent bonding of the vinyl-terminated, optically active PHIC macromonomers.

In the present system, the chiral PHIC macromonomer aggregated to form a "head-to-head" (vinyl-to-vinyl group) covalently aggregated state after graft copolymerization, as shown in Scheme 2. Due to steric hindrance of the bulky rod-polymer side chains, the syndiotactic structure was the most favorable for the graft copolymers.[32] In the covalently aggregated state, two PHIC chains are aligned opposite to each other, resulting in a longer chain that contains the same chiral moiety ((*S*)-C*t*) at both ends, as shown in the dotted-line box of Scheme 2. This extended PHIC chain has a covalent linkage (backbone of graft copolymer), in the exact middle, as shown in the dark-lined box of Scheme 2. In the noncovalently aggregated state, the polyisocyanates have high CD intensity due to adoption of more energetically favored

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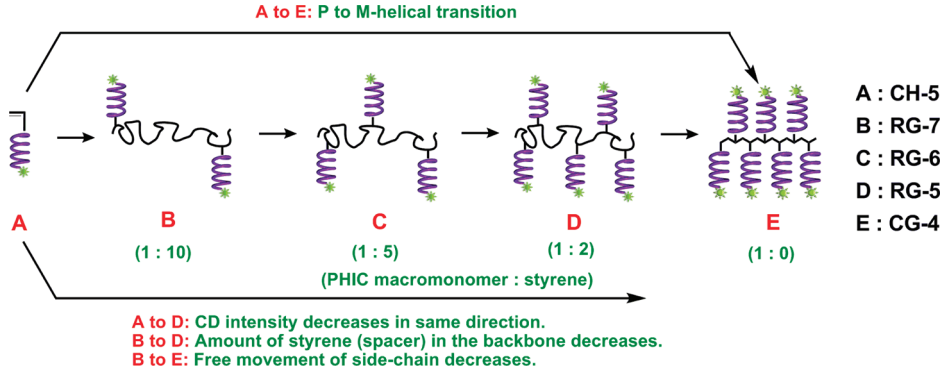
Scheme 3. Representation of the Modal Structures Chiral Random Graft Copolymers with Varying Amount of Styrene in Backbone



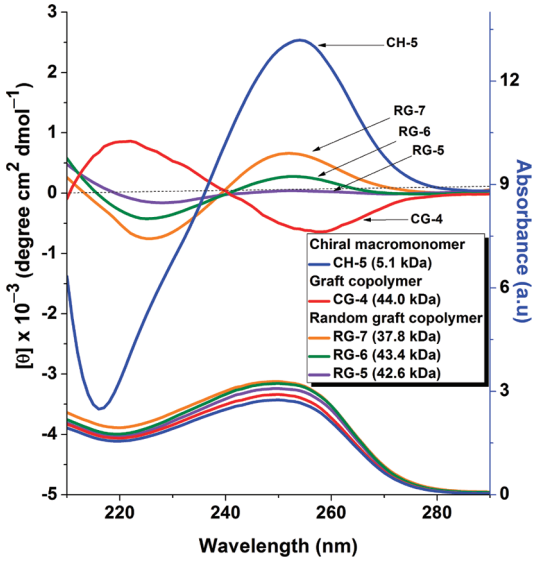


Figure 4. CD (upper) and UV (lower) spectra of chiral macromonomers of poly(*n*-hexyl isocyanate) (CH-5), the chiral graft copolymers (CG-4), and chiral random graft copolymers (RG-5 to 7) (all CD and UV spectra were measured in hexane at 1 mg/mL, with a cell path length of 0.1 cm at 25 °C).

conformations.[26] Therefore, it was assumed that the adoption of a conformation with opposite helical sense (P to M) and a lower CD intensity in the covalently aggregated state was due to the effect of covalent linkage on the extended chain containing (*S*)-C*t* at both ends. The covalent linkage creates an obstacle against the driving force applied by (*S*)-C*t* toward helicity induction. Moreover, it increases the steric hindrance and restricts the movement of PHIC chains.

In order to confirm the extended chain effect, several random graft copolymerizations of chiral PHIC macromonomers with styrene were conducted in different ratios. In the random graft copolymer, some space was created by styrene between two chiral PHIC chains; therefore, there were no consecutively aggregated chiral PHIC chains as were obtained by graft copolymerization of chiral PHIC macromonomers as shown in the dotted-line box in Scheme 2. Moreover, as the amount of styrene increases the space between consecutively chiral PHIC chains increases and as the amount of styrene decreases the space between PHIC side-chains decreases and they come closer to each other as shown in Scheme 3. The random graft copolymers (RG-5 to 7) of PHIC macromonomer and styrene showed positive Cotton effect at 255 nm and owned a P-helical conformation like PHIC macromonomer. Therefore, both PHIC macromonomer and its random graft copolymer with styrene had the same helical conformation, and the random graft copolymer did not adopt a conformation with an opposite helical sense even in covalently aggregated state. This strongly supported our assumption that the graft copolymer adopted a conformation with opposite helical sense compared with the chiral PHIC macromonomer due to the double covalent chiral domino effect of the extended PHIC chain containing chiral moieties at both ends and a covalent linkage in the middle of the chain.

Furthermore, in random graft copolymers, the CD intensity increased from RG-7 > RG-6 > RG-5, as shown in Figure 4. It can be interpreted like, as the amount of styrene increased in the backbone of the random graft copolymer the CD intensity increased, and as the amount of styrene decreased CD intensity decreased. However, all the random graft copolymer had lower CD intensity compared with chiral PHIC macromonomer. RG-5 had the low space between consecutive PHIC side-chains as it had 1:2 ratio of PHIC macromonomer:styrene. In such case, PHIC side-chains were close to each other, which caused high steric effect on the PHIC chain and reduced the free movement, as a result the chiral influence by (*S*)-C*t* on the PHIC domain decreased significantly. In RG-7, more space was created between consecutive PHIC side-chains compared with RG-5 as it had 1:10 ratio of PHIC macromonomer:styrene. Such a high space increased the free movement of PHIC chains, and increased the chiral influenced domain by (*S*)-C*t*, which increased the helicity induction. It can be interpreted that the reduced CD intensity in the graft copolymers was due to steric hindrance at the backbone of the graft copolymer chains, which restricted free movement of the PHIC chain. This effect was termed as a "spacer effect in chiral graft copolymers". Higher the space between two consecutive side-chain, higher the CD intensity and vice versa.

Adoption of opposite helical sense due to a covalent linkage of the extended PHIC chain in graft copolymers can be attributed to the adoption of opposite helical sense as observed in different types of liked or kinked biomacromolecules. The polypeptide chain containing a covalent linkage created by

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short linkers adopted opposite helical sense as an effect of linkage.[35] The simulation models of homochiral and heterochiral helices with kinked structures exhibit a conformation with an opposite helical sense when energy is minimized.[36]

The above explanation supported our assumption that covalently aggregated chiral PHIC adopts a conformation with opposite helical sense due to the linkage effect in the extended PHIC chain of the graft copolymer. The detailed studies of the effect of the side-chain length on CD intensity, as well as solvent and temperature effects on the graft copolymers will be presented in future publications.

CONCLUSIONS

Living anionic polymerization of *n*-hexyl isocyanate has been successfully performed using the functional initiator sodium 4-*N*-(4-vinylphenyl)benzamide (Na−4VPBA), which serves both as a chain initiator and an additive to prevent the backbiting reaction. This dual function was confirmed by the clear difference between initiation efficiency (∼20%) and an estimation of anion content (∼95%) for Na−4VPBA. Chiral poly(*n*-hexyl isocyanate) (PHIC) macromonomers with varying and controlled molecular weight (MW) were successfully synthesized using Na−4VPBA initiation and pyridine-catalyzed termination of living PHIC chains with (*S*)-2-acetoxypropionyl chloride ((*S*)-C*t*). The formation of chiral PHIC macromonomers was confirmed by ^{1}HNMR, SEC−MALLS and CD. Maximum optical rotation of the macromonomer is obtained when M_n = 5.0 kDa, i.e., DP ∼ 36. Graft copolymers of optically active PHIC were also successfully synthesized by free radical polymerization and fractional precipitation. The graft copolymerization was confirmed by a shift in the SEC curve due to an increase in the MW and the disappearance of the vinyl group peaks in ^{1}H NMR spectra. CD spectra showed that the graft copolymers had an opposite helical sense compared with chiral macromonomers, which was due to effect of the extended chain containing the same ((*S*)-C*t*) chiral moieties at the both ends and covalent linkage in the middle. Moreover, we have established a "spacer effect" in chiral random graft copolymers. Higher the amount of spacer in backbone, higher is the CD intensity and vice versa. The present work will be greatly useful in understanding helical behavior and transmission of stereochemical information in biomacromolecules and synthetic helical polymers through covalently aggregated states of these polymeric chains.

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