Synthesis of a Chiral Nonracemic Segmented Screwlike Oligomer. An Unusual Form of Molecular Chirality

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Many organic polymers possess helical backbones; however, with both antipodes usually present in nearly equivalent molar ratios, the bulk materials are racemic. When a chiral monomer is employed, there often results a preference for helix formation in one direction because there is registry between the consecutive repeat units. As a result of the registry-induced helicity, the optical rotations of the polymer show enormous enhancements over that of the individual monomers used.[1] Conceptually, there could be other new and interesting types of helicity in polymers, for example, a rigid-rod polymer whose backbone is linear but with a helical arrangement mapped out by the functional groups emanating from that linear backbone (Figure 1). But again, registry along the backbone exists to form a contiguous helical arrangement. If we consider, however, a linear polymer with restricted registry between the consecutive chiral units by utilizing segmental spacer groups that are freely rotating along the axis of the linear backbone (Figure 2), the optical rotations may be monomerlike rather than reflective of a long-range screwlike ordering. We describe here routes to either antipode of a chiral nonracemic soluble rigid-rod conjugated oligomer with such segmented screwlike properties. With this new molecular framework, we demonstrate that even highly aligned chiral groups along a common axis are insufficient for large optical rotational enhancements if there is no repeat unit registry.

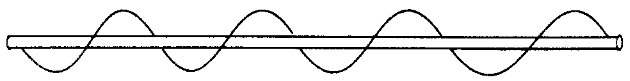

Figure 1. Screw arrangement that has a linear backbone with a helical twist emanating from the backbone.

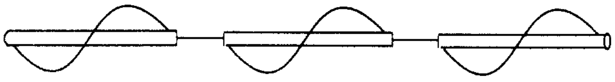

Figure 2. Segmented screw that has a helix interrupted at regular intervals along the linear backbone.

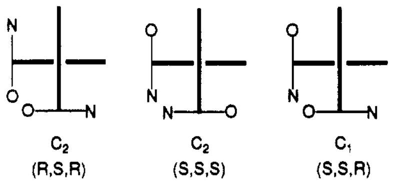

Figure 3. Representations of the three isomeric possibilities. The dark lines represent the binaphthyl system, while the carbonyl oxygen is represented by the O and the $N(i\text{-}Pr)_2$ group is represented by the N.

We sought to synthesize the required segmented screw framework by using a chiral binaphthyl-containing monomer for induction of the helical domains along the linear backbone while metal-promoted 1,4-disubstituted benzene couplings would permit the high chemical yields needed for the oligomerization.[2] The synthesis is outlined in Scheme 1. (*S*)-(−)-Binaphthol (**1**) (>99% ee)[3] was obtained by selective hydrolysis of the diester,[4] and then **1** was dimethylated to form **2**.[5] Use of electrophilic aromatic substitution reactions to cleanly introduce further functionality was not successful. We therefore utilized successive bis(orthometalation)[6] reactions to first dicarboxylate the binaphthyl unit to form **3** and then affix the pinacolboronic esters to form **5** via the bisamide **4**.[7] The enantiomeric purities of **2**, **3**, **4**, and **6** were determined by addition of the chiral ^{1}H NMR shift reagent (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol ((*S*)-(+)-TFAE) and monitoring of the methoxy methyl resonances at −50 °C (500 MHz).[8] While the isopropyl methyl groups on **4** (without (*S*)-(+)-TFAE) appeared as a multiplet in the ^{1}H NMR at room temperature, the isopropyl methyl resonances in **5** were far sharper and appeared as a triplet (6 H) and overlapping doublets (6 H), presumably due to carbonyl oxygen donation into the boron to form a conformationally restricted pseudo-5-membered ring. Direct oligomerization of **5** by metal-catalyzed cross coupling with aryl dibromides was unsuccessful probably due to the steric encumbrance around the naphthylboronic esters.[9] In order to provide both a less sterically hindered coupling moiety and the segmental spacer group needed, we affixed bromophenyl groups to the naphthyl system.[10] While **5** was a single isomer (one set of signals in the ^{13}C NMR), this was not the case in the bromophenyl systems; a diastereomeric mixture consisting primarily of two compounds, **6** and **7**, formed which were separable by column chromatography. One of the two compounds had C_2 symmetry, substantiated by its four isopropyl methyl doublets and one methoxy methyl singlet; therefore, its two carbonyls must be arranged as shown in **6** to give the (*R*,*S*,*R*) stereoisomer (three axes of atropisomerism) (Figure 3). Conversely, **6** could be the (*S*,*S*,*S*) isomer; however, this would force the eight bulky diisopropyl methyl groups to be in the same cleft, therefore, undoubtedly higher energy than the (*R*,*S*,*R*) stereochemistry where the two carbonyl oxygens occupy the same cleft (Figure 3). The second compound isolated was not C_2 symmetric, but C_1 symmetric, since we observed eight isopropyl methyl doublets and two methoxy methyl singlets. Thus, the two carbonyl oxygens must be pointing as shown in **7** to give the (*S*,*S*,*R*) stereochemistry (again, three axes of atropisomerism) (Figure 3). Unfortunately, at subsequent coupling temperatures, the asymmetry about the aryl–carbonyl bond was not retained; isomerization of the aryl–carbonyl carbon occurred at elevated temperatures so that either **6** or **7** in DMF at 100 °C for 4 h afforded an identical 2.8:4.3:1.0 mixture of the three isomers **6**, **7**, and the sterically least favored (*S*,*S*,*S*) isomer (one new methoxy methyl signal), respectively (Figure 3).[11] However, the stereochemical integrity about the central binaphthyl unit is preserved at these temperatures.[12]

Oligomerization of **6** under nickel(0)-promoted coupling conditions[13] (70–80 °C) afforded the desired segmented screwlike oligomer **8** in 90% yield after fractional precipitation from MeOH (M_n = 7000; M_w = 14 700 by size exclusion chromatography (SEC) relative to polystyrene).[14,15] We have also prepared the oligomer of **7** as well as the enantiomers of **6**–**8** starting with the enantiomer of **1** obtained by saponification of the ester remaining after the enzymatic hydrolysis.[16] Again, stereochemical isomerization about the aryl–carbonyl bond was not retained; therefore, both **6** and **7** afforded the same oligomer **8**.[16,17]

Unlike most chiral nonracemic polymers,[1] the segmented screwlike oligomer described here does not exhibit such

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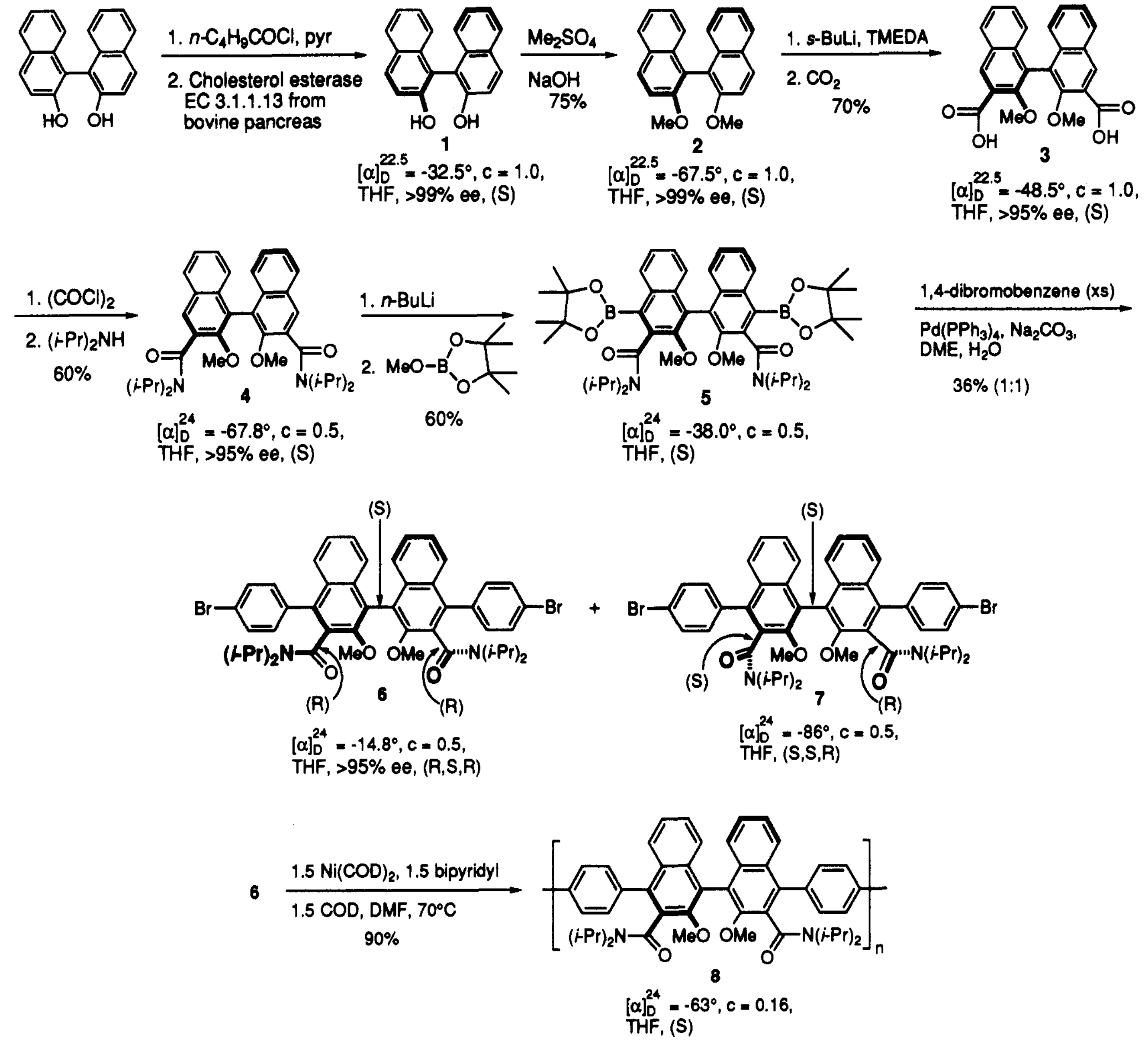
Scheme 1



large enhancements in the degrees of optical rotation. Even though the chiral monomer units are aligned along a common axis, the lack of repeat unit registry prevents large increases in the optical rotations. Indeed, $[\alpha]^{24}{}_D = -63°$ for **8** is a value between the optical rotational values of **6** and **7**, yet skewed in the direction of the more stable stereoisomer **7**. Also consistent with the near 90° twist of the binaphthyl ring system,[12b,18] the optical absorbance of the oligomer is nearly unchanged from that of the monomer ($\lambda = 305$ for a 4,4′-diphenylbinaphthyl monomer to $\lambda = 320$ nm for **8**).

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Supplementary Material Available: Detailed experimental procedures for the synthesis and characterization of both antipodes of 1–8 (6 pages). Ordering information is given on any current masthead page.

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(2) Though high degrees of asymmetric induction for the couplings of naphthalene units can be achieved with chiral metal complexes, the steric bulk around substituted naphthyl ring systems causes chemical yields to be inadequate for a direct step-growth process. See: Hayashi, T.; Hayashizaki, K.; Kiyoi, T.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8153.

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(7) We have also quenched the dilithio species derived from **4** with 1,2-dibromoethane to afford the corresponding binaphthyl dibromide; however, all attempts to carry out Pd(0)- or Pd(0)/Cu(I)-coupling reactions of this dibromide with arylmetals or 1-alkynes were unsuccessful. Thus, this naphthyl system is particularly hindered.

(8) Racemic **2** showed two methoxy methyl singlets (4.0-Hz separation) in the presence of (*S*)-(+)-TFAE, while the nonracemic **2** showed only one methoxy methyl singlet (>20:1) in the presence of the same shift reagent. This trend was consistent throughout the ^{1}H NMR analyses of **2**, **3**, **4**, and **6** and their respective antipodes. The Lewis acidic boron sites in **5** and the overlap of the isopropyl methinyl proton with the methoxy methyl protons in the non-C_2 symmetric **7** hindered our efforts to firmly quantify their enantiomeric purities. However, enantiomeric excesses of >95% can be inferred for compounds **5** and **7** based on the stereochemical purity of **6**. For original use of this chiral NMR shift reagent, see: (a) Pirkle, W. H.; Boeder, C. W. *J. Org. Chem.* **1977**, *42*, 3697. (b) Pirkle, W. H.; Sikkenga, D. L.; Paulin, M. S. *J. Org. Chem.* **1977**, *42*, 384.

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(14) Polymerization of the racemic analog on a larger scale afforded a higher molecular weight material with M_n = 14 900 and M_w = 29 800. Calcd for $(C_{48}H_{50}N_2O_4)_n$: C, 80.19; H, 7.01; N, 3.90. Found: C, 78.29; H, 7.16; N, 3.62; Br, <0.5.

(15) Since SEC is a measure of the hydrodynamic volume and not the molecular weight (MW), significant errors in M_n and M_w may result when comparing rigid-rod polymers with the flexible coils of the polystyrene standards. Therefore, the values recorded here are given simply as a reference. However, using analytical SEC, we have been able to resolve the discrete oligomers, monomer (confirmed with an authentic monomer sample) through octamer, on the late retention end of the SEC distribution plots. The crest in the modal distribution occurs at 8 repeat units in **8** which corresponds to a MW of approximately 6000 and equals 32 contiguous aryl units.

(16) (−)-**7** ($[\alpha]_D$ = −86°, *c* = 0.5, THF, 23 °C) afforded (−)-**8** ($[\alpha]_D$ = −56°, *c* = 0.15, THF, 23 °C) in 85% yield. (+)-**6** ($[\alpha]_D$ = +13°, *c* = 0.5, THF, 23 °C) afforded (+)-**8** ($[\alpha]_D$ = +53°, *c* = 0.06, THF, 23 °C) in 80% yield. (+)-**7** ($[\alpha]_D$ = +85°, *c* = 0.5, THF, 23 °C) afforded (+)-**8** (+62°, *c* = 0.25, THF, 23 °C) in 85% yield.

(17) Interestingly, while an identical binaphthyl screw arrangement will result regardless of the direction of insertion from the C_2 symmetric segments, the C_1 symmetric binaphthyl segments possess differing directional helicities due to their inherent symmetry restraints.

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