Supporting information for

Investigation of Secondary Amine-Derived Aminal Bond Exchange towards the Development of Covalent Adaptable Networks

Albert Chao and Donghui Zhang*

Department of Chemistry and Macromolecular Studies Group, Louisiana State University, Baton Rouge, Louisiana 70803, United States

* Corresponds to: Donghui Zhang (dhzhang@lsu.edu)

EXPERIMENTAL CONSIDERATION

Materials. All chemicals were purchased from Sigma-Aldrich. All chemicals were used without further purification. Deuterated solvents (*e.g.*, $CDCl_3$, THF-d_8 and TOL-d_8) were purchased from Fisher Scientific. Model aminal compound **1**, **2** (Figure 1) and those shown in Scheme 2 were prepared by adapting a literature procedure[S1] and stored under nitrogen before use. Tris[2-(methylamino)ethyl]amine (TA, Scheme 4) was synthesized by a literature procedure.[S2] Aluminum molds [triangle 55 mm (L) × 5 mm (T); disc 60 mm (D) × 5 mm (T); square 50 mm (L) × 5 mm thickness] were made by the LSU machine shop. THF-d_8 was dried with molecular sieves overnight before use in the kinetic studies. TOL-d_8 and THF-d_8 were dried by stirring over calcium hydride and purified by vacuum transfer.

NMR spectroscopy. ^{1}H NMR, ^{13}C NMR, and HSQC NMR spectra were recorded on a Bruker AV-500 spectrometer, and the chemical shifts in parts per million (ppm) were referenced relative to protio and ^{13}C impurities in $CDCl_3$ or THF-d_8.

FT-IR spectroscopy. FT-IR spectra were collected on ATR-FTIR spectrometer (Bruker Alpha). Progression of the condensation polymerization was tracked by monitoring the disappearance of the IR absorption due to the N-H bending (720-800 cm^{-1}) mode over time. FT-IR spectrum of the TA/DA solution (Entry 1-5, Table 1) without paraformaldehyde was measured as reference. After the addition of paraformaldehyde, the mixture was heated until homogenous at which point the FT-IR spectrum of the THF gel was measured again. The aminal conversion was determined as the percentage change of the integrated area of IR absorption due to the N-H bending mode.

MALDI-TOF mass spectrometry. Experiments were conducted on a Bruker UltrafleXtreme tandem time-of-flight (TOF) mass spectrometer. The instrument was calibrated with Peptide Calibration Standard II consisting of standard peptides Angiotensin I, Angiotensin II, Substance P, Bombesin, ACTH clip 1-17, ACTH clip 18-39, and Somatoratin 28 (Bruker Daltonics, Billerica, MA) prior to experiment. A saturated methanol solution of α-cyano-4-hydroxycinnamic acid was used as matrix. Samples were prepared by mixing a CH_2Cl_2 solution of polymers (10 mg/mL) with the matrix at 1:1 volume ratio, which were then deposited onto a 384-well ground-steel sample plate using a pipette and dried in air. Experiments were done in positive linear mode. The data analysis was performed with FlexAnalysis software.

Dynamic mechanical analysis (DMA). Tensile tests were conducted using dogbone shaped samples (ca. 1 mm (T) × 5 mm (W) × 12 mm (L) and a gauge length of 14 mm). The samples were stored for 24 – 48 h at room temperature in a desiccator prior to the tensile test. Stress-strain curve

experiments were performed using TA instruments DMA Q800 under uniaxial tensile mode. The experiments were conducted with a controlled force, 0.500 N/min at room temperature with a preload force 0.001 N until the sample yielded. Young's moduli (E') were determined from the slope of the linear stress-strain curve in the 0 to 0.5 % strain range. Stress relaxation analysis (SRA) experiments were conducted in tensile mode with a controlled strain and a preload force 0.001 N at specified temperatures (50 – 75 °C). The samples were kept at isothermal conditions (50 – 75 °C) for 10 min. Subsequently, each sample was subjected to an instantaneous 1% strain. The stress relaxation was monitored, while maintaining a 1 % constant strain until the stress relaxation modulus had relaxed to at least 37% (1/e) of its initial value. The activation energy of the stress relaxation (ΔE_a) was calculated using the method reported in the literature.[S4] Fracture samples from the initial tensile test were placed into an aluminum dogbone shaped mold under vacuum (< 30 mm Hg) at 70 °C for ~16 h. Each reprocessed sample was subjected to the same tensile test procedure as described above. A triplicate to quintuplicate of each sample was subjected to the tensile tests or SRA to determine the mean values of relevant parameters and standard deviations.

Thermal analysis. Differential scanning calorimetry (DSC). DSC analysis of the cross-linked polyaminal samples (Entry 1-5, Table 1) was conducted using a TA DSC 2920 instrument. The polymer (10 mg) was hermetically sealed in standard aluminum pans. An empty pan was used as reference. The sample was kept at -120 °C for 2 min and then heated to 100 °C at 10 °C·min^{-1}. Heat flow was recorded during the heating and cooling cycles, and normalized by the sample mass. TGA experiments were carried out on a TA 2950 TGA under a nitrogen atmosphere with a heating rate of 10 °C·min^{-1}. The scanned temperature range was r.t. – 600 °C. Data were analyzed with Thermal Advantage Software.

Synthesis of secondary amine-derived aminal model compound 1 and 2.[S1] A representative synthetic procedure for compound **1** is given as followed. Paraformaldehyde (0.882 g, 29.4 mmol) and $MgSO_4$ (50-100mg) were added to piperidine (5.0 g, 58.7 mmol) in neat. The mixture was vigorously stirred for 3 h at 55°C followed by vacuum distillation to afford a clear liquid (5.0 g, 93% yield).

Synthesis of linear or crosslinked polyaminals. Linear polyaminal was prepared by mixing *N,N'*-dimethyl-1,6-hexanediamine (DA) and paraformaldehyde at room temperature and heating at 70 °C under ambient pressure until the reaction mixture became homogenous (~90 min) and then at 120 °C in vacuum (< 30 mm Hg) for 12 h to remove any volatile. Cross-linked polyaminals (entry 1-5) were prepared by mixing TA/DA and paraformaldehyde in THF at a 45 wt% total monomer concentration. A representative procedure for the synthesis of polyaminal network (Entry 2, Table 1) is

given as followed. TA (0.5 g, 2.66 mmol), DA (0.575 g, 3.98 mmol) and paraformaldehyde (0.239 g, 7.97 mmol) were dissolved in THF (2.9 mL) in a closed vial. The heterogenous solutions were heated to 70 °C until all paraformaldehyde disappeared. The reaction was cooled down to room temperature and allowed THF to evaporate overnight followed by drying in the vacuum oven at 70 °C for ~16 h. Entries 1, 3, and 4 were made in a similar manner; Entry 5 was rid of solvents by rotavap before placement in the vacuum oven. The polymers were then molded in aluminum molds at 70 °C for ~16 h in the vacuum oven (< 30 mm Hg).

Kinetics of the aminal bond exchange reaction using model compounds. Preheat the Bruker AV-500 to 310K before inserting the sample. Compound **1** (21 mg, 0.115 mmol), **2** (21 mg, 0.115 mmol) and internal standard 1,3,5-trimethoxybenzene (19 mg, 0.115 mmol) were dissolved in THF-d_8 (0.5 mL) under N_2 atmosphere. The mixture was transferred into a J. Young NMR tube at room temperature. ^{1}H NMR spectra of the reaction mixture were collected over time (*c.a.* 120 time points). Each spectrum was collected with 10 scans and 2 s relaxation time (*c.a.* 1 min per spectrum). The kinetic studies were conducted at different temperatures (310, 320, 330, and 340 K) in the same manner. The reaction equilibrium was reached at 340 K after 24 h. All kinetic experiments were repeated three times to obtain the mean and standard deviation for the rate constant of the exchange reaction. The pseudo-first order rate constant of the aminal exchange reaction (k_{obs}) and the activation energy (ΔE_a) were determined by using the reported method.[S3]

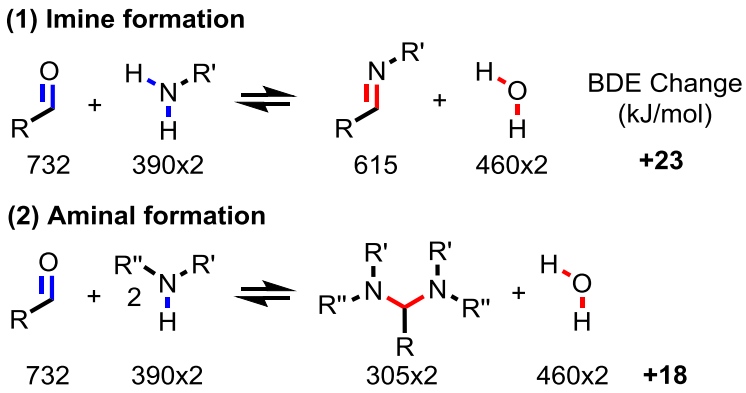
Equilibrium constants for the dissociation of aminal model compounds. A representative procedure to determine the K_{eq} of aminal dissociation into iminium ion and secondary amine is given as followed. Di-(piperidin-1-yl)methane (21 mg, 0.115 mmol) and 1,3,5- trimethoxybenzene (19 mg, 0.115 mmol), an internal standard was dissolved in TOL-d_8 (0.5 mL) followed by the addition of 1 equiv. TFA (13 mg, 9 μL) in an oven-dried vial. The mixture was then transferred into a J. Young NMR tube at room temperature. ^{1}H NMR spectra of the reaction mixture were collected at different temperature (300, 310, 320, 330, and 340 K) (Figure S2 and S3). Each spectrum was collected with 8 scans and 2 s relaxation time. The sample was allowed to equilibrate for 10 min at each temperature prior to the NMR spectral acquisition. All NMR experiments were repeated three times to obtain the mean value of the equilibrium constant (K_d). The enthalpy (ΔH_d) and entropy (ΔS_d) for each equilibrium reaction were determined by the van't Hoff plot analysis.

Gel content analysis. A measured amount of crosslinked polyaminals (8.2 – 11.2 mg) was soaked in an anhydrous toluene/DBU solution (0.23 M, 100 μL) in a Caplock polypropylene centrifuge tube inside the glovebox for 24 h at room temperature. The crosslinked polyaminals were removed

from the toluene/DBU solution and washed with anhydrous toluene (0.5 mL) to remove any residual DBU. The polymer was first dried in air and then *in vacuo*. The mass change of the polymer sample was determined by gravimetric analysis from which the gel content (=1-mass change/original polymer mass)×100 was calculated. (Note: DBU was dried over molecular sieves for 48 h prior to use. DBU was added to inhibit the dissociation of aminal bonds in the polymer network during the soaking process. Toluene was dried over CaH_2 overnight and separated by vacuum transfer).

Characterization of self-healing and recycling properties of polyaminal thermosets. Cross-linked polyaminal samples were cut into pieces with a razor blade and were remolded in a triangular shape mold at 80 °C in air. Disc-shaped samples were cut with a razor blade and re-attached at the cut-interface followed by heating the material to 80 °C for 1 h in the mold. Red disc-shape sample was prepared by the standard method and using a rhodamine B (0.05 wt%) / THF solution as the polymerization media. Square-shaped bi-moduli sample was prepared by holding two disc-shaped samples with different modulus together under 80 °C in air for 1 h.

Scheme S1.



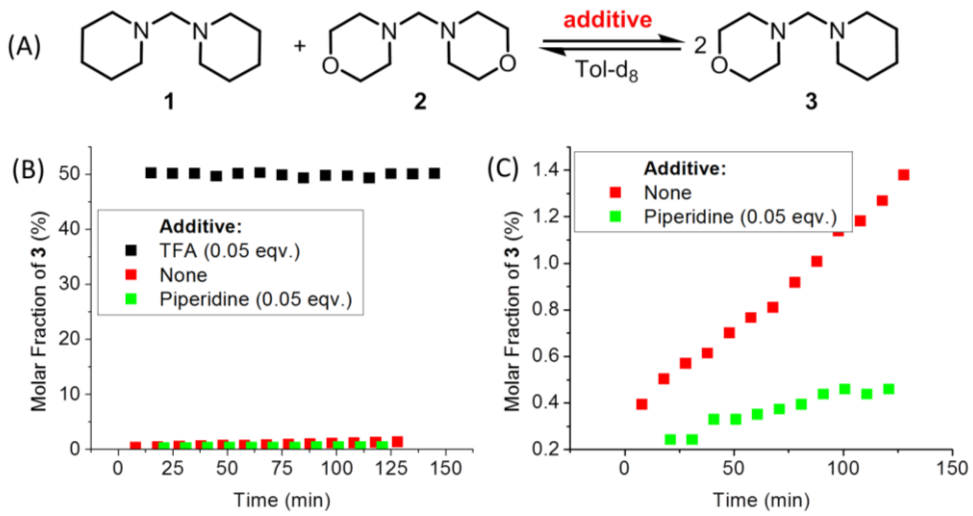


Figure S1. (A, B) Plots of molar fraction of the mixed aminal product **3** versus reaction time for the exchange reaction of piperidine-derived aminal **1** and morpholine-derived aminal **2** without any external additive (red ■), in the presence of TFA (black ■) or piperidine (green ■). (Note: 1,3,5-Trimethoxybenzene (TMB) is added as an internal standard for concentration determination; $[\mathbf{1}]_0=[\mathbf{2}]_0=[\text{TMB}]_0= 0.23$ M, in THF-d_8 at room temperature; $[\text{TFA}]_0$ or $[\text{piperidine}]_0$ is 0.05 equivalent relative to $[\mathbf{1}]_0$). In the presence of TFA, the equilibrium was reached rapidly. By contrast, the equilibrium was reached more slowly in the presence of piperidine than that without it. These results are consistent with a protic acid-catalyzed aminal exchange mechanism.

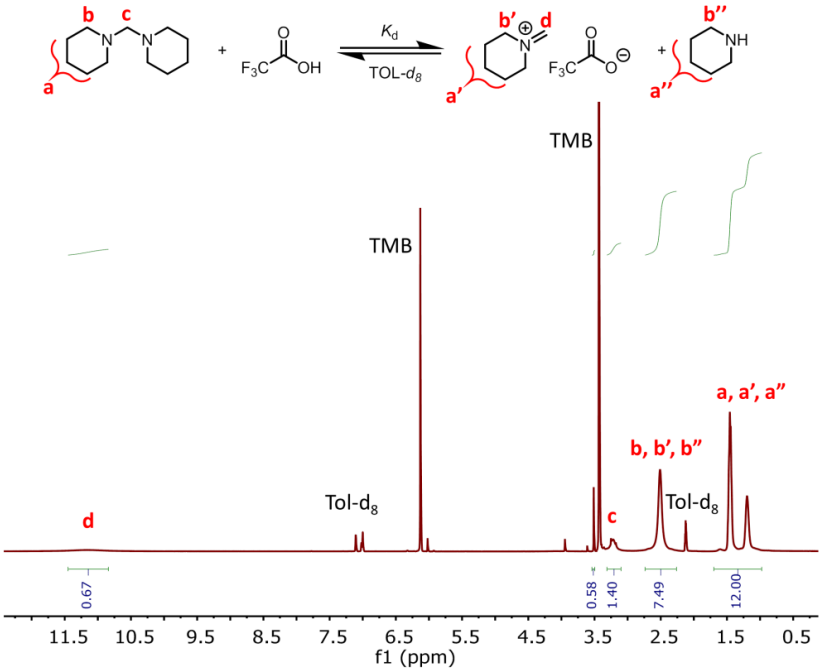


Figure S2. Representative ^{1}H-NMR spectrum of the dissociation equilibrium of piperidine-derived aminal compound **1** into the corresponding iminium species in the presence of TFA at 330 K in toluene-d_8 (Tol-d_8). 1,3,5-Trimethoxybenzene (TMB) is added as an internal standard for concentration determination.

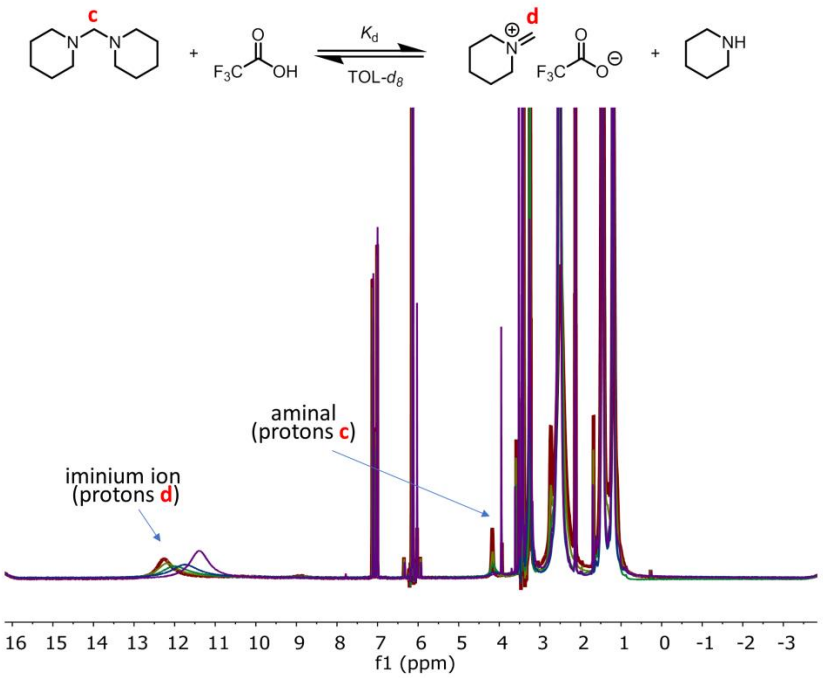


Figure S3. Vertically expanded ^{1}H-NMR spectra of the dissociation equilibrium of piperidine-derived aminal compound **1** into the corresponding iminium species in the presence of TFA in toluene-d_8 at different temperatures (*i.e.*, 300, 310, 320, 330, 340 K) showing the characteristics methylene protons due to the iminium species. 1,3,5-Trimethoxybenzene is added as an internal standard for concentration determination.

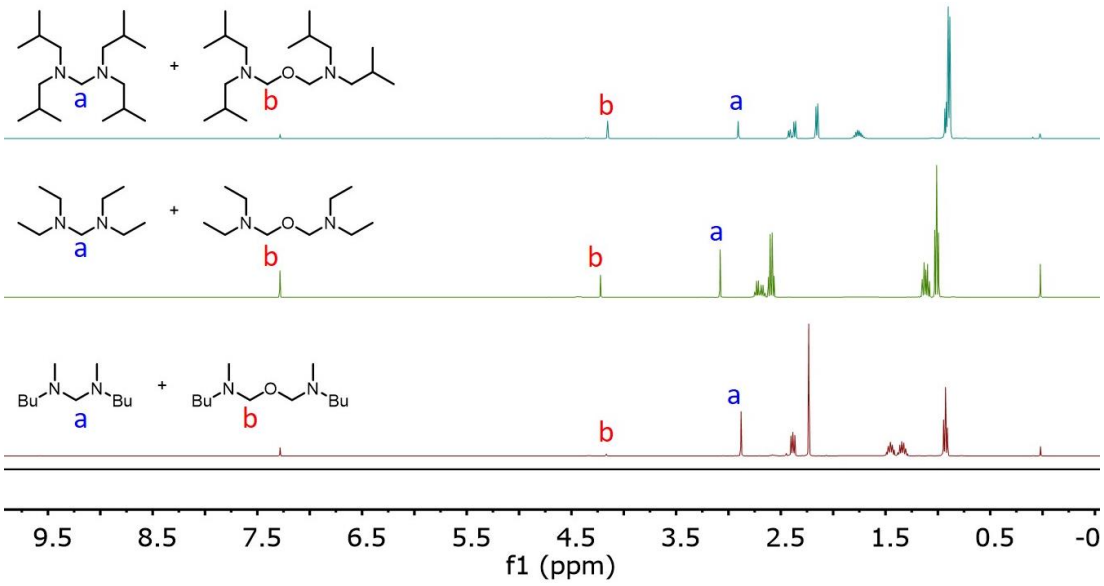
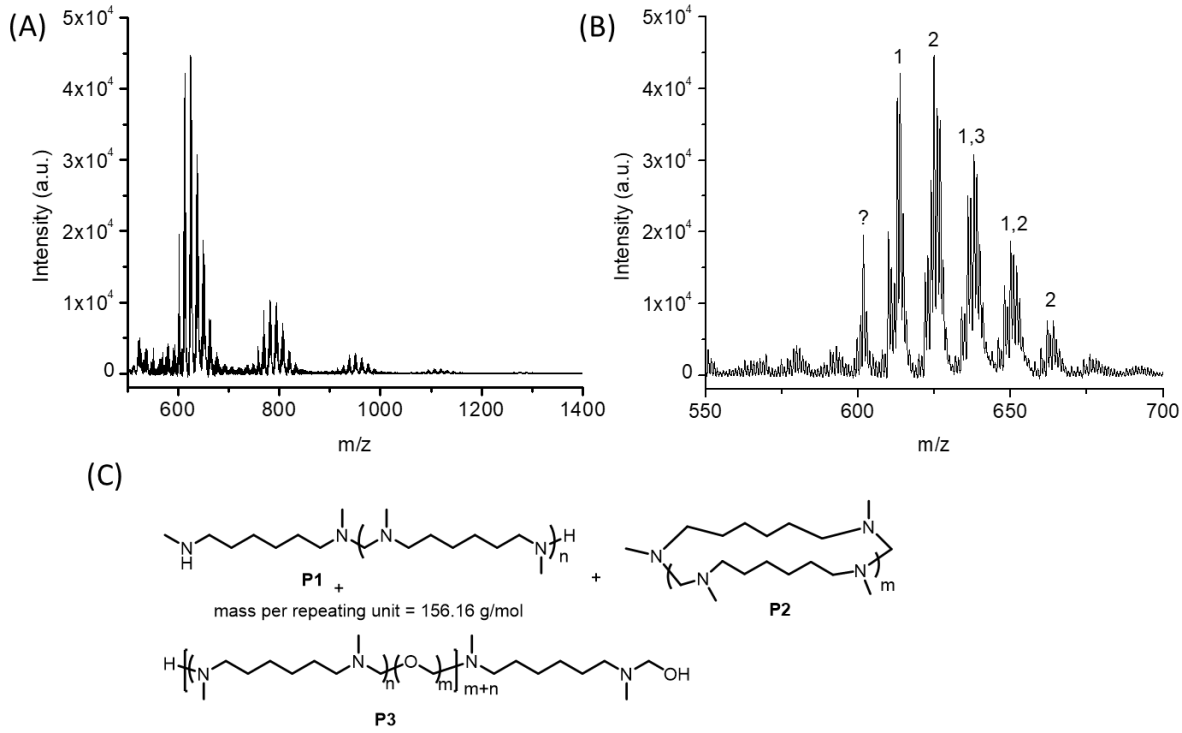


Figure S4. ^{1}H NMR spectra of the aminal and hemiaminal ether products formed from the respective reaction between formaldehyde and different mono-functional secondary amines. All ^{1}H NMR spectra were conducted in $CDCl_3$.



P1+H^+ (613.72 m/z experimental): 156.16×3+144.16+1.01=613.65 (theo.)
P1+Na^+ (635.93 m/z experimental): 156.16×3+144.16+22.99=635.63 (theo.)
P1+K^+ (651.93 m/z experimental): 156.16×3+144.16+38.96=651.60 (theo.)
P2+H^+ (625.89 m/z experimental): 156.16×4+1.01=625.65 (theo.)
P2+Na^+ (647.93 m/z experimental): 156.16×4+22.99=647.63 (theo.)
P2+K^+ (663.93 m/z experimental): 156.16×4+38.96=663.60 (theo.)
P3+H^+ (637.93 m/z experimental): 156.16×2+324.21+1.01=637.54 (theo.)

Figure S5. (A) Full and (B) expanded MALDI-TOF MS spectra of the polyaminal products formed from condensation of paraformaldehyde and *N*,*N*-dimethylhexylamine together with (C) the structural assignment and mass ion calculation. Note: the mass ion (?) refers the targeted polyaminal polymer with unknown end-group structures.

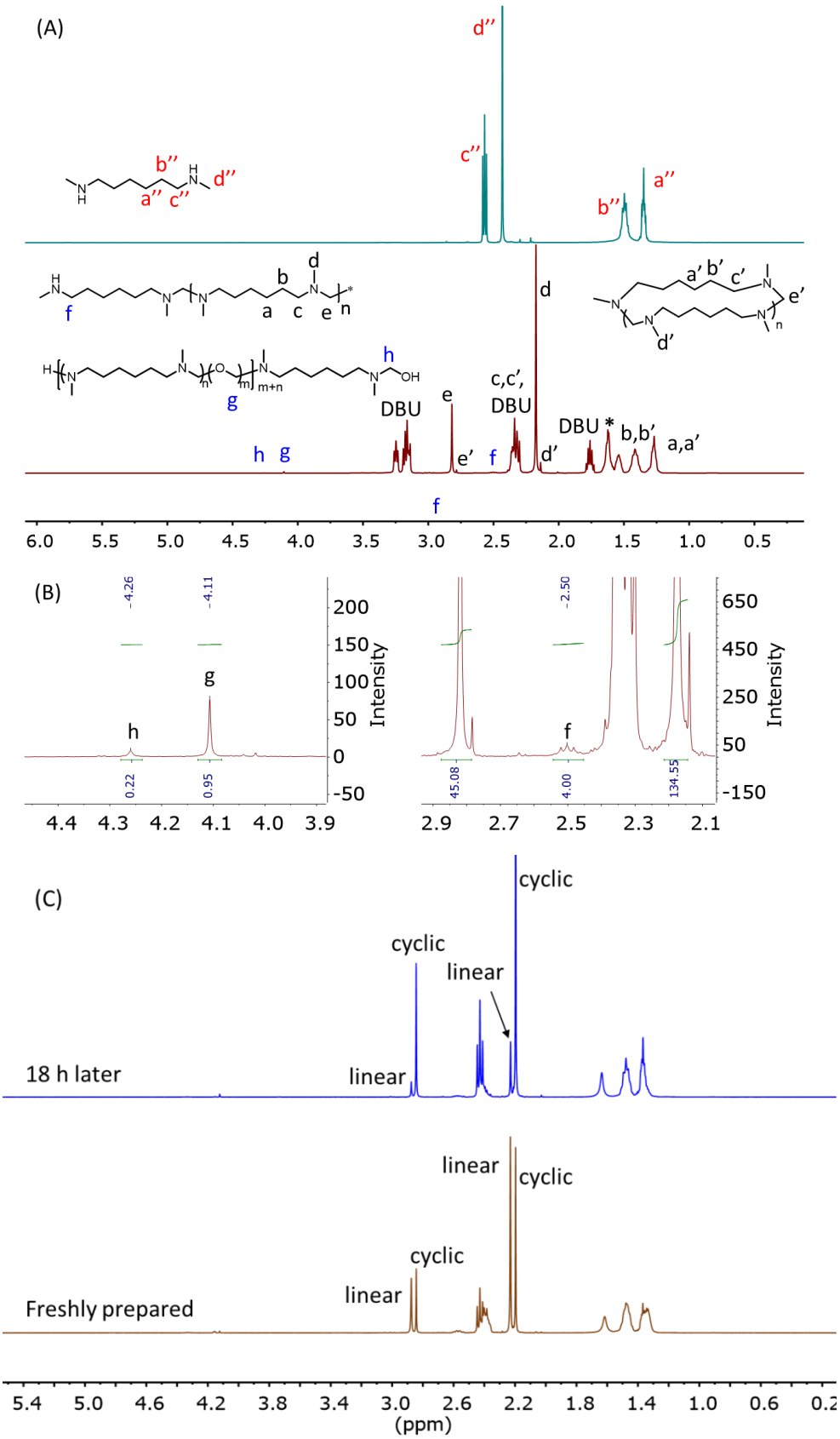


Figure S6. (A) ^{1}H NMR spectra of *N*,*N*-dimethylhexylamine (teal curve) and the polyaminal product (maroon curve) formed by polymerization of paraformaldehyde and *N*,*N*-dimethylhexylamine in

$CDCl_3$ with a 0.23 M DBU, and (B) expanded ^1H NMR spectra showing the corresponding end-group structures (f, h) and the hemiaminal ether linkages (g). (C) ^1H NMR spectra of the polyaminal product that was freshly prepared (blue curve) or allowed to stand at room temperature in $CDCl_3$ for 18 h (brown curve). It is clear that the linear polyaminal was slowly converted into the cyclic polymers due to intermolecular chain transfer, consistent with the dynamic nature of the aminal bonds. Note: DBU addition in (A) is to inhibit conversion of linear into cyclic polyaminals during the NMR analysis.

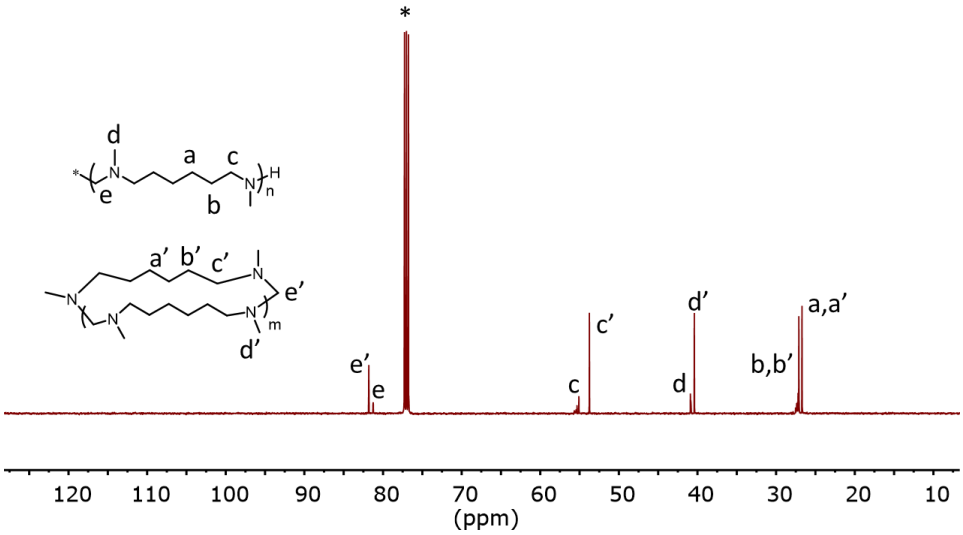


Figure S7. $^{13}C\{^1H\}$ NMR spectra of polyaminal products formed from condensation of paraformaldehyde and *N*,*N*-dimethylhexylamine. All $^{13}C\{^1H\}$ NMR spectra were conducted in $CDCl_3$. The asterisk (*) corresponds to the $CDCl_3$.

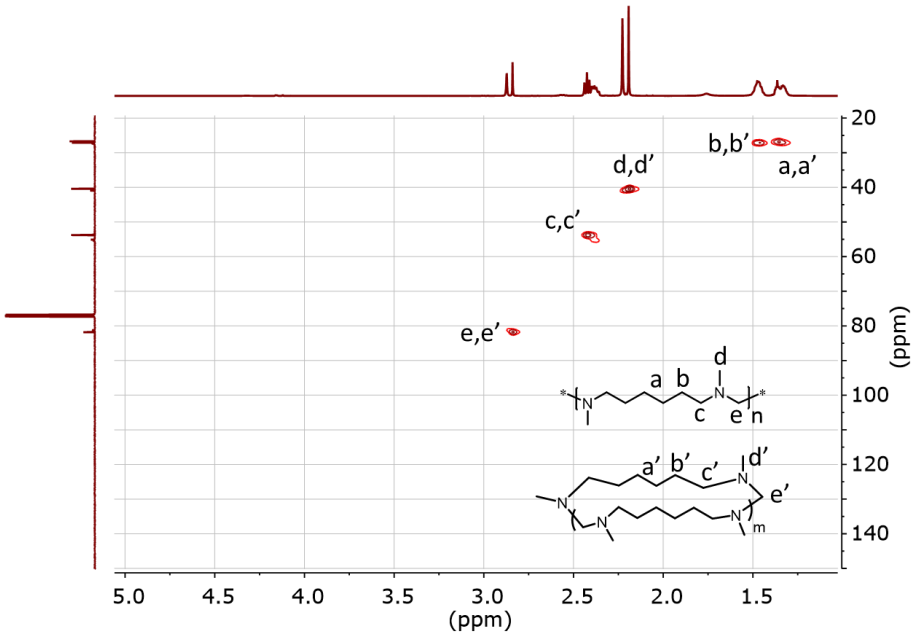


Figure S8. HSQC NMR spectrum of linear polyaminal products formed from condensation of paraformaldehyde and *N*,*N*-dimethylhexylamine. HSQC NMR spectrum was conducted in $CDCl_3$.

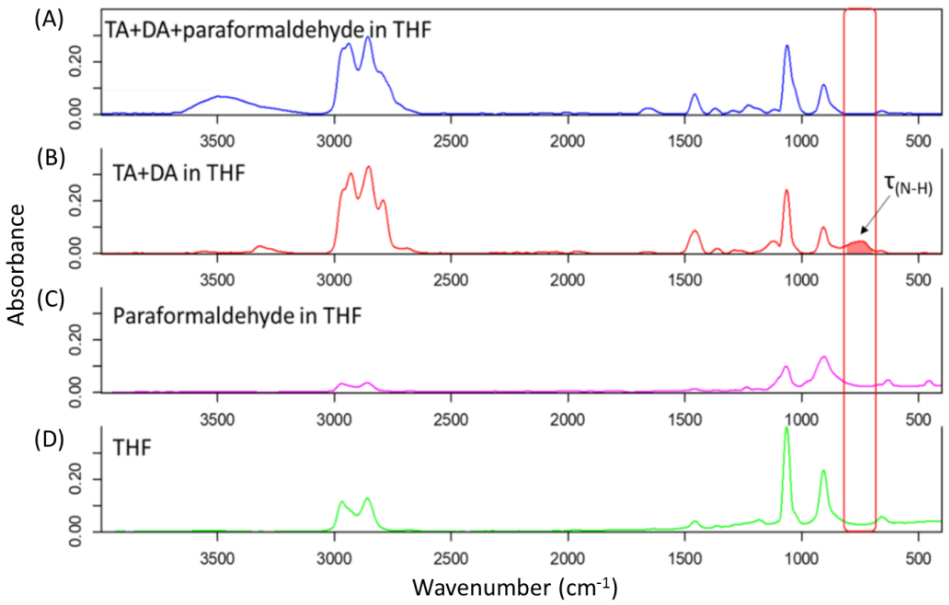


Figure S9. Representative FT-IR spectra of (A) the reaction product from TA, DA (together at 45 wt%) and paraformaldehyde in THF, (B) the TA and DA monomers (45 wt%) in THF, (C) paraformaldehyde (8 wt%) in THF, and (D) the neat THF. The conversions were calculated from the disappearance of fingerprint absorbance at 720-800 cm^{-1} due to N-H bending mode.

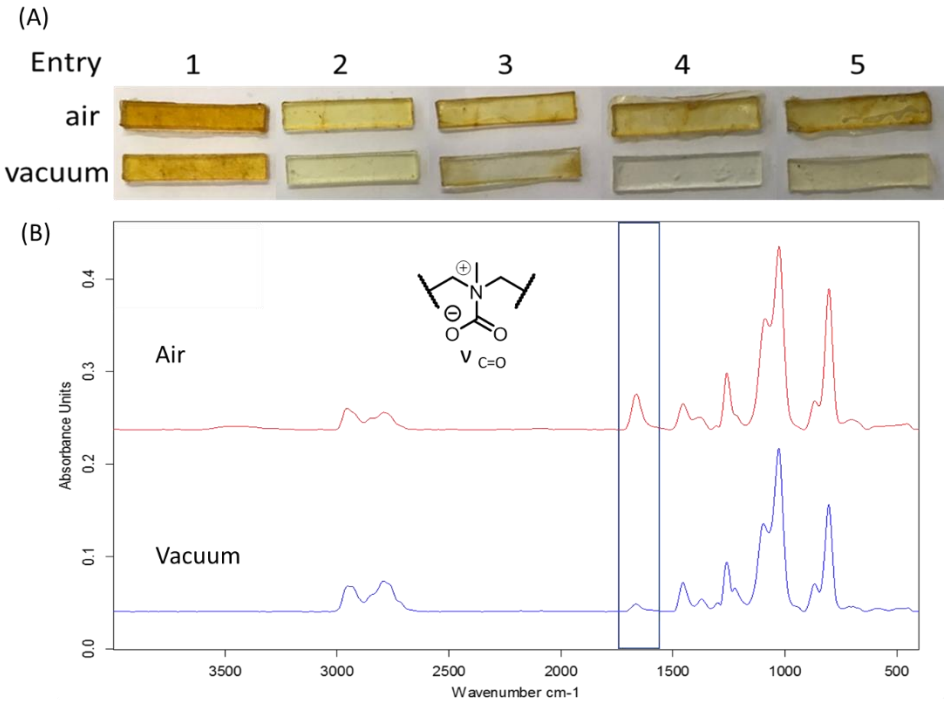


Figure S10. (A) Crosslinked polyaminal films synthesized in air or under vacuum. (B) FT-IR spectra of the crosslinked polyaminal films made in air (red curve) or vacuum (blue curve) where the C=O stretching band due to the carbamic acid group is more pronounced for the film prepared in air than that under vacuum.

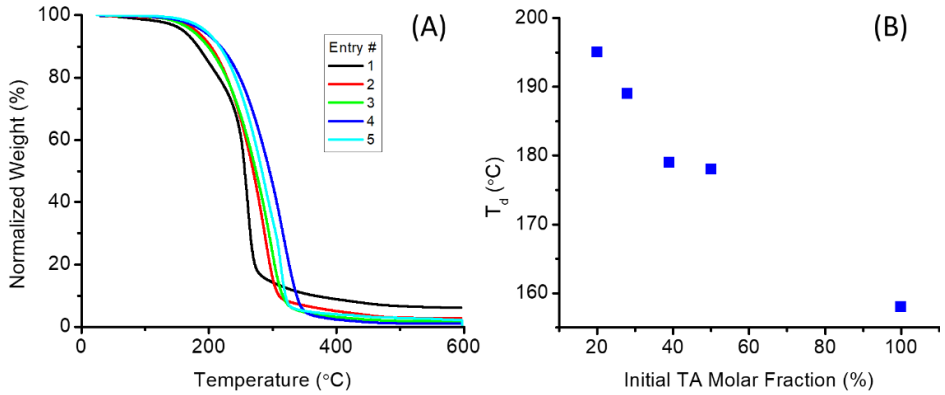


Figure S11. (A) TGA thermograms of the crosslinked polyaminal polymers (Entry 1-5, Table 1) obtained under nitrogen. (B) plot of onset decomposition temperature (T_d) versus the initial TA molar fraction in various crosslinked polyaminal polymers. T_d is defined at the onset decomposition temperature at 5 weight % loss.

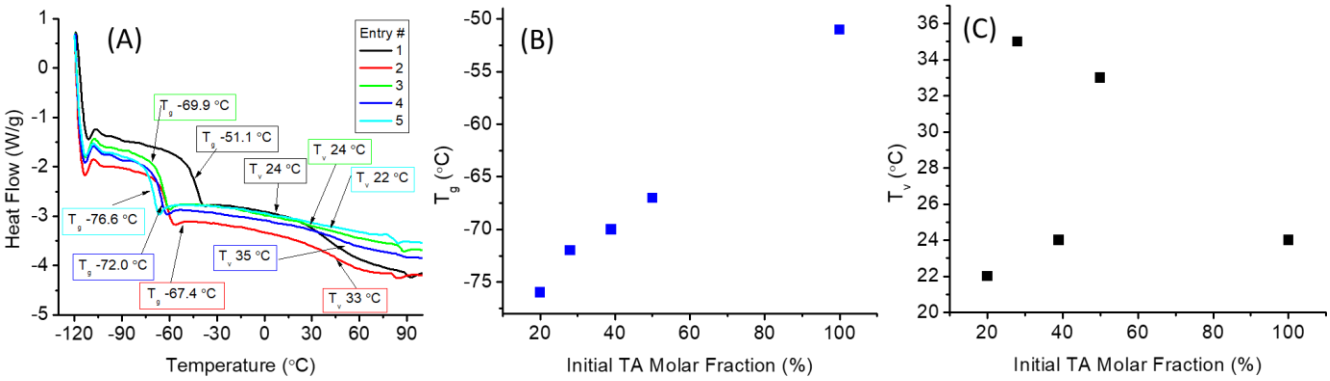


Figure S12. (A) DSC traces of the crosslinked polyaminal polymers (Entry 1-5, Table 1) and (B) plot of glass transition temperature (T_g) versus the initial TA molar fraction in various crosslinked polyaminal polymers. (C) Plot of the topology-freezing temperature (T_v) versus the initial TA molar fraction in various crosslinked polyaminal polymers.

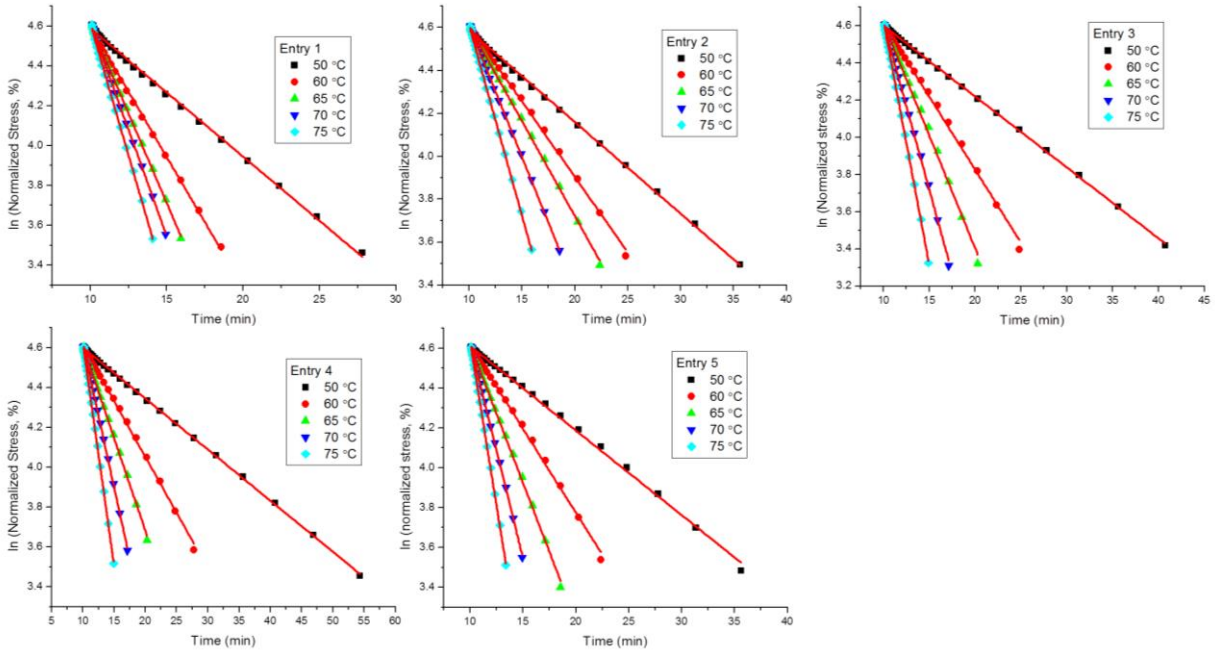


Figure S13. Plots of ln (normalized stress) versus time for the crosslinked polyaminal polymers with different crosslinker contents (Entry 1-5, Table 1) at different temperatures (50 °C, 60 °C, 65 °C, 70 °C, and 75 °C) obtained from the stress-relaxation experiments.

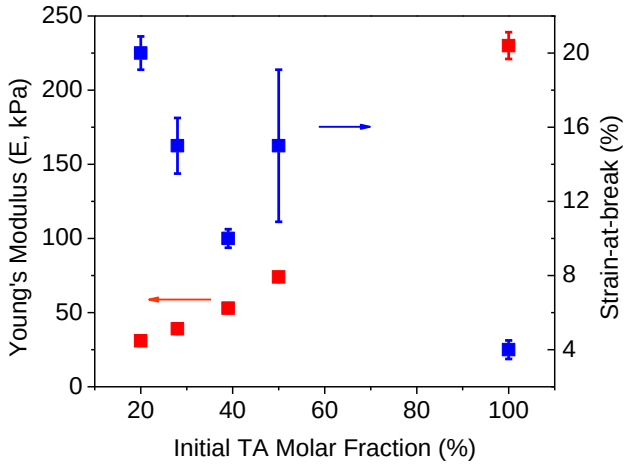
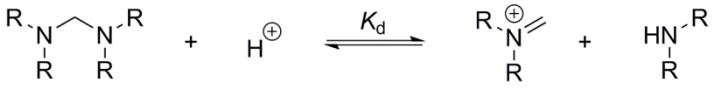


Figure S14. Plots of the Young's modulus and strain-at-break of the crosslinked polyaminal polymers versus the initial TA molar fraction in various crosslinked polyaminal polymers.

Table S1. Critical pHs at which depolymerization occurs (Column G), the extent of aminal dissociation at pH 4 or 7 (Column H and I) respectively for the polyaminal networks at their corresponding decomposition temperature (Entry 1-5, Table 1).

	A	B	C	D	E	F	G	H	I
1	Entry	1-p (%)	p (%)	$[aminal]_0$ (M)	T_d (°C)	K_d at T_d	pH (depoly.) *	p (%), pH 4 **	p (%), pH 7 **
2	1	83	17	15.6	164	4.94	1.0	0.56	0.018
3	2	91	9	13.0	156	4.15	1.6	0.56	0.018
4	3	93	7	12.6	179	6.74	2.0	0.73	0.023
5	4	96	4	12.1	155	4.06	2.3	0.58	0.018
6	5	97	3	11.9	195	9.18	2.9	0.88	0.028
7	Column A is the entry number for the respective polyaminal network and corresponds to those in Table 2								
8	Column B is the gel point determined by Carother equation for the respective polyaminal network								
9	Column C is the theoretical extent of aminal dissociation required for depolymerization to occur								
10	Column D is the molar concentration of aminal groups in the respective polyaminal network								
11	Column E is the decomposition temperature of the respective polyaminal network as determined by TGA								
12	Column F is the aminal dissociation constant at the respective decomposition temperature								
13	Column G is the pH at which the depolymerization can occur at the respective decomposition tempearature								
14	Column H is the extent of dissociation at pH 4 for the polyaminal network at the respective decomposition tempearature								
15	Column I is the extent of dissociation at pH 7 for the polyaminal network at the respective decomposition tempearature								



At equlibrium: $[Aminal]_0(1-p)$ $[H^+]$ $[Aminal]_0p$ $[Aminal]_0p$

$$K_d = \frac{([Aminal]_0p)^2}{[Aminal]_0(1-p)[H^+]} = \frac{[Aminal]_0p^2}{(1-p)[H^+]} \quad \text{eq. 1}$$

$$\ln K_d = \frac{-\Delta H^o}{RT} + \frac{\Delta S^o}{R} \quad \text{eq. 2}$$

* Rearrange eq. 1 into eq. 3 to obtain the depolymerization pH at T_d:

$$pH = -\log[H^+] = -\log\left(\frac{[Aminal]_0p^2}{(1-p)K_d}\right) = -\log\left(\frac{(\text{Column D})(\text{Column C}/100)^2}{(\text{Column B}/100)(\text{Column F})}\right) \quad \text{eq.3}$$

** Rearrange eq. 1 into eq. 4 and 5 and then solve the quadratic equation 5 to obtain the extent of dissociation of aminal at a specific pH (e.g. 4) at T_d:

$$[Aminal]_0p^2 + K_d[H^+]p - K_d[H^+] = 0 \quad \text{eq. 4}$$

$$(\text{Column D})p^2 + (\text{Column F})\times10^{-4}p - (\text{Column F})\times10^{-4} = 0 \quad \text{eq. 5}$$

References

(S1) Heaney, H.; Papageorgiou, G.; Wilkins, R. F. *Tetrahedron* **1997**, *53*, 14381-14396.

(S2) Comby, S.; Imbert, D.; Vandevyver, C.; Bünzli, J.-C. G. *Chem. Eur. J.* **2007**, *13*, 936-944.

(S3) Liu, W.-X.; Zhang, C.; Zhang, H.; Zhao, N.; Yu, Z.-X.; Xu, J. *J. Am. Chem. Soc.* **2017**, *139*, 8678-8684.

(S4) Brutman, J. P.; Delgado, P. A.; Hillmyer, M. A. *ACS Macro Letters* **2014**, *3*, 607-610.