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Supporting Information

Zinc Diethyldithiocarbamate as a Catalyst for Synthesising Biomedically-relevant Thermogelling Polyurethanes

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Figure S1A. ¹³C NMR spectra of ZDTC-catalysed PU (CDCl₃). Inset shows expanded carbonyl region showing the absence of any significant peaks arising from urea, allophanate and cyanurate linkages. The more complex aliphatic region of this polymer's spectrum compared to those catalyzed by DBTL (Figure S1B) may be a result of the significantly longer polymer structure, resulting in more diverse magnetically inequivalent carbon environments.



Figure S1B. ¹³C NMR spectra of DBTL-catalysed PU (CDCl₃).



Figure S2. GPC profiles of polyurethanes synthesised using different catalysts (data in Table 1). GPC analyses were performed on a Waters GPC machine at 40 °C, equipped with a 515 HPLC pump, Waters Styragel columns and Waters 2414 refractive index detector. HPLC grade THF was used as the eluent at a flow rate of 1.0 mL/min.



Figure S3. Oscillatory temperature sweep showing the changes in storage (*G*') and loss modulus (*G*'') as a function of temperature, as well as the gelation temperature of 10 wt % PU catalysed by various catalysts at a ramp rate of 5.0 °C·min⁻¹, under constant strain of 1.0 %, and angular frequency of 10.0 rad·s⁻¹. All polymer solutions have a concentration of 10 wt/v %.

Table S1. Rheological properties of the hydrogels containing different weight percentages of PU synthesised by ZDTC and DBTL.^a

S/N	PU	ZDTC catalyst				DBTL catalyst			
	content/	T _c / ⁰C	G' at	η* at 37	Axial	T _c / ⁰C	G' at	η* at 37	Axial
	wt %		37 °C/	°C/ Pa.s	force at		37 °C/	°C/ Pa.s	force at
			Pa		37 °C/ N		Pa		37 °C/ N
1	10.0	8.7	4950	500	14.90	21.9	559	59	0.67
2	7.5	8.9	3950	631	15.70	23.4	195	21	0.16
3	5.0	9.8	1830	291	9.33	27.7	28	3.4	<0.001
4	2.5	11.4	562	90	4.30	No gelation observed			
5	1.5	12.6	145	4.2	0.72				



Figure S4. Oscillatory temperature sweep showing the changes in storage (*G*') and loss modulus (*G*'') as a function of temperature, as well as the gelation temperature of 2.5 wt/v % PU solutions catalysed by ZDTC at different reaction temperatures and with different solvents (temperature ramp rate of 5.0 $^{\circ}$ C·min⁻¹, under constant strain of 1.0 %, and angular frequency of 10.0 rad·s⁻¹). Data is summarised in Table S1.



Figure S5. Oscillatory temperature sweep showing the changes in storage (G') and loss modulus (G'') as a function of temperature for the DBTL-catalysed PU at different concentrations in water. Data is summarised in Table S1.

Table S2. Properties of the PUs synthesised in the presence of ZDTC catalyst under different reaction conditions and the resulting hydrogels (2.5 wt/v %). ^a

^a All reactions performed on 5 g scale using identical quantities of PEG-diol, PPG-diol, HMDI and ZDTC catalyst. ^b As the reaction with DMF formed a very viscous solution after 2 hours which

S/N	Solvent	Solvent volume/	T/ ∘C	Polymer properties		2.5 wt/v % Hydrogel rheological properties ^e			Solvent physical properties	
		mL		M _n /kg	Ðď	T₀/ ºC	G' (37	η* (37 ºC)/	Dielectric	Gutmann Donor
				mol ^{-1 d}			°C)/ Pa	Pa∙s	constant ɛ	number
1	toluene	30	110	62.6	1.49	11.4	562	90	2.38 ¹	0.1 ¹
2	toluene	30	90	57.2	1.40	13.1	370	37		
3	toluene	30	70	33.7	1.36	40.2	Below T _c			
4	DMF⁵	35	110	40.3	1.36	16.3	90.4	9.1	36.7 ¹	30.9 ¹
5	xylenes	30	110	51.9	1.34	17.5	69.7	7.0	2.60 ²	-
6	chlorobenzene	30	110	50.0	1.46	10.2	600	60	5.71 ¹	NA

presented difficulties stirring, an additional 5 mL of anhydrous DMF was added to the reaction to ensure sufficient mixing.



Figure S6. Oscillatory temperature sweep showing the changes in storage (G') and loss modulus (G'') as a function of temperature for the PUs catalysed by ZDTC under different reaction conditions as specified in Table S2. All polymer solutions have concentrations of 2.5 wt/v%.



Figure S7. Stacked ¹H NMR spectra of (top) HMDI, (middle) equimolar quantities of HMDI + ZDTC and (bottom) ZDTC in d₇-toluene.



Figure S8. Stacked ¹H NMR spectra of ZDTC in d₇-toluene before and after heating at 110 °C for 24 hours.

Synthesis of PUs under non-anhydrous conditions

The synthesis was performed analogous to that reported in the main manuscript text, except that the PEG and PPG diols were not dried by azeotropic distillation prior to the reaction, and that non-anhydrous toluene was used. Briefly, 3.33g of PEG and 1.67 g of PPG were dissolved in non-anhydrous toluene (30 mL) at 110 °C, before DBTL or ZDTC (0.0067 mol equivalents with respect to each hydroxyl/ isocyanate group present) was added, followed by HMDI (0.40 mL, to maintain a 1:1 isocyanate: hydroxyl mole ratio). After stirring at 110 °C for 24 hours under an Argon atmosphere, 5 mL of ethanol was added to the reaction and stirred for a further 15 minutes to quench any unreacted isocyanate groups present. The polymer solution was then precipitated by pouring into vigorously-stirred diethyl ether (400 mL), and the polymer particles were collected by filtration to give white solids.

GPC results:

 M_n of DBTL-catalysed PU = 25.9 kDa, D = 1.54

 M_n of ZDTC-catalysed PU = 48.3 kDa, D = 2.12



Figure S9. GPC profiles of thermogelling PUs synthesised under non-anhydrous conditions catalysed by either DBTL (black curve) or ZDTC (red curve). GPC analyses were performed using an Agilent GPC machine at 40 °C, equipped with a 1260 Infinity II Isocratic Pump, PLgel 5µm MIXED-D 300 x 7.5 mm column and 1260 Infinity II refractive index detector, against polystyrene standards. HPLC grade THF was used as the eluent at a flow rate of 1.0 mL/min.

	ZDTC catalysis								
Time/	Relative	¹ H NMR	Mole ratio						
min	Integ	ration							
	PPG ^[a]	HMDI ^[b]	PPG	HMDI					
10	5.21	1	0.195	1					
20	6.38	1	0.250	1					
30	7.23	1	0.284	1					
40	7.76	1	0.304	1					
50	7.91	1	0.310	1					
60	7.86	1	0.309	1					
90	0 7.90		0.310	1					
120	8.13	1	0.319	1					

Table S3. Relative Integration of PPG and HMDI resonances at different durations of reaction catalysed by either DBTL or ZDTC.

[a] Resonance at 1.10-1.15 ppm; average molecular weight = 2000 [b] Resonance at 3.10-3.15 ppm; molecular weight = 168.



Figure S10. Size distribution of micelles formed by ZDTC-PUs (red curve) DBTLC-PUs (black curves), determined by dynamic light scattering of the aqueous polymer solutions (0.10 wt %) at 25 °C.

Determination of CMC by the Dye-Solubilisation Method

The aqueous polymer concentration was varied between the range of 0.001 to 0.5 mg/mL of polyurethane in water at a constant concentration of 1,6-Diphenyl-1,3,5-hexatriene (DPH). As DPH shows a higher absorption coefficient in a hydrophobic environment than in water, with increasing polymer concentration, the absorbances at 344, 358, and 378 nm increased (Figure S9), as more polymer molecules are available to self-assemble into micelles. The point where the absorbance suddenly increases corresponds to the concentration at which micelles are formed, as DPH partitions preferentially into the hydrophobic micellar core formed in the aqueous solution. The CMC was determined by extrapolating best fit curves between the difference in absorbances between 378 nm and 400 nm (A378 – A400) as a function of logarithmic concentration (Figure 5, main manuscript text).



Figure S11. Absorbance of DPH at different concentrations of polyurethane in water, whose synthesis are catalysed by (A) DBTL or (B) ZDTC.

Synthesis of three-component PUs for cell viability studies

The three-component PUs were synthesised using an identical catalyst loading (0.67 mol% w.r.t each reactive OH/NCO pair) as described in the Experimental Section of the main text: PEG_{2050} (8.0 g), PPG_{2000} (2.0 g) and PCL_{2000} (0.10 g) were mixed together and dried by azeotropic distillation with anhydrous toluene (2 x 30 mL). Following which, the mixture was re-dissolved in toluene (55 mL) whereupon the catalyst (24 mg ZDCT or 42 mg DBTL) and HMDI (0.85 mL) was added portionwise. The reaction was stirred at 110 °C for 24 hours before it was cooled down to ambient temperature, and the PU polymers were precipitated by slowly pouring the reaction mixture into vigorously-stirred diethyl ether (500 mL) and filtered. The resulting white polymers were dried in a vacuum oven at 30 °C for 3 days (yields: ZDTC-catalysed = 86 %; DBTL-catalysed = 82 %). ¹H NMR (CDCI₃, 500 MHz): 4.89 (br. s, OCON<u>H</u>), 4.19 (m, C<u>H</u>₂OCONH); 4.04 (m, OC<u>H</u>₂ of PCL); 3.63 (br. s, OC<u>H</u>₂ of PEG); 3.53 (m, OC<u>H</u>₂ of PPG); 3.39 (m, C<u>H</u>CH₃ of PPG); 3.14 (m, NC<u>H</u>₂CH₂CH₂); 2.28 (m, C<u>H</u>₂C=O of PCL); 1.47 (m, NCH₂C<u>H</u>₂CH₂); 1.31 (m, NCH₂CH₂C<u>H</u>₂); 1.13 (m, CHC<u>H</u>₃ of PPG).



Figure S12. Partial ¹H NMR spectra of poly(PEG/PPG/PCL/urethane) catalysed by ZDTC (CDCl₃, 500 MHz).

References

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