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**by**

**Peter V. Bedworth and James M. Tour**

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## **Synthesis of a Chiral Non-Racemic Segmented Screw-Like Oligomer. An Unusual Form of Molecular Chirality\*\***

**By Peter V. Bedworth and James M. Tour\***

### **Abstract**

Described is the synthesis of a chiral non-racemic conjugated organic oligomer that possesses a linear backbone but has segmented helical functional groups emanating from the backbone. Both antipodes were independently synthesized. The monomer is based upon a chiral non-racemic binaphthalene core with *p*-bromophenyl groups at the 4 and 4'-positions of the binaphthalene. The monomer was prepared using successive bis(orthometallation) reactions on chiral non-racemic binaphthol. The *p*-bromophenyl groups were affixed via a Pd(0)-catalyzed cross coupling of 1,4-dibromobenzene and the 4,4'-bis(boronic ester) of the binaphthalene. The final oligomerization was affected by a Ni(0)-promoted coupling of the arylbromides. The new oligomeric framework demonstrates that even highly aligned chiral groups along a common axis are insufficient for large optical rotational enhancements if there is no repeat unit registry.

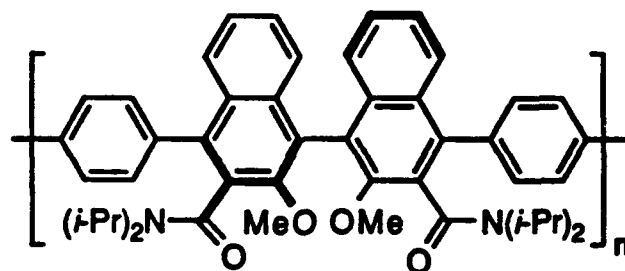
[\*] Prof. J. M. Tour, P. V. Bedworth

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Text for the table of contents:

Described is the synthesis of a chiral non-racemic conjugated organic oligomer that possesses a linear backbone but has segmented helical functional groups emanating from the backbone. Such a form of molecular helicity has been hitherto unreported. Both antipodes were independently synthesized. The monomer is based upon a chiral non-racemic binaphthalene core with *p*-bromophenyl groups at the 4 and 4'-positions of the binaphthalene. The monomer was prepared using successive bis(orthometallation) reactions on chiral non-racemic binaphthol. The final oligomerization was affected by a Ni(0)-promoted coupling of the arylbromides. The new oligomeric framework demonstrates that even highly aligned chiral groups along a common axis are insufficient for large optical rotational enhancements if there is no repeat unit registry.



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.<sup>[1]</sup> 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).

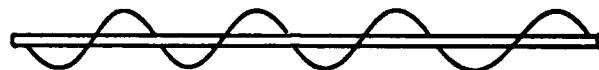


Figure 1. A screw arrangement that has a linear backbone with a helical twist emanating from the backbone.

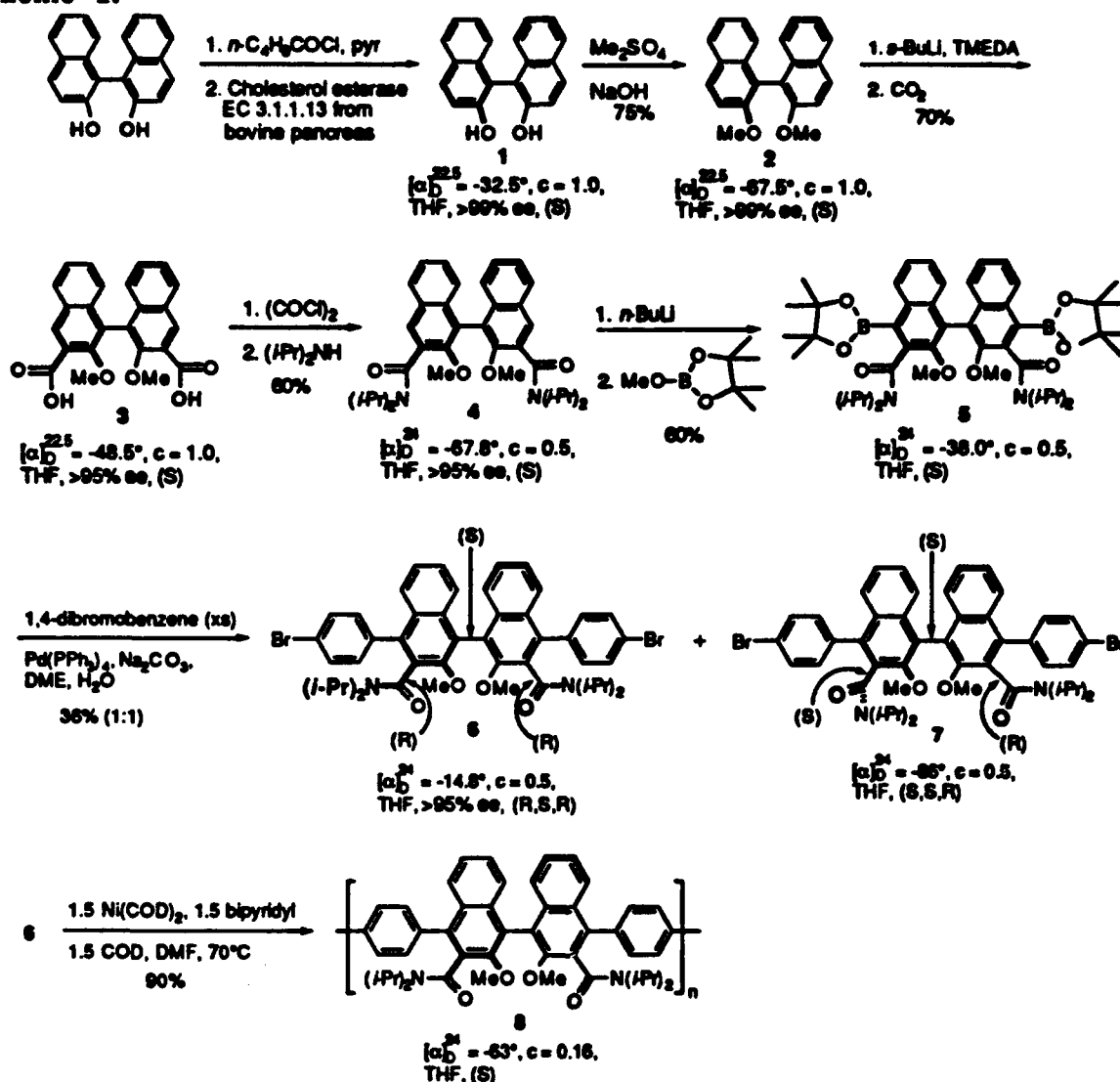


Figure 2. A segmented screw that has a helix interrupted at regular intervals along the linear backbone.

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 monomer-like rather than reflective of a long range screw-like ordering. We describe here routes to either antipode of a chiral non-racemic soluble rigid rod conjugated oligomer with such segmented screw-like 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.

Though high degrees of asymmetric induction for the coupling 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.<sup>[2]</sup> We therefore sought to synthesize the required segmented screw framework by using a chiral binaphthyl-containing

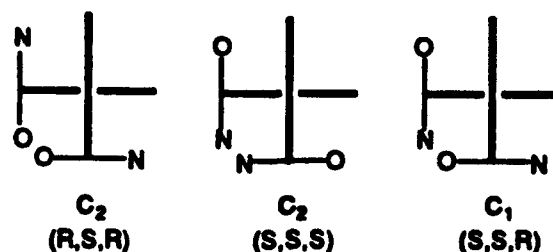
Scheme 1.



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. The synthesis is outlined in Scheme 1. (S)-(-)-Binaphthol (1) (>99% ee)<sup>[3]</sup> was obtained by selective hydrolysis of the diester,<sup>[4]</sup> and then 1 was dimethylated to form 2.<sup>[5]</sup> Use of electrophilic aromatic substitution reactions to cleanly introduce further functionality was not successful. We therefore utilized successive bis(orthometallation)<sup>[6]</sup> reactions to first dicarboxylate the binaphthyl unit to form 3 and then affix the pinacol boronic esters to form 5 via the bisamide 4. 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 systems is particularly hindered. The enantiomeric purities of **2**, **3**, **4**, and **6** were determined by addition of the chiral  $^1\text{H}$  NMR shift reagent (S)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol ((S)-(+)-TFAE) and monitoring of the methoxy methyl resonances at  $-50^\circ\text{C}$  (500 MHz).<sup>[7]</sup> Racemic **2** showed two methoxy methyl singlets (4.0 Hz separation) in the presence of (S)-(+)-TFAE while the non-racemic **2** showed only one methoxy methyl singlet (>20:1) in the presence of the same shift reagent. This trend was consistent throughout the  $^1\text{H}$  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- $\text{C}_2$  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**. While the isopropyl methyl groups on **4** (without (S)-(+)-TFAE) appeared as a multiplet in the  $^1\text{H}$  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. Indeed, less hindered phenyl pinacol boronic esters can couple in high efficiencies for a step growth polymerization.<sup>[8]</sup> 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.<sup>[9]</sup> While **5** was a single isomer (one set of signals in the  $^{13}\text{C}$  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  $\text{C}_2$  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) (Fig 3).





**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  $\text{N}(i\text{-Pr})_2$  group is represented by the N.

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) stereoisomer where the two carbonyl oxygens occupy the same cleft (Fig 3). The second compound isolated was not  $\text{C}_2$  symmetric, but  $\text{C}_1$  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) (Fig 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  $100^\circ\text{C}$  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 (Fig 3).<sup>[10]</sup> However, the stereochemical integrity about the central binaphthyl unit is preserved at these temperatures.<sup>[11]</sup>

Oligomerization of **6** under nickel(0)-promoted coupling conditions<sup>[12]</sup> ( $70\text{--}80^\circ\text{C}$ ) afforded the desired segmented screw-like oligomer **8** in 90% yield after fractional precipitation from MeOH ( $M_n = 7,000$ ;  $M_w = 14,700$  by size exclusion chromatography (SEC) relative to polystyrene). Note that polymerization of the racemic analog on a larger scale afforded higher molecular weight material with  $M_n = 14,900$ ;  $M_w = 29,800$ .<sup>[13]</sup> 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 authentic monomer sample) through octamer, on the late retention end of the SEC distribution plots. The crest in the modal distribution occurs at eight repeat units in **8** which corresponds to a MW of approximately 6,000 and equals 32 contiguous aryl units. 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.<sup>[14]</sup> Again, stereochemical isomerization about the aryl-carbonyl bond was not retained, therefore, both **6** and **7** afforded the same oligomer **8**.

Unlike most chiral non-racemic polymers,<sup>1</sup> the segmented screw-like oligomer described here does not exhibit such 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,  $[\alpha]_D^{24} = -63^\circ$  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**. 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. Also consistent with the near  $90^\circ$  twist of the binaphthyl ring system,<sup>[11]</sup> 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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[14] (-)-7 ( $[\alpha]_D = -86^\circ$ ,  $c = 0.5$ , THF,  $23^\circ\text{C}$ ) afforded (-)-8 ( $[\alpha]_D = -56^\circ$ ,  $c = 0.15$ , THF,  $23^\circ\text{C}$ ) in 85% yield. (+)-6 ( $[\alpha]_D = +13^\circ$ ,  $c = 0.5$ , THF,  $23^\circ\text{C}$ ) afforded (+)-8 ( $[\alpha]_D = +53^\circ$ ,  $c =$

0.06, THF, 23°C) in 80% yield. (+)-7 ( $[\alpha]_D = +85^\circ$ ,  $c = 0.5$ , THF, 23°C) afforded (+)-8 ( $+62^\circ$ ,  $c = 0.25$ , THF, 23°C) in 85% yield.