Advances in the Synthesis of Polymeric, Enantiomerically Enriched Helicenes and Acenes

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Abstract

Helicene molecules have enormous potential utility. Helicenes are foreseen to act as organic semiconductors, components of fast optical switches, asymmetric catalysts, and molecular actuators. Acene molecules have potential utility as organic semiconductors due to their linear, conjugated pi-electron system. Yet despite this multitude of uses, there has been no method of preparing polymeric helicenes until recently and there remains no method of preparing enantiomerically enriched helicenes or polymeric acenes. We have developed a new synthetic strategy consisting of a ring closing olefin metathesis [2], which has proven to be very successful and, thus, progress towards enantiomerically enriched, polymeric helicenes is continuing with little hindrance. The synthetic route employed to obtain polymeric acenes did not yield promising results, so progress toward polymeric acenes has slowed until a new synthetic strategy is developed.

Introduction

Helicene molecules consist of ortho-fused benzene rings, similar to coronene. However, the sixth benzene ring is not fused to the first in helicene molecules, but rather to the seventh, and so on. Figure 1 is a depiction of [13.3.1]helicene (consisting of 13 ortho-fused benzene rings). The steric hindrance of the molecule causes it to twist out of the plane, creating a screw-shape. Thus, helicenes are chiral even though they do not possess any chiral carbons; they can form clockwise or counter-clockwise screws.
Helicene molecules have enormous potential utility. Helicenes are foreseen to act as organic semiconductors, components of fast optical switches, asymmetric catalysts, and molecular actuators. Helicenes are potentially useful to the fields of nano-electronics, nano-mechanics, medicinal chemistry, and to the pharmaceutical industry. Due to their conjugated pi-electron system, they can conduct electricity. Helicenes can rotate light almost 10000°, a quality that makes them ideal components of fast optical switches [3]. The length of functionalized helicenes has been shown to be a function of pH, a quality that allows the molecule to stretch and contract, producing motion [6]. To produce a significant amount of force as molecular actuators, it is desirable to produce polymeric helicenes that can develop a larger amount of motion and stretch larger distances. The electronic properties of organic semiconductors are a function of the purity of the compound [1], thus enantiomerically pure portions are needed. Also, to act as asymmetric catalysts and be useful to medicinal chemistry, a sample of helicene containing only one enantiomer must be prepared.
Acene molecules consist of benzene rings linearly fused, creating a linear molecule (figure 2), rather than the helical shape of the ortho-fused rings of the helicene.

![Diagram of Acene molecule](image)

**Figure 2.** A depiction of a general polymeric helicene, consisting of \( n \) monomer units.

Acene molecules have potential utility as organic semiconductors due to their conjugated pi-electron system. The larger acenes are already employed as supercapacitors called polyacene batteries (www.wikipedia.com). Many desirable properties of the acene molecule are enhanced with increasing length: decreasing reorganization energy and exciton binding energy and increasing carrier mobility and band width [1]. However, heptacene (consisting of 7 benzene rings) is the largest acene thus synthesized and due to its instability, had to be isolated within a poly (methyl methacrylate) (PMMA) matrix [1]. Stability of the acene decreases with increasing length.

Yet despite this multitude of uses, there has been no method of preparing polymeric helicenes until recently and there remains no method of preparing enantiomerically enriched helicenes or polymeric acenes. Until recently, the largest helicene to be produced was [14.3.1]helicene, synthesized by photocyclization in 1975 by Martin and Baes. In 2005, King and Bonifacio synthesized the first polymeric helicene by utilizing a ring closing olefin metathesis reaction. However, characterization of the helicene was difficult due to the presence of both enatiomers. Thus, there remains a need for syntheses of polymeric, enantiomerically enriched helicenes and acenes.
Results and Discussion

Progress was made toward synthesis of polymeric, enantiomerically enriched helicenes. It is thought that if a few chiral monomers are introduced into a larger polymeric backbone of non-chiral monomers, then the resulting molecule will organize itself according to the chirality of the chiral monomers; this is called the “soldiers and sergeants” effect. Thus, the synthesis of a chiral monomer for production of a polymeric helicene was undertaken. The first strategy (scheme 1) employed a Sonogoshira coupling reaction to attach chiral alkynes to 1,3-Dibromobenzene. The subsequent reduction of the alkynes would yield 4-[2,4-Dibromo-5-(3-hydroxy-but-1-enyl)-phenyl]-but-3-en-2-ol (3) that could act as a monomer for the synthesis of the polymeric helicene.

Scheme 1. Route to synthesizing chiral monomer to produce polymeric helicene.
A = I₂ / H₂SO₄
B = Diisopropylamine + CuI + Pd(PPh₃)₄ + 3-butyn-2-ol / THF
C = LiAlH₄

The synthetic route depicted in scheme 1 experienced a bottleneck after the synthesis of (2). The subsequent reduction of the alkynes to yield (3) was more difficult that initially expected. Thus, another approach was taken. A 4,6-Dibromobenzene-1,3-dicarbaldehyde molecule (5) was synthesized (scheme 2) and will be reacted with a Wittig reagent (4) to produce several stereoisomers. These isomers will be reacted with diphenyl disulfide to yield the desired chiral monomer (6). The production of (4), was
more troublesome than predicted; however, a synthesis was eventually discovered to create the desired chiral salt with about 90% yield (figure 2). The predicted soup of stereoisomers to be obtained after the Wittig reaction has yet to be synthesized and the step of this synthetic route currently being performed is the production of (4).

![Figure 2. Synthesis of (2-Methyl-butyl)-triphenyl-phosphonium bromide.](image)

**Scheme 2.** A synthetic strategy to achieving a chiral monomer to produce polymeric helicenes. (Stereochemistry is shown as unknown in (6) because a racemic reagent is being used.)

- A = Br₂ / I₂
- B = Br₅ / CH₂Cl₂
- C = AgNO₃ / EtOH
- D = (4) + KOT-Bu / THF
- E = Diphenyl disulfide
Another synthetic strategy was devised involving the synthesis of a 4,6-Dibromobenzene-1,3-dicarbaldehyde (5), followed by a Grignard reaction to create a diol (scheme 3). The dehydration of the diol molecule would yield a non-chiral monomer (7) to assist with polymerization by acting as a “soldier” in the aforementioned “soldiers and sergeants” effect. The dehydration was performed with phosphoryl chloride, but isolation of the desired product was not achieved.

**Scheme 3.** A synthetic route to producing non-chiral monomers to assist in the production of polymeric helicenes.
A = Br₂ / I₂
B = Br₃ / CH₂Cl₂
C = AgNO₃ / EtOH

Progress was also made toward synthesis of polymeric acenes. A strategy was devised utilizing a benzyne intermediate. The benzyne was generated using 1,2,4,5-Tetrabromo-3,6-dimethylbenzene and n-butyllithium and was reacted with perylene in toluene. The desired product was a pentacene molecule with bromine functionalization to assist in further polymerization (by subsequent reaction with additional perylene, for example). However, the product was not synthesized. The mono-adduct is thought to have been isolated, though not yet fully characterized. The product mixture fluoresced
very intensely (even under visible light), which is taken as evidence to support the belief that some product was synthesized that contained a conjugated pi system capable of such fluorescence.

Scheme 4. A synthetic route to obtaining bromine functionalized pentacenes.

Experimental

1,5-Dibromo-2,4-diiodobenzene

12.0g (51mmol) of 1,3-Dibromobenzene and 150mL of concentrated sulfuric acid were heated to 90°C. Very slowly, for 25 minutes, 30.0g (118.2mmol) of molecular iodine was added. The reaction was heated to 115°C for 11 hours. The mixture was poured on ice (~50g) and stirred overnight. The solution was filtered and the brown precipitate obtained was dissolved in toluene. The mixture was extracted three times with a mixture of Na₂SO₃ and Na₂CO₃. The mixture was extracted with brine and water until the pH of both phases was neutral. The organic phase was dried with MgSO₄ and the solvent was evaporated. The creamy solid obtained was recrystallized in toluene with 51% yield of (1). NMR spectra were identical to those previously listed for this compound.

4-[2,4-Dibromo-5-(3-hydroxy-but-1-ynyl)-phenyl]-but-3-yn-2-ol

3.2g (6.6mmol) of (1) and 0.97g of 3-butyn-2-ol was added to 110mL of diisopropylamine and evacuated, then back filled with nitrogen. This was repeated three
times to ensure that the reaction would not be disturbed by air or water. 0.15g of CuI was added under nitrogen and again, the reaction was evacuated and back filled with nitrogen. Anhydrous THF was added to the flask. 0.1526g of Pd(PPh$_3$)$_4$ was added to the flask under nitrogen. The reaction was stirred at room temperature for 24 hours. The inorganic material was removed by flash chromatography using silica dioxide. The solvent was evaporated and the product was recrystallized in dichloromethane to yield 65% of (2).

**1,5-Dibromo-2,4-dipropenyl-benzene**

To a three-necked flask was added 25mg (0.07mmol) 1-[2,4-Dibromo-5-(1-hydroxy-propyl)-phenyl]-propan-1-ol and 1mL pyridine (scheme 3). While stirring, 430mg (0.28mmol) phosphoryl chloride was added through a septum very slowly (1 drop every 1-2 seconds). The reaction refluxed at 120°C for three hours. A volume of water equal to the volume of pyridine (1mL) was added. The solution was extracted with diethyl ether and brine and the organic phase was dried over sodium sulfate. The solvent was evaporated and the product purified with flash chromatography using hexane: diethyl ether as an eluent in a 1:1 ratio. The solvent was evaporated, but the proton NMR spectrum did not show any aliphatic peaks. It was concluded that the desired product (7) was not synthesized.

**(2-Methyl-butyl)-triphenyl-phosphonium Bromide**

0.730g (4.84mmol) of 1-bromo-2-methylbutane (racemic) was combined with 1.27g (4.84mmol) of triphenylphosphine and refluxed at 130°C for 48 hours. The white, solid substance obtained was washed with ether to yield 1.74g (87%) of the desired product (4); a very elegant synthesis. $^1$H NMR (CD$_3$COCD$_3$) δ: 3.82, 3.83, 3.79, 3.78, 1.69, 1.65,
1.52, 1.50, 1.49, 1.48, 1.47, 1.45, 1.44, 1.39, 1.09, 1.07, 1.05, 0.97, 0.96, 0.84, 0.83, 0.82 ppm.

**2,3,9,10-Tetrabromo-1,4,8,11-tetramethyl-((5,6,7)(12,13,14))-tetraphenyl-pentacene**

135mg (0.32mmol) of 1,2,4,5-Tetrabromo-2,6-dimethylbenzene, 10mg (0.04mmol) of perylene, and 20mL of toluene were combined in a Schlenck flask, cooled to -15°C with an ethylene glycol / dry ice bath. The flask was then evacuated and back-filled with nitrogen three times. 0.12mL of 2.67M n-BuLi was added (0.32mmol) very slowly so that the temperature did not rise more than 2 or 3°C. The reaction was then brought to room temperature and quenched with methanol, the solvent was evaporated, and the mixture was separated on the Kugelrohr at 220°C. Analysis by atmospheric pressure photoionization (APPI) mass spectrometry of the portion of material that did not move on the Kugelrohr contained a peak around 512.0u. This peak is thought to correspond to the mono-adduct of the desired product (8).

**Conclusions**

Progress towards enantiomerically enriched, polymeric helicenes is continuing with little hindrance. Now that the racemic (2-Methyl-butyl)-triphenyl-phosphonium bromide has been produced, we will synthesize the enantiomerically pure phosphonium bromide and perform a Wittig reaction on (5). This will yield a chiral monomer (6) for production of enantiomerically enriched, polymeric helicenes. A different synthetic route toward enantiomerically enriched, polymeric helicenes (scheme 1) is also moving forward. Progress toward polymeric acenes has slowed until a new synthetic strategy is developed.
References


