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## COMMUNICATION

Unexpected stereomutation dependence on the chemical structure of helical vinyl glycopolymers<sup>†‡</sup>

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**A small change in chemical structure causes a remarkable influence on the stereostructure stability and mutarotational rate of helical vinyl polymers bearing laterally attached *p*-terphenyl pendants with an achiral butoxy terminal and a chiral galactosyloxy terminal.**

Switchable helical polymers, which adapt to the surrounding environment *via* stereomutation, are stimuli-responsive materials with a broad range of applications, such as in asymmetric synthesis,<sup>1</sup> chiral separation,<sup>2</sup> biosensors,<sup>3</sup> and electrooptical devices.<sup>4</sup> To fully explore their fascinating potential, delicate molecular design and in-depth understanding of the mechanism and dynamics of stereostructure change are essential. Glycopolymers, as a type of interesting functional materials, have been attracting great attention due to the unique recognition abilities of clustered saccharide groups.<sup>5</sup> They are also of interest in inducing a tunable helical polymer backbone and subsequently providing asymmetric geometric patterns of saccharide groups.<sup>6</sup>

Recently, we reported a helical vinyl glycopolymer, poly{2,5-bis[4'-(β-D-galactosyloxy)phenyl]styrene} (PGPS), which undergoes the transition from kinetically controlled conformation (KCC) to thermodynamically controlled conformation (TCC) when annealed in dimethylsulfoxide (DMSO).<sup>7</sup> Each repeating unit of PGPS has two glycosyl groups at the ends of the side *p*-terphenyl pendant. In the present work, we designed and synthesized four novel helical vinyl glycopolymers, poly{2-(4'-butoxyphenyl)-5-[4'-(2,3,4,6-tetra-*O*-acetyl-β-D-galactosyloxy)phenyl]styrene} (**P1**), poly{2-(4'-butoxyphenyl)-5-[4'-(β-D-galactosyloxy)phenyl]styrene} (**P2**), poly{2-[4'-(2,3,4,6-tetra-*O*-acetyl-β-D-galactosyloxy)phenyl]-5-(4'-butoxyphenyl)styrene} (**P3**), and poly{2-[4'-(β-D-galactosyloxy)phenyl]-5-(4'-butoxyphenyl)styrene} (**P4**). All these polymers consist of one chiral glycosyl terminal and one achiral butoxyl terminal at the end of the terphenyl group. **P2** and **P4** are deacetylated products of **P1** and **P3**. **P1** and **P2** differ from **P3** and **P4** only by the position where the side-group is linked to the polymer main chain.

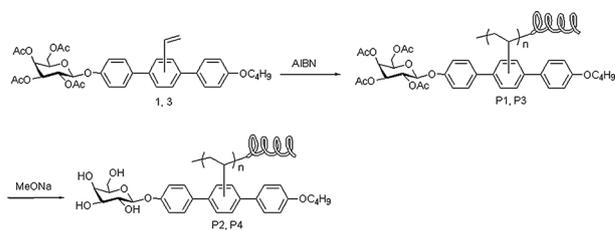
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<sup>‡</sup> Electronic supplementary information (ESI) available: Experimental details, <sup>1</sup>H NMR spectra of monomers and polymers, FT-IR spectra of **P1** and **P2**, conformation models of **P2** and **P4**. See DOI: 10.1039/c2cc00036a

To our surprise, such a small structure modification exerts a remarkable influence on the stereostructure stability and stereorotational rate of the polymer.

The two monomers, 2-(4'-butoxyphenyl)-5-[4'-(2,3,4,6-tetra-*O*-acetyl-β-D-galactosyloxy)phenyl]styrene (**1**) and 2-[4'-(2,3,4,6-tetra-*O*-acetyl-β-D-galactosyloxy)phenyl]-5-(4'-butoxyphenyl)styrene (**3**), were prepared *via* multistep synthetic routes (Schemes S1 and S2, ESI<sup>†</sup>). They were converted to **P1** and **P3** with radical polymerization. Whereas, **P2** and **P4** were obtained by deacetylation of **P1** and **P3** in methanol, a poor solvent for the four polymers, respectively (Scheme 1).

The monomers **1** and **3** show specific optical rotations ( $[\alpha]_{365}^{20}$ ) of 90° and 72° in THF, respectively. After radical polymerization, the resultant polymers **P1** and **P3** display  $[\alpha]_{365}^{20}$  values of 1203° and 1124°, separately (Table 1). Such large increments in optical rotation power indicate that the optical activities of the polymers do not solely arise from the configurational chirality of the side group, but also a chiral secondary structure, most likely helical

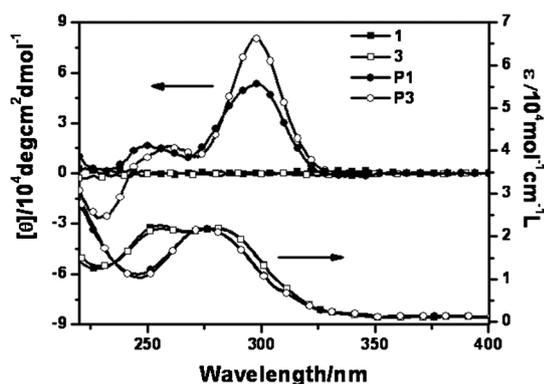


**Scheme 1** Synthesis of **P1**, **P2** and their deacetylated products **P3**, **P4**.

**Table 1** Polymerization results and chiroptical properties of the resultant polymers<sup>a</sup>

Polymer	Yield (%)	$M_n \times 10^{-4}{}^b$	$M_w/M_n{}^b$	$[\alpha]_{365}^{20} / ^\circ$
<b>P1</b>	87	7.8	1.71	1203
<b>P2</b>				1344
<b>P3</b>	84	6.9	1.65	1124
<b>P4</b>				23

<sup>a</sup> Polymerization conditions: temperature, 60 °C;  $[M]/[AIBN] = 300$ ; reaction time, 24 h. **P2** and **P4** were obtained from **P1** and **P3** *via* deacetylation in methanol, respectively. <sup>b</sup> Number-average molecular weight ( $M_n$ ) and weight-average molecular weight ( $M_w$ ) were estimated by GPC in THF calibrated against a series of standard polystyrene. <sup>c</sup> Specific optical rotation in units of degrees was measured in a 1 dm cell at a concentration of *ca.* 2.0 mg mL<sup>-1</sup> in DMSO at 20 °C.

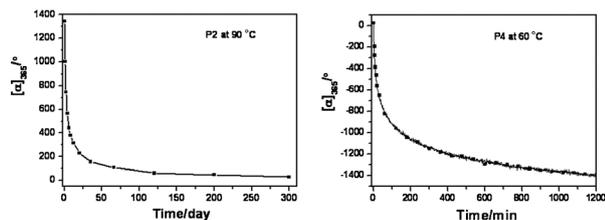


**Fig. 1** CD and UV-vis absorption spectra of **1**, **3**, **P1**, and **P3** in THF at a concentration of  $2 \times 10^{-5}$  mol L $^{-1}$ .

conformation, of the polymer main chain is generated.<sup>8</sup> After deacetylation of **P1** in methanol, the resultant polymer **P2** has an  $[\alpha]_{365}^{20}$  value of  $1344^\circ$ , slightly larger than that of **P1**, probably indicating the reservation of the original stereostructure of **P1**. The deacetylated product of **P3**, *i.e.*, **P4**, shows a dramatically decreased optical rotation (from  $1124^\circ$  to  $23^\circ$ ). This might be attributed to the drastically increased mutability.<sup>9</sup>

Fig. 1 presents the UV-vis absorption and CD spectra of the acetylated monomers and their polymers. The monomers **1** and **3** have two absorption peaks centered at 256 and 279 nm, respectively, which are assigned as the electronic transitions of vinyl groups and side *p*-terphenyl. The absorption of the vinyl group disappears completely after polymerization. Compared to the weak signals of monomers in CD spectra, the polymers display intensive Cotton effects: **P1** shows two intensive positive Cotton bands centered at 250 and 297 nm, respectively; while **P3** exhibits two CD bands centered at 255 and 297 nm, as well as a negative signal centered at 230 nm. These observations imply a twisting arrangement of the side *p*-terphenyl groups along the polymer backbone. This is consistent with the speculation on the formation of the helical polymer main chain.

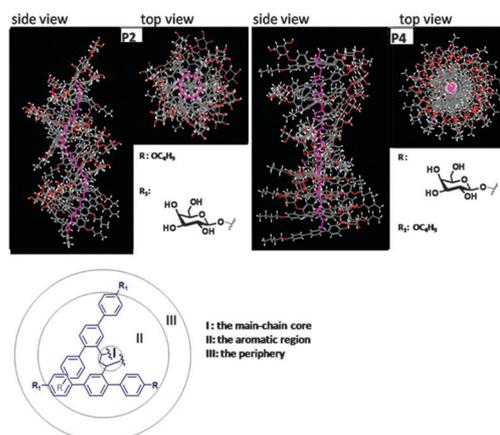
All the polymers were first annealed in DMSO at  $90^\circ\text{C}$  to investigate their optical stabilities. Both **P1** and **P3** display no obvious change in optical rotation, indicating the stable stereostructures. However, the removal of acetyl groups enables **P2** and **P4** to adjust their stereostructures. It is interesting to note that the stereostructure stability and mutarotational rate greatly depend on the position of the glycosyl group. As shown in Fig. 2, it takes as long as 300 days for **P2** to change its optical rotation from  $1344^\circ$  to almost zero at  $90^\circ\text{C}$ . In sharp contrast, the mutarotation of **P4** at  $90^\circ\text{C}$  is too fast to track its change in optical rotation, and thus, instead the mutarotation was tracked at a lower temperature, *i.e.*,  $60^\circ\text{C}$ . Its specific optical rotation changes from  $23^\circ$  to  $-800^\circ$  within 68 min. After annealing for



**Fig. 2** Annealing time dependence of specific optical rotation of **P2** at  $90^\circ\text{C}$  (a) and **P4** at  $60^\circ\text{C}$  (b) in DMSO,  $c = 0.2$ .

24 h, the  $[\alpha]_{365}^{60}$  value reaches a constant value of about  $-1574^\circ$ . The CD spectrum of **P4** after annealing in DMSO also shows a negative Cotton effect, opposite to the positive one before annealing, implying the mutation of helical structure again (Fig. S1, ESI $^\ddagger$ ).<sup>7,8</sup>

To shed light on the interplay between the stereostructure and the glycosyl position, the conformational analyses of **P2** and **P4** were carried out by computer simulation,<sup>10</sup> based on energy minimization with the Compass forcefield followed by MD at 298 K. Both polymers adopt pine-like helices in which side chains connected at given tilt angles occupy equably the space around the backbone no matter they are isotactic, syndiotactic, or atactic (Tables S1–S3, ESI $^\ddagger$ ). Fig. 3 shows the computer simulated conformations of atactic **P2** and **P4**. The column of the rigid chain can be divided into three parts: the twisting main-chain core, the aromatic region with high electron density, and the periphery. The glycosyl groups of **P2** sit in the periphery of the polymer chain while those of **P4** in the aromatic region. The exterior groups have more freedom to rotate, but interior ones are restricted by each other within the chiral environment. These conformational models can find evidence from CD and NMR experiments. **P3** exhibits a negative band at around 230 nm, corresponding to the absorption of acetyl groups since its acetyl groups are close to the helical polymer backbone, but **P1** does not (Fig. 1). In **P1**, the protons of glycosyl and attached acetyl groups exhibit considerable sharp peaks and their chemical shifts are close to those of the corresponding monomer while the peaks of the protons on the butoxy group become relatively broad (Fig. S2, ESI $^\ddagger$ ). Moreover, the peak of the protons **d** shifts from 4 ppm to 3 ppm, implying a shield effect of the high electron-intensity atmosphere. The protons on butoxyl of **P3** show comparatively sharp resonance peaks (as that of **e**) while those on glycosyl exhibit broad signals. These signal changes indicate that the glycosyl of **P3** and the butoxyl of **P1** are restricted in the dense electron atmosphere of *p*-terphenyl, the aromatic region of the chain column, while the glycosyl of **P1** and the butoxyl of **P3** are located in the periphery. After deacetylation, the peaks of the protons on acetyl disappear and those on glycosyl are shifted to 3.4–3.8 ppm. Similar results are observed for **P4**: the peaks of the protons on butoxyl of **P2** are relatively weak and broad while those of **P4** are strong and sharp. Moreover, the peaks of **d** can be observed in **P4** but not in **P2** because they shift to the high field where they are covered by the signals of the protons on glycosyl.



**Fig. 3** Computer simulated conformations of atactic **P2** and **P4**.

To further confirm the position of hydrophilic glycosyl groups, the contact angle measurements of glycopolymers were carried out. The acetylated polymers, **P1** and **P3**, show contact angles of 75° and 79°, respectively, while deacetylated compounds, **P2** and **P4**, reveal more hydrophilic values of 54° and 63°, separately (Fig. S6, ESI†). The similar contact angles of acetylated polymers illuminate the nature of similar hydrophobicity. In comparison, the contact angle of **P4** is obviously larger than that of **P2**. Such a result indicates that the hydrophilic glycosyls are indeed exposed outside for **P2** but shielded inside for **P4**.

On the basis of the above discussion, a possible explanation of the stereomutation mechanism of **P2** and **P4** is proposed. **P1** and **P3** have helical conformations with a dominant screw sense stabilized by the steric repulsion of side groups. The freshly prepared **P2** and **P4** in methanol inherit the conformations of **P1** and **P3**, respectively. Given the fact that the two polymers obtained *via* direct radical polymerization of 2-(4'-butoxyphenyl)-5-[4'-(β-D-galactosyloxy)phenyl]styrene (**2**) and 2-[4'-(β-D-galactosyloxy)phenyl]-5-(4'-butoxyphenyl)styrene (**4**) in DMF, which is a good solvent for the monomer but not a solvent for the polymer and may trap the polymer stereostructure once formed, display almost the same optical rotation as that of **P2** and **P4**, we speculate that both **P2** and **P4** adopt KCCs due to the steric interactions of side-groups (Table S4, ESI†).<sup>7</sup> These KCCs are different from their TCCs, unlike **P1** and **P3**, and just stable at low temperature. At the elevated temperature, KCC-to-TCC transition takes place. In the case of **P4**, the bulky glycosyl groups are confined in the close-packed aromatic region, which gives rise to strong steric repulsion. As a result, KCC of the chain is unstable and thus the mutarotation is accelerated. The movement of glycosyl groups makes H-bonding between OH of glycosyl groups possible, which may exert new induction power to the helical conformation. On the other hand, the big glycosyl residues of **P2** extend to the periphery. They are less crowded than **P4** and of weaker stabilizability to the helical conformation. Such a subtle balance finally leads to transition to TCC, *i.e.*, the slow racemization of the helix. Novak *et al.* have reported the solvent- and temperature-driven dynamic conformational changes of polycarbodiimides to the reversible shutter-like reorientation of the aromatic pendant groups without inversion of the static helical backbone.<sup>11</sup> They thought that the secondary layer of chirality created during the polymerization by the constricted arene pendant groups gives rise to the dramatic chiro-optical changes. Considering the severe restriction to the main chain rotation caused by the bulky side-groups, it is reasonable to exclude the helix–helix transition of polymer backbones for **P2** and **P4**. A low-energy concerted realignment of terphenyl pendant groups influenced by solvent and temperature might induce the observed stereomutation. More evidence is needed before an adequate explanation can be made.

In summary, we have demonstrated the synthesis and chiroptical properties of four novel helical vinyl glycopolymers with an excess of screw-sense. Although the KCCs and TCCs are identical for both **P1** and **P3**, they are different for **P2** and **P4**. The KCCs of the latter two polymers transform irreversibly to TCCs when annealed in DMSO at elevated temperature. The mutarotational rate shows

an unexpected dependence on the position where the *p*-terphenyl group is linked to the polymer backbone. The strong steric repulsion between side-groups of **P4**, the glycosyl groups of which are confined in the crowded inner part of the helix, accelerates the mutarotation. Whereas the relatively weak steric repulsion between side-groups of **P2** with glycosyl groups in the exterior part of the helix leads to a slower mutarotation. By taking advantage of isolation and ready transition of KCCs, **P2** and **P4** may find applications in chiral separation, asymmetric catalysis, and sensors.

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