CHAPTER 6

Synthesis of an Amphiphilic, Non-ionic Poly(*para*-phenylene ethynylene) Derivative with a Remarkable Quantum Yield in Water

Poly(*para*-phenylene ethynylene)s derivative have been synthesized via our A_2+BB' polycondensation method. The polymer backbone is appended with branched oligoethyleneglycol side chains that efficiently encapsulate the non-polar backbone within a polar shell to provide both solubility and site-isolation to allow for exceptionally high photoluminescence efficiency in aqueous environments.

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Introduction

Conjugated polymers have attracted significant attention in last few decades. Poly(*para*-phenylene ethynylene) represent one class of such conjugated polymers. The tremendous interest in these materials is due to their remarkable electronic and optical properties and hence their use in organic electronics and molecule-based -so called "plastic"- devices. One attractive application of these polymers is in the field of chemo and biosensing. The detection of biologically relevant analytes can be achieved in high sensitivity using sensory materials based on conjugated organic polymers.[1-2] However, the tendency of P*p*Es to self assemble in supramolecular architectures in particular in water due to the hydrophobic nature of the backbone limits its scope in the sensing of biologically relevant analyte. To render these polymers water-soluble, the common strategy involves the introduction of ionizable groups on the backbone.[3] For example, Carboxylic, ammonium and sulfonic groups have been used in side chains for this purpose.[3] The disadvantage of this approach is the precise adjustment of solution pH to avoid aggregation and

more importantly, undesirable interactions of these polyelectrolyte with charged biomolecules and/or counterions. Alternative strategies to provide these polymers with water-solublility include incorporation of polyhydroxylated[4] or carbohydrate-based[5] substituents. However, In this case, the free hydroxyl groups are not chemically inert and potentially give rise to undesirable side reactions.

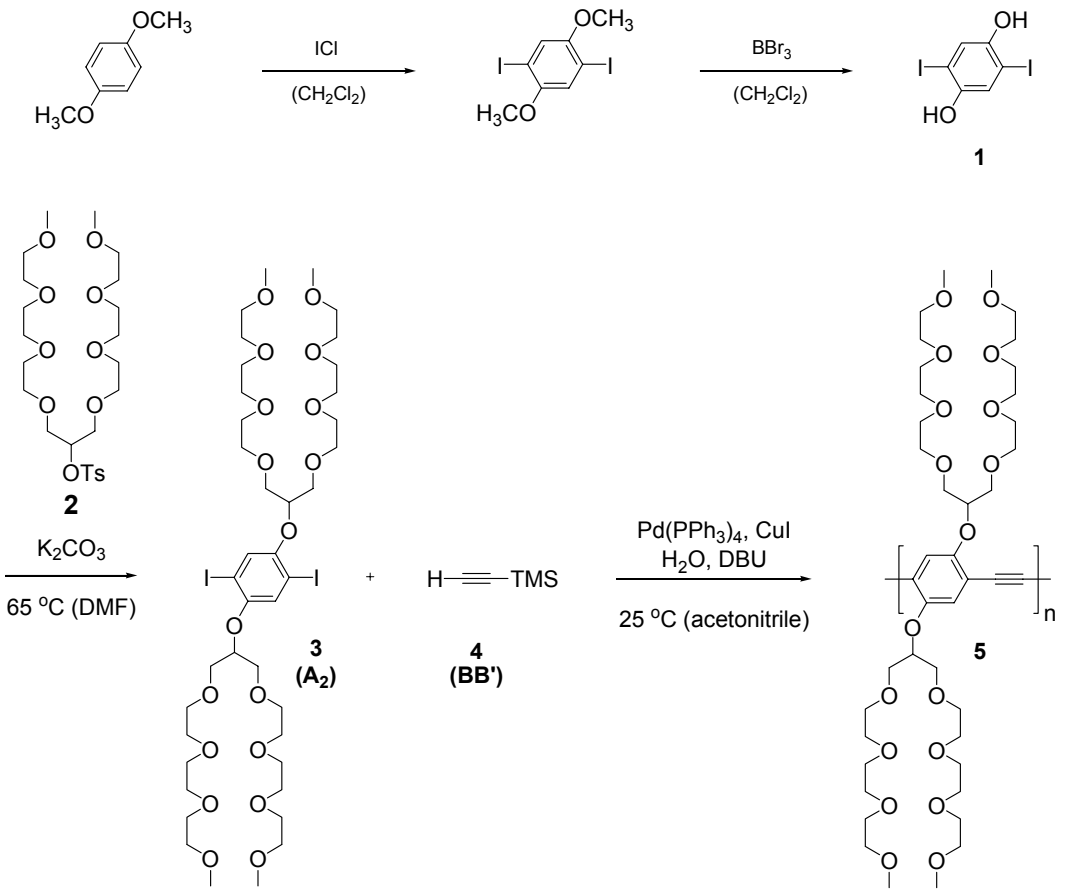
Motivation

We aimed to utilize our *in-situ* deprotection/coupling polycondensation protocol to synthesize amphiphilic, site-isolated, and inert P*p*PEs from readily available monomer building blocks.[6,7] In order to efficiently suppress aggregation arising from ionic substituents and their associated counter-ions or from hydrogen-bonding protic residues, *two branched* oligoethyleneglycol (OEG) side chains[8,9] were introduced at *every* repeat unit. The polar, non-ionic, and non-protic side chains were chosen to render the backbone soluble in a variety of media including water and provide a chemically inert scaffold.

Polymer Synthesis

Monomer synthesis was accomplished by alkylation of 2,5-diiodohydroquinone **1**[10] with branched OEG tosylate **2**[8] (Scheme 1). Applying our A_2+BB' polycondensation protocol,[6] involved stoichiometric reaction of diiodide **3** (A_2 monomer) with trimethylsilylacetylene **4** (TMSA, BB' monomer) in the presence of 5 mol% freshly prepared $Pd(PPh_3)_4$ catalyst, 10 mol% CuI cocatalyst, 6 equiv. of diazabicyclo[5.4.0]undec-7-ene (DBU), and 10 equiv. of water in acetonitrile at room temperature for 3 d. The commercial availability of TMSA and the rapid synthetic access to monomer **3** make this synthesis of polymer **5** highly practical.

Scheme 1



Polymer **5** was obtained in 83% isolated yield after single precipitation into diethyl ether and extraction to remove residual inorganic impurities. GPC analysis[11] of polymer **5** indicated reasonable degrees of polymerization (DP ~ 30) and polydispersities (PDI ~ 2.0) typical for polycondensation processes. ^{1}H-NMR showed successful incorporation of the monomer repeat units into polymer **5** with no discernable end-groups, while in ^{13}C-NMR no diacetylene defects could be detected.[6]

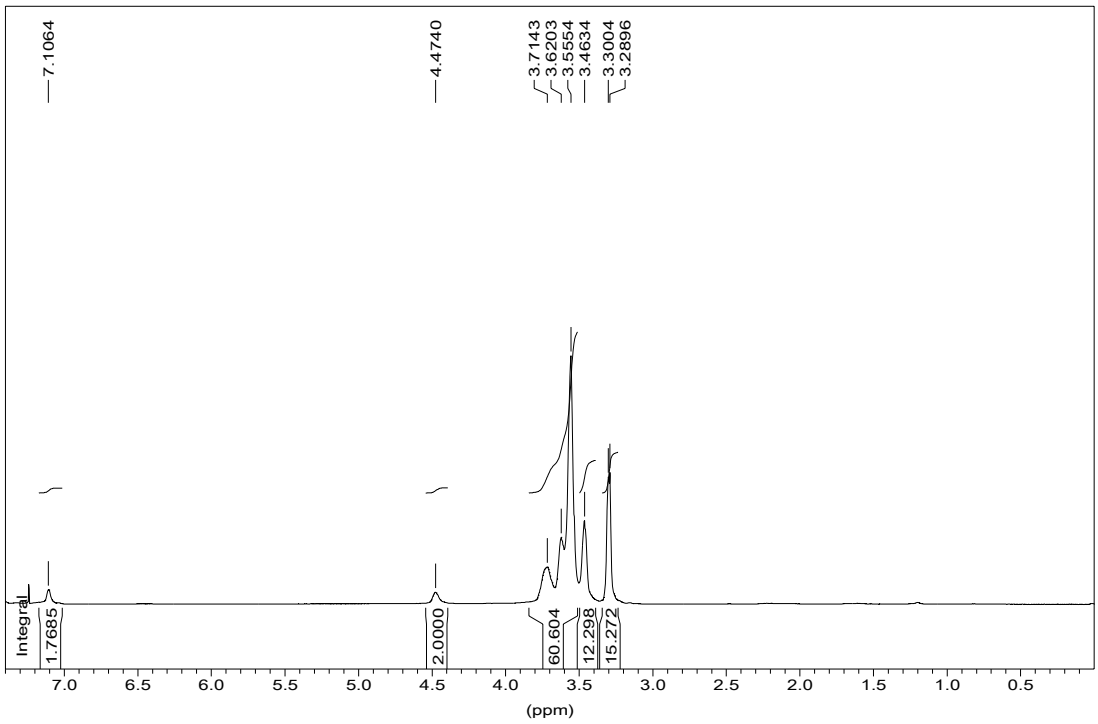


Figure 1. ^{1}H NMR spectrum of polymer **5** (500 MHz, $CDCl_3$, 25 °C).

Optical Properties

Polymer **5** displayed good solubility in a wide range of different solvents, most importantly in water (0.7 mg/mL). UV/vis spectra of polymer **5** in various organic solvents exhibit typical absorption maxima λ_{max} = 437–441 nm (Figure 2, Table 1) suggesting that the full effective conjugation length has been reached.[7]

Table 1 Absorption and emission characteristics of polymer **5.**

Solvent	$\lambda_{abs}{}^{a}$ / nm	$\lambda_{em}{}^{a}$ / nm	$\Phi_f{}^{b}$
chloroform	437	465	0.53
acetonitrile	441	468	0.63
methanol	438	466	0.57
water	427	464	0.43

[a] λ_{max} of absorption and emission bands, respectively; [b] using quinine sulfate as reference standard.[12]

In water however, a considerable hypsochromic shift (λ_{max} = 427 nm) was observed, similar to the reported case of an ionic P*p*PE.[3d] Since the data suggest a negligible polarity effect of the medium, water seems to cause certain structural reorganization and/or induce some degree

of aggregation, both potentially distinguishable by emission spectroscopy. Corrected and normalized fluorescence spectra of polymer **5** in the same solvents were qualitatively similar yet showed distinctly different photoluminescence efficiencies (Figure 2). Calibration using quinine sulfate as reference standard[12] yielded the corresponding quantum yields (Table 1) that do not scale with solvent polarity. Interestingly, in chloroform serving as a good solvent for both the polar side chains and the non-polar core, less intense emission is observed as compared to acetonitrile that preferentially solvates the polar corona. Increasing solvent polarity from acetonitrile via methanol to water caused a decrease in photoluminescence efficiency.

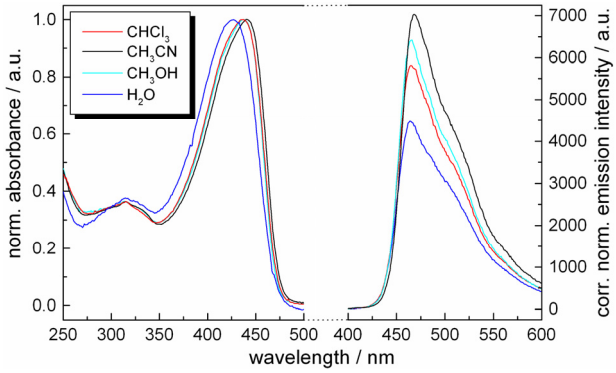


Figure 2. UV/vis absorption and fluorescence emission spectra of polymer **5** in various solvents (25 °C). Absorption spectra are scaled to the same optical density, while emission spectra are corrected and normalized

In order to span the entire emission intensity range, the solvent was systematically varied from acetonitrile to water (Figure 3). Fluorescence emission was found to decrease with increasing amount of water in a non-linear fashion (inset Figure 3).

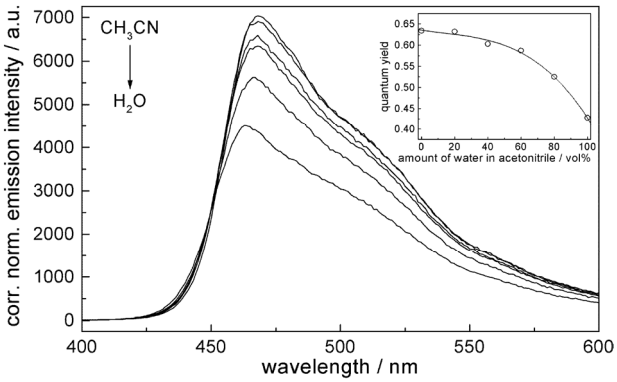


Figure 3. Fluorescence emission spectra of polymer **5** in acetonitrile/water solvent mixtures (25 °C). The inset shows the calculated quantum yields as a function of solvent composition (the line obtained from the non-linear least squares fit of the data is included as a guide to the eye).

It is important to note that the shape of the fluorescence band did not change considerably, indicating almost negligible aggregation that would have causes a broad, red-shifted, excimer-like emission. This finding is furthermore supported by UV/vis absorption measurements on annealed films that did not show any sign of aggregation, such as narrower and bathochromically shifted absorption bands (Figure 4).[8] Therefore, the observed solvent effects are most likely due to different solvation of the amphiphilic polymer, causing structural reorganization of the backbone chromophores in polar/aqueous environments.

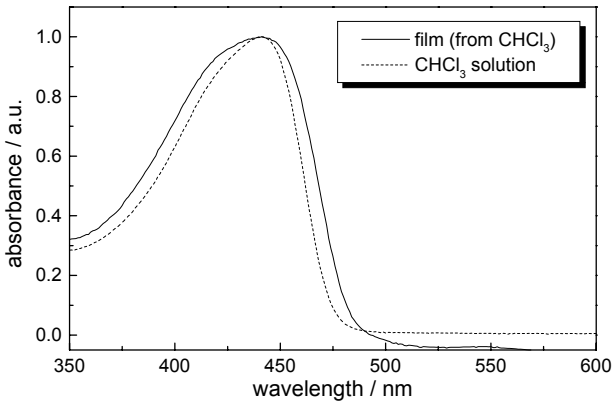


Figure 4. UV/vis absorption spectra of polymer **5** in $CHCl_3$ solution and in the annealed, i.e. heated, film prepared by drop casting from $CHCl_3$ (25 °C).

In general, the quantum yields in solution are high and even in water, which imposes an enormous hydrophobic effect to drive aggregation, remarkably efficient photoluminescence has

been observed. In fact, to the best of our knowledge polymer **5** exhibits by far the highest quantum yield in water (Φ_f = 0.43) of any known P*p*PE derivative (ionic P*p*PEs:[3] Φ_f = 0.03-0.10; polyhydroxylated P*p*PE:[4] Φ_f = 0.07). This exceptional behavior is attributed to the significant steric demand of the employed side chains that are attached twice per repeat unit and place their branch points in close proximity of the backbone. Thereby, an efficient shielding of the P*p*PE core is achieved as indicated by molecular mechanics calculations (Figure 5).

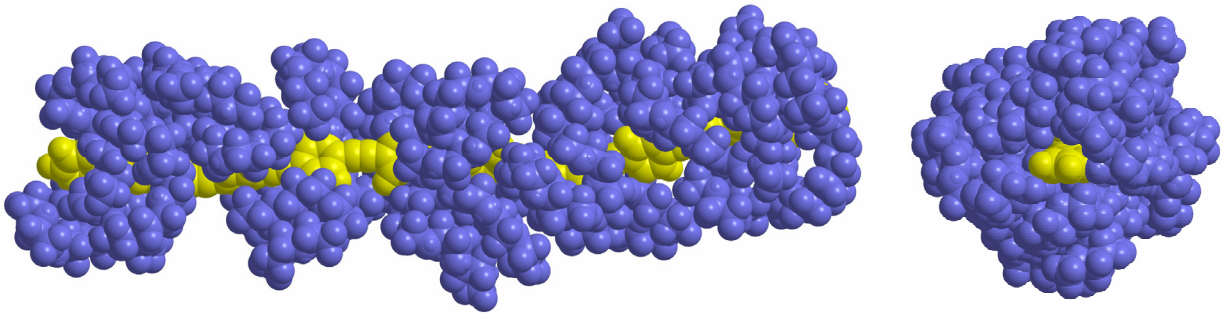


Figure 5. Molecular model (MM2) of decamer resembling polymer **5** (side and top views; P*p*PE-backbone is shown in yellow, branched OEG side chains in blue.

In related poly(*para*-phenylene)s, these branched OEG side chains were found to efficiently prevent aggregation in the solid state.[8] In addition to the chosen substituents, the observed high quantum yields can be explained by the absence of diacetylene defects due to our method of polymer preparation.[3a,6]

Conclusion

The utility of our A_2+BB' polycondensation approach[6] arising from its practicality due to rapid monomer availability as well as the quality of the obtained materials has successfully been demonstrated by the synthesis of a chemically inert, water-soluble, and highly emissive P*p*PE derivative, which could potentially be used in ultrasensitive biosensing. The described approach should be generally applicable to the design of conjugated polymers both soluble and emissive in aqueous environments.

Experimental

General Methods. 2,5-Diiodohydroquinone **1**[10] and 1,3-Bis(3,6,9-trioxadecyl)glycerol-2-toluenesulfonate **2**[14] were synthesized as described in the literature. $Pd(PPh_3)_4$ was freshly prepared,[15] all other chemicals were commercial and used as received. Acetonitrile was distilled prior to use under N_2 atmosphere over calcium hydride. Column chromatography was carried out with 130-400 mesh silica gel. NMR spectra were recorded on Bruker AC500 as well as Delta JEOL Eclipse 500 (500 and 126 MHz for ^1H and ^{13}C, respectively) spectrometers at 23 ± 2 °C using residual protonated solvent signal as internal standard (^1H: $\delta(CHCl_3)$ = 7.24 ppm, δ(DMSO) = 2.49, $\delta(CH_3CN)$ = 1.94 ppm and ^{13}C: $\delta(CHCl_3)$ = 77.0 ppm, δ(DMSO) = 39.7 ppm). Mass spectrometry was performed on Perkin-Elmer Varian Type CH5DF (FAB) instruments. IR spectra were recorded as KBr pellets on a Nicolet 5SXC FTIR-Interferometer. Elemental analyses were performed on a Perkin-Elmer EA 240. GPC measurements in THF as the mobile phase were performed on a Polymer Laboratories PL-GPC 120 system equipped with a built-in refractive index detector at 40 °C using a flow rate of 1 mL/min. The samples were separated through a series of three columns (l = 300 nm, d = 8 nm), PS-DVB gel with 10 µ bead sizes, which were calibrated with several narrow polydispersity polystyrene samples. The HPLC system consisted of a Knaur Eurosphere 7µm C18, 4·120 mm silica gel column and UV-detection at 254 nm with an eluent flow of 1 mL/min.

Optical spectroscopy. UV/visible absorption and fluorescence emission/excitation spectra were recorded in various solvents of spectroscopic grade using quartz cuvettes of 1 cm path length on a Cary 50 Spectrophotometer and a Cary Eclipse Fluorescence Spectrophotometer, respectively, both equipped with Peltier thermostated cell holders (ΔT = ± 0.05 °C). Unless stated otherwise, all experiments were carried out at 25 ± 0.05 °C. For quantum-yield determinations using quinine sulfate (9.98 10^{-10} M in 2.0 M H_2SO_4) as standard, Melhuish´s value[12] of Φ_f = 0.546 for 365 nm excitation was used. The samples were excited at λ_{exc} = 365 nm, slit widths were set to 2.5 nm bandpass for excitation and 5 nm bandpass for emission. Fluorescence spectra were corrected for variations in photomultiplier response over wavelength using correction curves generated on the instrument. The corrected fluorescence spectra were normalized by the exact optical density OD_{365nm}. For UV-visible absorption $OD(\lambda_{max})$ ~ 0.8 (~ 20 mg/L) and for fluorescence measurements $OD(\lambda_{max})$ ~ 0.1 were used. Influence of metal cations (Li^+, Mg^{2+}, Ca^{2+}, Ba^{2+},

Zn^{2+}) was investigated by adding varying amounts of the respective acetate salts to the aqueous solution. Variation of pH (4-11) was achieved by using buffer solutions.

Molecular Modeling. Molecular mechanics calculations were carried out using the MM2 force field. Reasonable starting geometries for the decamer resembling polymer **5** were obtained by minimization of shorter oligomer fragments that were obtained from monomer units minimized by molecular dynamics simulations.

Synthesis

Monomer: 1,4-Bis(1,3-bis(3,6,9-trioxadecyl)-2-glyceryl)-2,5-diiodobenzene (3): Compound **1**[10] (1.44 g, 4.0 mmol), **2**[2] (5.1 g, 9.6 mmol), and K_2CO_3 (2.21 g, 16 mmol) were dissolved in 8 mL of dry DMF and heated at 65 °C for 2 days. Then the reaction mixture was diluted with dichloromethane and washed with saturated ammonium chloride and brine solutions. The resulting crude product was purified by column chromatography (10 % methanol in ethyl acetate) to give **3** as orange oil (3.0 g, 69 % yield). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.22 (s, 2 H, Ar-H), 4.20-4.10 (m, 2 H, O-CH_2), 3.50-3.40 (m, 48 H, O-CH_2), 3.30-3.28 (m, 8 H, O-CH_2), 3.13 (s, 6 H, O-CH_3), 3.11 (s, 6 H, O-CH_3); ^{13}C NMR (500 MHz, $CDCl_3$): δ 153.09, 125.78, 87.67, 80.57, 71.72, 70.97, 70.61, 70.45, 70.42, 70.36, 70.28, 58.77; FAB-MS (MNBA, 3 kV): *m/z* = 1117.3 (calcd 1117.27 for $C_{40}H_{72}O_{18}I_2Na^+$), Anal. C: 45.26, H: 6.79 (calcd C: 43.88, H: 6.63); HPLC (85 % MeOH / 15 % H_2O, 1 mL/min): 98.6 % peak area.

Polymer 5: Monomer **3** (0.438 g, 0.40 mmol), CuI (0.008 g, 0.04 mmol), and $Pd(PPh_3)_4$ (0.028 g, 0.02 mmol) were loaded in a flame-dried 10 mL Schlenk tube, which was evacuated and refilled with argon. Dry and degassed acetonitrile (1.7 mL) was submitted to the tube via a syringe, then 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 0.36 mL, 2.40 mmol) and trimethylsilylacetylene **4** (TMSA, 0.057 mL, 0.40 mmol) were added, immediately followed by addition of distilled water (0.070 mL, 4.0 mmol). The tube was covered with aluminum foil and the reaction mixture was allowed to stir at rt for 3 d. The reaction mixture was precipitated in 500 mL of diethyl ether, the resulting solid was dissolved in chloroform and washed with water, brine, saturated ammonium chloride, 1 M HCl, water, and $NaHCO_3$ solution to give the desired polymer **5** (0.29 g, 83 %) as yellow solid. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.10 (broad s, 2 H, Ar-H), 4.47 (broad s, 2 H, O-CH), 3.71 (broad s, 8H O-CH), 3.62-3.46 (broad m, 48 H, O-CH), 3.30 (broad s, 6 H, O-CH_3), 3.28 (broad s, 6H, O-CH_3); ^{13}C-NMR (500 MHz, $CDCl_3$): δ 133.74, 131.88, 131.60, 131.28, 128.71, 128.65, 128.56, 106.32, 105.41, 84.53, 71.10, 70.29, 69.70, 69.61, 69.44, 61.18, 57.84;

GPC (THF, 40 ^{o}C): M_w = 46500, M_n = 22700, PDI (M_w/M_n)= 2.0; Anal. C: 57.74, H: 7.50 (calcd for $(C_{42}H_{72}O_{18})_n$ C: 58.32, H: 8.39); IR (KBr): 3419, 2924, 2872, 2811, 2724, 2200, 2143, 1642, 1488, 1421, 1350, 1271, 1210, 1108, 1041, 851, 543 cm^{-1}.

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