Induction of one-handed helical oligo(*p*-benzamide)s by domino effect based on planar-axial-helical chirality relay[†]

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One-handed helical oligo(*p*-benzamide)s were induced *via* the domino effect based on the planar-axial-helical chirality relay triggered by a planar chiral transition-metal complex at the terminal position as the single chiral source.

Helical chirality is one of the most important and central conformational motifs, such as found in DNA and the secondary structure of proteins. Recent studies have focused on the induction of one-handed helical chirality in polymers.¹ One efficient and attractive method for the induction of helical chirality in polymers and oligomers is the control of whole helical chirality of a dynamic helix by the site-specific action of an external stimulus upon a terminal position.² Inai et al. reported the outstanding domino effect on the helical screw sense of chiral peptides possessing a terminal chiral residue as the single chiral source.³ On the other hand, we previously reported the stereoselective synthesis of axial chiral benzamides or anilides induced by planar chiral transition-metal complexes.⁴ Thus, it is expected that the fixation of terminal axial chirality of amide in a dynamic helix composed of oligoamides could induce chirality in the whole helix via the domino effect. In this communication, we report the details of the induction of a one-handed helix by the domino effect based on a planar-axial-helical chirality relay triggered by a planar chiral ferrocene as a single chiral source (Scheme 1).

As the achiral and dynamic helical backbone, *N*-alkylated poly(*p*-benzamide)s recently reported by Kobayashi and Yokozawa were used.⁵ Initially, (*S*)-*N*,*N*-methylphenyl-2-iodoferroceneamide **1** was synthesized and its axial chirality corresponding to the first stage of chiral induction by the planar chirality of **1** was studied (Fig. 1). It has been reported that *N*-alkylated benzamides exhibit *cis* conformation in solution and the solid phase.^{6,7} Thus, it is expected that ferroceneamide **1** would also exhibit *cis* conformation (*i.e.*, ferrocenyl and phenyl groups lie on the same side). Furthermore the axial chirality of ferroceneamide would determine

the direction of helicity, namely, right- or left-handed. X-Ray crystal structure analysis‡ indicated that ferroceneamide 1 exhibits *cis* conformation and has a CpFe fragment located at the opposite side of the phenyl group, thus inducing (*S*)-axial chiral amide. On the other hand, examination of the conformation of ferroceneamide 1 in solution by variable-temperature NMR revealed that 1 showed only one isomer from room temperature to -60 °C. Thus, ferroceneamide 1 retains the thermodynamically stable conformation even in solution.

We next examined the second stage of the one-handed helical induction of oligobenzamides by axial chirality. N-Alkylated poly(p-benzamide)s required three benzamides units for one turn.⁵ We synthesized the trimer, the tetramer and the hexamer of oligo N-methyl-p-benzamides and (S)-2 was attached to the terminal position of each oligobenzamides. As shown in Fig. 2, the circular dichroism (CD) spectra of 3b, 3c and 3d indicated a negative Cotton effect at 260 nm in the wavelength region of the benzamide unit and a positive Cotton effect at 310 nm in CHCl₃. These differences in CD patterns from that of the monomer 3a clearly indicate that the observed CDs of 3b, 3c and 3d are induced circular dichroisms (ICDs) by an induced one-handed helix based on an oligoamide unit in CHCl₃.⁸ In addition, these observed ICD spectra were in agreement with the reported right-handed oligobenzamides with a chiral *N*-alkyl group in each monomer unit.⁵ Thus, fixation of axial chirality of an amide would allow for control of the second stage of chiral induction, *i.e.*, the whole helical chirality and the direction of the one-handed helix.

Although X-ray crystal structure analysis of **3** met with an unsuccessful result, theoretical calculation indicates a righthand helical structure as the most stable conformation shown in Fig. 3. Positive and negative CD bands that give rise to the net electronic transition moment in oligo(p-benzamide)s would associate with the moments that are parallel and perpendicular to the helix axis, respectively.⁵ Based on these



Scheme 1 Chirality relay in a dynamic helix.

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Fig. 1 X-Ray crystal structure of ferroceneamide 1 with axial chirality of amide.





aspects, a decrease of the positive CD band in 3c and 3d compared with that in 3b would indicate a decrease in a diastereomeric excess in the helical propensity. In connection with the above, to discuss the limitations of a chiral transmission in solution, it is necessary to introduce a marker that acts as a diastereotopic probe at the another terminal.⁹ Thus, whether the overlapping of ICDs in 3c and 3d is an indication of the limitation of chiral transmission in our system, needs further investigation.¹⁰



Fig. 3 RHF/3-21G optimization of ferroceneamides

On the other hand, when **3b** and **3d** were dissolved in CH₃CN, "clear-cut" ICDs were not observed in contrast with the case where they were dissolved in CHCl₃. One possibility is that the helical conformation partially changed in CH₃CN, which might be caused by the difference in solvent polarity (see ESI† for details). As our aim was to explore effective chiral transfer systems, we next examined *p*-tris(benzamide)s with 2-methyl- and 2-naphthyl-substituted planar chiral ferrocene carboxylic acids as the chiral source (Fig. 4). In the 2-methyl-substituted derivatives **4a** and **4b**, the negative CD bands at ~270 nm would be due to the planar chirality and no ICD was observed.

However, as the positive CD band at 310 nm in **4b** is assigned to a newly generated CD band, we surmise that **4b** might adopt a loosely folded conformation. On the other



Fig. 4 (a) CD and (b) UV spectra of 4 and 5 in CHCl₃.

hand, 2-naphthyl-substituted derivative **5b** did not show any significant ICD. Thus, we could not obtain systems that are more effective than 2-iodo-substituted ferrocene derivatives at the present stage.

In summary, we have succeeded in inducing one-handed helical oligo(*p*-benzamide)s *via* the domino effect based on the planar-axial-helical chirality relay triggered by a planar chiral transition-metal complex as the single chiral source. Studies of the stereocontrol of ultra-remote sites *via* communication of chiral information¹¹ through the planar-axial-helical chirality relay are under way.

Notes and references

‡ *Crystal data* for 1: C₁₈H₁₆NOFeI, M = 445.08, tetragonal, $P4_{1}2_{1}2$, a = 11.742(3), b = 11.742(3), c = 24.521(6) Å, $V = 3381.0(1)^3$ Å³, Z = 8, $D_c = 1.749$ g cm⁻³, μ (Mo-K α) = 2.718 mm⁻¹, F(000) = 1744.00, T = 296 K, 32 883 reflections collected, 3878 unique ($R_{int} = 0.026$), $R_1 = 0.0308$ ($I > 2\sigma(I)$), $wR_2 = 0.0827$ (all data), S = 1.029, Flack parameter -0.01(3). Data collection was carried out using the RIGAKU RAXIS RAPID, and SHELXL97 programs were used for the structure solution and refinement.

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