Supporting Information

Development of Dual Acid/Visible Light-Degradable Core-Crosslinked Nanogels with Extended Conjugate Aromatic Imines for Enhanced Drug Delivery

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Figure S1. ^{13}C NMR spectrum of M3 in DMSO-d_6.

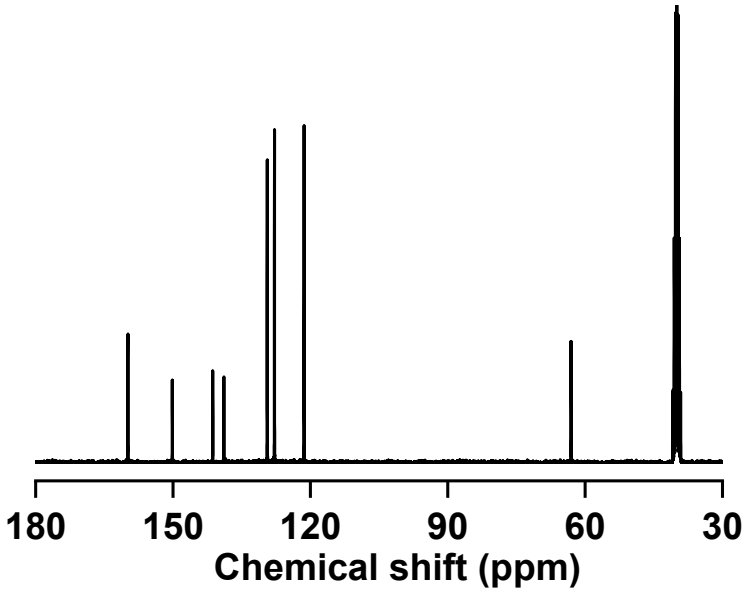

Figure S2. HR-MS spectrum of M3.

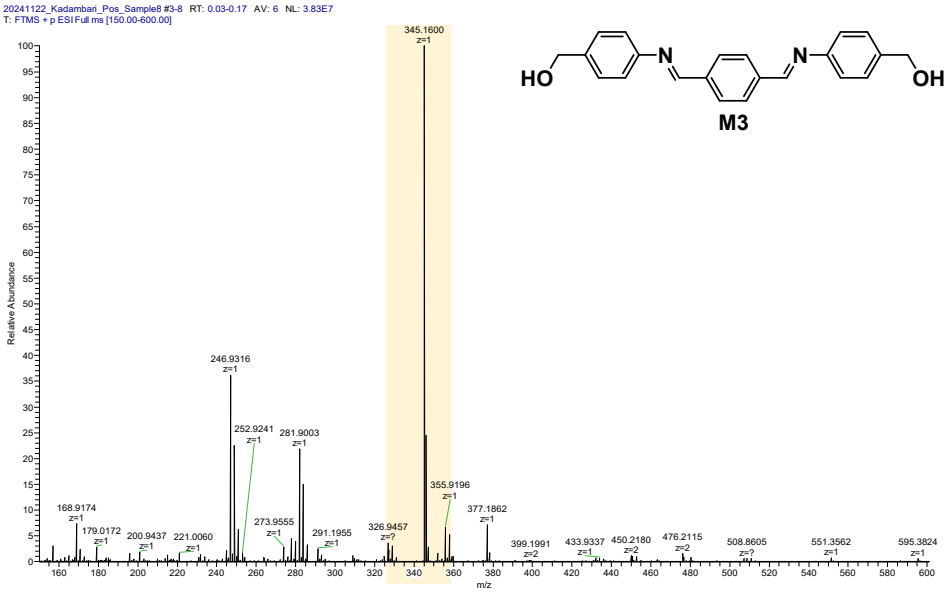

Figure S3. Overlaid UV/Vis spectra (a) and absorbance at λ_{max} = 355 nm (b) of M3 over its concentration in DMSO.

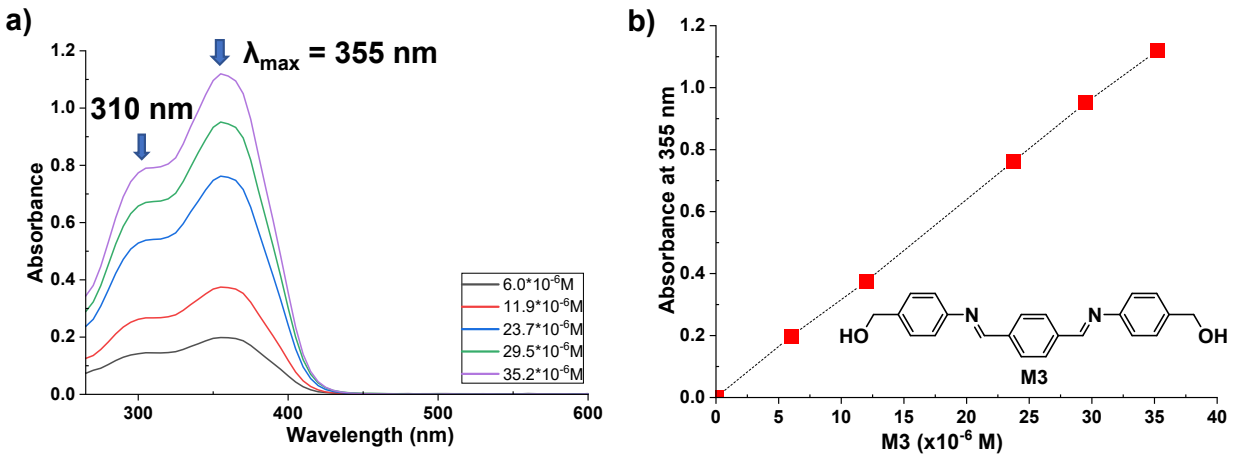

Figure S4. ^{1}H NMR spectrum of P-Im3-DMSO swollen in DMSO-d_6. The spectrum shows no peaks presenting M3 and PEG-b-PCIMA.

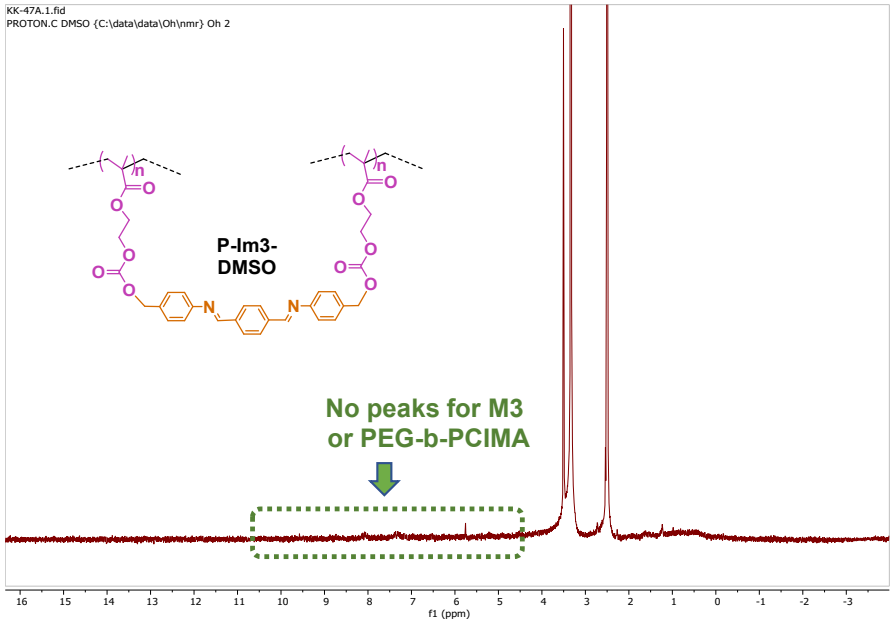

Figure S5. ^{1}H NMR spectrum of the supernatant in DMSO-d_6 after P-Im3-DMSO was precipitated from cold diethyl ether. The spectrum shows peaks presenting free imidazole as a side product that is generated by CDI-mediated crosslinking reactions.

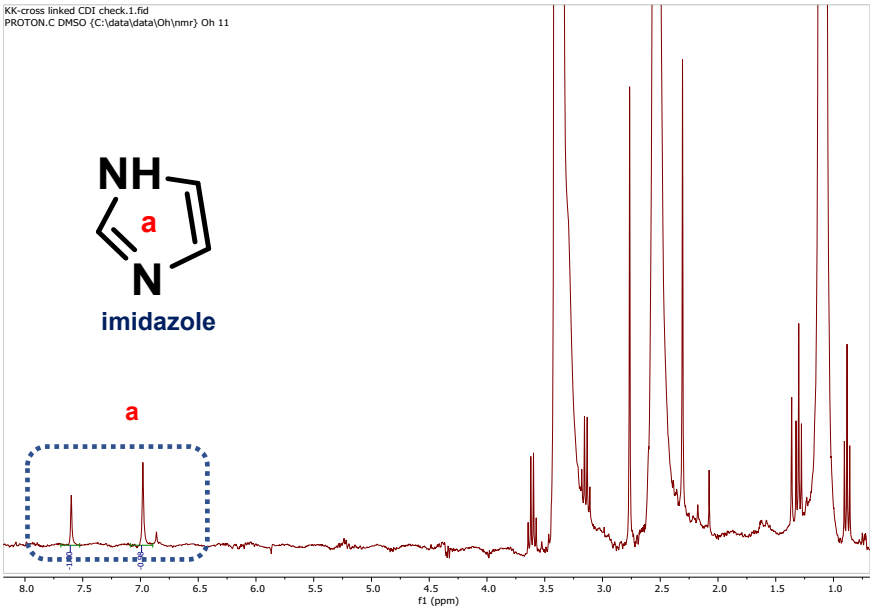

Figure S6. DSC thermogram of P-Im3-DMSO.

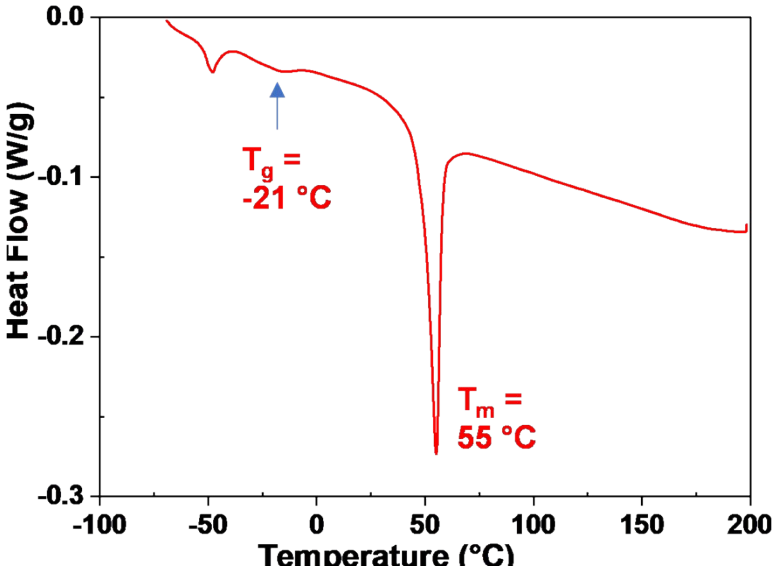

Figure S7. TGA thermogram of P-Im3-DMSO.

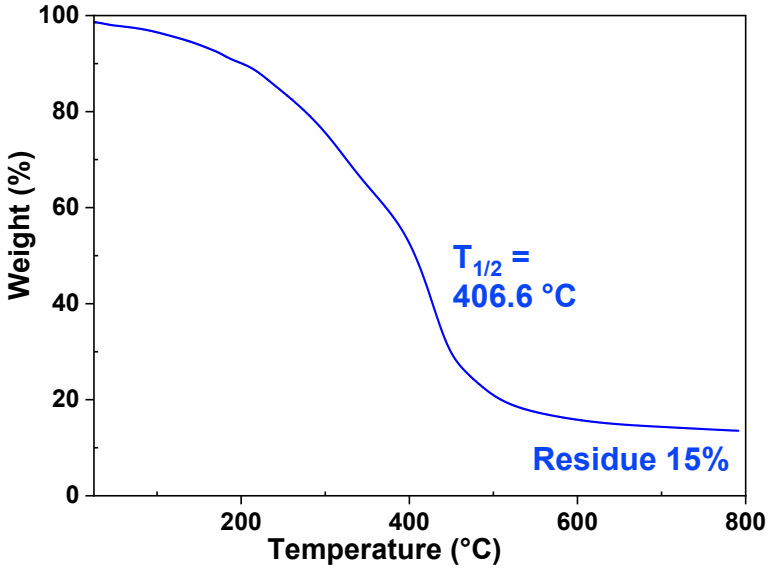

Figure S8. Digital images of aqueous dispersion fabricated through a conventional *in situ* crosslinking approach before (a) and after (b) dialysis, followed by filtration (c); DLS diagram of the dispersion after dialysis and filtration (d).

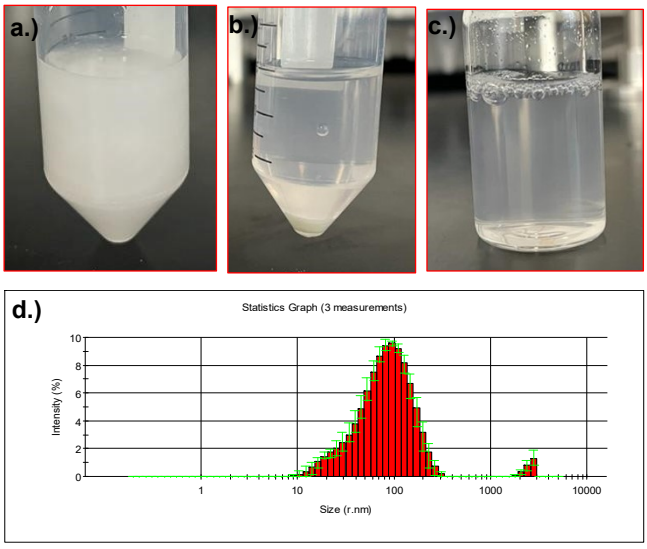

Figure S9. Schematic presentation for acid-catalyzed hydrolysis of benzoic imine bond in P-Im3-DMSO crosslinked polymer (a) and overlaid ^{1}H NMR spectra of the polymer in DMSO-d_6 before (b) and after (c) treatment with HCl. Insets: digital images of NMR tubes.

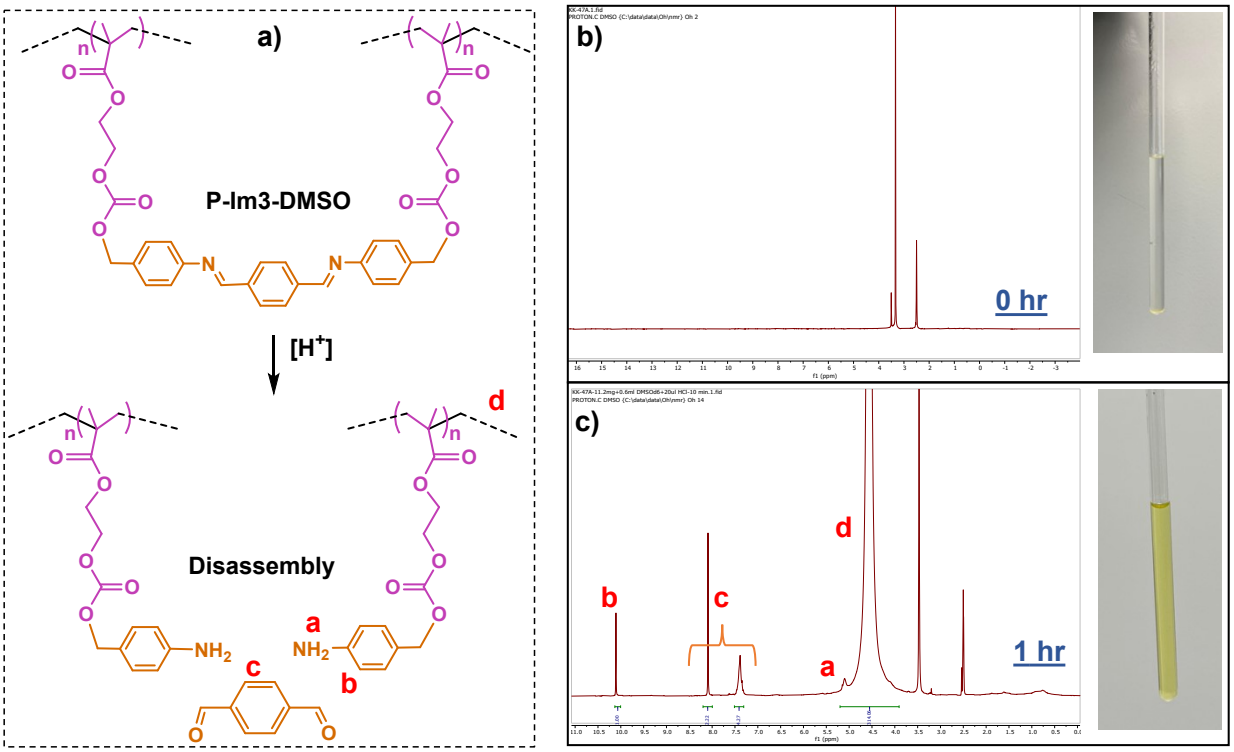

Figure S10. Overlaid DLS diagrams of aqueous P-Im3-Aq nanogels upon irradiation of visible light at λ = 420 nm over 10 hrs (a) and their TEM images before (scale bar = 500 nm) (b) and after (scale bar = 100 nm) (c) irradiation of light.

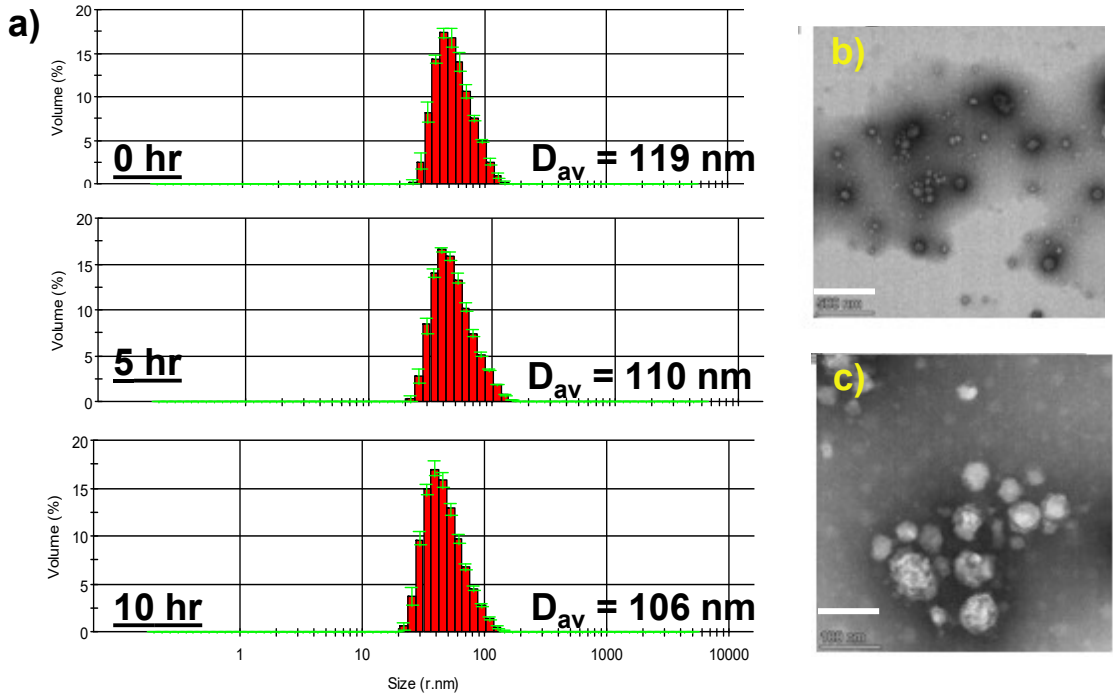

Figure S11. Relative free energy profile of EE to EZ and EZ to ZZ isomerization. TS denotes the transition state.

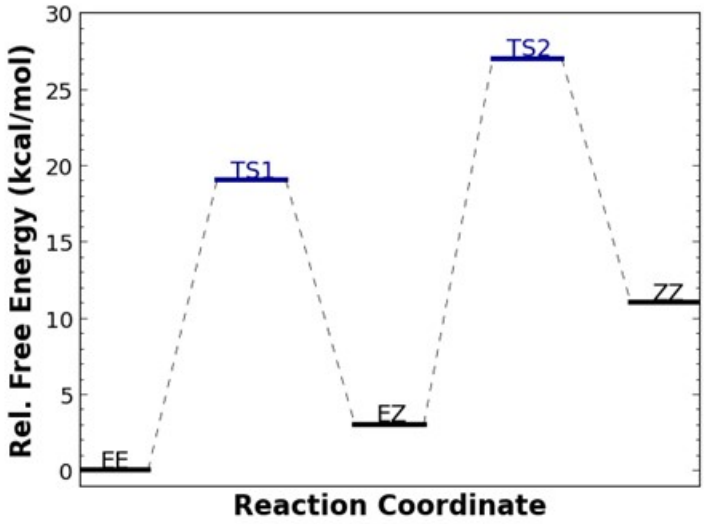

Figure S12. M3 molecular orbital configuration with possible electron transitions.

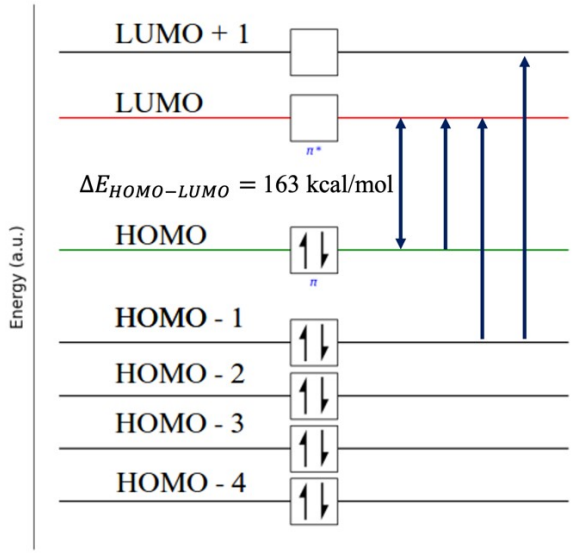

Figure S13. The FMOs, HOMO-1 (a), HOMO(b), LUMO(c) and LUMO+1 (d), of EE configuration obtained via the ωB97XD/6–311++G(d,p) model chemistry.

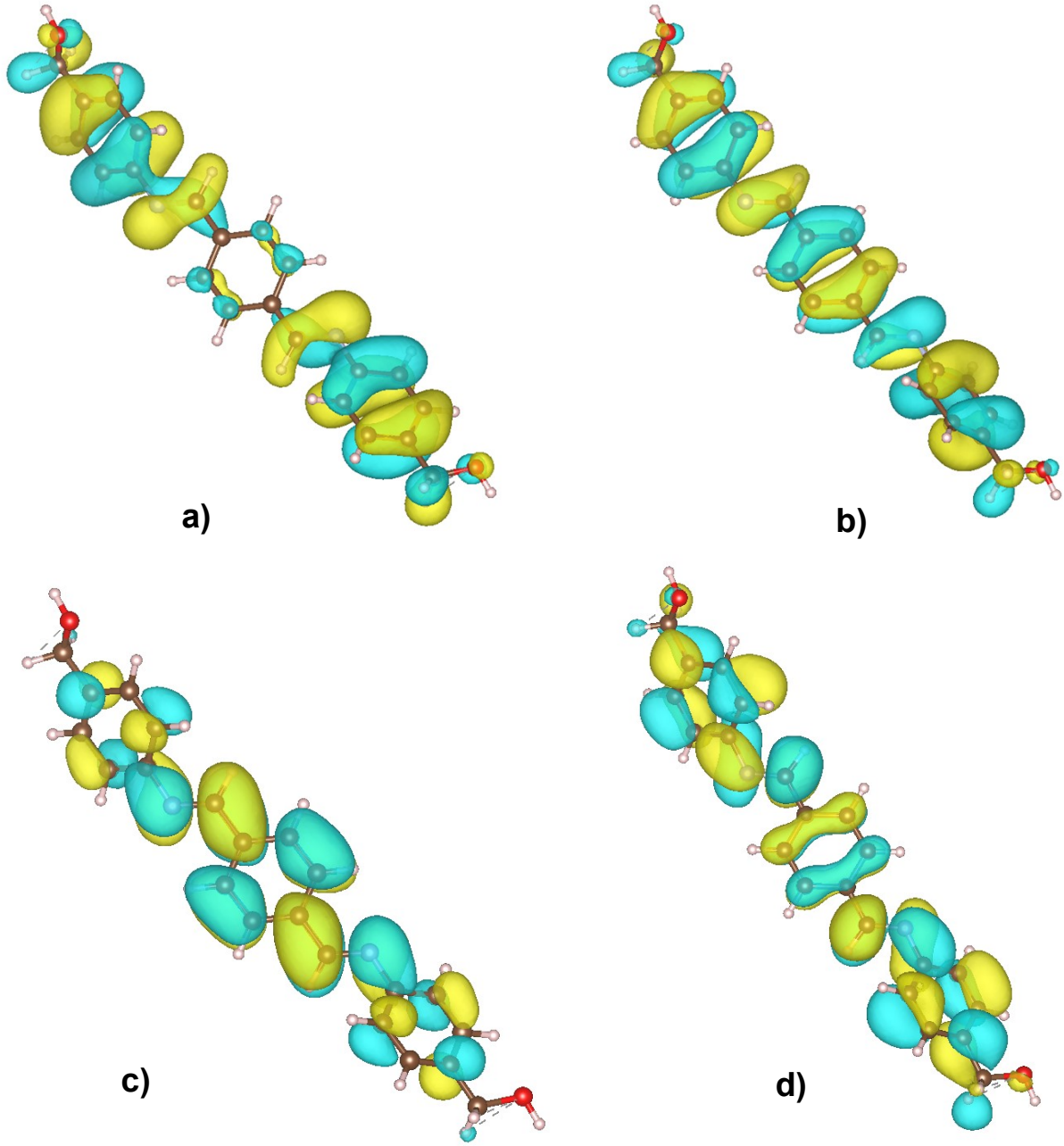

Figure S14. Overlaid UV/Vis spectrum (a) and absorbance at λ_{max} = 430 nm (b) of Cur over its concentration in water/THF (1/1 v/v).

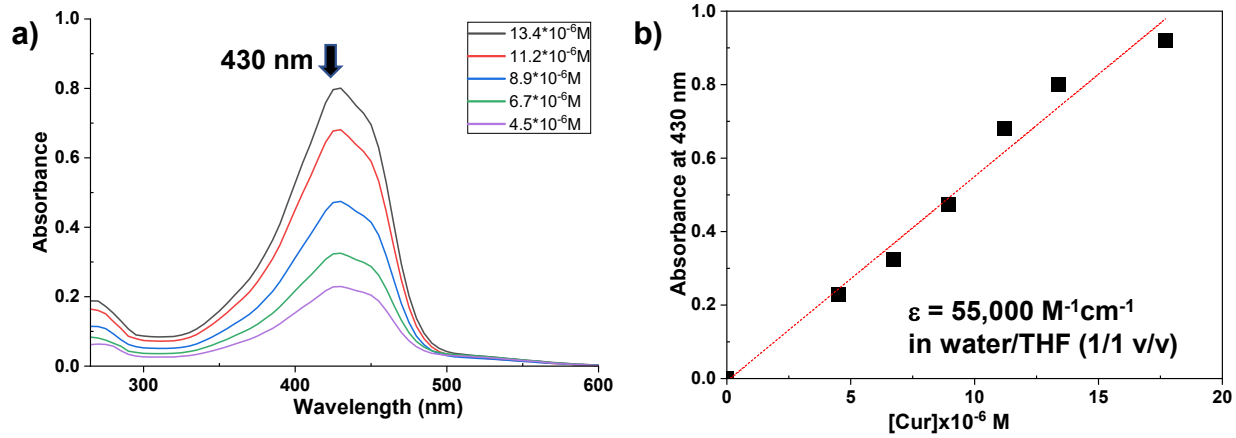

Figure S15. UV/Vis spectrum of aqueous P-Im3-Aq/Cur nanogels at 0.27 mg/mL in water/THF (1/1 v/v).

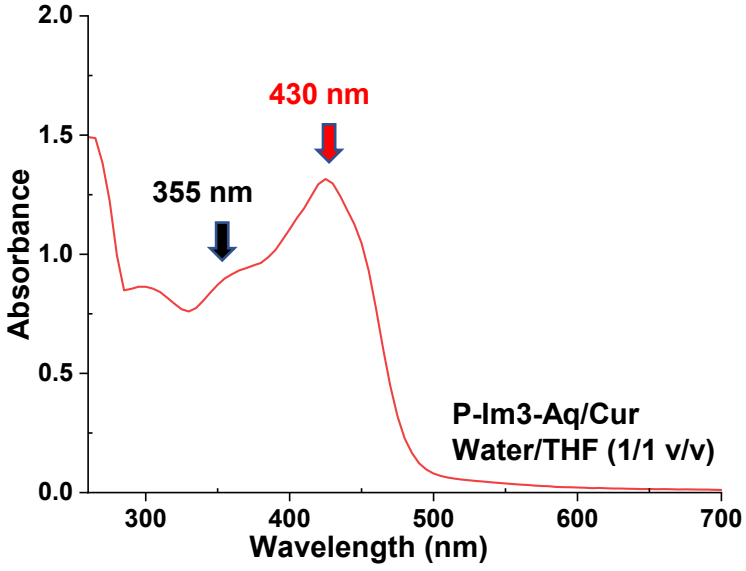

Figure S16. Overlaid UV/Vis spectra for release of Cur from aqueous P-Im3-Aq/Cur nanogels under visible light at λ = 420 nm (a) and in dark as a control (b).

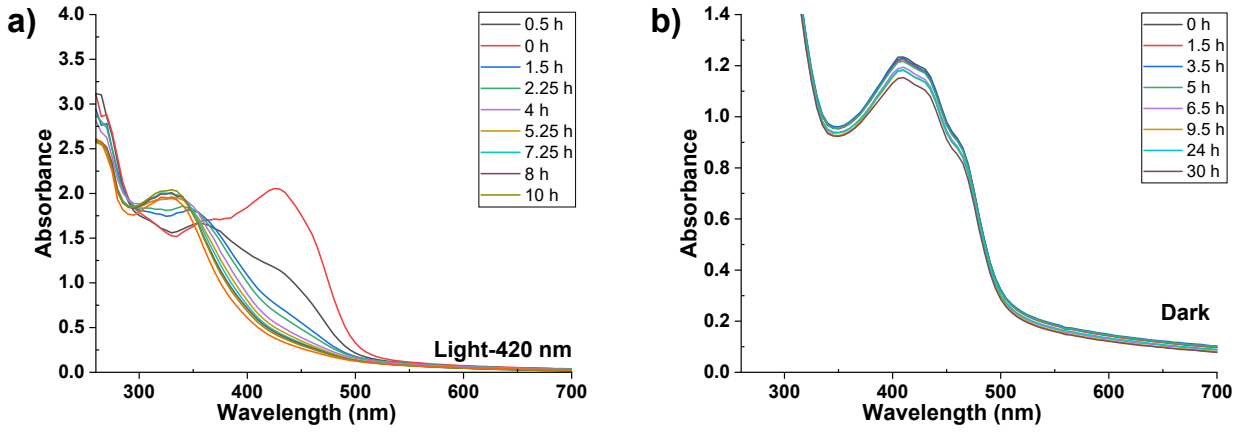

Figure S17. Overlaid UV/Vis spectra for the release of Cur from P-Im3-Aq/Cur nanogels in pH = 7.4 (a) and acidic pH = 5.0 (b).

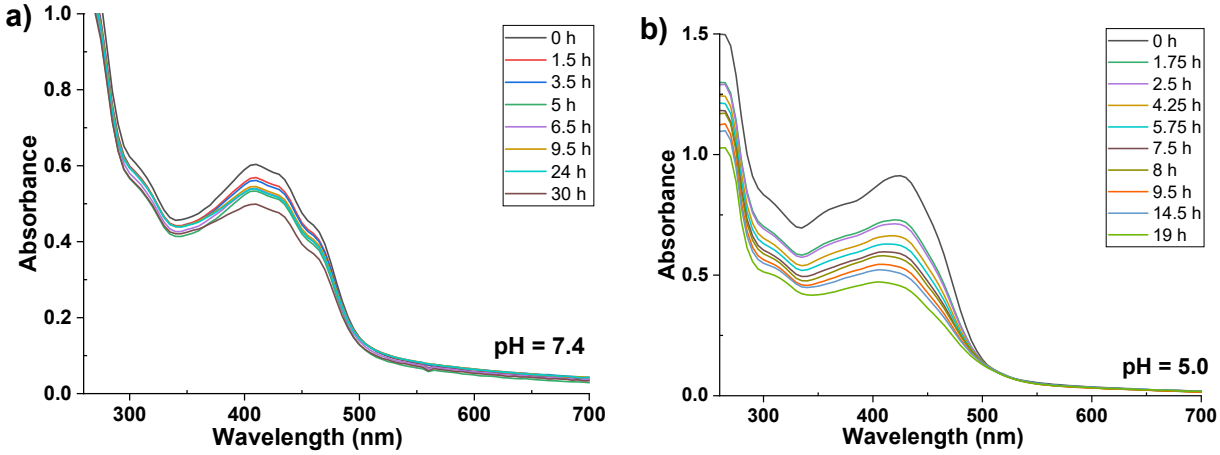

Figure S18. Overlaid UV/Vis spectrum for the release of Cur from P-Im3-Aq/Cur nanogels in acidic pH = 5.0 under exposure to visible light at λ = 420 nm.

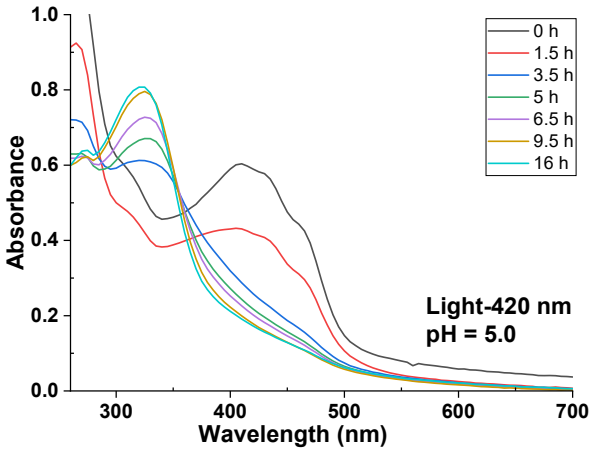

Table S1. Recipes for a series of aqueous P-Im3-Aq nanogels.

Entry	M3 (mg)	PEG-b-PCIMA (mg)	DBU (mg)	DMSO (mL)	Water (mL)
P-Im3-aq	1.7	3.5	0.3	2	10
P-Im3-aq-A	1.7	3.5	0.3	3	9
P-Im3-aq-B	1.7	3.5	0.3	4	8
P-Im3-aq-C	1.7	3.5	0.3	5	7
P-Im3-aq-D	1.1	3.5	0.2	2	10
P-Im3-aq-E	0.8	3.5	0.1	2	10

Table S2. Calculated thermochemistry values with electronic energy (E_{DFT}), zero-point energy (ZPE), thermal enthalpy correction (H_{corr}) and thermal correction to free energy G_{corr} (all units are in kcal/mol).

Isomer	E_{DFT}	ZPE	H_{corr}	G_{corr}
EE	-696665	234	249	198
TS1	-696644	232	248	196
EZ	-696661	234	249	197
TS2	-696636	232	248	196
ZZ	-696654	234	249	198

$$\Delta H^{o}(298) = \Sigma\left(E_{DFT} + H_{corr}\right)_{product} - \Sigma\left(E_{DFT} + H_{corr}\right)_{reactants} \quad (1)$$

$$\Delta G^{o}(298) = \Sigma\left(E_{DFT} + G_{corr}\right)_{products} - \Sigma\left(E_{DFT} + G_{corr}\right)_{reactants} \quad (2)$$

Note: E_{DFT} refers to the electronic energy calculated via DFT, while H_{corr} and G_{corr} represent the thermal corrections to enthalpy and Gibbs free energy at room temperature, respectively

Table S3. Excited state, λ_{max}, excitation energy (E), oscillator strength (f) and electronic configurations for EE, EZ and ZZ conformers of M3.

Conformer	λ		oscillator strength (f)	transition component	$MO_{contribution}$*
	eV	nm			
EE	3.68	337	1.2	H → L	75%
EZ	3.7	334	0.18	H → L	65%
ZZ	3.73	331	0.11	H → L	56%

$MO_{contribution} = 2 \times (C_{H\rightarrow L})^2$ where $C_{H\rightarrow L}$ is the coefficient of the excited state wavefunction in terms of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO)

Table S4. Cartesian coordinates of calculated structures (M3)

EE

C	-1.39413600	-0.84454200	0.06289700
C	-0.63823100	0.30771100	-0.16135800
H	-1.15218900	1.25068200	-0.30407900
C	0.74337400	0.23120300	-0.19722200
H	1.32871900	1.12902600	-0.37080900
C	1.39656600	-0.99088400	-0.01264000
C	2.86585400	-1.03622400	-0.05807700
H	3.37007900	-0.07857500	-0.24858900
N	3.52056100	-2.10877200	0.12462800
C	4.92341400	-2.08314700	0.01589700
C	5.67139900	-2.79369200	0.95728800
H	5.15047600	-3.32751700	1.74360900
C	7.05438100	-2.79134900	0.89298100
H	7.62283500	-3.32905700	1.64660400
C	7.72412700	-2.11868700	-0.12991100
C	9.22862300	-2.18216600	-0.20076400
H	9.64184200	-2.02914100	0.80549200
H	9.52742900	-3.18690600	-0.53234000
O	9.71237600	-1.20106500	-1.09722300
H	10.64820500	-1.34388600	-1.23482300
C	6.97801200	-1.43838600	-1.08476600
H	7.49092800	-0.92359200	-1.88756100
C	5.58985200	-1.41756000	-1.01348400
H	5.01854500	-0.90562500	-1.78049800
C	0.64060600	-2.14336400	0.21031200
H	1.15453200	-3.08654600	0.35180900
C	-0.74095700	-2.06659900	0.24775500
H	-1.32629200	-2.96425100	0.42250600
C	-2.86343400	-0.79833700	0.10816100

H	-3.36876200	-1.75898500	0.28098600
N	-3.51526400	0.28260700	-0.02833500
C	-4.92194000	0.24323200	-0.02151100
C	-5.60808100	1.23886500	0.67326200
H	-5.03625700	2.00171200	1.18894400
C	-6.99475800	1.24395600	0.71356200
H	-7.52214900	2.01366000	1.26292800
C	-7.72633300	0.27681400	0.02895300
C	-9.23300600	0.24896000	0.07397900
H	-9.61884700	0.00644600	-0.92536000
H	-9.55308800	-0.55183400	0.75617900
O	-9.72687700	1.49894400	0.51460100
H	-10.66715100	1.42055600	0.67243100
C	-7.04047400	-0.69178500	-0.69992900
H	-7.59524500	-1.43318100	-1.26801700
C	-5.65347200	-0.71768700	-0.72453700
H	-5.13505500	-1.45965200	-1.32213700

TS1

C	1.42604300	-1.51787500	0.23622300
C	1.14819300	-0.17541000	-0.01690000
H	1.97023100	0.52174500	-0.13787000
C	-0.16577100	0.25140100	-0.11061500
H	-0.38191500	1.29672100	-0.30835300
C	-1.22018600	-0.65251500	0.04664900
C	-2.60567700	-0.16733400	-0.05785700
H	-2.72547500	0.90833500	-0.24733900
N	-3.60588000	-0.94155900	0.04912800
C	-4.90361200	-0.39983600	-0.01160500
C	-5.87297900	-1.09137500	-0.74123500

H	-5.59297600	-2.00996300	-1.24360800
C	-7.16080200	-0.59192900	-0.83502600
H	-7.89771200	-1.12838300	-1.42604300
C	-7.52545200	0.58121200	-0.17310000
C	-8.95014600	1.06754200	-0.25296200
H	-9.29629200	0.99373800	-1.29286400
H	-9.58576300	0.40836000	0.35542400
O	-9.03240300	2.40086700	0.21089900
H	-9.95423500	2.64659500	0.28152000
C	-6.56831500	1.25116800	0.57958100
H	-6.84740500	2.15554700	1.10556600
C	-5.26735600	0.76801600	0.65946200
H	-4.53718900	1.28535100	1.27266600
C	-0.93979200	-1.99685400	0.30060200
H	-1.76477900	-2.68854900	0.42176200
C	0.37434500	-2.42242400	0.39318400
H	0.59301400	-3.46764400	0.59069600
C	2.82665800	-2.00053000	0.34284200
H	2.92379400	-3.08252900	0.54323500
N	3.83103200	-1.28321600	0.22371300
C	4.91476800	-0.50389100	0.09540600
C	5.50741200	-0.30105900	-1.16468000
H	5.08267100	-0.78733700	-2.03459500
C	6.62206000	0.51171000	-1.28022000
H	7.06891400	0.64955600	-2.26029800
C	7.18479200	1.14984400	-0.17669000
C	8.41800900	1.99077900	-0.31365900
H	8.43779600	2.46073100	-1.30595400
H	8.40694000	2.79046900	0.43888000
O	9.56875800	1.16631600	-0.13730600
H	10.34937200	1.71535000	-0.22511500

C	6.59001400	0.94172500	1.06624400
H	7.01164800	1.42019900	1.94516600
C	5.47507500	0.13534400	1.21697600
H	5.02528800	-0.01316100	2.19128200

EZ

C	-1.12355100	-0.70959000	-0.15680500
C	-0.31451400	0.33710000	-0.60703700
H	-0.75343400	1.26671700	-0.94305600
C	1.06344100	0.18620100	-0.63518200
H	1.68173900	1.00407200	-0.99179900
C	1.66504100	-0.99832800	-0.20922300
C	3.13095100	-1.11684100	-0.24203000
H	3.67569700	-0.24053800	-0.61984600
N	3.73711800	-2.15940100	0.15470800
C	5.13918400	-2.22113700	0.04855500
C	5.85734900	-2.76642700	1.11496600
H	5.31567300	-3.11011200	1.98851900
C	7.23865100	-2.84104800	1.05796000
H	7.78499000	-3.24564800	1.90530800
C	7.93417200	-2.41527200	-0.07440100
C	9.43364200	-2.56207800	-0.12501400
H	9.85820900	-2.23975200	0.83546000
H	9.68299000	-3.62459500	-0.25762400
O	9.95891800	-1.79387600	-1.18993100
H	10.88557800	-2.00654400	-1.29572400
C	7.21618000	-1.90250800	-1.14818400
H	7.74878900	-1.58077600	-2.03440000
C	5.83090200	-1.80328700	-1.08884800
H	5.28054900	-1.42659800	-1.94442500

C	0.85920400	-2.05089800	0.23008600
H	1.32955400	-2.97305500	0.54965700
C	-0.51596800	-1.90706600	0.24149400
H	-1.13836600	-2.73393500	0.56949900
C	-2.60715300	-0.66222600	-0.11317800
H	-3.07894200	-1.64688200	-0.16932200
N	-3.40723700	0.31783900	-0.01575000
C	-2.96544000	1.64319800	0.15280600
C	-3.19899000	2.57966100	-0.85447800
H	-3.68986700	2.26043800	-1.76687300
C	-2.78461600	3.89400700	-0.69635900
H	-2.93962100	4.61088000	-1.49405300
C	-2.15928400	4.30843800	0.47799700
C	-1.75747400	5.74647200	0.67493400
H	-2.61465200	6.31053800	1.06988800
H	-0.95331900	5.80027000	1.42045800
O	-1.33855900	6.29780700	-0.56243300
H	-1.26408400	7.24699600	-0.46542400
C	-1.95998100	3.37523000	1.49169100
H	-1.47423200	3.67769400	2.41486500
C	-2.36207100	2.05570000	1.34046200
H	-2.19109100	1.33341100	2.13063600

TS2

C	-1.64848400	-0.87286000	0.96413000
C	-1.07285500	0.39421000	1.09206900
H	-1.67151900	1.28495800	0.95752900
C	0.27597200	0.51618900	1.38894100
H	0.71662800	1.50380200	1.48500300
C	1.07057600	-0.61383200	1.57075200

C	2.50997800	-0.45150600	1.90089900
H	2.84542400	0.59782300	1.98276500
N	3.30080600	-1.38985700	2.07722700
C	4.15759300	-2.40237600	2.27630400
C	4.89075100	-2.94292500	1.20378200
H	4.76221100	-2.52797700	0.21133900
C	5.76396400	-3.99388600	1.42524200
H	6.31643200	-4.40065700	0.58351400
C	5.94816400	-4.54243600	2.69294200
C	6.86326000	-5.71038100	2.90537800
H	7.69932000	-5.66057300	2.19521800
H	7.27961800	-5.67513700	3.92082300
O	6.12978300	-6.91952700	2.71649200
H	6.72553800	-7.65778800	2.85281100
C	5.21768600	-3.99876300	3.74766900
H	5.33731000	-4.40935500	4.74582000
C	4.33620400	-2.94784100	3.56098200
H	3.77822500	-2.53689200	4.39369200
C	0.50456800	-1.88059600	1.43155700
H	1.12779000	-2.75835600	1.56406200
C	-0.83722600	-2.00357000	1.11839300
H	-1.27221800	-2.99063400	0.99680300
C	-3.07600700	-1.10985500	0.62591900
H	-3.25642500	-2.06487600	0.12551800
N	-4.10652100	-0.39764200	0.82673400
C	-4.06257200	0.81694700	1.53671000
C	-4.38895600	2.00363300	0.88324600
H	-4.63940000	1.97573800	-0.17100000
C	-4.35809200	3.20702400	1.57519100
H	-4.58393400	4.12810100	1.04586400
C	-4.05005100	3.24800700	2.93240700

C	-4.08193200	4.55288200	3.68371900
H	-3.91711000	5.38078600	2.98181900
H	-5.07782700	4.68876000	4.12926100
O	-3.09044300	4.54317300	4.69720500
H	-3.24296500	5.28492100	5.28245200
C	-3.76525900	2.05181100	3.58809600
H	-3.51964300	2.07247900	4.64329400
C	-3.76939800	0.84756500	2.90138900
H	-3.53254900	-0.07786700	3.41442200

ZZ

C	-1.75054200	-0.58992900	-0.21472200
C	-0.94621700	0.39369400	0.36728000
H	-1.38795600	1.28425600	0.79364400
C	0.42995200	0.23964900	0.38744300
H	1.04454900	1.01930300	0.82624400
C	1.04121900	-0.90484700	-0.13176500
C	2.52278500	-0.97775100	-0.05161400
H	3.01091600	-0.00066400	-0.00661400
N	3.30183900	-1.97860600	-0.01925400
C	2.82711000	-3.30327100	0.02247500
C	3.09532100	-4.16295100	-1.04252800
H	3.64004500	-3.78484100	-1.90025200
C	2.64801500	-5.47584600	-1.01088400
H	2.83114100	-6.13165700	-1.85374800
C	1.95468500	-5.96614600	0.09380500
C	1.51544500	-7.40552300	0.15719100
H	2.33032200	-8.01353200	0.57577400
H	0.65526000	-7.49319300	0.83382200
O	1.18459700	-7.86084200	-1.14386900

H	1.08642900	-8.81249100	-1.12004300
C	1.72056000	-5.11092800	1.16726300
H	1.18233900	-5.47376900	2.03813700
C	2.15450600	-3.79327300	1.14168100
H	1.95665400	-3.13164600	1.97742700
C	0.23906500	-1.87739100	-0.73489700
H	0.68184000	-2.76102300	-1.17468000
C	-1.13415100	-1.70547300	-0.78831900
H	-1.74399700	-2.45859500	-1.27732500
C	-3.23007900	-0.50788700	-0.31612500
H	-3.64547600	-1.06957100	-1.15696000
N	-4.07968800	0.09386300	0.40927200
C	-3.71956900	0.78548400	1.58113200
C	-3.92069800	2.16274400	1.65282300
H	-4.32017800	2.68475000	0.79090600
C	-3.57899300	2.85401900	2.80715800
H	-3.71179700	3.93159300	2.83785500
C	-3.07773100	2.18761600	3.92250500
C	-2.77249700	2.94516800	5.18816300
H	-2.52026800	3.98395900	4.93772000
H	-3.67086900	2.96544500	5.82177100
O	-1.70386400	2.31649900	5.87504000
H	-1.64138400	2.69096800	6.75349500
C	-2.91773300	0.80524100	3.85720600
H	-2.52413200	0.27743800	4.71771300
C	-3.23309500	0.10839500	2.70066500
H	-3.09210100	-0.96559600	2.65126700