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# Rigid Hydrophilic Structures for Improved Properties of Conjugated Polymers in Water

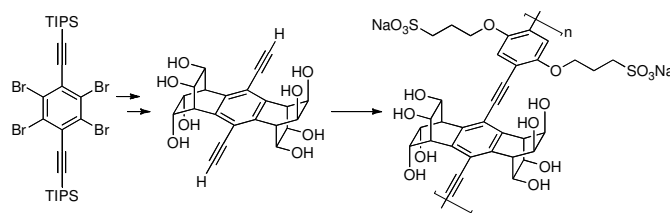
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## ABSTRACT



This paper describes the synthesis of a hydrophilic monomer bearing a three-dimensional noncompliant array of hydroxyl groups that prevents water driven aggregation of hydrophobic poly(*p*-phenylene ethynylene) polymer backbones.

Fluorescent conjugated polyelectrolytes (CPEs) are made water soluble by pendant ionic functionalities along the polymer backbone. CPEs have seen application in a variety of chemical and biological sensing schemes<sup>1</sup> because the intra- and interchain migration of excitons along the polymer backbone results in the amplification of fluorescence signals relative to small-molecule fluorophores.<sup>1a,2</sup> However, the rigid hydrophobic main chains of CPEs are prone to interpolymer  $\pi$ - $\pi$  interactions leading to self-quenching and reduced luminescence.<sup>3</sup> Supramolecular and macromolecular approaches to mitigate these effects have been developed that effectively isolate polymer chains from each other.<sup>4,5</sup> However, these strategies can result in large interpolymer separation that can reduce energy transfer between chains, which is the basis of some transduction schemes.<sup>1b</sup>

The three-dimensional, noncompliant structure of iptycene-type monomers (**2**, Figure 1) has been shown by our laboratory to prevent strong quenching interactions between polymer chains while still promoting productive interpolymer energy transfer necessary for amplification.<sup>6</sup> We hypothesized that monomer **1**, with its three

dimensional hydrophilic architecture, might impart the same properties to water soluble polymers as **2** does in non-polar media.

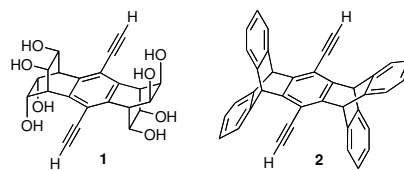
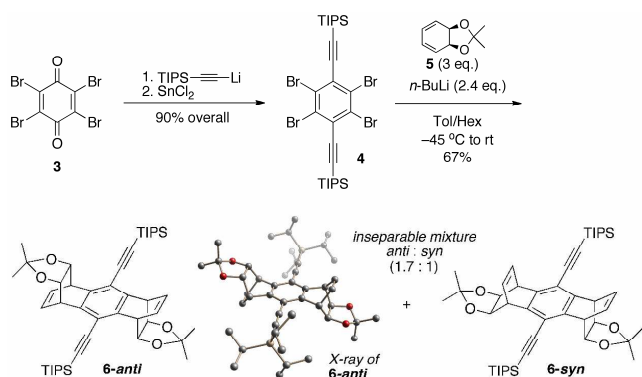


Figure 1. Three dimensional monomers

The synthesis of **1** began with *p*-bromaniil (**3**); double addition of TIPS acetylide to **3** followed by SnCl<sub>2</sub> reductive aromatization provided **4**.<sup>7</sup> We envisioned the three dimensional carbon framework might be established in one step via a double aryne-cycloaddition protocol.<sup>8</sup> In the event, addition of *n*-BuLi to dienophile precursor **4** at -45

°C produces a benzyne intermediate after initial lithium-halogen exchange. This putative dienophile underwent [4+2] cycloaddition with **5**<sup>9</sup> to provide a mixture of **6-anti** and **6-syn** cycloaddition products in a ratio of 1.7:1. The reaction was evaluated under a variety of solvent and temperature conditions (a more detailed discussion can be found in the Supporting Information), but the ratio of isomers varied only slightly. The isomers were not easily separated so the mixture was carried on to the next step; however, sufficient quantities of **6-anti** could be isolated to confirm the stereochemistry by X-ray crystallography (Scheme 1). The structure of **6-syn** was determined from a dioxo-diosmium bridged species isolated in a subsequent step (*vide infra* Scheme 2). Despite a modest yield, this procedure creates considerable complexity in a single step. Further, this transformation can be performed on multigram scales (>5 g).

**Scheme 1.** Synthesis of the carbon framework

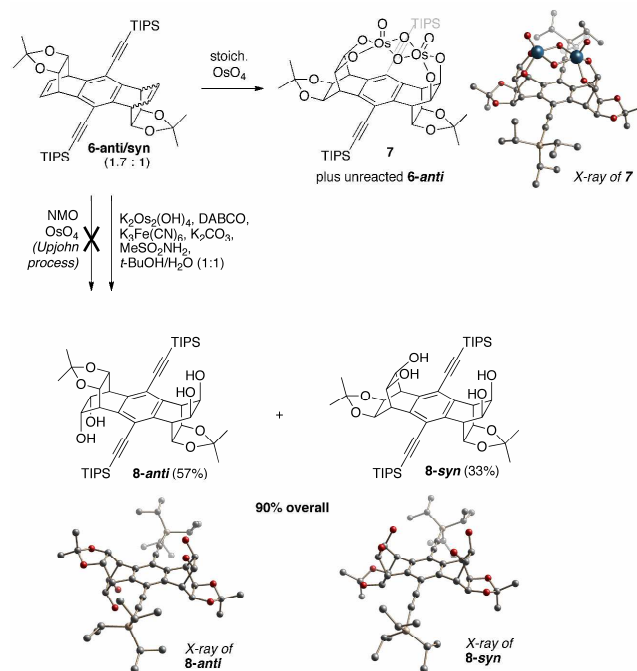


Modeling studies suggested the double dihydroxylation of **6** would occur on the less hindered face of the alkene in **6-anti/syn** to produce the corresponding isomers **8-anti** and **8-syn** (Scheme 2). Unfortunately, all attempts with a variety of NMO mediated osmium tetroxide dihydroxylation conditions (Upjohn process)<sup>10,11</sup> showed no conversion of starting material. However, <sup>1</sup>H NMR analyses of the crude reaction mixtures revealed the amount of **6-syn** diminished relative to **6-anti** with increasing OsO<sub>4</sub> loadings. To investigate this observation further, a reaction using a stoichiometric amount of OsO<sub>4</sub> was performed and **7** was obtained. While dioxo-diosmium type species are known,<sup>12</sup> the *cis*-dioxo variant **7** demonstrates remarkable stability in a variety of solvents and can be purified by silica gel chromatography. The steric bulk surrounding the osmium in this system likely prevents re-oxidation by NMO, thus trapping the osmium catalyst and halting the catalytic cycle.

These observations led us to examine the Sharpless asymmetric dihydroxylation (SAD), where conditions allow for hydrolysis of the osmate ester before reoxidation.<sup>13</sup> After some modification of the SAD conditions (see Supporting Information), separable isomers of **8-anti** and **8-syn** were isolated in excellent yield and the geometry of

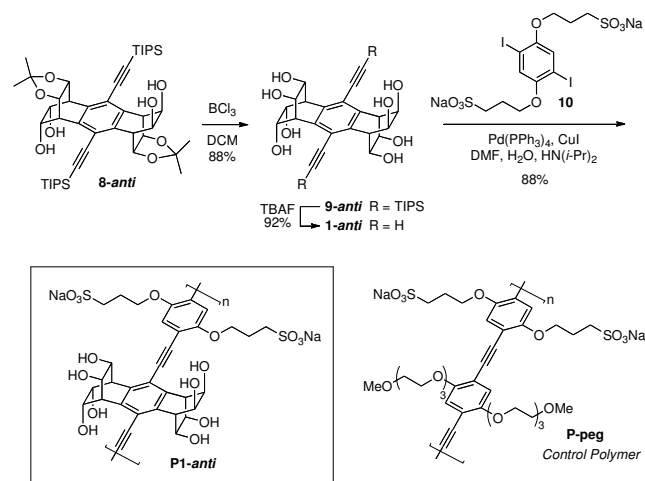
dihydroxylation was confirmed by X-ray crystallography (Scheme 2).

**Scheme 2.** Dihydroxylation

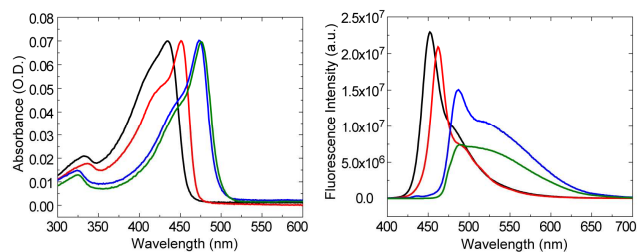


Global deprotection of **8-anti** (see Supporting Information for **8-syn**) with BCl<sub>3</sub> to remove the acetonide groups followed by TBAF to remove the TIPS groups provided **1-anti** (Scheme 3). Unfortunately, homopolymerization of **1-anti** using palladium mediated oxidative homocoupling of acetylenes<sup>14</sup> was not possible and only insoluble material could be isolated.

**Scheme 3.** Deprotection and polymerization



Attempts to polymerize diol protected versions of **1-anti** and then deprotect after polymerization also failed to yield water soluble homopolymers. These observations suggest the rigid structure of **1-anti** may not provide enough favorable entropic interactions with water to produce a soluble homopolymer. Copolymerization however, with the sulfonated diiodide **10**<sup>3a,15</sup> by Sonogashira polymerization produced high molecular weight ( $M_n = 14,500$ , PDI = 1.7, DP = 18) and highly water-soluble (>8 mg/mL) polymers in good yield.



**Figure 2.** UV-vis absorbance and fluorescence spectra of **P1-anti** in water (black); **P1-anti** in 1X PBS (red); **P-peg** in water (blue); **P-peg** in 1X PBS (green).

The immediate effects of incorporating a monomer such as **1-anti** with its non-compliant three dimensional architecture can be seen in Figure 2. The emission characteristics of **P1-anti** in comparison to an analogous control polymer (**P-peg**)<sup>5a</sup> lacking a deaggregating structure<sup>16</sup> is evident by the sharper emission features. Further, sensing of biological analytes will likely not take place in pure water but in higher ionic strength solutions like phosphate buffered saline. Indeed, **P1-anti** shows the same sharp emission features in 1X PBS with a quantum yield within the error of measurement (Table 1). The control polymer however, shows a complete loss of emission features, consistent with aggregate formation. Peak analysis data in Table 1 shows numerically what is visually represented in Figure 2. The presence of **1-anti** (**P1-anti**) produces distinctly sharper fluorescence signals with visible vibrational features.

**Table 1.** Peak analysis from Figure 2

	$\Phi_F$	peak height <sup>a</sup>	FWHM <sup>a,b</sup>	ratio <sup>c</sup>
<b>P1-anti</b> , water	19%	41.81	32.50	1.30
<b>P1-anti</b> , 1X PBS	17%	36.99	24.82	1.50
<b>P-peg</b> , water	19%	22.10	92.47	0.24
<b>P-peg</b> , 1X PBS	12%	10.86	100.29	0.11
<b>P1-anti</b> , water:glycerol <sup>d</sup>	49%	143.7	28.48	5.04

<sup>a</sup> arbitrary units. <sup>b</sup> FWHM = full width at half maximum.

<sup>c</sup> ratio = (peak height):(FWHM). <sup>d</sup> (1:1).

Interestingly, despite evidence for the deaggregating effects of **P1-anti**, there is not an observed increase in

quantum yield often seen when bulky side chains are used. It may be that in addition to deaggregation, bulky side chains might also serve to rigidify the polymer back bone through intrachain steric interactions. To test this, **P1-anti** was dissolved in 1:1 water:glycerol. This higher viscosity solution increased the quantum yield of **P1-anti** to 49% relative to 19% in pure water (Table 1) indicating that chain rigidification may be playing a role (see Supporting Information for spectra).

In summary, we have developed an expedient synthesis of monomer **1-anti** (and **1-syn**, see Supporting Information). Further, the hydrophilic three-dimensional structure of **1-anti** was shown to promote deaggregation when incorporated into a CPE and improved spectral properties were observed in both water and 1X PBS. Work towards observing interpolymer energy transfer for sensing applications is underway.

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**Supporting Information Available** Experimental procedures and characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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