Electronic Supplementary Material (ESI) for RSC Advances


# Supporting Information

## Well-controlled Synthesis of Boronic-Acid Functionalised Poly(lactide)s: A Versatile Platform for Biocompatible Polymer Conjugates and Sensors

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# Experimental Section

## General procedures and starting materials.

All experimental manipulations were performed under an atmosphere of dry, oxygen-free argon, using standard Schlenk and glovebox techniques unless otherwise stated. All solvents were degassed, eluted over activated alumina columns and stored under argon prior to use. Zinc hexamethyldisilazide [$Zn(HMDS)_2$], 4-(hydroxymethyl)phenylboronic acid, *N*-methyldiethanolamine, phenol, catechol Alizarin Red S and pinacol were bought from Aldrich and used without further purification. Compounds **1**[1] and **2**[2] have been prepared according to literature procedures. $^1$H NMR spectra were recorded on a Bruker 300 MHz, 400 MHz or 500 MHz spectrometers at room temperature and referenced to residual protio solvent peaks, unless otherwise stated. Coupling constants *J* are given in Hertz. Gel Permeation Chromatography (GPC) analyses were performed on a Polymer Laboratories PL-GPC 50 integrated system using a PLgel 5 μm MIXED-D 300×7.5 mm column at 35 °C, THF solvent (flow rate, 1.0 ml/min). The polydispersity index (PDI) was determined from $M_w/M_n$, where $M_n$ is the number average molecular weight and $M_w$ the weight average molecular weight. The polymers were referenced to 11 narrow molecular weight polystyrene standards with a range of $M_w$ 615 – 5680000 Da. A correction factor of 0.58 was applied to the $M_n$ values determined against polystyrene standards.[3]

## Polymerisation Reactions.

In a typical run complex **1** (64 mg, 0.1 mmol) was dissolved in $CH_2Cl_2$ (10 ml) to which **2** (23 mg, 0.1 mmol) was added and left to stir at room temperature for 15 min inside the glovebox. Then, *rac*-lactide (720 mg, 5 mmol) was added to the reaction vessel and left to stir for 15 min. The vessel was then exposed to air and the polymerisation reaction terminated by the addition of 1 mL of MeOH, a small aliquot (*ca.* 0.5 mL) was taken at this stage to evaluate the reaction conversion by $^1$H NMR ($C_6D_6$) (typical

1 Chamberlain, B. M.; Cheng, M.; Moore, D. R.; Ovitt, T. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2001**, *123*, 3229–3238.
2 Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2008**, *130*, 14084–14085.
3 a) Save, M.; Schappacher, M.; Soum, A. *Macromol. Chem. Phys.* **2002**, *203*, 889–899. b) A. Duda, A. Kowalski, S. Penczek, *Macromolecules* **1998**, *31*, 2114– 2122.

conversions were found to be consistently higher than 95%). Then, the solvent was almost completely removed under reduced pressure and the polymer was precipitated on pouring into n-hexane (50 mL), washed with hexane to remove any excess of monomer and dried in vacuo to yield a white solid. $^{1}$H NMR spectroscopy ($CDCl_3$) and GPC (THF) were used to determine the end groups and molecular weights ($M_n$ and $M_w$) of the polymers produced. A correction factor of 0.58 was applied to the $M_n$ values determined against polystyrene standards.[3] Representative $^{1}$H NMR spectra of these polymers is provided in Figure S1 with a peak assignment.

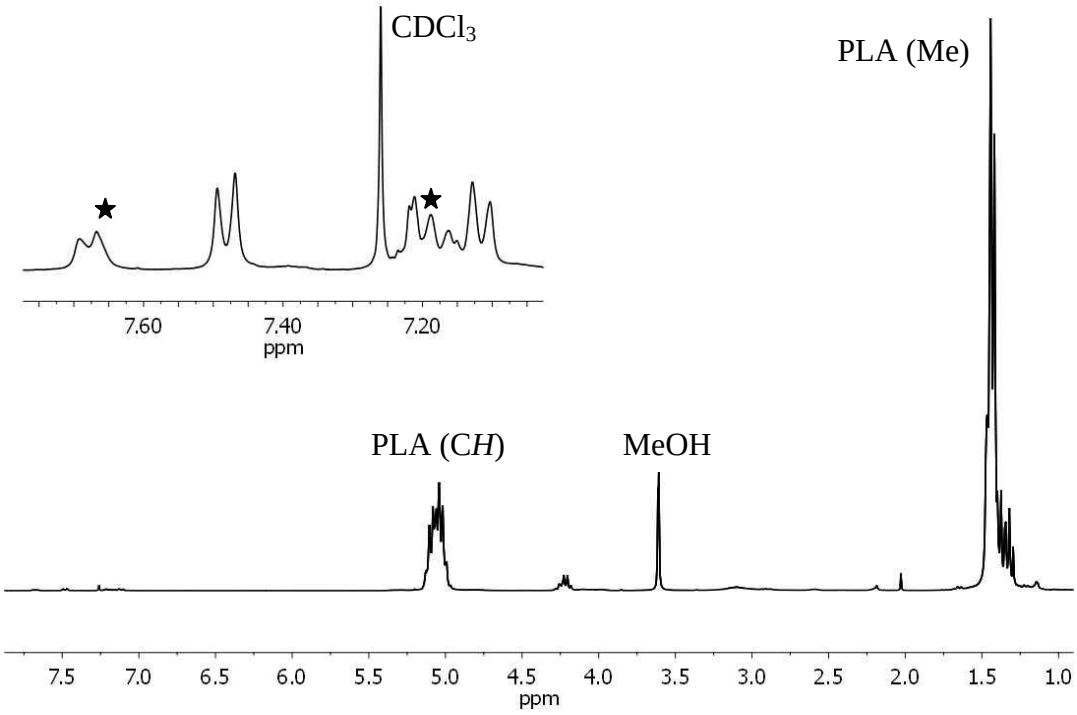


**Fig. S1** $^{1}$H NMR of boronic acid-ended polymers [★ signals corresponding to the anhydride cyclic trimer $(PLA\text{-}OCH_2PhB)_3(\mu\text{–}O)_3$].

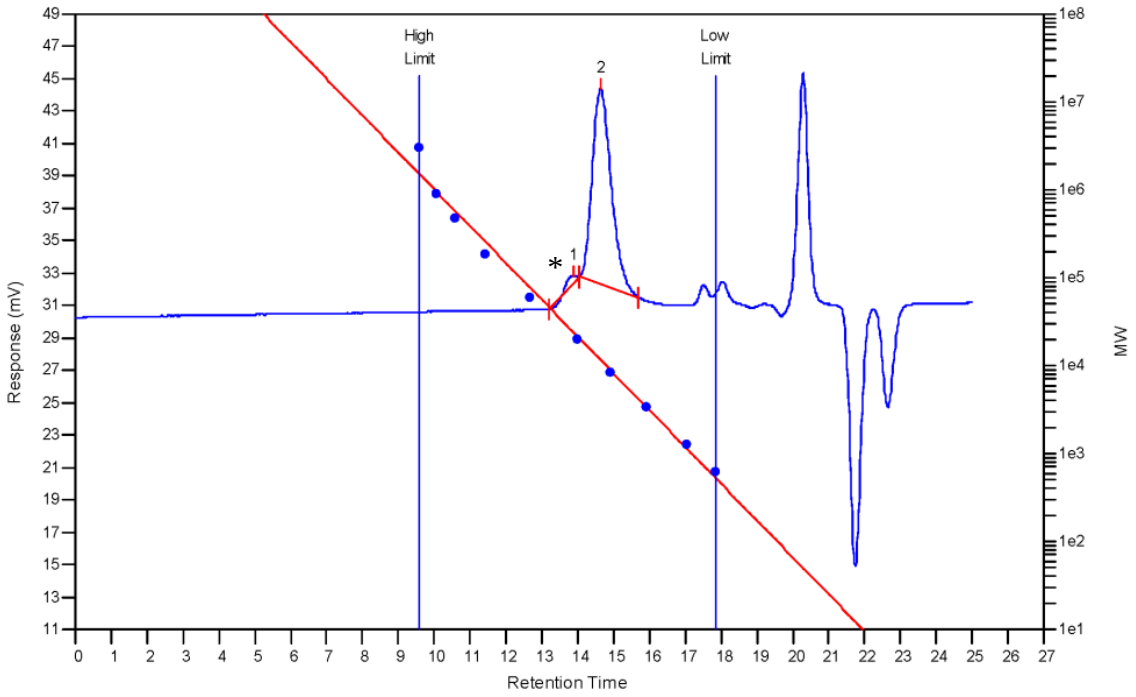


**Fig. S2** Typical GPC trace of polymer **4**. *Band corresponding to the presence of small amounts of the anhydride cyclic trimer $(PLA\text{-}OCH_2PhB)_3(\mu\text{–}O)_3$.

**Preparation of ARS-coupled polymers.**

In a typical preparation 200 mg of the boronic acid ended polymer, **4**, was dissolved in 15 mL of $CH_2Cl_2$ in a round bottom flask to which an excess of Alizarin Red S was added and left to stir at room temperature overnight. Then the solution was cannula-filtered to yield a clear bright orange solution which was concentrated to about 2 mL and then MeOH (50 mL) was added. The vessel was then left at -20 ºC overnight to induce the precipitation of the polymer, which was then collected as a pale orange solid (64 mg). This material has been used for all the titration experiments.

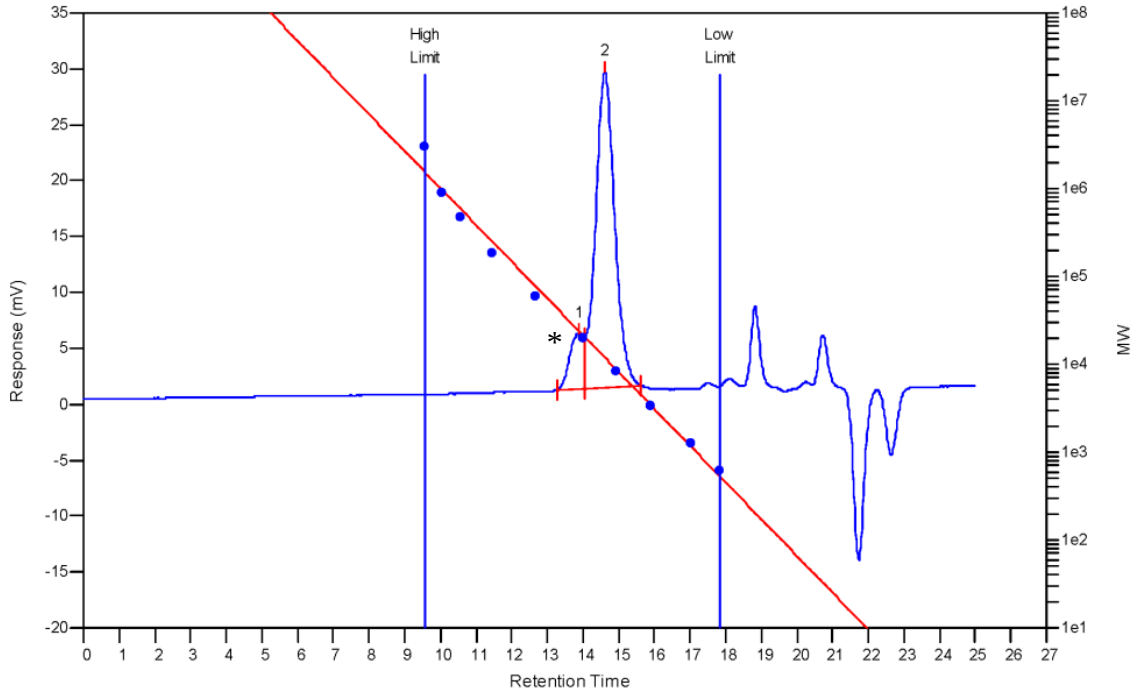


**Fig. S3** Typical GPC trace after ARS coupling of the polymer. *Band corresponding to the presence of small amounts of the anhydride cyclic trimer $(PLA\text{-}OCH_2PhB)_3(\mu\text{–}O)_3$.

**Titration experiments.**

Fluorescence measurements were recorded on a Perkin Elmer LS 50 B Fluorimeter using quartz cuvettes with 10 mm path length. For all the measurements we have used an excitation wavelength of $\lambda_{ex}$ = 495 nm and a scan rate of 60 nm/min.

The titration experiments were carried out dissolving 10 mg of the ARS-coupled polymer, **5**, in 2 mL of laboratory grade tetrahydrofuran. The solution was then transferred to the quartz cuvette recording the initial fluorescence spectrum. Then titration curves were obtained by recording the fluorescence spectrum of the same sample after successive additions of the analytes.

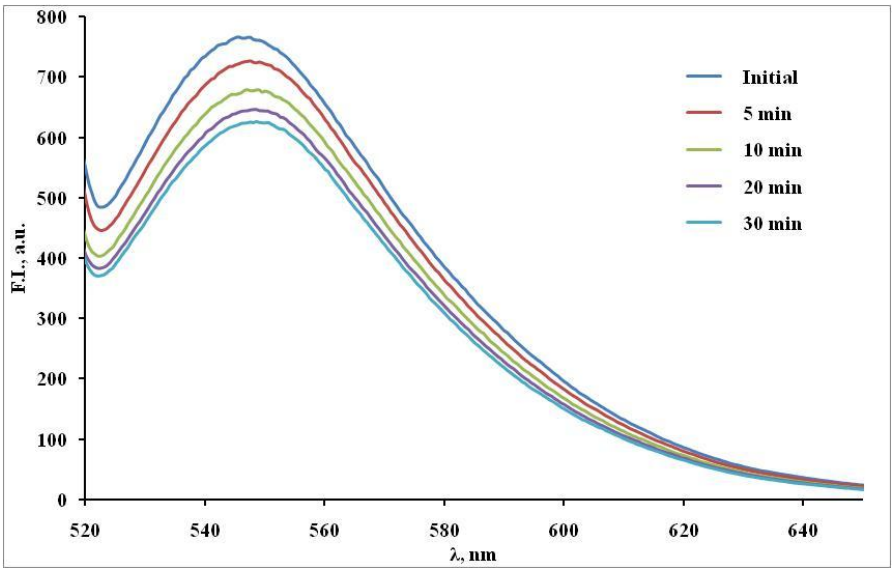


**Fig. S4** Fluorescence Intensity (F.I.) time-evolution of ARS-coupled polymers.

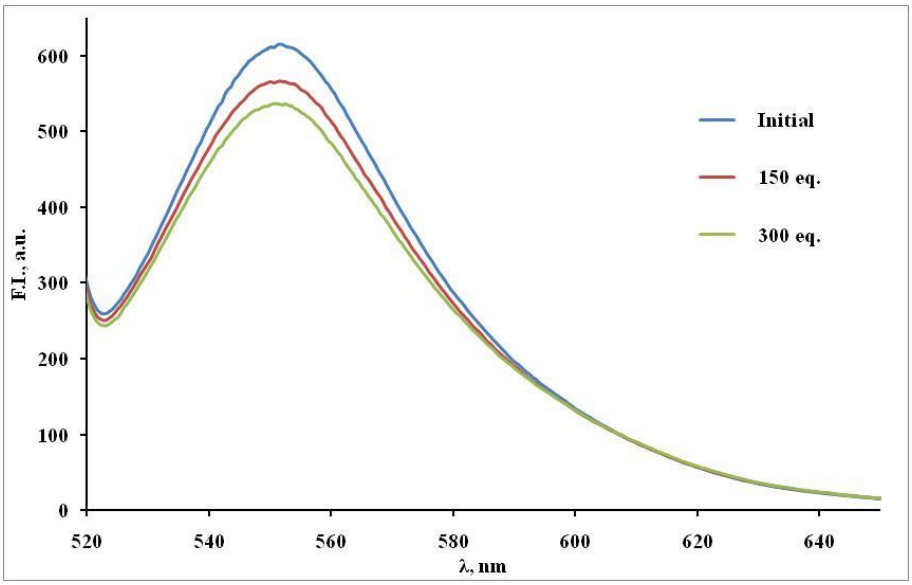


**Fig. S5** Fluorescence Intensity (F.I.) of ARS-coupled polymers with increasing concentration of EtOH.

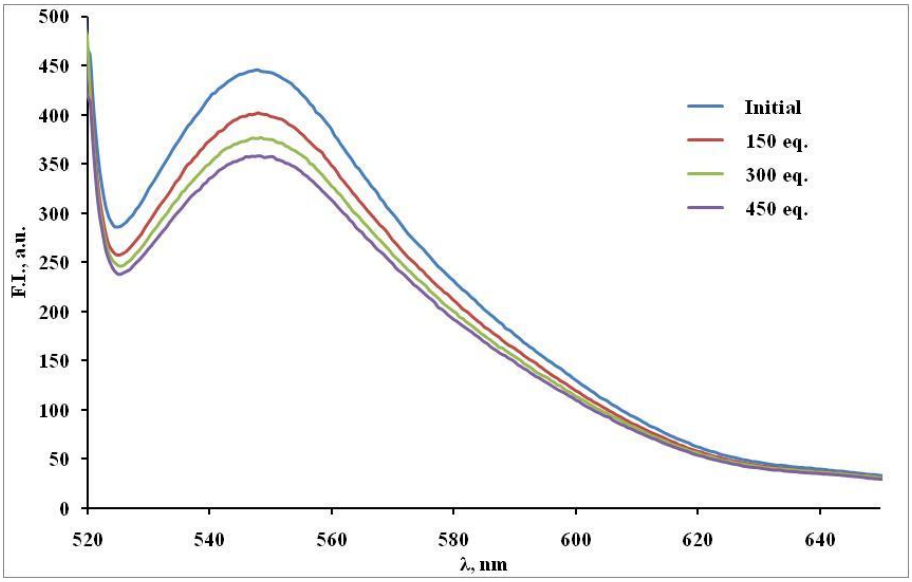


**Fig. S6** Fluorescence Intensity (F.I.) of ARS-coupled polymers with increasing concentration of phenol.

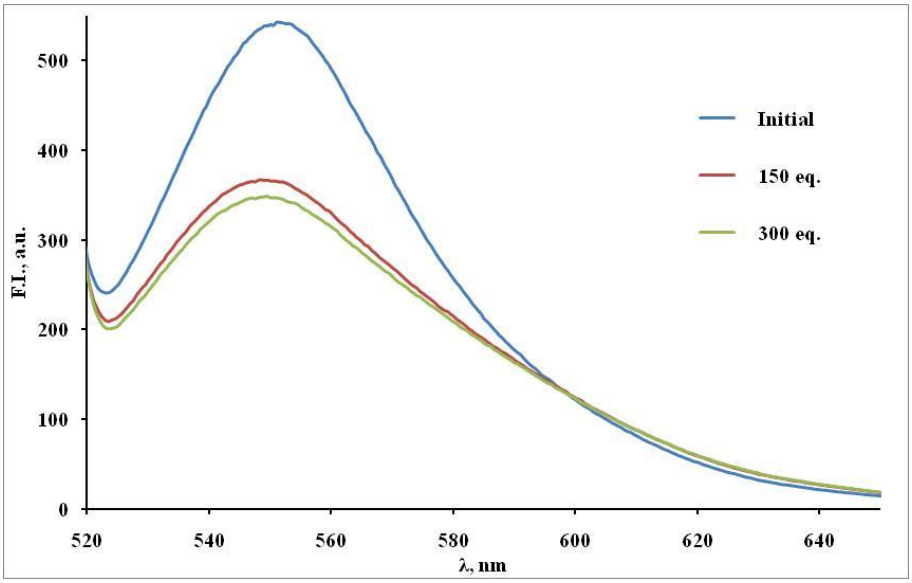


**Fig. S7** Fluorescence Intensity (F.I.) of ARS-coupled polymers with increasing concentration of pinacol.

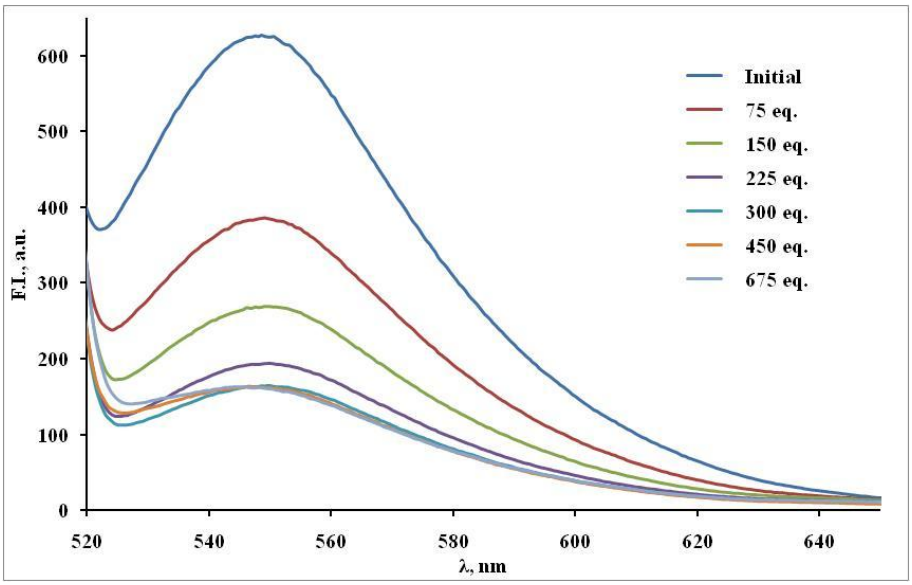


**Fig. S8** Fluorescence Intensity (F.I.) of ARS-coupled polymers with increasing concentration of catechol.

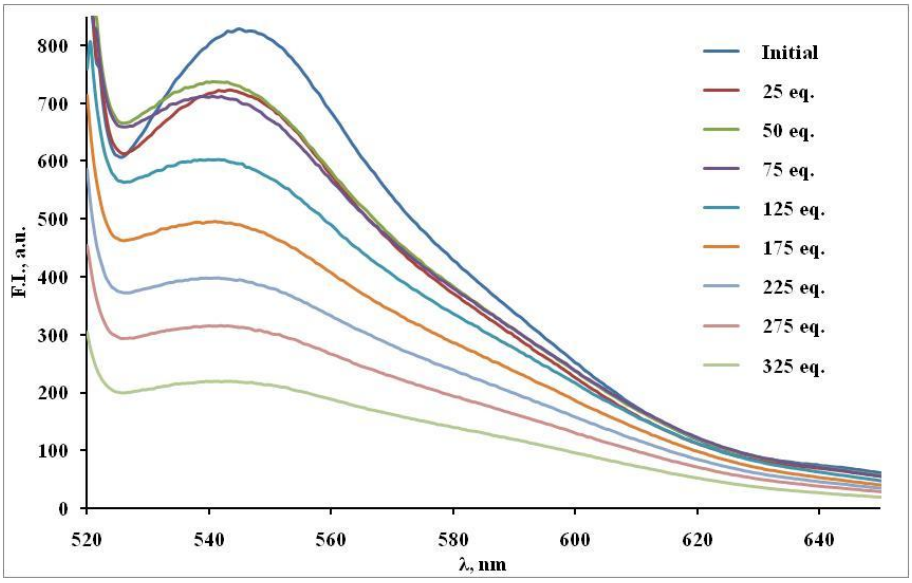


**Fig. S9** Fluorescence Intensity (F.I.) of ARS-coupled polymers with increasing concentration of BOC-protected L-DOPA.

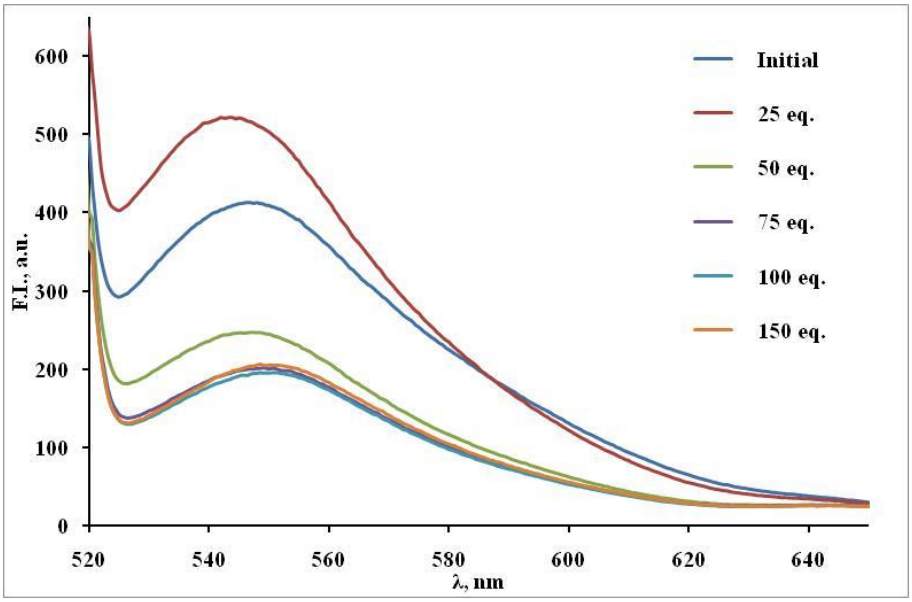


**Fig. S10** Fluorescence Intensity (F.I.) of ARS-coupled polymers with increasing concentration of D/L-Lactic Acid.