Conjugated Polymers

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Fluorous Biphase Synthesis of a Poly(*p*-phenyleneethynylene) and its Fluorescent Aqueous Fluorous-Phase Emulsion**

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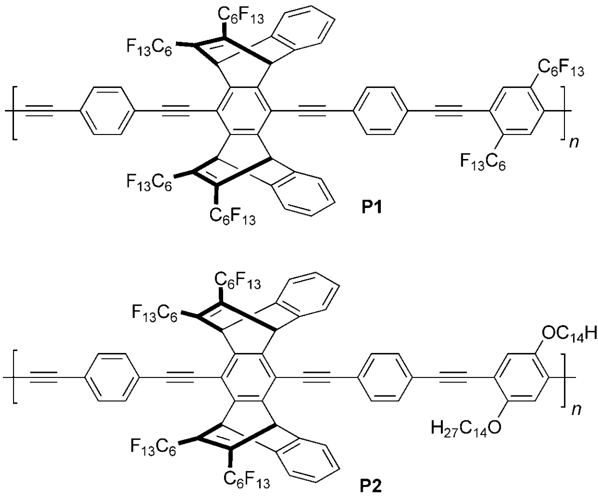
Highly fluorinated materials display a variety of interesting properties such as thermal and chemical stability, low surface energy, and high resistance to oxidation.[1] These materials can display orthogonal solubility by dissolving in fluorous solvents with limited solubility in organic solvents, thus allowing for facile purification by liquid-to-liquid extraction and/or fluorous solid-phase extraction.[2] Fluorous small molecules, materials, and solvents have been utilized in areas such as fluorous biphase chemistry,[3] liquid crystals,[4] electronics,[5] and as arrays for biosample screening.[6] Conjugated polymers that are soluble in fluorous phases have merit both in that they would allow for facile purification and processing and in that they could provide nontoxic platforms for fluorescence-based bioimaging and detection. Furthermore, the introduction of rigid perfluoroalkyl chains to the backbone of a conjugated polymer is expected to enhance the quantum yield of the material both in solution and in the solid state. Herein we report the syntheses and the properties of two highly fluorinated poly(*p*-phenylene ethynelene)s (PPEs), **P1** and **P2** (Scheme 1). Both polymers are highly fluorescent in solution and in thin films. Furthermore, **P1**, which displays a selective solubility in fluorous solvents, can be synthesized by fluorous biphase polymerization, thus allowing for facile isolation and purification of the polymer after polymerization (Figure 1). The alkoxylated counterpart, **P2**, shows good solubility in organic solvents but is not soluble in the fluorous phase. The selective solubility of **P1** in fluorous solvents allows for the creation of a highly fluorescent and stable emulsion in water.

The design principle of **P1** was based on the qualitative guidelines of fluorous compatibility outlined by Horváth et al.[3] and consists of 1) a majority fluorine content by weight and 2) long perfluoroalkyl chains that form a sheath around the PPE backbone. Furthermore, a rigid, bulky architecture was desired to discourage aggregation of the polymer both in solution and in solid state. The syntheses of monomer **1** and of polymers **P1** and **P2** from **1** are outlined in Scheme 2.



Scheme 1. Chemical structures of the PPE polymers **P1** and **P2**.

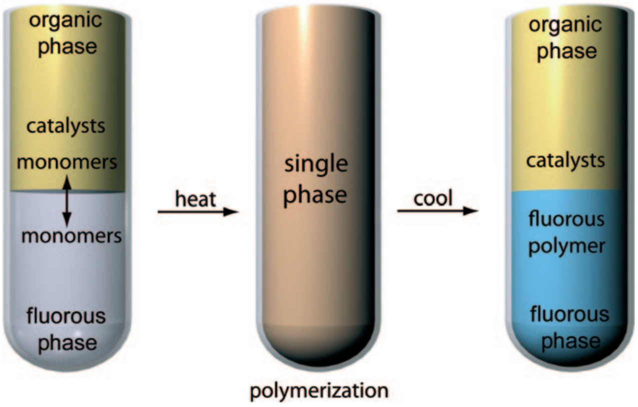


Figure 1. Fluorous biphase synthesis of fluorescent fluorous polymers.

When the pentacene derivative **5** was treated with an excess of perfluoro(7-tetradecyne) in xylenes at 145 °C, no reaction was observed after 4 days. This lack of reactivity was attributed to the poor solubility of perfluoro(7-tetradecyne) in xylenes, even at elevated temperatures. When the reaction mixture was homogenized with a high-sheer mixer at 80 °C, before raising the temperature to 145 °C, the desired twofold Diels–Alder reaction took place to afford the corresponding di-adduct in 86 % yield. The reaction gave the *syn* isomer as the major product, with a 6:1 *syn*/*anti* ratio. This selectivity is in sharp contrast to the Diels–Alder reactions of **5** with hexafluorobutyne and dimethyl acetylenedicarboxylate (DMAD), where the *anti* isomers are observed as the major

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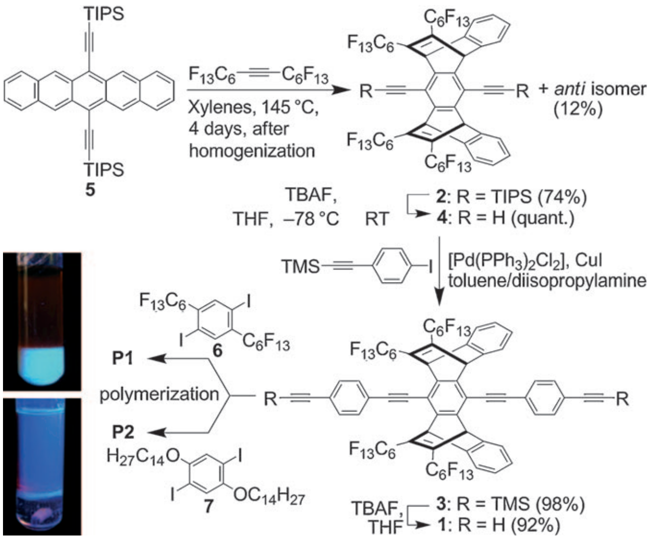


Scheme 2. Synthetic routes to PPE polymers **P1** and **P2**. Polymerization conditions: perfluoro(methylcyclohexane)/toluene/diisopropylamine 3:5:1, 5 mol% [Pd(PPh$_3$)$_4$], 7 mol% CuI, 85 °C, 4 days. The photographs show reaction mixtures at the end of the reaction irradiated with a hand-held long-wavelength UV lamp.

products.[7] The *anti* isomer had a poor solubility in most organic solvents, while the *syn* isomer was highly soluble; therefore the synthesis was carried out by using only the *syn* isomer.

Removal of the triisopropylsilyl (TIPS) moieties from **2** gave the corresponding diacetylene **4**. Sonogashira–Hagihara cross-coupling polymerization of **4** with diiodide **6** under various conditions gave only oligomeric products. The low degree of polymerization was attributed to the sterically demanding environment around the acetylene moieties of **4**. It was therefore envisioned that monomer **1**, with reduced steric hindrance around the acetylene functional groups, would provide polymers with higher molecular weights.

When monomer **1** was subjected to Sonogashira–Hagihara cross-coupling polymerization in toluene/diisopropylamine with **6**, higher-molecular-weight products were obtained, although the products were still soluble in organic solvents. It was expected that more fluorous solvent conditions for the Sonogashira–Hagihara cross-coupling reaction would produce polymers with higher molecular weights, which may subsequently render the material selectively soluble in fluorous solvents. When a solvent mixture of toluene/perfluoro(methylcyclohexane)/diisopropylamine (5:3:2) was heated, it was observed that the solvent mixture became monophasic at 82 °C, and, upon cooling, the fluorous phase separated neatly from the organic (toluene/diisopropylamine) phase. The Sonogashira–Hagihara cross-coupling polymerization between monomer **1** and diiodide **6** in this solvent system at 85 °C gave, upon cooling, a biphasic mixture in which the bright blue fluorescence was localized in the fluorous layer (photograph in Scheme 2). Removal of the organic layer, followed by washing of the fluorous layer with methanol, acetone, and ethyl acetate gave **P1** in 87% yield. This constitutes a first example of a fluorous biphase synthesis of a conjugated polymer. The polymer obtained in this manner was optically pure and was used without further purification for photophysical measurements.

When monomer **1** was treated with comonomer **7** under identical conditions, a complete reversal of the solubility was observed, with the fluorescence of the product biphasic mixture localized in the upper organic phase. Removal of the fluorous layer, followed by precipitation of the organic layer with ethanol and washing the resulting solid with acetone gave **P2** in 78% yield.

The normalized absorption and emission spectra of **P1** and **P2** are shown in Figure 2. The fluorous soluble **P1** displays a band edge and an emission maximum that are both blue-shifted relative to **P2**. A small (5–6 nm) Stokes shift and sharp absorption and emission spectra of **P1** suggest that the structure of the polymer in solution is highly rigid. Both **P1** and **P2** are highly fluorescent. Fluorous **P1** has a quantum yield of 0.95 in perfluorodecalin and **P2** has a quantum yield of 0.84 in toluene. Furthermore, both polymers exhibit high quantum yields in thin films (0.32 for **P1** and 0.42 for **P2**). The lower thin-film quantum yield of **P1** relative to that of **P2** could be associated with the flatter geometry of the comonomer **6** relative to **7**, which results in a higher degree of aggregation for **P1** in the solid state than for **P2**.

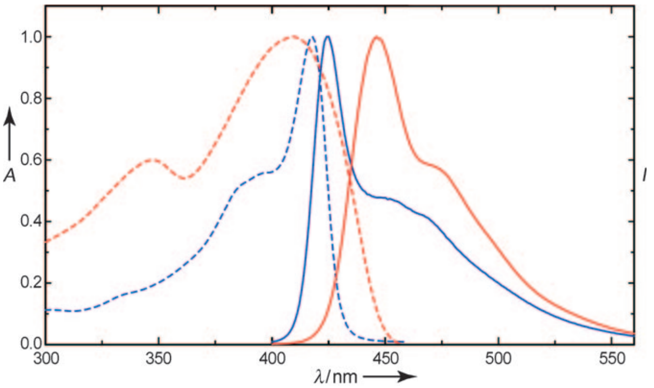
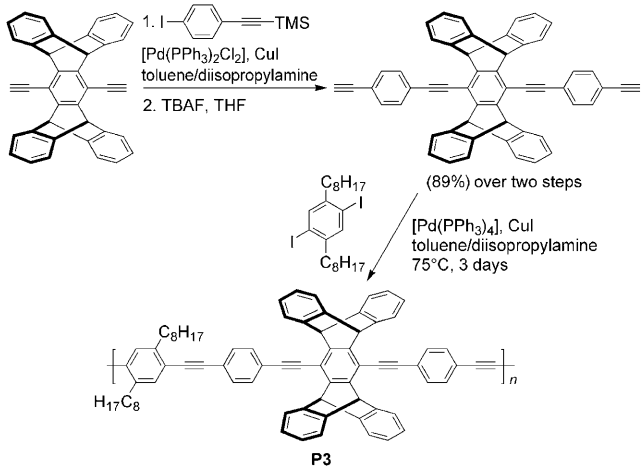


Figure 2. Absorption (dotted line) and emission (solid line) spectra of **P1** (blue, in perfluorodecalin; quantum yield 0.95) and **P2** (red, in toluene; quantum yield 0.84).

To compare these properties to those of a nonfluorinated polymer, a new polymer, **P3**, that features a rigid, three-dimensional architecture and a dialkylaryl moiety in the backbone, was synthesized (Scheme 3; see Figure S1 in the Supporting Information for the solution absorption and emission spectra). This polymer showed a reduced quantum yield in solution (0.48 in toluene) compared to **P1** and **P2**. The thin-film emission spectrum of **P3** showed a broad, red-shifted peak, suggesting a large degree of aggregation, whereas the thin-film emission spectra of **P1** and **P2** did not display significant shifts from their respective solution spectra (Figure S2 in the Supporting Information). Also, **P3** was insoluble in fluorous solvents.

Monomer **1** is soluble in organic solvents including acetone, hexane, chloroform, ethyl acetate, and THF, and insoluble in nonpolar fluorous solvents (such as perfluorohexane (FC-72), perfluoromethylcyclohexane, and perfluoro-



Scheme 3. Structure and synthesis of PPE polymer **P3**.

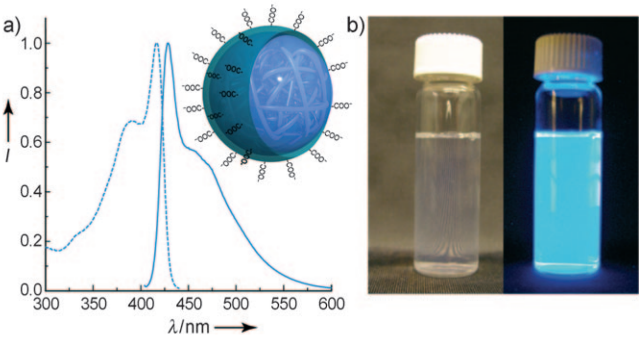


Figure 3. a) Absorption (dotted line) and emission (solid line) spectra of the emulsion of a perfluorodecalin solution of **P1** in pH 7.4 PBS buffer (quantum yield 0.58), and a schematic representation of the emulsion particle; b) photograph of the emulsion before (left) and after (right) irradiation with a hand-held UV lamp.

decalin). Polymer **P1** is soluble in these fluorous solvents, but is insoluble in organic solvents. The exclusive solubility of **P1** in fluorous solvents made it difficult to determine the degree of polymerization by gel permeation chromatography (GPC) analysis. Dynamic light scattering (DLS) analysis showed that the average length of **P1** is 16 nm, a value that corresponds to the typical persistence length of long PPEs.[8] DLS measurements in perfluorodecalin also showed similar length distributions. When **P1** was end-capped with 1-bromo-4-*tert*-butylbenzene, no signals corresponding to the *tert*-butyl group were observed in the ^{1}H NMR spectrum, indicating a high degree of polymerization (>20). Polymer **P2**, which is soluble in organic solvents, could be analyzed by GPC, and was shown to have $M_n = 520$ kDa, $M_w = 2850$ kDa, and PDI = 5.48.

In order to facilitate the imaging and sensory applications of our fluorous-phase soluble fluorescent polymer, we processed fluorous solutions of **P1** into a stable emulsion in water with easily modifiable functional groups on the surface. Perfluorodecalin,[9] which has been approved by the US Food and Drug Administration (FDA) for use as a component in human blood surrogate, was chosen as the fluorous component of the emulsion. When a solution of **P1** in perfluorodecalin was added slowly to a hot aqueous solution of 2*H*,2*H*,3*H*,3*H*-perfluorononanoic acid under probe sonication, a turbid and strongly fluorescent emulsion formed. Upon cooling, a relatively monodisperse emulsion was obtained with an average diameter of 245.8 nm and a polydispersity index (PdI) of 0.099 as determined by DLS. The emulsion displayed absorption and emission spectra (Figure 3) identical to those of **P1**. The emulsion prepared in phosphate-buffered saline (PBS) buffer was highly fluorescent, with a quantum yield of 0.58. The Z-potential is a useful method for the measurement of the stability of colloids in water, because a higher surface charge discourages the aggregation of particles. Colloids with a surface potential of ±40 mV and higher are considered to have a good stability.[10] An emulsion of the perfluorodecalin solution of **P1** in water had a Z-potential of −57 mV with 13.2 mV deviation, thus indicating that the surfaces of the emulsion are sufficiently charged to confer good stability to the overall emulsion.

We have synthesized two PPEs from a novel, highly fluorinated building block **1** and have demonstrated that, depending on the choice of the comonomer, the solubility properties of the materials could be changed drastically. Both polymers were highly fluorescent both in solution and in thin films. The fluorous-phase-soluble PPE, **P1**, could be processed into a stable emulsion in PBS buffer (pH 7.4). The emulsion involves a nontoxic fluorous solvent, is highly fluorescent, and has functional groups on the surface, which could be further modified. Further work on the attachment of biologically active molecules to the surface of the emulsion is under way.

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