# Supporting Information

# Reactive Degradable Linear Poly(aminoamide)s: Synthesis, Post-Polymerization Modification and Layer-by-Layer Coating

Sulbha Kumari and Subrata Chattopadhyay*

*Department of Chemistry, Indian Institute of Technology Patna, Bihta, Patna 801106, Bihar, India*.

** Corresponding authors.*

*E-mail addresses:* sch@iitp.ac.in

## 1. Materials

N, N'-methylene bisacrylamide 3× cryst. extrapure AR (99.5%), benzylamine (99%), dodecylamine (98%), 1,4-diazobicyclo[2.2.2]octane (99%), furfural (99%) and dimethylformamide (DMF) was purchased from Sisco Research Laboratories Pvt. Ltd. (SRL). Diphenyl carbonate (DPC, 99%), tryptamine (97%), 4,4'-methylenebis(phenyl isocyanate) (98%), ethyl carbazate (97%), octylamine (99%), octadecylamine (≥99%), (3-aminopropyl)trimethoxysilane, and deuterated dimethyl sulfoxide (DMSO-$d_6$, 99.9 atom % D) were purchased from Sigma Aldrich, bromine solution was purchased from Merck.

## 2. General characterization

**Nuclear Magnetic Resonance (NMR)** spectra were recorded on Brucker 400MHz spectrophotometers and JEOL JNM-ECZ500R spectrometer using TMS as internal standard and DMSO-$d_6$ as NMR solvent. For $^{13}$C-solid state NMR spectra, JEOL JNM-ECZ500R spectrometer was used.

**Fourier transform infrared (FTIR)** spectra were obtained using a PerkinElmer spectrum 400 FT-IR spectrophotometer in ATR mode at room temperature and the data were collected within wavelength ranged from 4000-600 $cm^{-1}$ with 64 scans.

**Size Exclusion Chromatography (SEC)** were performed on Shimadzu i-series plus integrated HPLC, equipped with a refractive index detector (Wyatt Optilab T-rEX). The measurement was performed at 40 ºC using DMF as eluent (containing 0.01%LiBr) and flow rate of 0.75 mL/min. The data was processes using ASTRA 7.3.0 software (Wyatt Technology Corporation).

**Thermogravimetric analyses (TGA)** were performed on a NEXTA STA300 (Hitachi) instrument under a $N_2$ flow, at a heating rate of 10 °C per minute within a temperature range of 30 to 800°C. For analysis, 6 mg of the samples were used.

**Differential Scanning Calorimetric (DSC)** were performed on DSC7020 (Hitachi) instrument under a $N_2$ flow, at a heating rate of 10°C per minute within a temperature range of -65 to 160°C. For analysis, 3 mg of the samples were used.

**Scanning Electron Microscopy (SEM)** surface morphology of the crosslinked polymers were recorded using a Gemini-500 Zeiss (Germany). All the sample were sputtered with gold using spin coater.

**Brunauer-Emmett-Teller (BET)** analysis were performed using Quantachrome Autosorb iQ2 analyzer. Before the analysis, all the sample were outgassed at 120°C for 8 hr. Surface area and porosity of the polymer samples were done at 77K.

**Atomic Force Microscopy (AFM)** topography images of coated polymer samples were taken in Agilent Technologies 5500 in non-contact mode. Silicon cantilever probes were used with a spring constant of 42 N/m at a resonance frequency of 300 kHz. For performing the thickness measurement, the coated sample was scratched and the data was recorded.

**Water Contact Angle (WCA)** measurements were carried out in CA Goniometer Ramé-Hart instrument Model 250 and the contact angle were measured using DROP image Advance CA software.

## 3. Synthesis

**3.1. Synthesis of indolized-poly(aminoamide) (PAA).** To a solution of N,N'-methylene bisacrylamide (0.5g, 3.243 mmol) in methanol (10 mL), tryptamine (0.519g, 3.243 mmol) was added under continuous stirring. The resulting solution was stirred at 50 °C for 48 h. After the completion of reaction, the obtained precipitate was separated, washed with methanol and dried using rotory evaporator. The product obtained as pale yellow solid in 89% yield. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 2.23 ($H^2$, $H^5$), 2.60-2.76 ($H^1$, $H^6$, $H^7$, $H^8$), 4.36 ($H^4$), 6.86-7.54 (ArH).

**3.2. Synthesis of mono-TADs.** The synthesis of mono-TADs is a two-step procedure, first step involved the synthesis of precursor urazole molecule and second step involved the oxidation of urazole to corresponding TAD.[1] Briefly, diphenyl carbonate (1g, 4.668 mmol, 1 eq.) was

melted at 85 °C and 1 eq. primary amine (benzylamine, octylamine, dodecylamine and octadecylamine) was added under continuous stirring. The mixture was continued to stir under inert atmosphere for 40 min. To this reaction mixture, ethyl carbazate (0.485g, 4.668 mmol, 1eq.) was added and stirred for 2.5 h at 140 °C. The reaction mixture was then additionally heated at 240 °C for 1.5 h. After the completion of the reaction, the mixture was cooled down to room temperature, washed with diethyl ether and dried. The product formed i.e., urazole was then oxidized to the corresponding mono-TAD using DABCO-Br as oxidizing agent.[2] The synthesized urazole precursor (0.6g, 1eq.) was taken in a 50 mL round bottom flask, 0.2 eq. of DABCO-Br and 10 mL of dried DCM was added and the mixture was stirred under inert atmosphere at room temperature for 5 h. The reaction mixture was filtered and the collected pink filtrate was concentrated to remove the DCM. The pink colored mono-TAD was obtained. All the precursor urazole and respective mono-TAD was characterized using NMR spectroscopy (Figure S3-S10).

*Synthesis of Benzyl-Urazole.* The compound was obtained as white solid in 92% yield. $^{1}$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 4.54 (2H, s, $CH_2$), 7.26-7.32 (5H, m, ArH), 10.22 (2H, s, NH-NH); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 41.77 ($CH_2$), 127.92 (CH), 129.01 (CH), 137.19(C), 155.20 (CO). HRMS (Q-TOF) anal. Calcd for $C_9H_{10}N_3O_2^+$[M+H]$^+$: 192.0768; found: 192.0772.

*Synthesis of Benzyl-TAD.* The compound was obtained as pink solid in 81% yield. $^{1}$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 4.69 (2H, s, $CH_2$), 7.32-7.38 (5H, m, ArH); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 44.50 ($CH_2$), 128.53 (CH), 129.03 (CH), 134.42 (C), 160.53 (CO).

*Synthesis of Octyl-Urazole.* The compound was obtained as white solid in 90% yield. $^{1}$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 0.85 (3H, t, $CH_3$), 1.23 (10H, m, 5×$CH_2$), 1.51 (2H, quint, $CH_2$), 3.33 (2H, t, $CH_2$), 10.00 (2H, s, NH-NH); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 14.44 ($CH_3$), 22.57 ($CH_2$), 26.53 ($CH_2$), 27.93 ($CH_2$), 28.97 ($CH_2$), 29.07 ($CH_2$), 31.69 ($CH_2$), 38.36 ($CH_2$), 155.61 (CO). HRMS (Q-TOF) anal. Calcd for $C_{10}H_{20}N_3O_2^+$[M+H]$^+$: 214.1550; found: 214.1561.

*Synthesis of Octyl-TAD ($C_8$-TAD).* The compound was obtained as purple solid in 80% yield. $^{1}$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 0.85 (3H, t, $CH_3$), 1.24 (10H, m, 5×$CH_2$), 1.56 (2H, quint, $CH_2$), 3.46 (2H, t, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 14.43 ($CH_3$), 22.58 ($CH_2$), 26.37 ($CH_2$), 27.18 ($CH_2$), 28.93 ($CH_2$), 29.01 ($CH_2$), 31.69 ($CH_2$), 41.16 ($CH_2$), 160.67 (CO).

*Synthesis of Dodecyl-Urazole.* The compound was obtained as white solid in 83% yield. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 0.85 (3H, t, $CH_3$), 1.23 (18H, br, 9×$CH_2$), 1.51 (2H, quint, $CH_2$), 3.33 (2H, t, $CH_2$), 10.00 (2H, s, NH-NH); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 14.41 ($CH_3$), 22.56 ($CH_2$), 29.18 ($CH_2$), 29.37 ($CH_2$), 29.42 ($CH_2$), 29.47 ($CH_2$), 29.49 ($CH_2$), 31.76 ($CH_2$), 38.30 ($CH_2$), 155.55 (CO). HRMS (Q-TOF) anal. Calcd for $C_{14}H_{28}N_3O_2^+$[M+H]$^+$: 270.2176; found: 270.2185.

*Synthesis of Dodecyl-TAD ($C_{12}$-TAD).* The compound was obtained as pink solid in 79% yield. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 0.85 (3H, br, $CH_3$), 1.24 (18H, br, 9×$CH_2$), 1.56 (2H, br, $CH_2$), 3.36 (2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 14.37 ($CH_3$), 22.58 ($CH_2$), 28.96 ($CH_2$), 29.22 ($CH_2$), 29.35 ($CH_2$), 29.45 ($CH_2$), 29.50 ($CH_2$), 29.53 ($CH_2$), 31.80 ($CH_2$), 41.09 ($CH_2$), 160.58 (CO).

*Synthesis of Octadecyl-Urazole.* The compound was obtained as white solid in 81% yield. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 0.85 (3H, t, $CH_3$), 1.23 (30H, br, 15×$CH_2$), 1.51 (2H, quint, $CH_2$), 3.31 (2H, $CH_2$), 10.00 (2H, s, NH-NH); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 14.41 ($CH_3$), 22.56 ($CH_2$), 26.50 ($CH_2$), 27.90 ($CH_2$), 28.98 ($CH_2$), 29.17 ($CH_2$), 29.49 ($CH_2$), 31.76 ($CH_2$), 38.30 ($CH_2$), 155.54 (CO). HRMS (Q-TOF) anal. Calcd for $C_{20}H_{40}N_3O_2^+$[M+H]$^+$: 354.3115; found: 354.2706.

*Synthesis of Octadecyl-TAD ($C_{18}$-TAD).* The compound was obtained as purple solid in 78% yield. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 0.85 (3H, br, $CH_3$), 1.23 (30H, br, 15×$CH_2$), 1.54 (2H, br, $CH_2$), 3.20 (2H, $CH_2$); $^{13}$C NMR (DMSO-$d_6$, 100 MHz): 14.42 ($CH_3$), 22.57 ($CH_2$), 28.92 ($CH_2$), 29.17 ($CH_2$), 29.36 ($CH_2$), 29.49 ($CH_2$), 31.74 ($CH_2$), 41.09 ($CH_2$), 160.53 (CO).

**3.3. Synthesis of 4,4'-(4,4'-diphenylmethylene)-bistriazolinedione (MDI-bisTAD).** The synthesis procedure was adapted as already described in literature.[2] The mixture of ethyl carbazate (1g, 9.605 mmol) in toluene (7.5 mL) is placed is an ice bath under inert condition. To this, the solution of 4, 4'-methylenebis(phenyl isocyanate) (1.2g, 4.802 mmol) in toluene (5 mL) was added dropwise with vigorous stirring. The resultant mixture was stirred at room temperature for 3 h and then at 90 °C for 2 h. After cooling it down to room temperature, the product 4,4'-(4,4'-diphenylmethylene)-bis-(carbethoxysemicarbazide) was filtered, washed with toluene and then dried (Yield 94%). To the synthesized bis-semicarbazide (1g, 2.182 mmol), 5mL of 4M aq. KOH solution was added and the mixture was refluxed for 2 h under inert atmosphere. The solution was warm filtered, cooled down to room temperature and

acidified till pH 1 using conc. HCl. The resultant precipitate (4,4'-(4,4'-diphenylmethylene)-bisurazole, MDI-bisurazole) was filtered, washed with water and dried under vacuum oven. In a 50 mL round bottom flask, MDI-bisurazole (0.8g, 2.183 mmol), DABCO-Br (2.03g, 1.288 mmol) and dried DCM (10 mL) was added and stirred for 5 h at room temperature under inert atmosphere. The solution was filtered and the residue was washed with DCM. The pink filtrate was collected and dried using rota vapour. The pink-coloured MDI-bisTAD was obtained (Yield ~90%). $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 4.10 (2H, s, $CH_2$), 7.3-7.6 (8H, m, ArH).

**3.4. Post-polymer modification of indolized-poly(aminoamide).** To the solution of indolized-PAA (0.2g, 0.636 mmol w.r.t the repeating unit) in DMF (2 mL), the solution of mono-TAD (1eq.) in DMF (1 mL) was added and the mixture was stirred for 20 min. After the completion of the reaction, the solution was precipitated in diethyl ether, dried and washed several times with water. The final post-modified product was then dried.

*Modification with $C_8$-TAD (PAA-$C_8$-TAD).* The product obtained as brown solid in 76% yield with modification degree of 64% (calculated from $^1$H-NMR). $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm), Figure 1a): 0.85 ($H^{13}$), 1.03-1.64 ($H^{12}$), 2.23 ($H^2$, $H^5$), 2.59-2.83 ($H^1$, $H^6$, $H^7$, $H^8$), 3.28 ($H^{11}$), 4.37 ($H^4$), 6.87-7.62 (ArH).

*Modification with $C_{12}$-TAD (PAA-$C_{12}$-TAD).* The product obtained as brown solid in 69% yield with modification degree of 45%. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm), Figure S12): 0.84 ($H^{13}$), 1.03-1.70 ($H^{12}$), 2.23 ($H^2$, $H^5$), 2.58-2.83 ($H^1$, $H^6$, $H^7$, $H^8$), 3.24 ($H^{11}$), 4.38 ($H^4$), 6.86-7.55 (ArH).

*Modification with $C_{18}$-TAD (PAA-$C_{18}$-TAD).* The product obtained as brown solid in 60% yield with modification degree of 85%. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm), Figure S13): 0.83 ($H^{13}$), 1.06-1.72 ($H^{12}$), 2.24 ($H^2$, $H^5$), 2.58-2.82 ($H^1$, $H^6$, $H^7$, $H^8$), 3.17 ($H^{11}$), 4.37 ($H^4$), 6.83-7.56 (ArH).

*Modification with Benzyl-TAD (PAA-benzyl-TAD).* The product obtained as brown solid in 79% yield. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm), Figure S14): 2.24 ($H^2$, $H^5$), 2.57-2.87 ($H^1$, $H^6$, $H^7$, $H^8$), 4.24-4.59 ($H^4$, $H^{11}$), 6.85-7.61 (ArH).

**3.5. Crosslinking of indolized-PAA with MDI-bisTAD.** Indolized-PAA (0.2g, 0.636 mmol) was dissolved in minimum amount of DMF. To this, solution of MDI-bisTAD (0.254, 0.318, 0.381, 0.445 and 0.508 mmol for 40, 50, 60, 70 and 80% crosslinking) in minimum amount of

DMF was added, an immediate gelation was observed. After 20 min, acetone (15 mL) was added to the gel and stirred. The obtained solid was filtered, washed with acetone and dried. All the crosslinked polymers were obtained in > 90% yield.

**3.6. Synthesis of Furan-2-yl-*N*-(3-(trimethoxysilyl)propyl)methanimine (FTMSPM).** To the solution of furfural (0.1g, 1.041 mmol) in methanol (4 mL), (3-aminopropyl)trimethoxysilane (0.373g, 2.080 mmol) was added and the mixture was stirred for 24 h at room temperature. The solvent was removed via rotory evaporator and the product was dried. The obtained product was yellow solid in 90% yield. $^1$H-NMR (400 MHz, DMSO-$d_6$, δ (ppm)): 0.54 ($H^2$), 1.37-1.64 ($H^3$), 2.46 ($H^4$), 3.34 ($H^1$), 6.58-6.85 ($H^6$, $H^7$), 7.77 ($H^8$), 8.06 ($H^5$).

**3.7. Preparation of indolized-PAA coated surface.** Silicon wafer was cleaned with acetone and water before activation. The substrate was immersed in the conc.$H_2SO_4$:$H_2O_2$ (30%) (2:1, piranha solution) for 1 h, washed thoroughly with water and dried under the stream of argon. The solution of 30 mM FTMSPM in methanol was stir for 3 h at 60 ºC, then the activated silicon wafer was transferred to this solution and stirred additionally for 18 h. The wafer was then rinsed with ethanol and water and dried under the stream of argon. The pre-prepared silicon wafer was then placed in the DMF solution of 0.1M MDI-bisTAD for 5 min. The wafer was taken out and then spin coated (3000 rpm, 60 s) with indolized-PAA (40 mg/mL) solution in DMF. 0.1M MDI-bisTAD (few drops) was then added at the polymer-coated silicon substrate and kept for 2 min. After 2 min the substrate was again spinned at 3000 rpm for 60 s. This procedure was repeated to get the desired number of layers. Lastly, after the last layer of polymer coating, a few drops of 0.1 M of $C_{18}$-TAD solution in DMF was added to the layered polymer coated silicon substrate and kept it for 2 min followed by spinning. The final polymer coated surface was washed with THF to remove excess $C_{18}$-TAD and dried at 60 ºC for 24 h.

**3.8. Thermoreversible studies.** The reversible kinetic experiment for studying transclick behaviour between benzyl-TAD modified PAA (PAA-benzyl-TAD) and *trans, trans*-2,4-hexadiene-1-ol (HDEO, a trapping agent for TAD) was performed as follows. To the solution of PAA-benzyl-TAD (0.06 g, 0.119 mmol) in 2.2 mL DMSO-$d_6$, HDEO (0.013 g, 0.131 mmol, 1.1 eq. w.r.t repeating unit) was added and the reaction mixture was stirred at 130 °C under closed condition. At different interval of time (t = 0 min, 6 h, 12 h and 24 h), the mixture (0.55 mL) was transferred to the NMR tube, cooled down in running water and then analyzed using $^1$H-NMR.

**3.9. Degradation studies.** The degradation of indolized-PAA and crosslinked PAA was analyzed gravimetrically. Briefly, 10 mg of the sample was taken in each glass vial containing 10 mL alkaline solution (0.01M and 0.1M NaOH solution). The resulting mixture was stirred with a rotation of 400 rpm at 40 °C. At various interval of time, the degraded polymer sample was separated from the alkaline solution washed with distilled water and dried at 100 °C. After cooling it down to room temperature, the sample was weighed and percentage degradation was calculated using the formula:

$$\Delta m\ (\%) = \frac{m_1 - m_2}{m_1} \times 100$$

Where Δm = degradation rate (wt %), $m_1$ and $m_2$ are the weight of the sample before and after degradation.

**Supporting Data-**

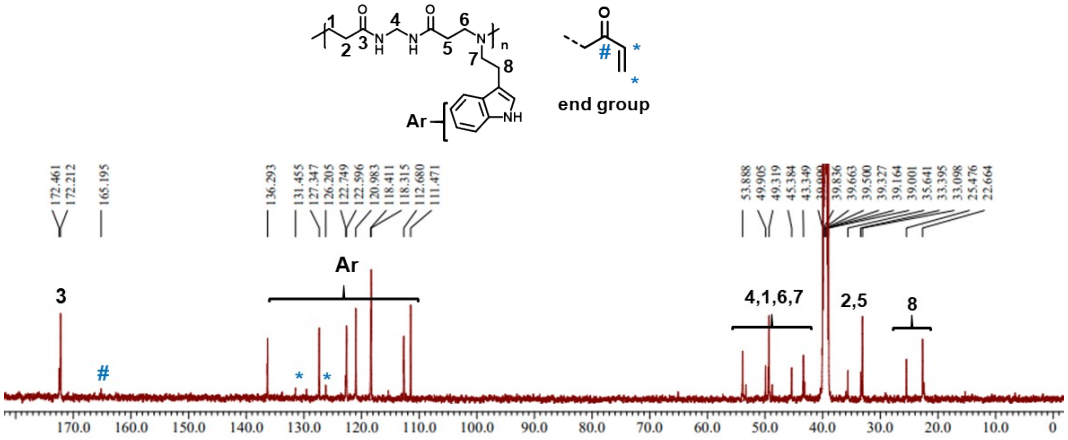


**Figure S1:** $^{13}$C-NMR spectra of indolized-PAA.

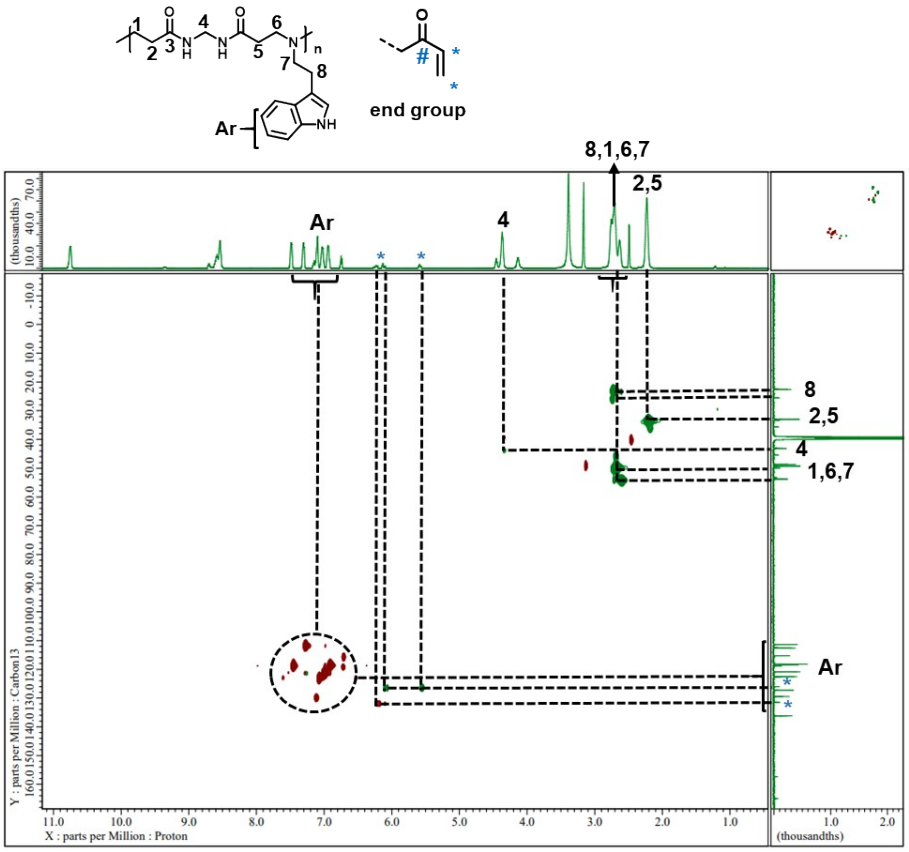


**Figure S2:** CH-HSQC of indolized-PAA.

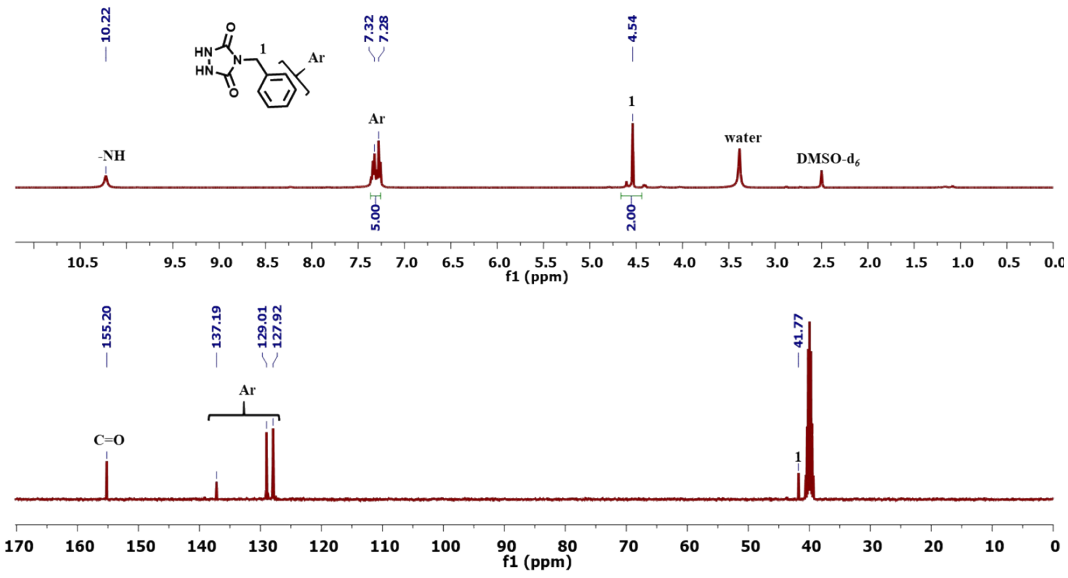


**Figure S3:** $^{1}$H & $^{13}$C-NMR spectra of Benzyl-urazole.

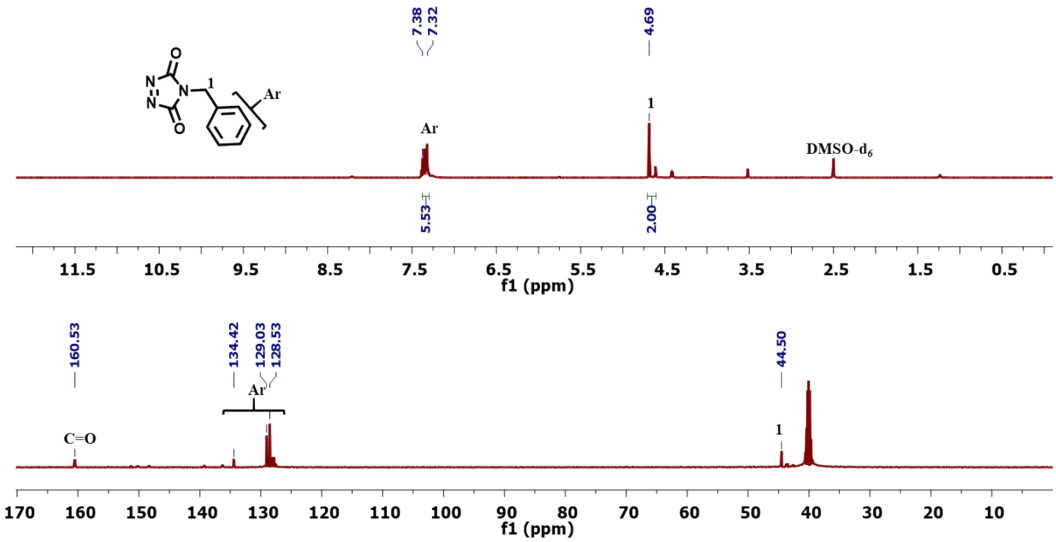


**Figure S4:** $^{1}$H & $^{13}$C-NMR spectra of Benzyl-TAD.

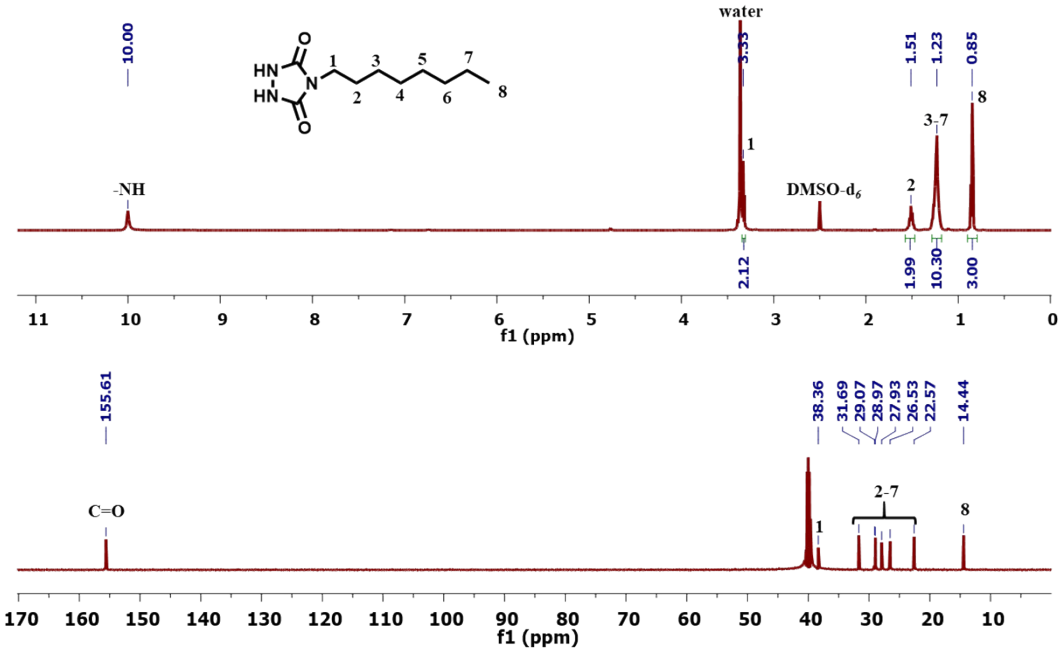


**Figure S5:** $^{1}$H & $^{13}$C-NMR spectra of $C_8$-urazole.

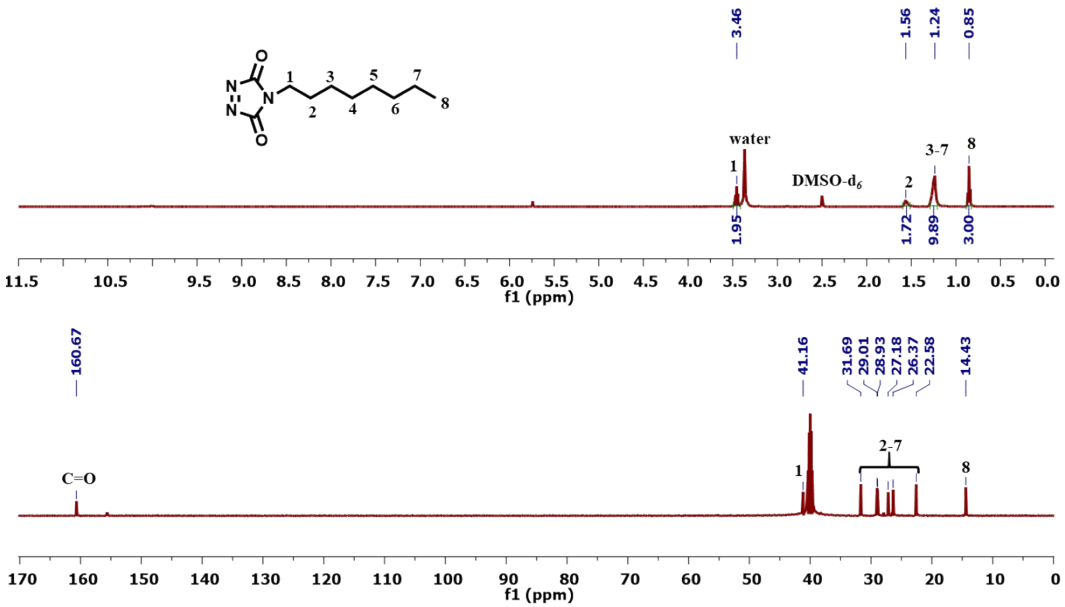


**Figure S6:** $^{1}H$ & $^{13}C$-NMR spectra of $C_8$-TAD.

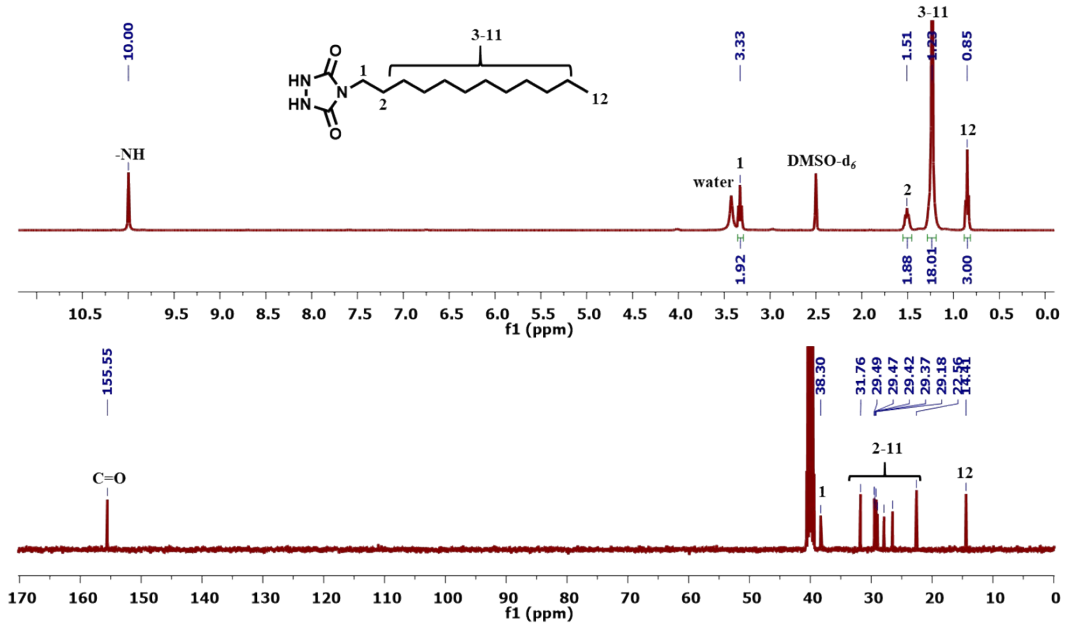


**Figure S7:** $^{1}H$ & $^{13}C$-NMR spectra of $C_{12}$-urazole.

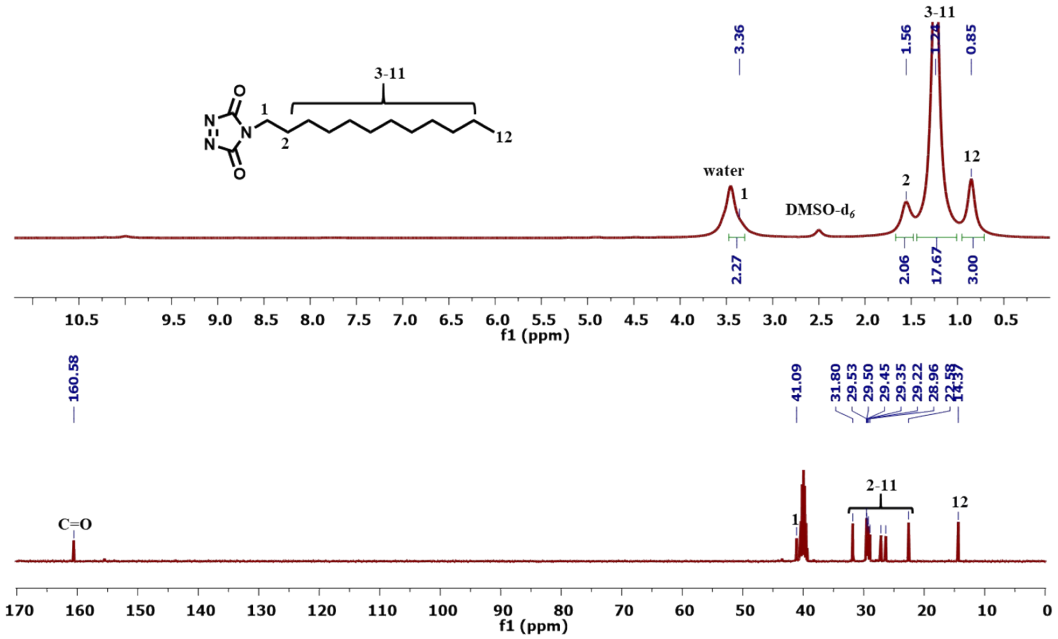


**Figure S8:** $^{1}H$ & $^{13}C$-NMR spectra of $C_{12}$-TAD.

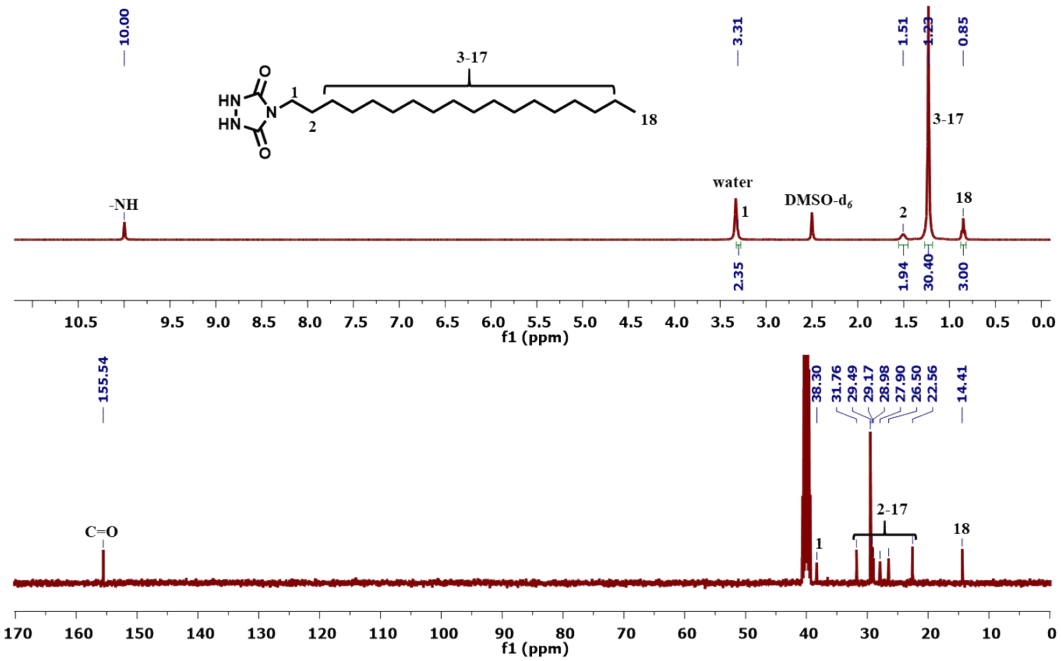


**Figure S9:** $^{1}H$ & $^{13}C$-NMR spectra of $C_{18}$-urazole.

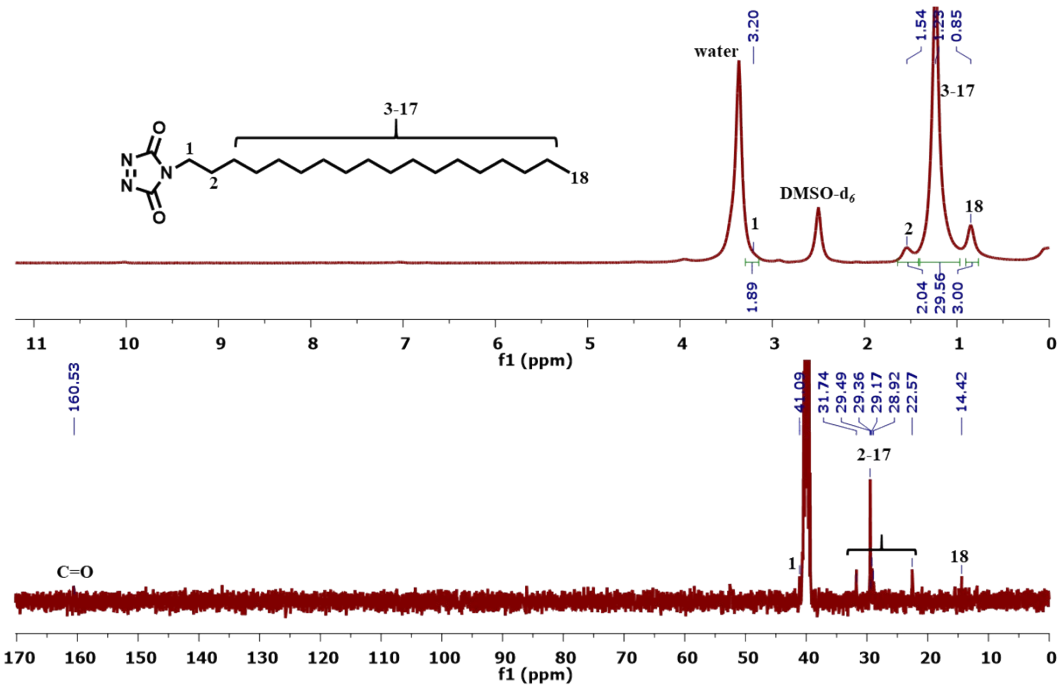


**Figure S10:** $^{1}$H & $^{13}$C-NMR spectra of $C_{18}$-TAD.

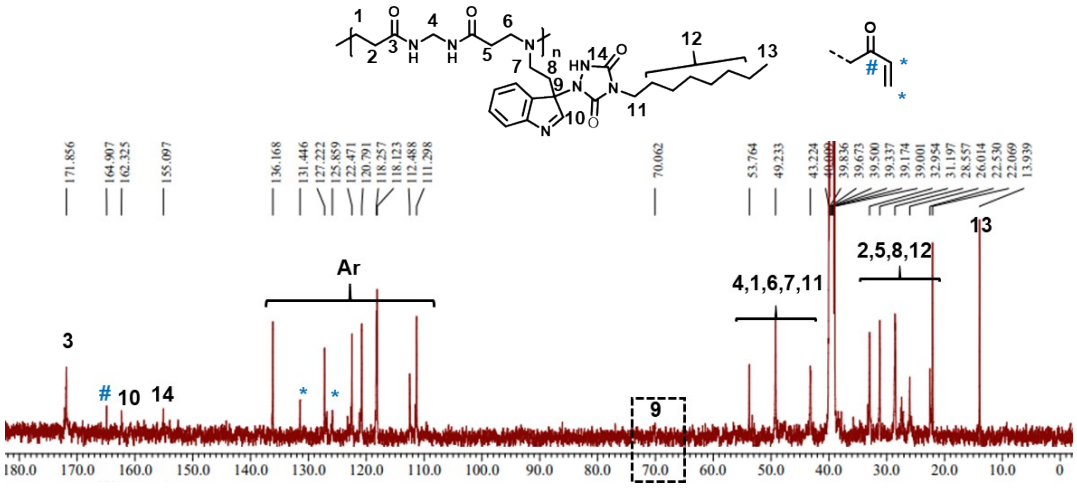


**Figure S11:** $^{13}$C-NMR spectra of PAA-$C_8$-TAD.

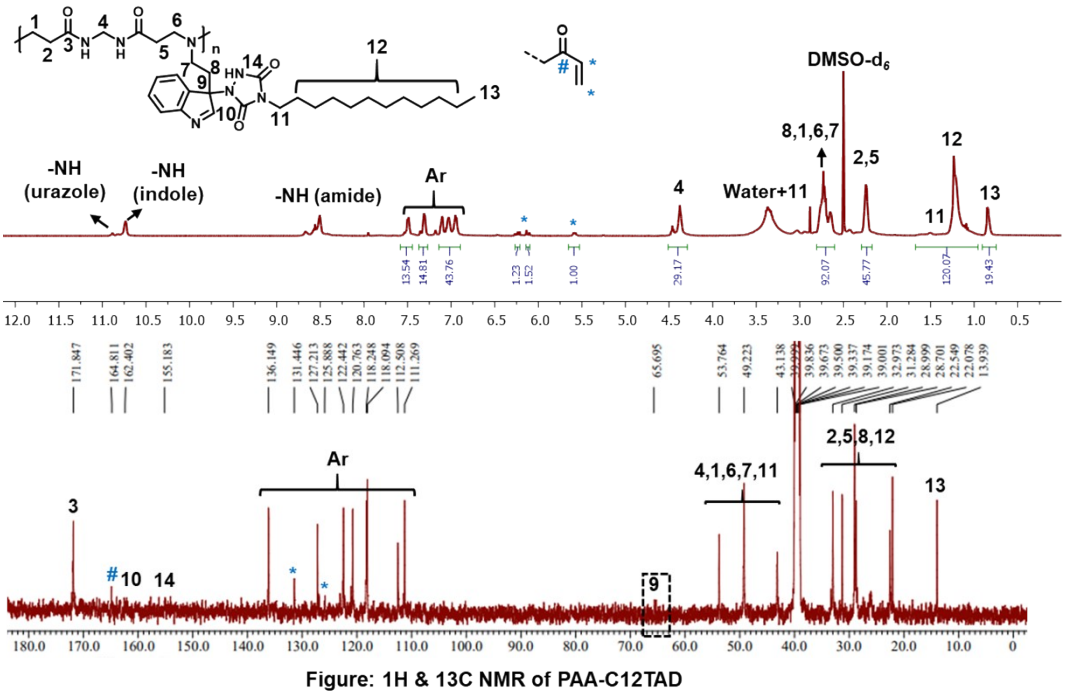


Figure: 1H & 13C NMR of PAA-C12TAD

**Figure S12:** $^{1}H$ & $^{13}C$-NMR spectra of PAA-$C_{12}$-TAD.

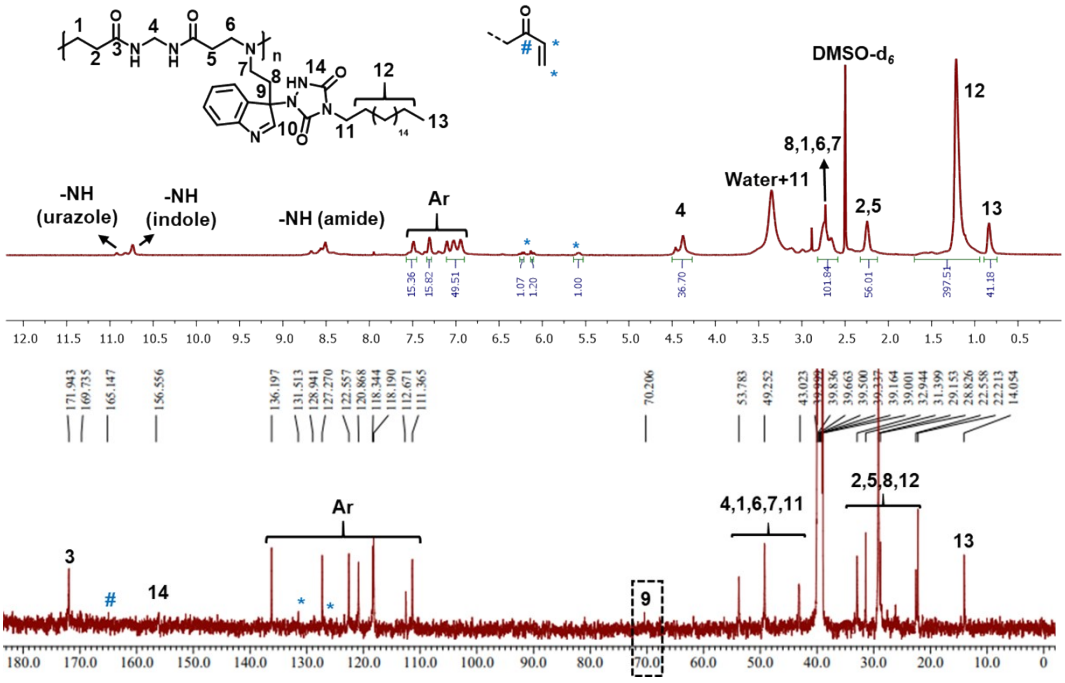


**Figure S13:** $^{1}H$ & $^{13}C$-NMR spectra of PAA-$C_{18}$-TAD.

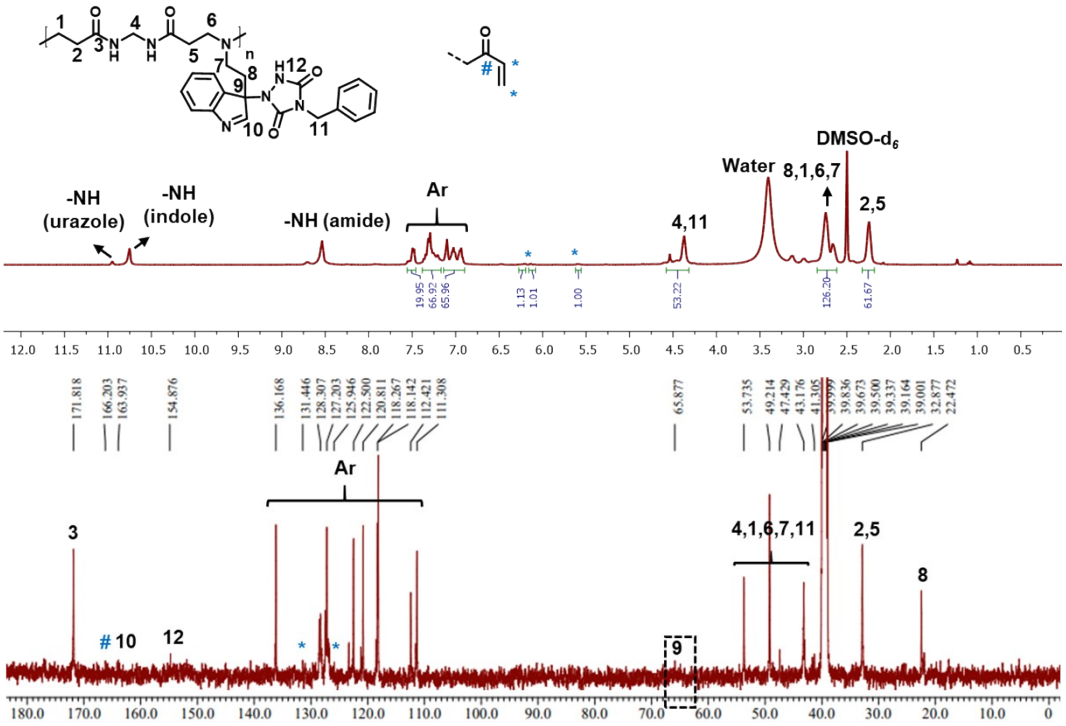


**Figure S14:** $^{1}$H & $^{13}$C-NMR spectra of PAA-Benzyl-TAD.

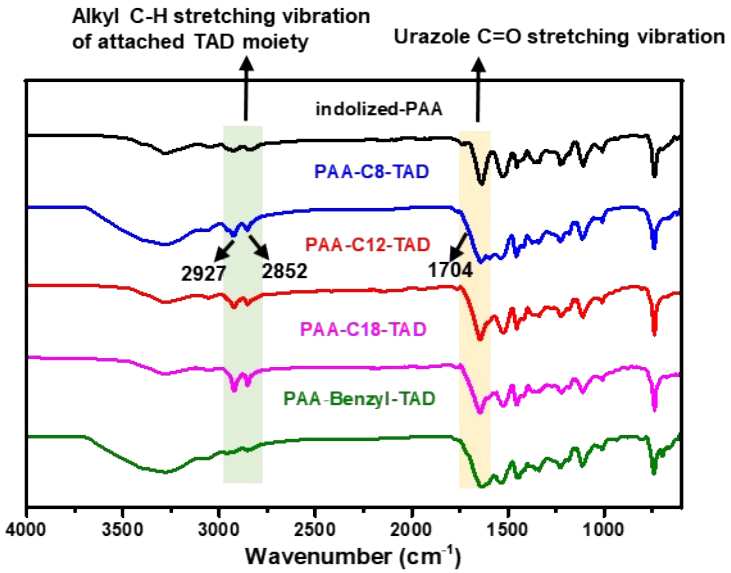


**Figure S15:** FTIR spectra of indolized-PAA and post-modified PAAs.

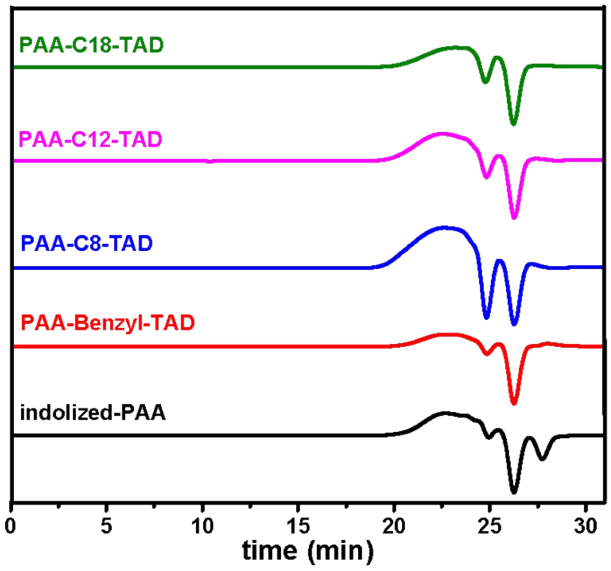


**Figure S16:** SEC of idolized-PAA and its post-modified PAAs.

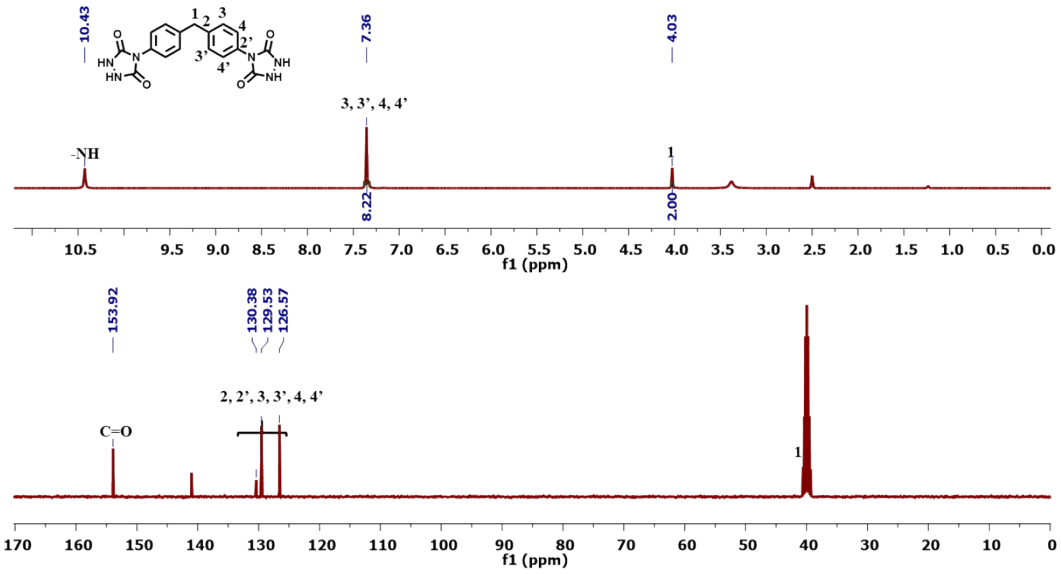


**Figure S17:** $^{1}$H & $^{13}$C-NMR spectra of MDI-bisurazole.

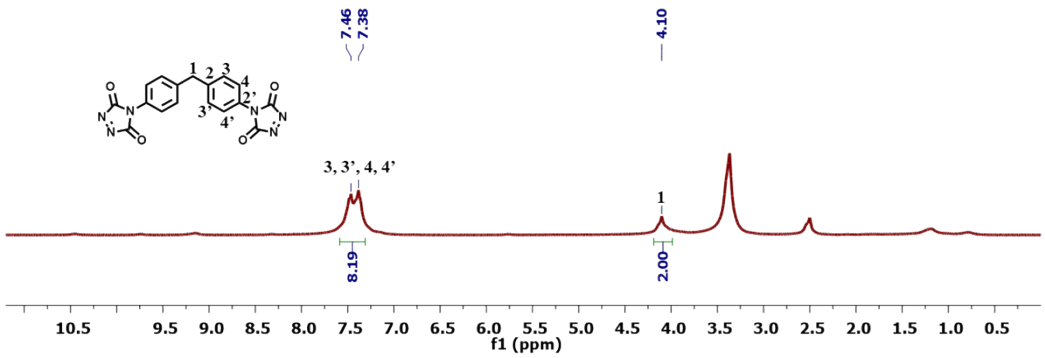


**Figure S18:** [1]H spectra of MDI-bisTAD.

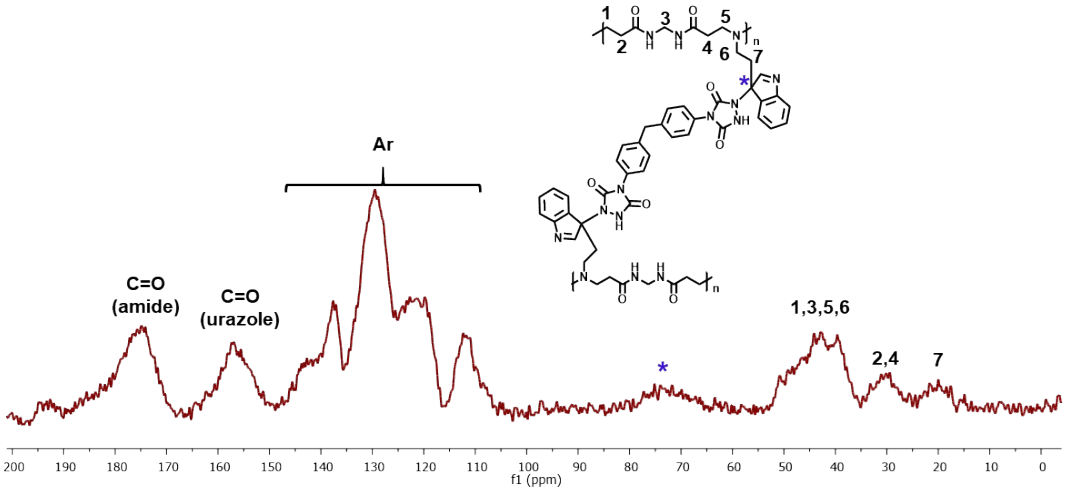


**Figure S19:** Solid-state NMR of crosslinked indolized-PAA (PAA-60%M).

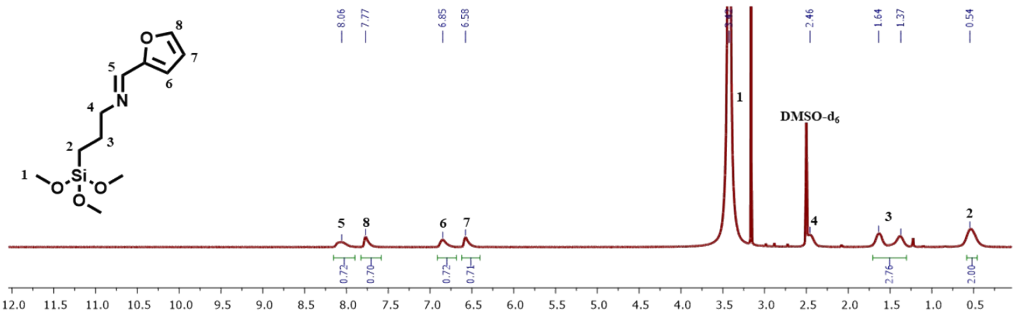


**Figure S20:** [1]H-NMR spectra of FTMSPM (Note: small fraction of starting material was observed. The FTMSPM coated surface was washed with ethanol to remove this unreacted material).

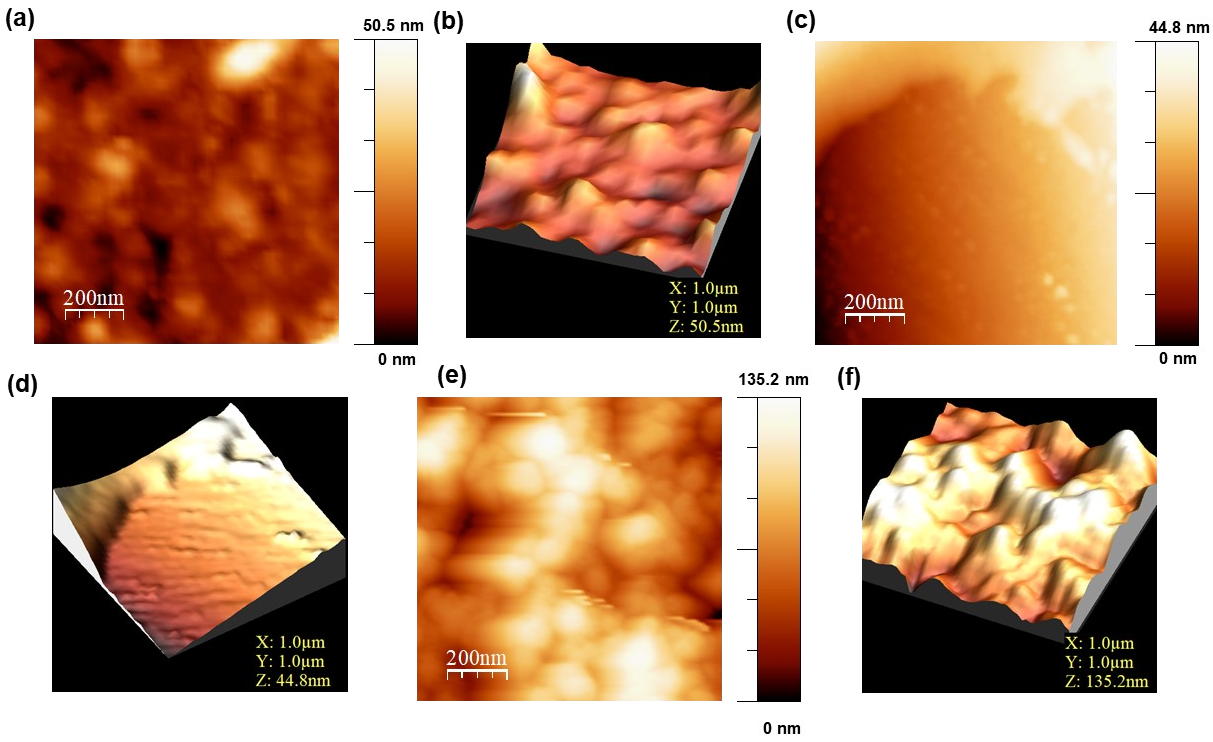


**Figure S21:** (a) & (c) are the 2D AFM image and (b) & (d) are the 3D AFM image of indolized-PAA coated surface at layer-2 and layer-3 respectively, (e) & (f) are the 2D and 3D AFM image of indolized-PAA coated surface (layer-1) functionalized with $C_{18}$-TAD.

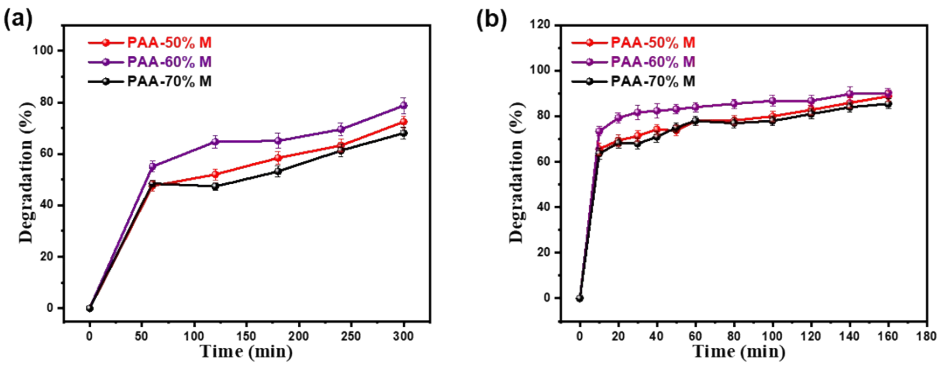


**Figure S22:** Degradation kinetics of crosslinked PAA (PAA-50% M, PAA-60% M and PAA-70% M) at (a) 0.01M NaOH solution (pH 12) and (b) 0.1M NaOH solution (pH 13) via gravimetric method.

## Reference

1. L. Vlaminck, B. Van de Voorde and F. E. Du Prez, *Green Chemistry*, 2017, **19**, 5659-5664.
2. S. Billiet, K. De Bruycker, F. Driessen, H. Goossens, V. Van Speybroeck, J. M. Winne and F. E. Du Prez, *Nature chemistry*, 2014, **6**, 815-821.