Supporting Information

On the stability of trithiocarbonate RAFT agents containing both a cyano and a carboxylic acid functional group.

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Materials and methods

2-phenylethanethiol, 1-dodecanethiol, 1-butanethiol, ethanethiol, carbon disulfide, potassium tert-butoxide, iodine, azobis(cyanovaleric acid) (ACVA), carbon disulphide, sodium thiosulphate, and magnesium sulphate were all used as received from Sigma Aldrich. *N*-hexane, ethyl acetate, dichloromethane, dimethylformamide, diethyl ether, pyridine, tetrahydrofuran, acetonitrile and methanol were used dry where applicable and of reagent grade quality. MilliQ water (18.2 mΩ/cm) was used throughout. 2,2'-Azobis(2-isobutyronitrile) (AIBN) was recrystallized from methanol and methyl methacrylate (MMA) was filtered through basic alumina to remove radical inhibitors before use.

*Synthesis of 4-cyano-4-(((phenylethylthio)carbonylthioyl)thio)pentanoic acid (**4**).* The synthesis of the RAFT chain transfer agent (CTA) was adapted from that previously published.[1-4] Briefly, 2-phenylethanethiol (10.3 g, 74.7 mmol) was added drop-wise to a stirred suspension of potassium tert-butoxide (8.3 g, 74.7 mmol) in 150 mL of diethyl ether over 10 mins at 5 ^{o}C. The reaction was left to stir for a further 30 mins after which carbon disulfide (5.68 g, 74.7 mmol) was added drop-wise over 10 mins and left to stir for a further hour. To this, iodine (9.47 g, 37.3 mmol) was added portion-wise and stirred and allowed to warm to room temperature overnight. The reaction mixture was washed three times with sodium thiosulfate (0.25 M), brine, and water, then dried over anhydrous magnesium sulfate.

After solvent removal, a yellow solid resulted (bis-((phenethylthio)carbonothioyl)thio) disulfide). Yield: >95 %.

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.31 – 7.16 (m, 5H), 3.59 (t, *J* = 7.7 Hz, 2H), 2.91 (t, *J* = 7.7 Hz, 2H).

ACVA (8.0 g, 28.5 mmol) and the above bis-((phenethylthio)carbonothioyl)thio) disulfide (10.2 g, 23.8 mmol) were dissolved in 100 mL of ethyl acetate and heated to reflux under an inert atmosphere overnight. The solvent was removed and the crude product was purified by silica gel column chromatography using *n*-hexane:ethyl acetate (50:50) as eluent. The second fraction afforded a viscous yellow oil (**4**). Yield: 12.1 g (75%).

1H NMR (500 MHz, DMSO-d6) δ 12.44 (s, 1H), 7.35 – 7.15 (m, 5H), 3.64 (t, J = 7.7 Hz, 2H), 2.96 (t, J = 7.7 Hz, 2H), 2.45 – 2.20 (m, 4H), 1.85 (s, 3H).

Synthesis of Poly(methyl methacrylate) (PMMA_1 and PMMA_4). Methyl methacrylate (0.50 g, 5.0 mmol), 2,2′-Azobis(2-methylpropionitrile)(1.07 mg, 0.0065 mmol) and CTA **1** (13.1 mg, 0.0325 mmol, 4) (or CTA **4** in the case of PMMA_4, 11.0 mg, 0.0325 mmol) were combined in a Schlenk tube and dissolved in THF (1 mL). This was degassed with nitrogen for 10 minutes then sealed and placed in a thermostated oil bath at 75 ^{o}C for 4.5 hrs. At the conclusion of the polymerization, the polymer was precipitated out in an excess of *n*-hexane (200 mL). The polymer was filtered, washed further with *n*-hexane and dried. CTA concentrations of polymers synthesised with doped amounts of either **1a** or **4a**, were adjusted accordingly so that the molar ratio of total CTA in the polymerisation remained at 5:1 (CTA:Initiator).

All NMR experiments were undertaken on a Bruker Avance 500 high-resolution NMR spectrometer. Diffusion-weighted spectra were collected at a gradient strength (gpz6) of 95% for a minimum of 128 scans.

SEC-MALLS chromatographic system consisted of 1515 isocratic pump (Waters), a 717 auto sampler (Waters), Styragel HT 6E and Styragel HT 3 columns (Waters), 2414 differential refractive index detector (Waters) and a Dawn Heleos laser light scattering detector (Wyatt). THF was used as the mobile phase with a flow rate of 1 mL/min.

ESI-MS measurements were recorded using a Waters Micromass Quattro mass spectrometer in positive mode using filtered methanol as solvent.

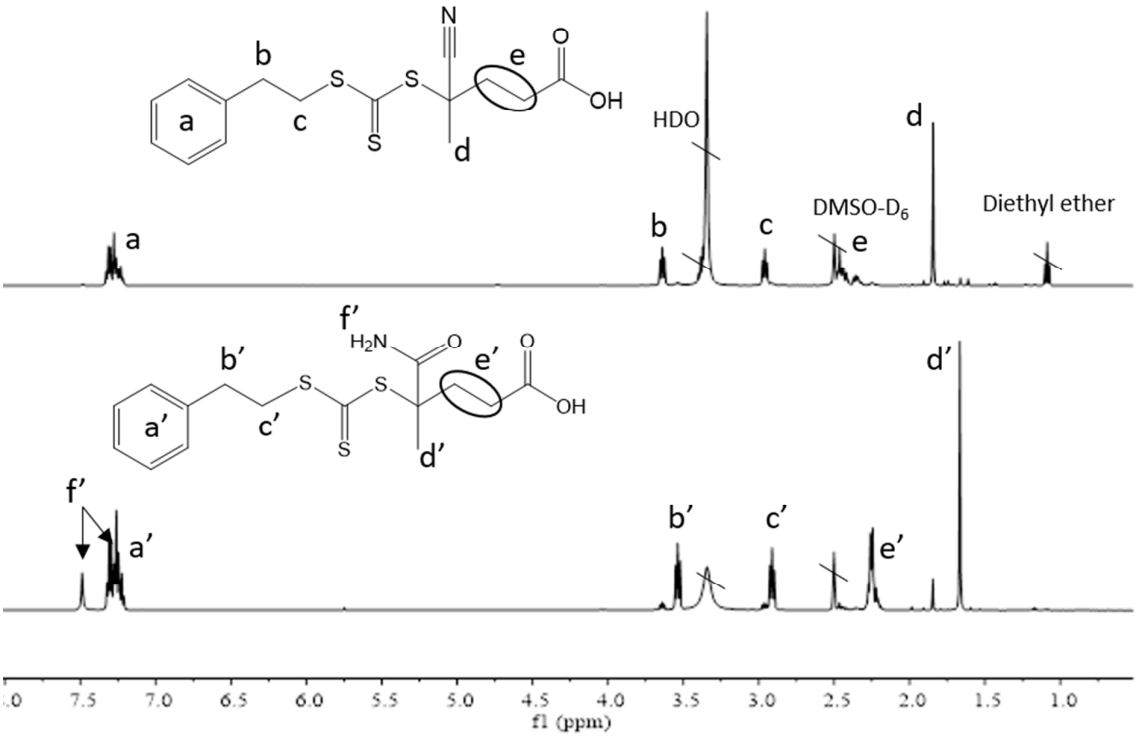

Figure S1. ^{1}H NMR spectrum of **4** (top) and the isolated degradation product **4a** (bottom) in DMSO-D_6. It should be noted that there remains a small amount of **4a** in the top spectrum and **4** in the bottom spectrum.

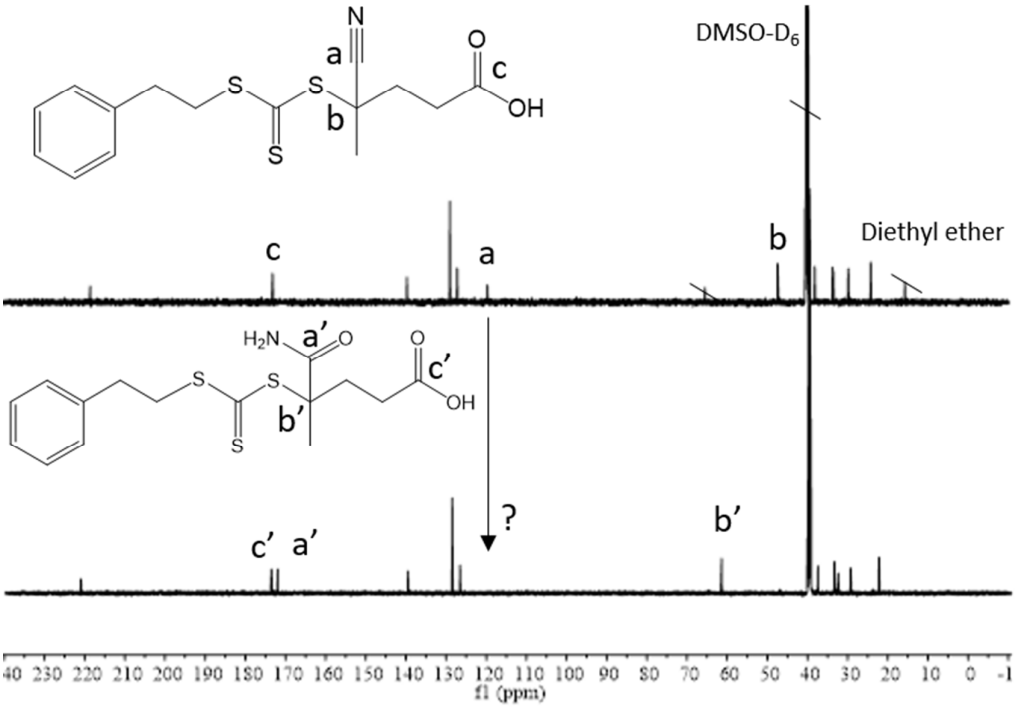

Figure S2. ^{13}C NMR spectrum of **4** (top) and the isolated degradation product **4a** (bottom) in DMSO-D_6.

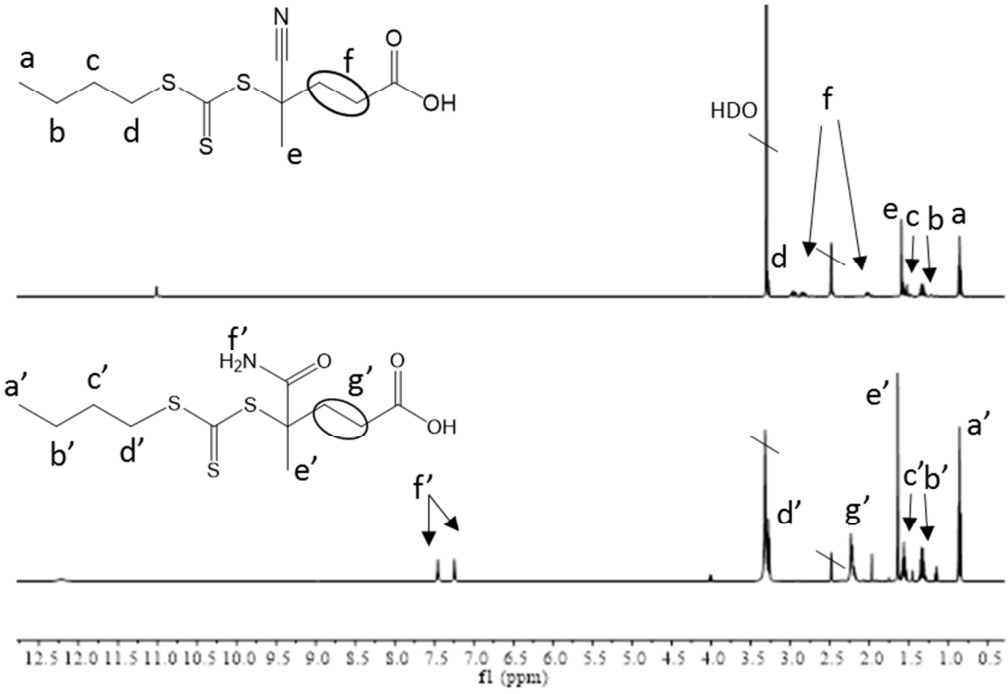

Figure S3. ^{1}H NMR spectrum of **2** (top) and the isolated degradation product **2a** (bottom) in DMSO-D_6.

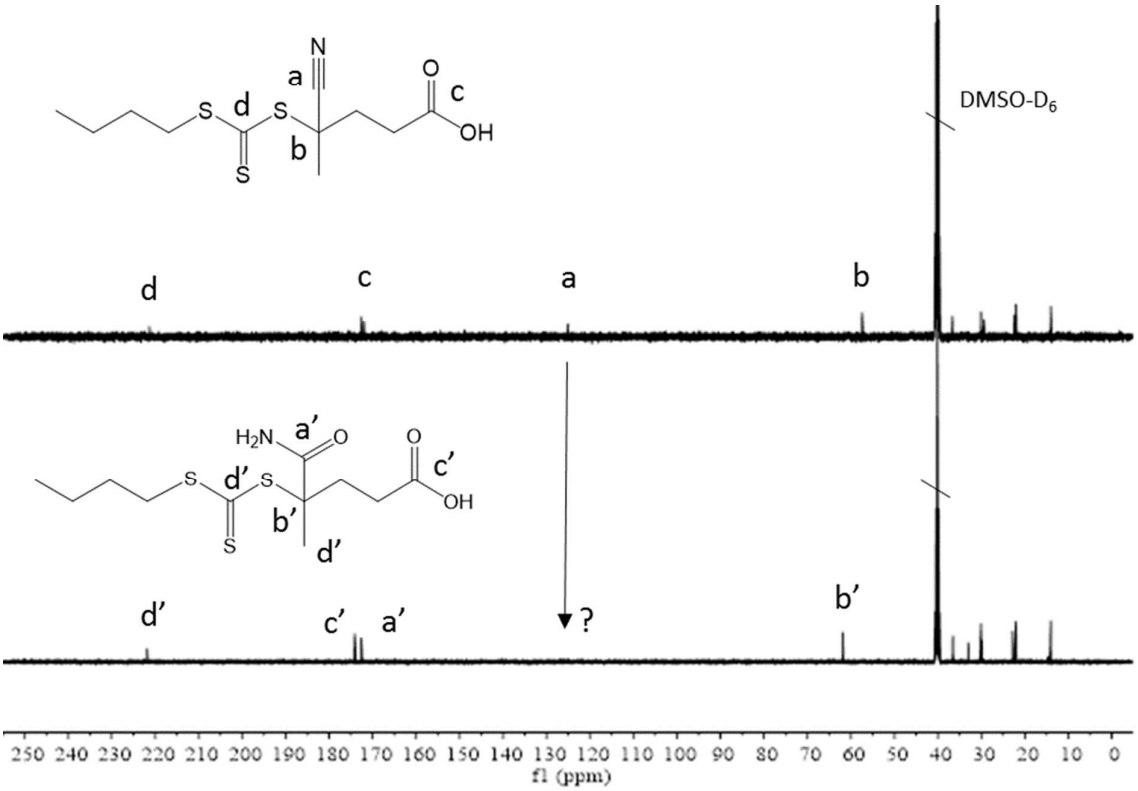

Figure S4. ^{13}C NMR spectrum of **2** (top) and the isolated degradation product **2a** (bottom) in DMSO-D_6.

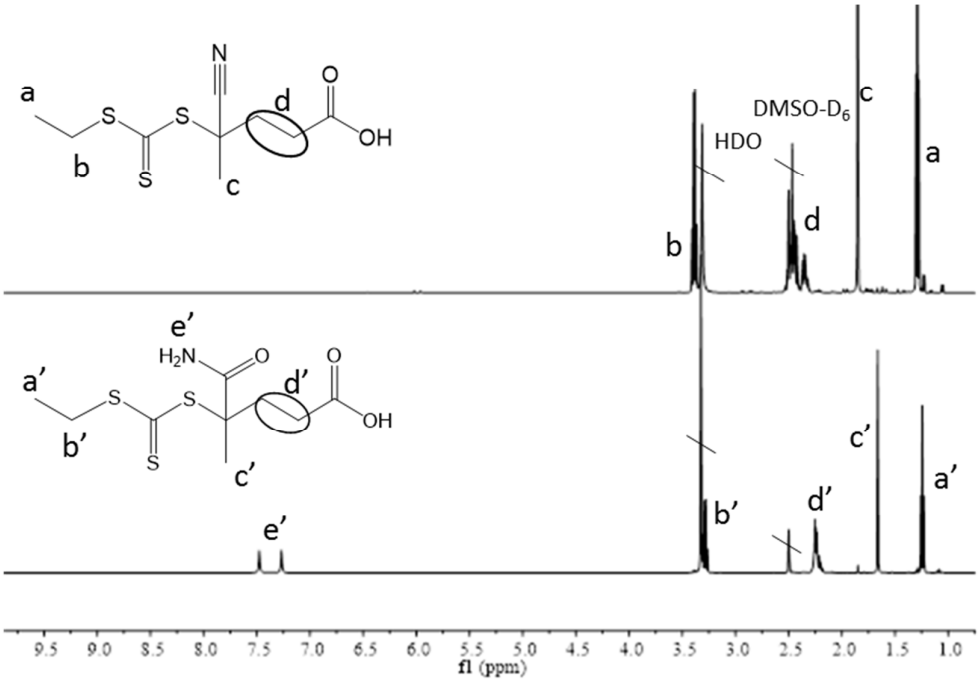

Figure S5. ^{1}H NMR spectrum of **3** (top) and the isolated degradation product **3a** (bottom) in DMSO-D_6.

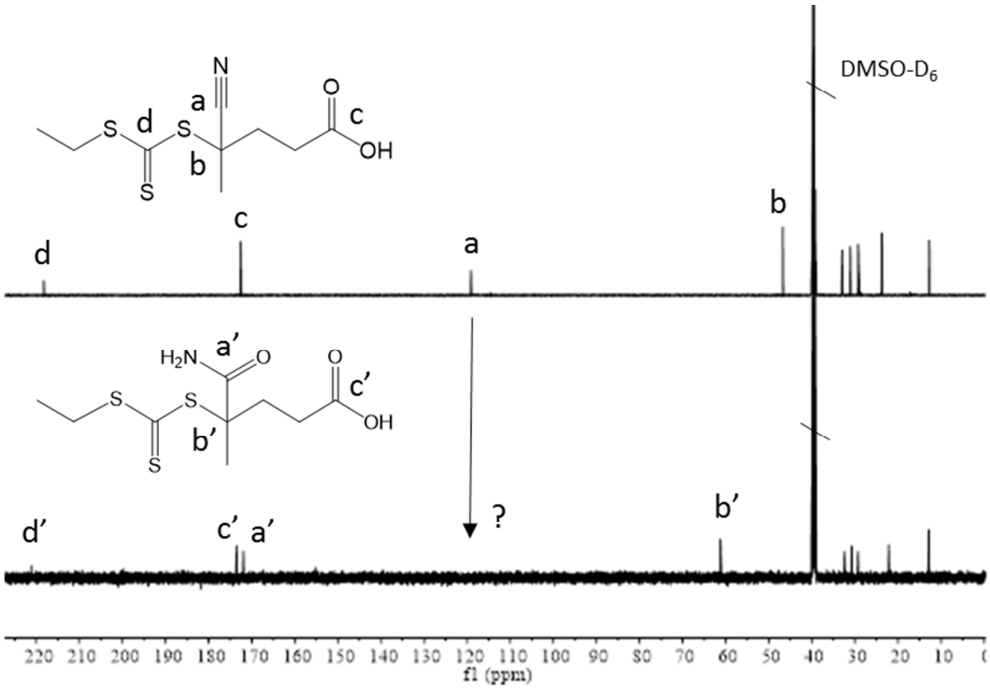

Figure S6. ^{13}C NMR spectrum of **3** (top) and the isolated degradation product **3a** (bottom) in DMSO-D_6.

Table S1. The ESI-MS of all of RAFT agents and their hydrolysis products versus theoretical mass/charge values.

	Theory				Experimental			
RAFT agent	$[M+H]^+$	$[M+Li]^+$	$[M+Na]^+$	$[M+K]^+$	$[M+H]^+$	$[M+Li]^+$	$[M+Na]^+$	$[M+K]^+$
1	404.17	410.18	426.16	442.13	404.26	410.26	426.24	442.24
1A	422.18	428.19	444.17	460.14		428.44	444.42	460.38
2	292.05	298.06	314.03	330.01		298.31	314.29	330.30
2A	310.06	316.07	332.04	348.02		316.31	332.30	348.28
3	264.02	270.03	286.00	301.97	265.09			
3A	282.03	288.04	304.01	319.98	282.12		304.25	
4	340.04	346.06	362.03	378.01			362.30	378.29
4A	358.05	364.07	380.04	396.02			380.10	

References

(1) Moad, G.; Chong, Y. K.; Postma, A.; Rizzardo, E.; Thang, S. H. Advances in RAFT Polymerization: The Synthesis of Polymers with Defined End-Groups. *Polymer* 2005, *46*, 8458-68.
(2) Roth, P. J.; Wiss, K. T.; Zentel, R.; Theato, P. Synthesis of Reactive Telechelic Polymers Based on Pentafluorophenyl Esters. *Macromolecules* 2008, *41*, 8513-19.
(3) Scarano, W.; Duong, H. T. T.; Lu, H.; De Souza, P. L.; Stenzel, M. H. Folate Conjugation to Polymeric Micelles via Boronic Acid Ester to Deliver Platinum Drugs to Ovarian Cancer Cell Lines. *Biomacromolecules* 2013, *14*, 962-75.
(4) Fuchs, A. V.; Tse, B. W. C.; Pearce, A. K.; Yeh, M.-C.; Fletcher, N. L.; Huang, S. S.; Heston, W. D.; Whittaker, A. K.; Russell, P. J.; Thurecht, K. J. Evaluation of Polymeric Nanomedicines Targeted to PSMA: Effect of Ligand on Targeting Efficiency. *Biomacromolecules* 2015, *16*, 3235-47.