

Supporting Information

Ambient Oxygen-Doped Conjugated Polymer for pH-Activatable Aggregation-Enhanced Photoacoustic Imaging in the Second Near-Infrared Window

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Supporting figures; chemical synthesis routes and characterization data (e.g., NMR and HPLC)

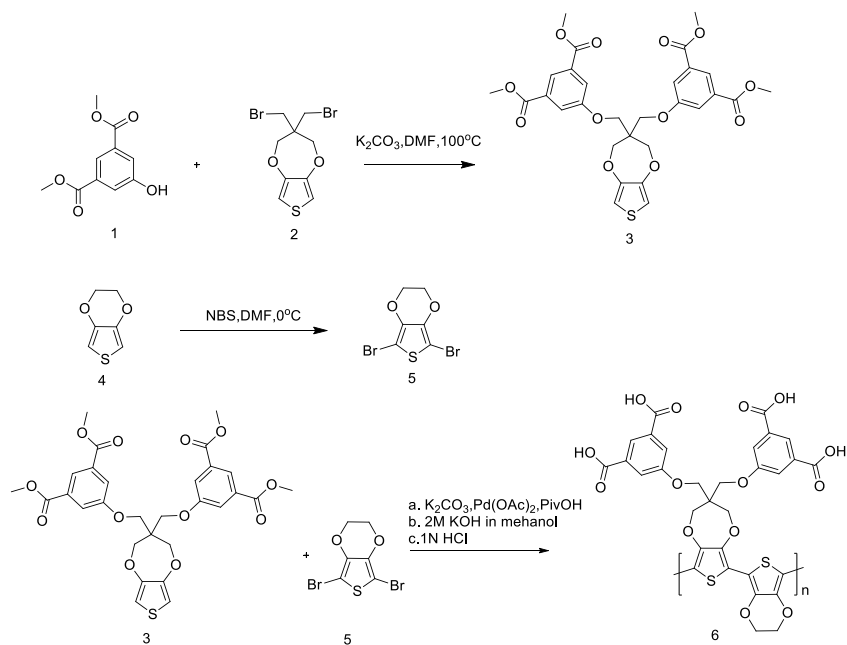


Figure S1. Synthetic routes for Compound 6 (PPE).

All reagents purchased from suppliers were used without further purification. **PPE** was synthesized according to the previous literature.^[1] ^1H and ^{13}C NMR spectra were recorded on a mercury 300 at 293 K with deuterated chloroform as the solvent.

(Compound 3): To a 250 mL flask was charged with a stir bar, dimethyl 5-hydroxyisophthalate (compound 1, 2.8 g, 13.3 mmol), 3,3-bis(bromomethyl)-3,4-dihydro-2H-thieno[3,4-b][1,4]dioxepine (compound 2, 2 g, 5.8 mmol) and K_2CO_3 (4 g, 29 mmol). 40 mL DMF was added and heated to 100 °C, allowing reaction for 18h. Then the solution was cooled to room temperature and added with 200 mL water and 50 mL DCM to extract the product. The DCM layer was collected and rotovap to remove solvent, and then submitted to silica gel column to purify compound 3. White solid 2.5 g was got. (Y = 70%). ^1H NMR (300 MHz, CDCl_3) δ (ppm): 8.28 (s, 2H), 7.75 (s, 4H), 4.30 (d, 8H), 3.93 (s, 12H).

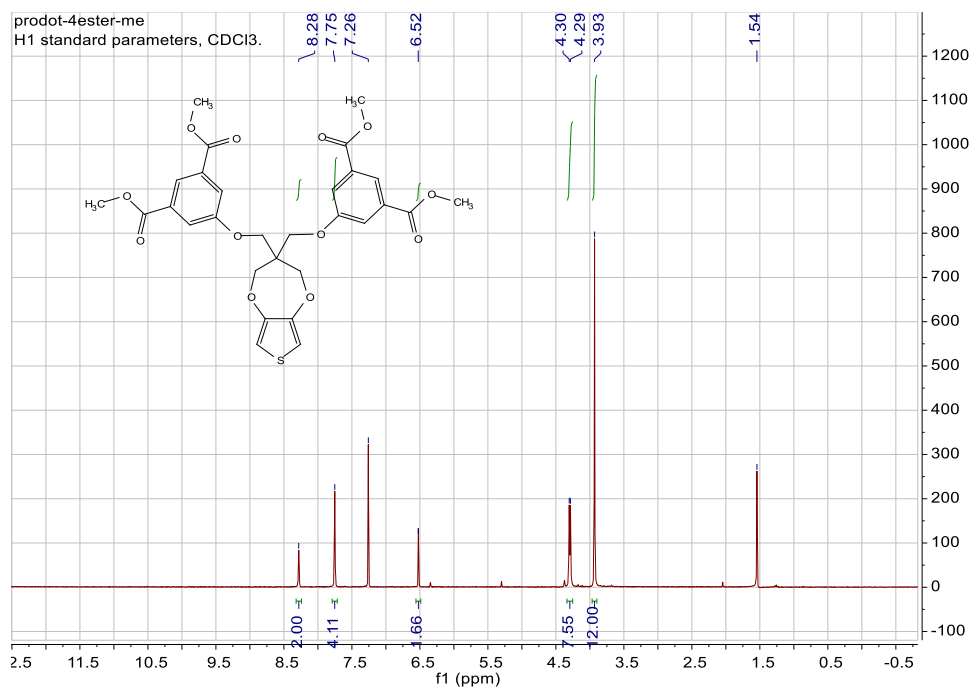


Figure S2. ¹H NMR of Compound 3 (ProDOT)

(Compound 5): To a 250 mL flask was charged with a stir bar, EDOT (compound 4, 2.0 g, 14 mmol) and DMF 8mL then cool to 0 °C. NBS (5.13 g, 28.8 mmol) was dissolved into 20 mL DMF and then was added into the flask dropwise. After reacting at 0 °C for 30 min, 40 mL water was added into the flask with the temperature below 10 °C. It was then filtered and washed with MeOH/water=1/2 solution 20 mL to get white solid 4 g (Y = 95%). ¹H NMR (300 MHz, CDCl₃) δ (ppm): 4.27 (s, 4H).

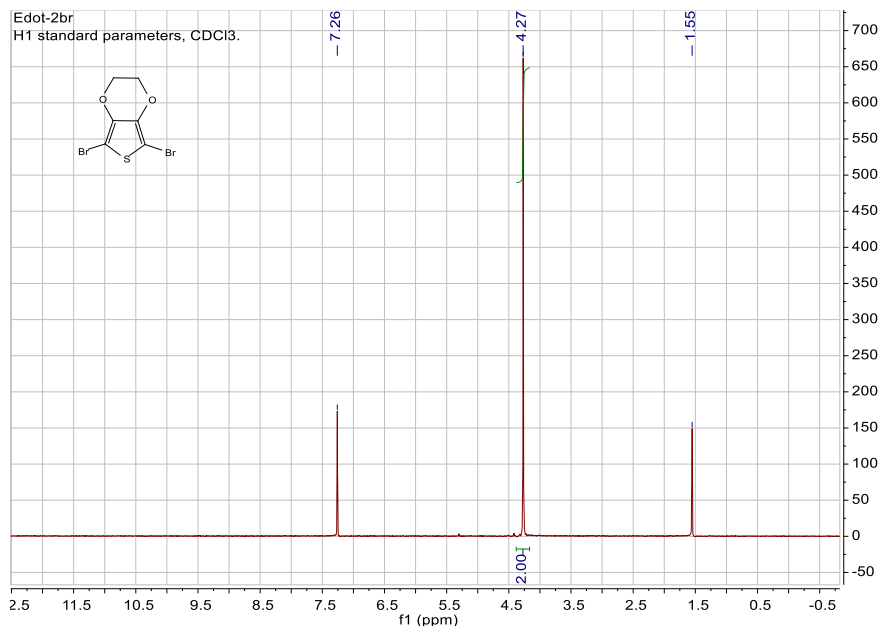


Figure S3. ^1H NMR of Compound 5 (EDOT)

(Compound 6): To a Schlenk tube charged with a stir bar, compound 3 (0.5 g, 0.83 mmol), compound 5 (0.25 g, 0.83 mmol), PivOH (25 mg, 0.25 mmol), $\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol) and K_2CO_3 (0.3 g, 2.2 mmol). The mixture was vacuumed and refilled with nitrogen for three times. Degas DMAc 5 mL was added with syringe and the solution was heating to 140 °C for 18 h. Then the product was precipitated out from the solution with 100 mL methanol/1M HCl (1/1). It was filtered and washed with methanol to get solid. The solid was suspended into 50 mL 2 M KOH methanol solution and heated to reflux overnight. Next, the solution was cooled to room temperature and filtered to get the polymer solid. The polymer solid was dissolved into 20mL water and filter to remove the insoluble impurities. The filtrate was collected and neutralized with 6M HCl to pH = 2. Solid precipitate from the solution was filter and dry to get the desired polymer compound 6. (0.58 g, Y = 90%)

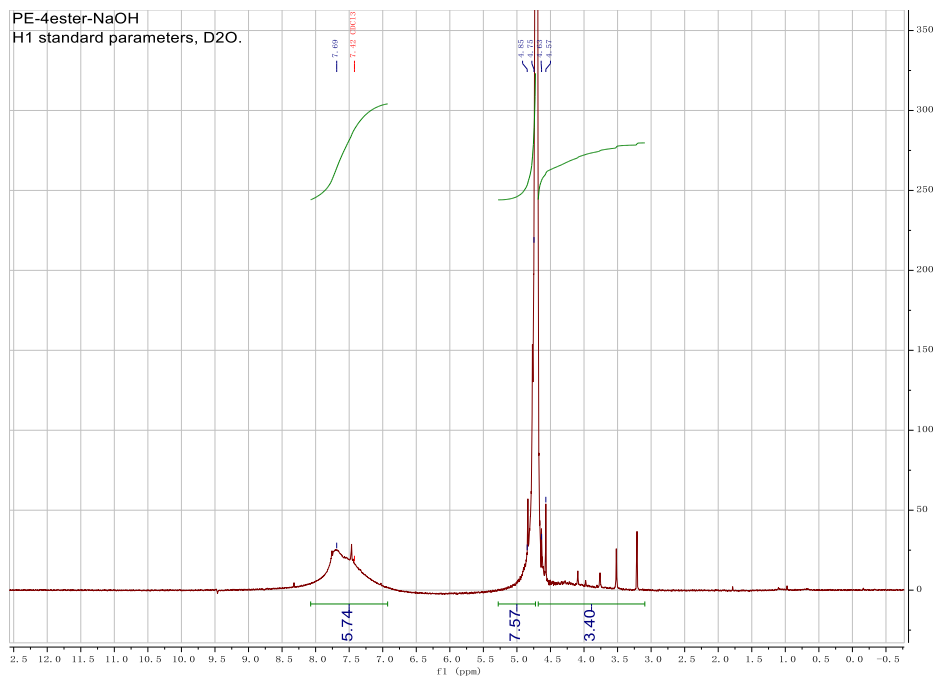


Figure S4. ^1H NMR of Compound 6 (PPE). Because the water peak in D_2O (at 4.8ppm) overlay with the $-\text{CH}_2$ peak, we roughly get the proton integral ratio between aromatic and aliphatic protons is 6/11.

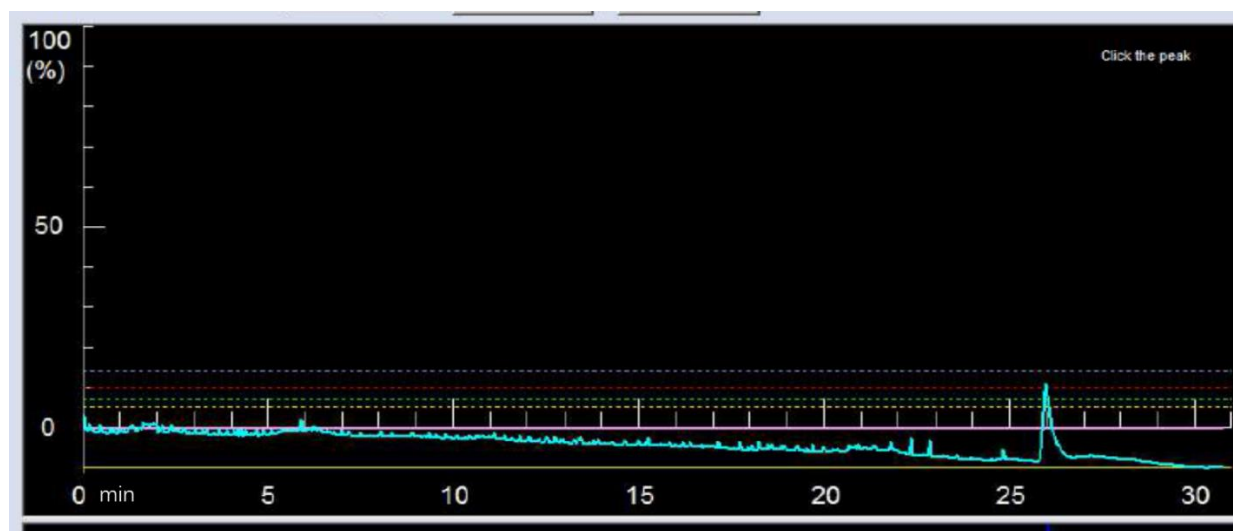


Figure S5. HPLC of Compound 6 (PPE) show only one main peak of the polymer.

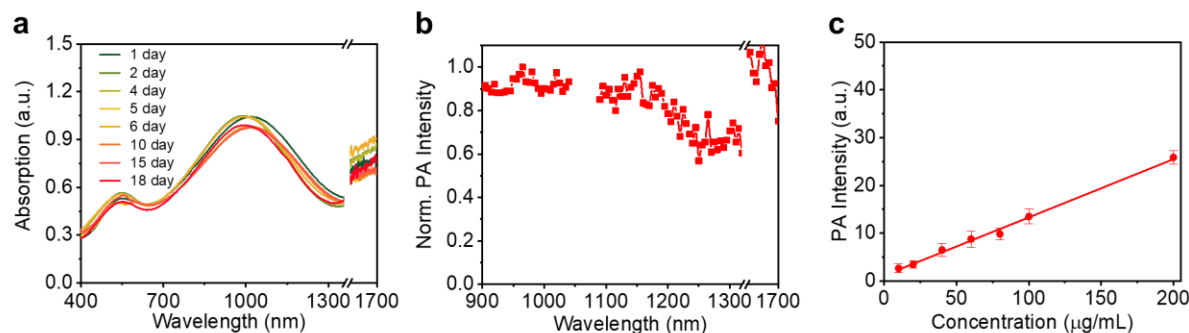


Figure S6. Stability and optical properties of doped PPE in MEM cell culture medium. a) Absorption spectra of doped **PPE** in MEM cell culture medium (pH = 7.4, 10% Fetal Bovine Serum) over time. b) PA spectrum of doped **PPE** in MEM cell culture medium (pH = 7.4, 10% Fetal Bovine Serum). c) PA intensity of doped **PPE** at 1100 nm as a function of mass concentration in MEM cell culture medium (pH = 7.4, 10% Fetal Bovine Serum). $R^2 > 0.99$. Error bars represent for standard deviations.

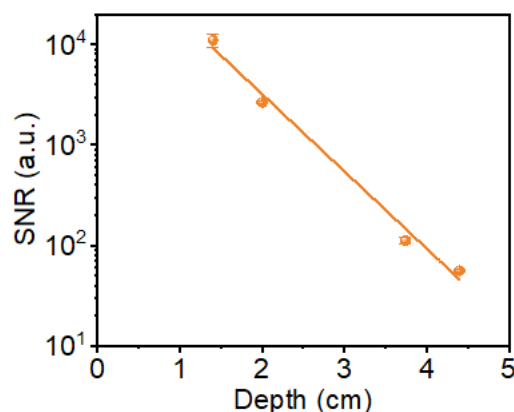


Figure S7. SNR of 0.5 mg mL^{-1} doped PPE contained in a polyurethane tube as a function of depth from illuminated tissue surface. Laser energy density was tuned to 45 mJ cm^{-2} at 1064 nm.

References

- [1] J. F. Ponder Jr, A. M. Österholm, J. R. Reynolds, *Chemistry of Materials* **2017**, 29, 4385