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Macromolecular Helicity

Molecular Transmission: Controlling the Twist Sense of a Helical Polymer with a Single Light-Driven Molecular Motor**

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The transmission of chiral information from the molecular to the macromolecular or supramolecular level is a topic of intense current interest.[1] Research ranges from fundamental studies on asymmetric autocatalysis,[2] which probe the origin of homochirality in nature, to more practical applications focusing on sensing and the analysis of chiral compounds.[3] In all of this work the so-called amplification of chirality is the key parameter. In dynamic supramolecular systems this amplification of chirality can be achieved in, for example, liquid crystals,[4] chiral aggregates and gels,[5] and synthetic helical foldamers[6] and polymers.[7] Prominent examples of dynamic chiral polymers are polyisocyanates.[8] These polymers adopt stiff helical conformations in solution, in which equal amounts of *P* and *M* helical segments exist on a long chain. A subtle chiral induction, for example, substitution of deuterium for hydrogen in the side chain,[9] can result in a disproportionately high preference for one helical sense owing to the large cooperativity between the nonchiral monomeric units.

In previous systems[10,11] the chiral information of multiple photochromic units randomly distributed along the polymer chain was transferred to the polymer backbone. In the molecular design presented here a single chiral photochromic unit—a light-driven molecular motor—is situated at the terminus of a dynamically racemic helical polymer (containing equal amounts of left- and right-handed helices; Figure 1). Effective chiral induction by the molecular motor allows fully reversible control of the preferred helical sense of the polymer and a three-state switching cycle with racemic, *P*, and *M* helicity of the polymer.[12]

We introduced a modified version of the light-driven molecular motors developed in our group[13,14] at the α-chain-end of a poly-(*n*)-hexylisocyanate (PHIC). To the best of our knowledge, this is the first example of the use of a switchable chiral initiator to prepare these helical polymers. Unidirectional rotation in these systems is achieved in a four-step cycle by a combination of two photochemically induced *cis–trans* isomerizations, each followed by an irreversible thermal isomerization (see Figures 3 and 4).[14] The *cis* isomers of the motor (Figure 2a) are anticipated to induce a large preference for a *P* or *M* helical sense of the polymer backbone as the naphthalene moiety in the upper half of the motor is in close proximity to one specific side at the start of the polymer chain, whereas the *trans* isomer (Figure 2b) is less suited to induce a preference for one helical twist sense in the polymer (Figure 1).

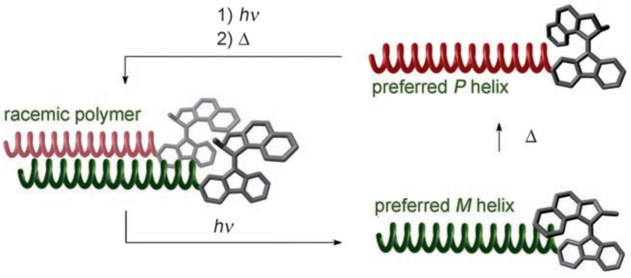
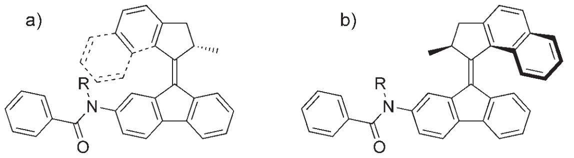


Figure 1. Schematic illustration of the reversible induction and inversion of the helicity of a polymer backbone by a single light-driven molecular motor positioned at the terminus. Irradiation of the photochromic unit leads to a preferred helical sense of the polymer backbone. A thermal isomerization of the rotor unit inverts the preferred helicity of the polymer chain. A subsequent photochemical and thermal isomerization step establishes the original situation with a random helicity of the polymer backbone.



(2′*S*)-(*M*)-*cis*-**1** (R=H)
(2′*S*)-(*M*)-*cis*-**2**-PHIC (R=PHIC)
(2′*S*)-(*M*)-*cis*-**3** (R=COCH$_3$)

(2′*S*)-(*M*)-*trans*-**1** (R=H)
(2′*S*)-(*M*)-*trans*-**2**-PHIC (R=PHIC)
(2′*S*)-(*M*)-*trans*-**3** (R=COCH$_3$)

Figure 2. Structures of a) *cis* and b) *trans* isomers of the benzamide-functionalized motor **1**, chain-end motor functionalized poly-(*n*)-hexylisocyanate **2**, and *N*-acetylated motor **3**.

We appended a benzamide function onto motor molecule **1** (Figure 2) with the intention that its sodium salt can act as an initiator for the polymerization of (*n*)-hexylisocyanate, yielding poly-(*n*)-hexylisocyanate (PHIC).[15] The resulting polymers are functionalized at the α-chain-end with a single enantiomer of a molecular motor (Figure 2). We reasoned that in order to induce the largest change in the chiral environment of the chain end of the polymer, owing to the different stages of the upper rotor part, the amide function-

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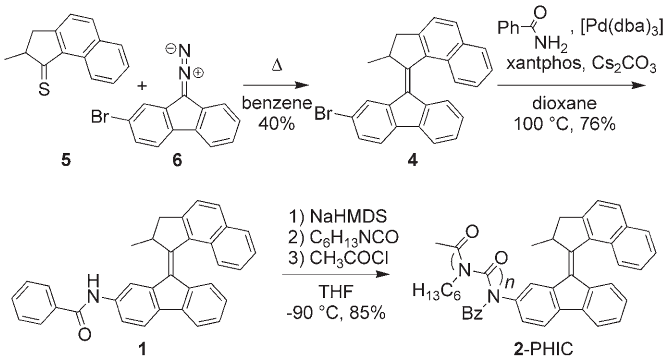
ality must be introduced at the 2-position of the lower (stator) half of the motor.

Synthesis of motor **1** was achieved using a diazo–thioketone coupling as a key step, generating bromine-functionalized precursor **4**, after which palladium-catalyzed amidation was successfully used to introduce the amide functionality[16] (Scheme 1). Detailed studies of the photochemical and thermal isomerization using low-temperature circular dichroism (CD) and ^{1}H NMR spectroscopy proved that **1** operates as a molecular motor.[17] Polymerization was achieved through the generation of the initiator by deprotonation of the amide in **1** using sodium hexamethyldisilazide in THF at −90 °C, followed by the addition of (*n*)-hexylisocyanate and end-capping with acetyl chloride. Acetylation of **1** afforded motor molecules **3** (Figure 2), which were used as CD reference compounds. The CD spectra of the different isomers of **3** allowed the discrimination between the CD absorptions of the helical polymer and those of the motor molecule connected to it.



Scheme 1. Synthesis of benzamide-functionalized motor **1** and formation of **2**-PHIC ((2′*S*)-(*M*)-*trans*-**2**-PHIC: M_w = 19 700; (2′*S*)-(*M*)-*cis*-**2**-PHIC: M_w = 28 700). Bz = benzoyl, dba = *trans,trans*-dibenzylideneacetone, HMDS = hexamethyldisilazide, xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene.

First, the photoisomerization of (2′*S*)-(*M*)-*trans*-**2**-PHIC was followed using CD spectroscopy, and the results were compared to those obtained using (2′*S*)-(*M*)-*trans*-**3** (Figure 3). Initially, nearly identical spectra were obtained for the polymer and the acetylated motor, indicating that for this isomer the CD signals of the polymer–motor hybrid originate solely from the attached motor molecule (see also the near-zero CD difference absorption spectrum in Figure 3 d). Upon irradiation of a sample of (2′*S*)-(*M*)-*trans*-**2**-PHIC in Et_2O at −20 °C (λ = 365 nm), providing (2′*S*)-(*P*)-*cis*-**2**-PHIC[18] (step 1 in Figure 3), a dramatic change in the CD spectrum of the polymer was observed, with new absorption maxima appearing around 220 and 260 nm (Figure 3 b). Irradiation under the same conditions of a sample of (2′*S*)-(*M*)-*trans*-**3** resulted in an inversion of the CD absorptions, in accordance with the helix inversion of the acetylated motor to provide (2′*S*)-(*P*)-*cis*-**3**. Subtraction of the CD spectrum obtained after irradiation of the acetylated motor from the

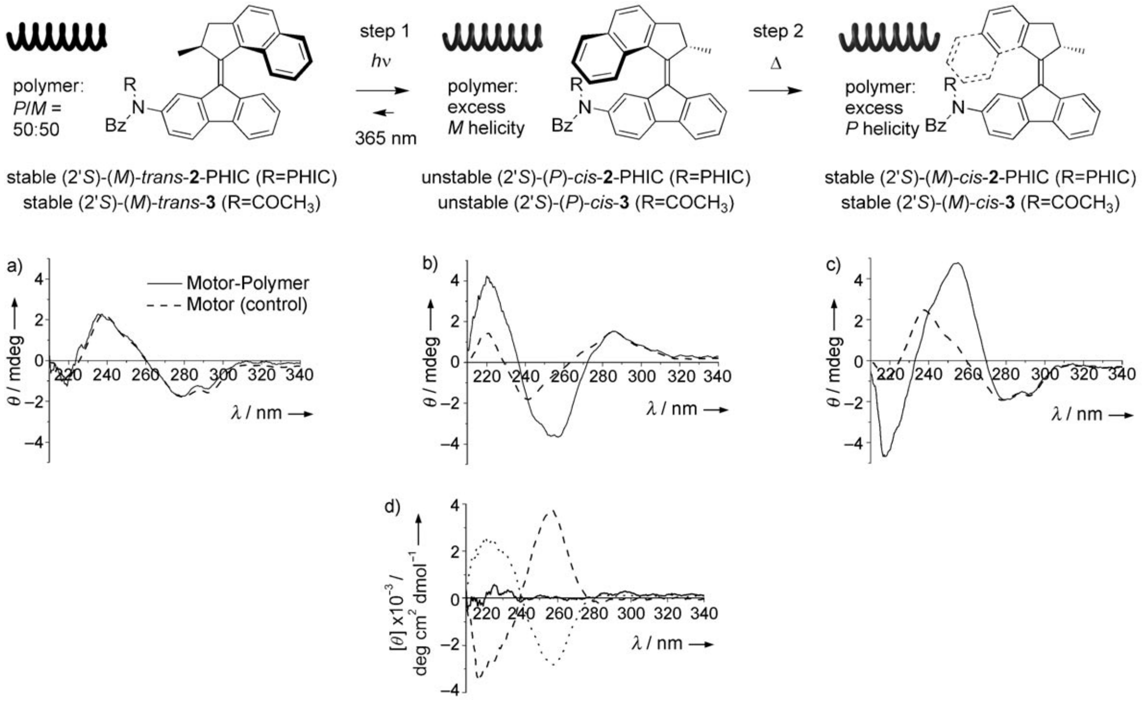


Figure 3. CD spectra (Et_2O, −20 °C) of a) (2′*S*)-(*M*)-*trans*-**2**-PHIC (15.0 mg L^{-1}; solid line) and (2′*S*)-(*M*)-*trans*-**3** (1.11 μм; dotted line); b) step 1: the PSS mixture with (2′*S*)-(*M*)-*trans*-**2**-PHIC and (2′*S*)-(*P*)-*cis*-**2**-PHIC (solid line), and the PSS mixture with (2′*S*)-(*M*)-*trans*-**3** and (2′*S*)-(*P*)-*cis*-**3** (dotted line) after irradiation (365 nm); c) step 2: the mixture of (2′*S*)-(*M*)-*trans*-**2**-PHIC and (2′*S*)-(*M*)-*cis*-**2**-PHIC (solid line) and the mixture of (2′*S*)-(*M*)-*trans*-**3** and (2′*S*)-(*M*)-*cis*-**3** (dotted line) after irradiation and storage in the dark at 20 °C for 30 min. d) Molar ellipticity spectra of the polymer backbone (CD difference spectra: polymer **2**−acetylated motor **3**) for the stable (2′*S*)-(*M*)-*trans* isomer of the motor (solid line), after irradiation (dotted line), and after irradiation and storage in the dark at 20 °C (dashed line).

CD spectrum of the polymer yielded a CD difference spectrum typical of PHIC with an excess of the *M* (left-handed) helical sense of the backbone (Figure 3 d).[19]

When (2′*S*)-(*P*)-*cis*-**2**-PHIC was kept in the dark for 30 min at 20 °C, it thermally converted into (2′*S*)-(*M*)-*cis*-**2**-PHIC[20] (step 2 in Figure 3), which resulted in a change of sign of the main CD absorptions of the polymer. In contrast, the CD spectrum of the acetylated motor nearly returned to the original spectrum of (2′*S*)-(*M*)-*trans*-**3** after the conversion of (2′*S*)-(*P*)-*cis*-**3** to (2′*S*)-(*M*)-*cis*-**3** (the CD spectra of (2′*S*)-(*M*)-*trans*-**3** and (2′*S*)-(*M*)-*cis*-**3** are nearly identical). The most notable feature is the inversion of the CD difference spectrum (Figure 3 d), indicating that the chirality of the polymer backbone has switched from a predominant *M* to *P* helical sense.

Irradiation ($\lambda = 365$ nm) of a sample of (2′*S*)-(*M*)-*cis*-**2**-PHIC at −20 °C generated a photostationary state (PSS) mixture predominantly consisting of (2′*S*)-(*P*)-*trans*-**2**-PHIC[21] (step 3 in Figure 4). Although this was expected to lead to a depletion of the CD absorptions corresponding to the polymer backbone (as only the *cis* isomers of the motor were anticipated to induce a preferred helicity), a slight increase in the intensity of the CD signals of the polymer was observed (Figure 4 a,b). A sample of (2′*S*)-(*M*)-*cis*-**3** was irradiated under the same conditions, resulting in an inversion of the CD absorptions, again in accordance with the helix inversion of the acetylated motor to provide (2′*S*)-(*P*)-*trans*-**3**. Also the CD absorptions in the CD difference spectrum increased slightly (Figure 4 d), indicating a somewhat higher induction of a *P* helical sense of the polymer backbone by the (2′*S*)-(*P*)-*trans* isomer than that by the (2′*S*)-(*M*)-*cis* isomer of the motor.

When (2′*S*)-(*P*)-*trans*-**2**-PHIC was kept in the dark for 30 min at 20 °C, it thermally converted into (2′*S*)-(*M*)-*trans*-**2**-PHIC (step in Figure 4), resulting in a strong decrease in the intensity of the main absorptions around 220 and 260 nm (Figure 4 c). The thermal conversion of acetylated motor (2′*S*)-(*P*)-*trans*-**3** to (2′*S*)-(*M*)-*trans*-**3** under similar conditions was accompanied by the formation of the original spectrum of (2′*S*)-(*M*)-*trans*-**3**. Also, the intensity of the absorptions in the CD difference spectrum strongly decreased (Figure 4 d; the remaining absorption is attributed to (2′*S*)-(*M*)-*cis*-**2**-PHIC present in the PSS mixture).

As anticipated, the (2′*S*)-(*M*)-*trans* isomer does not induce any preference for one specific helical sense in the polymer backbone. After a photochemical *trans*-to-*cis* isomerization, the naphthalene moiety comes in close proximity to the α-chain-end of the polymer chain, which results in a preferred *M* helical sense of the polymer backbone (step 1 in Figure 3). A thermal helix inversion in the motor molecule brings the naphthalene moiety to the opposite side of the polymer chain (Figure 1), which inverts the preferred helical sense of the polymer (step 2 in Figure 3). The subsequent photochemical *cis*-to-*trans* isomerization does not immediately lead to the anticipated loss of excess helical sense in the polymer backbone (step 3 in Figure 4). This can be understood if one realizes that the methyl substituent, which adopts an axial orientation and points away from the lower half of the motor

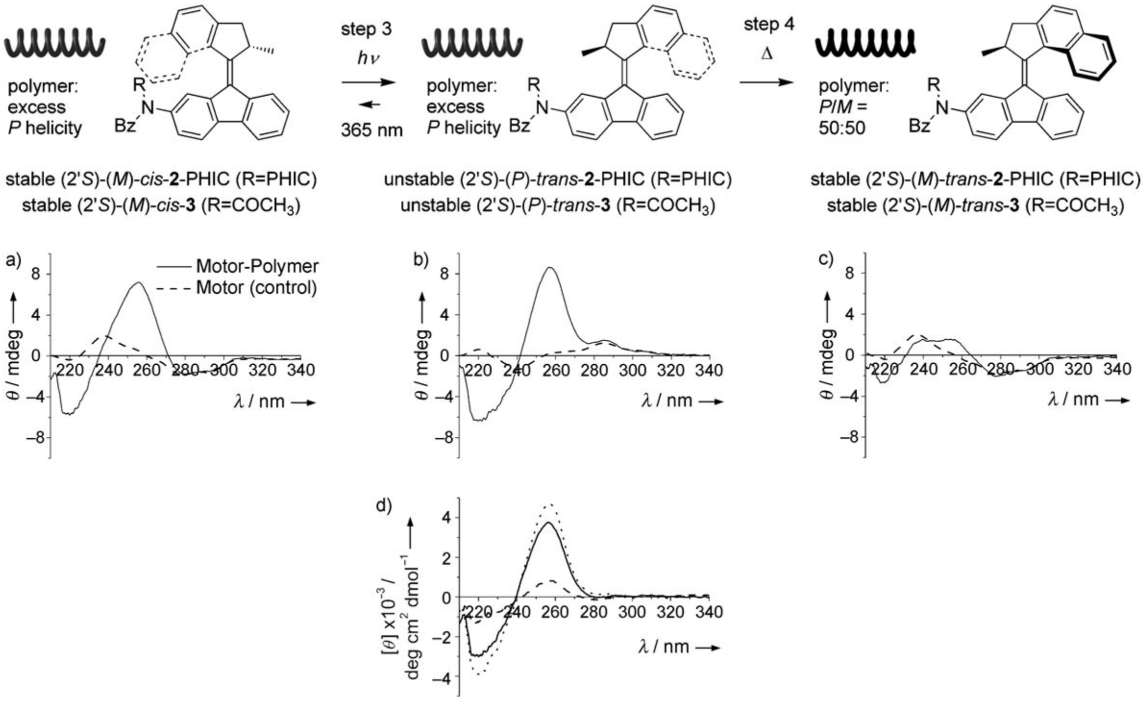


Figure 4. CD spectra (Et_2O, −20 °C) of a) (2′*S*)-(*M*)-*cis*-**2**-PHIC (23.3 mg L^{-1}; solid line) and (2′*S*)-(*M*)-*cis*-**3** (1.23 μM; dotted line); b) step 3: the PSS mixture with (2′*S*)-(*M*)-*cis*-**2**-PHIC and (2′*S*)-(*P*)-*trans*-**2**-PHIC (solid line), and the PSS mixture with (2′*S*-(*M*)-*cis*-**3** and (2′*S*)-(*P*)-*trans*-**3** (dotted line) after irradiation (365 nm); c) step 4: the mixture of (2′*S*)-(*M*)-*cis*-**2**-PHIC and (2′*S*)-(*M*)-*trans*-**2**-PHIC (solid line), and the mixture of (2′*S*)-(*M*)-*cis*-**3** and (2′*S*)-(*M*)-*trans*-**3** (dotted line) after irradiation and storage in the dark at 20 °C for 30 min. d) Molar ellipticity spectra of the polymer backbone (CD difference spectra: polymer **2**−acetylated motor **3**) for the stable (2′*S*)-(*M*)-*cis* isomer of the motor (solid line), after irradiation (dotted line), and after irradiation and standing in the dark at 20 °C (dashed line).

in (2′*S*)-(*M*)-*trans*-**2**-PHIC, is forced in an equatorial orientation in (2′*S*)-(*P*)-*trans*-**2**-PHIC, whereby it is in much closer proximity to the α-chain-end of the polymer and as a consequence locks the PHIC helicity. As the methyl substituent in (2′*S*)-(*P*)-*trans*-**2**-PHIC resides on the same side of the lower half of the motor as the naphthalene moiety in (2′*S*)-(*M*)-*cis*-**2**-PHIC, the polymer backbone retains its preference for the *M* helical sense. Another thermal helix inversion of the motor (step 4 in Figure 4) is required to regenerate the original stable *trans* isomer, completely eliminating the excess helical sense in the polymer backbone. Comparison of the molar ellipticity of these polymers (Figure 3 d and Figure 4 d) to that of poly((*R*)-2,6-dimethylheptylisocyanate)[9] reveals that the excess helical sense approximates 1/12th of the total amount of polymer.[22] The transmission of chirality, from a single chiral photochromic switch unit—a rotary molecular motor—to the backbone of a dynamically racemic helical polyisocyanate, allows for reversible induction and inversion of a preferred helical sense of the polymer.

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[17] See the Supporting Information.

[18] A photostationary state (PSS) mixture of (2′*S*)-(*M*)-*trans*-**2**-PHIC and (2′*S*)-(*P*)-*cis*-**2**-PHIC is obtained. For **1** the PSS ratio was determined at (2′*S*)-(*M*)-*trans*-**1**/(2′*S*)-(*P*)-*cis*-**1** = 21:79 (see the Supporting Information); for **2** a similar PSS mixture is anticipated.

[19] Poly((*R*)-2,6-dimethylheptylisocyanate), which is known to exist as an *M* helix (see Ref. [8a]), has the opposite CD absorption (see Ref. [9]).

[20] A mixture of (2′*S*)-(*M*)-*trans*-**2**-PHIC and (2′*S*)-(*M*)-*cis*-**2**-PHIC is obtained, the ratio of which is identical to that of the PSS mixture obtained after step 1.

[21] A PSS mixture of (2′*S*)-(*M*)-*cis*-**2**-PHIC and (2′*S*)-(*P*)-*trans*-**2**-PHIC is obtained. For **1** the PSS ratio was determined at (2′*S*)-(*M*)-*cis*-**1**/(2′*S*)-(*P*)-*trans*-**1** = 21:79 (see the Supporting Information); for **2** a similar PSS mixture is anticipated.

[22] Helix reversals will rarely occur along the relatively short polymer chains (in hydrocarbon solvents at 20 °C, the population of helix reversals has been estimated at one per 600 monomeric units, see Ref. [8b]).