Synthesis and Helical Structure of Oligo(quinoline-2,3-diyl)s

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Oligo(quinoline-2,3-diyl)s having a terminal bromo group were synthesized by the Suzuki–Miyaura coupling of 5,8-disubstituted 2-bromoquinolin-3-ylboronic acid derivatives, and their helical structures were elucidated by a single-crystal X-ray analysis of the hexamer, UV measurements, and induction of a non-racemic helical sense by introduction of a chiral end group.

Helical organic polymers and oligomers attract much attention in organic chemistry, because they are expected to exhibit unique properties arising from their helical structures.[1] In particular, much effort has been devoted to selective synthesis of helical polymers that are capable of retaining non-racemic helical structures.[1,2] For further development in this field, it seems to be very important to explore new polymer scaffolds constituting stable helical structures.

We have been interested in the synthesis of aromatic polymers and oligomers in which naphthalene-like monomer units are linked together at their 2- and 3-positions.[3,4] Such polymers are not capable of adopting a planar structure because of steric repulsion between the rings; instead they adopt helical structures to minimize the steric repulsion in certain cases (Figure 1). It has also been demonstrated that the helical structure can be controlled by introduction of appropriate chiral groups at the terminus of the polymer and oligomers.[2c,3d] Herein, we report the synthesis of new quinoline oligomers,[5] in which quinoline units are linked at their 2- and 3-positions. The helical structure of the oligoquinolines was established by a single-crystal X-ray analysis. Moreover, the non-racemic helical sense was successfully induced in the oligoquinolines by introduction of optically active amide groups at the termini of the oligomers.

2-Bromoquinolin-3-ylboronic acid derivatives **1**[6] were subjected to the Suzuki–Miyaura coupling[7,8] under various reaction conditions (Figure 2). A reaction of the boronic acid **1a** in the presence of a $Pd(PPh_3)_4$ catalyst produced trimer **2** ($n = 3$) as the major product (34%) along with the higher oligomers up to the pentamer in 51% total yield (Entry 1).[9] We then switched the catalyst system to $Pd[P(t\text{-}Bu)_3]_2$ to obtain higher oligomers.[10] In the presence of KF as an additive, boronic acid **1a** produced higher oligomers up to the 12mer, which were detected by MS (Entries 2 and 3). In the reaction mixture after 10 h (Entry 2), a considerable amount (18%, not included in the total oligomer yield) of 2-bromo-5,8-dimethylquinoline **2** ($n = 1$), which may be derived by hydrolysis of **1**, was obtained. A longer reaction time resulted in the shift of the distribution toward higher oligomers ($n = 8$–12; 23%), giving a higher total yield (78%) of oligomers (Entry 3). In Entries 4 and 5, the corresponding pinacol boronate **1b** was used to minimize hydrolysis of the monomer. The boronate **1b** showed a significantly lower reactivity than **1a**. Only 19% of oligomers was obtained, along with a considerable amount of hydrolyisis product, in aqueous dioxane with KF as an additive (Entry 4). However, the use of anhydrous DMF as the solvent with use of $NaHCO_3$ as the base dramatically improved the yield of oligomers (94%) (Entry 5). The reaction produced higher oligomers ($n = 8$–12) in 10% total yield in addition to trimer to heptamer (18, 13, 20, 19, and 14% yield, respectively). Almost no hydrolysis product was detected in the reaction mixture. It should be noted that extension of the reaction time did not change the oligomer distribution.

On the basis of MS and NMR analysis, the oligomers were found to lack the terminal boryl groups, but retained the bromo group at the 2 positions of the oligomers.[9] The oligomers higher than trimer ($n \geq 4$) showed broadened ^1H NMR signals at room temperature (400 MHz). The pentamer showed a complicated NMR spectrum at room temperature in benzene-d_6, while sharp signals were observed at 55 °C. As for the hexamer, a well-resolved NMR spectrum could not be obtained even at 80 °C. The oligomers ($n = 3$–7) isolated as colorless solids showed almost constant λ_{max} (273 nm) and a shoulder (ca. 340 nm) in the UV spectra (Figure 3), suggesting that there is no significant conjugation along the oligoquinoline skeleton and that the oligomers do not adopt a planar structure.[11]

The oligo(quinoline-2,3-diyl)s were dissolved in acidic aqueous solution. Although 2 M hydrochloric acid hardly dissolved the hexamer at room temperature, 6 M hydrochloric acid

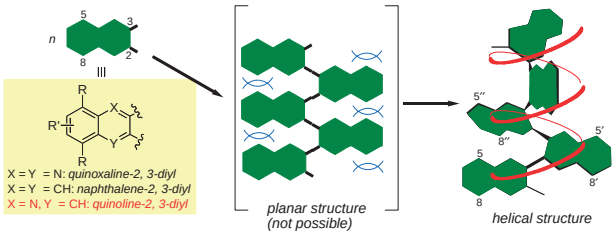


Figure 1. A concept of helix formation by linking 5,8-disubstituted naphthalene-2,3-diyl-like monomers.

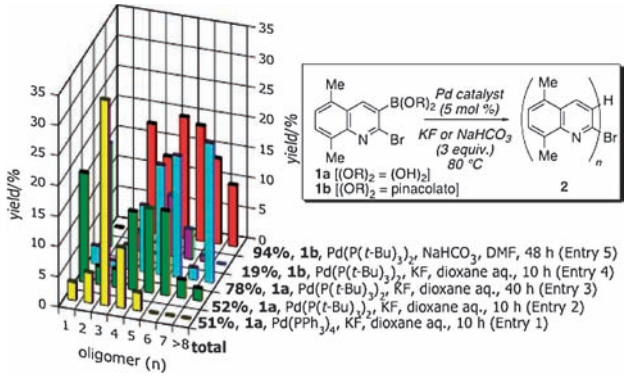


Figure 2. Synthesis of oligo(quinoline-2,3-diyl)s by Suzuki–Miyaura coupling of **1a** or **1b**.

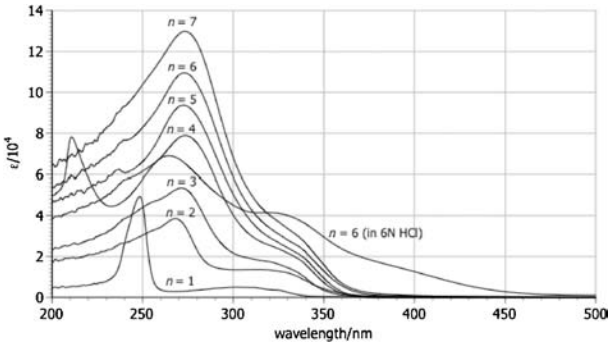


Figure 3. UV–vis spectra of **2** ($n = 1$–7). Solvent: $CHCl_3$ ($n = 1$–7) or 6 M hydrochloric acid ($n = 6$); Concentration: 4.6–7.4 × 10^{-6} M.

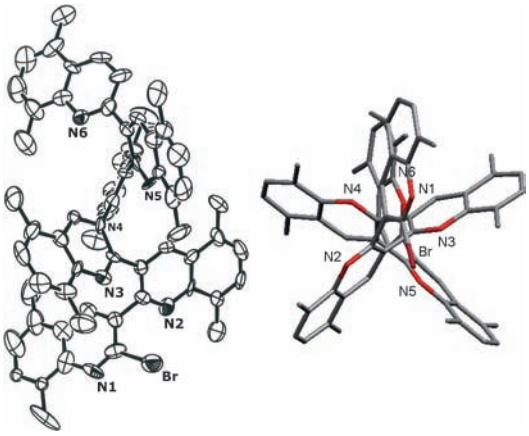


Figure 4. X-ray structure of hexamer **2** ($n = 6$). (left) Side view; (right) top view.

could dissolve it, albeit in low concentration [at least 2 mg **2** ($n = 6$) in 10 mL of 6 M HCl (aq)]. The protonated hexamer showed a UV spectrum significantly different from that of unprotonated **2** ($n = 6$) in $CHCl_3$ (Figure 3).[11] By neutralization of the acidic solution, the hexamer was recovered unchanged.

The helical structure was established by a single-crystal X-ray analysis of the hexamer (Figure 4). A single crystal suitable for the analysis was obtained by recrystallization from CH_2Cl_2–hexane. The oligomer adopted the 5/2 helix with an average dihedral angle of 127° between the adjacent quinoline rings.

The pentamer **2** ($n = 5$) was aminocarbonylated via a palladium-catalysed reaction with optically pure primary amines under a carbon monoxide atmosphere (eq 1).[12] The obtained oligomers having the optically active aminocarbonyl terminal group exhibited CD spectra with distinctive Cotton effect couplets (Figure 5). It is remarked that the intensity of the CD curve is greatly influenced by the optically active amino moiety. The aminocarbonylated pentamers (*R*)-**3a** and (*S*)-**3a** derived from the enantiomers of 1-cyclohexylethylamine exhibited CD spectra that were the mirror image of each other. Furthermore, the pentamer (*S*)-**3c** derived from the *t*-butyl-substituted optically active amine showed the most intense CD curve among the three examined. These results suggest that the chiral end group induced a non-racemic helical structure on the oligoquinoline backbone, although the degree of screw-sense induction as well as the sense of the helix is currently unknown.[3d]

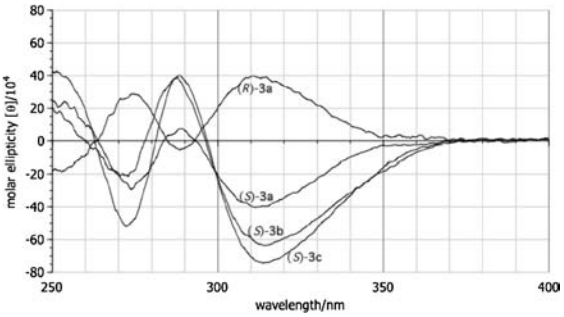
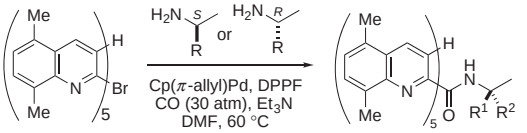


Figure 5. CD spectra of optically active quinoline pentamers **3a**–**3c**.



(1)

(*R*)-**3a** (R^1 = H, R^2 = Cy): 61%
(*S*)-**3a** (R^1 = Cy, R^2 = H): 41% (1 atm CO)
(*S*)-**3b** (R^1 = Ph, R^2 = H): 45%
(*S*)-**3c** (R^1 = *t*-Bu, R^2 = H): 39%

Further studies on improvement of the polymerization procedure to obtain higher polymers and properties of the new quinoline oligomers are now being undertaken in this laboratory.

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