Direct routes to functional RAFT agents from substituted *N*-alkyl maleimides

Rosa Catania,[a,b] Ruggero Foralosso,[a] Lampros Spanos,[a] Emanuele Russo,[a] Francesca Mastrotto,[c] Pratik Gurnani,[a] Kevin Butler[d], Huw Williams[d], Snow Stolnik,*[a] Giuseppe Mantovani *[a]

[a]Division of Molecular Therapeutics and Formulation, School of Pharmacy, University of Nottingham, Nottingham NG7 2RD, United Kingdom

[b]School of Life Sciences, University of Nottingham, Queens Medical Centre, Nottingham NG7 2UH, United Kingdom

[c]Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Padova 35131, Italy

[d]School of Chemistry, University of Nottingham, Nottingham NG7 2RD, United Kingdom

Materials and Methods.

All solvents were purchased from Fischer Chemicals and were of analytical grade. All chemicals were purchased from Sigma-Aldrich Company, Alfa Aesar or Fisher Scientific and utilised without further purification. Azoinitiator 2,2'-azobis[2- (2-imidazolin-2-yl)propane]dihydrochloride (VA-044) was purchased from Wako.

Thin layer chromatography (TLC) was performed using pre-coated silica gel 60 ALUGRAM SIL G/UV254 and developed in the solvent system indicated. Compounds were visualised by use of UV light (254 nm) or a basic solution (10% w/w K_2CO_3 in water) of $KMnO_4$. Acros Organics 60Å (0.035-0.070 mm) silica gel was used for column chromatography.

Agilent 971-FP Flash Purification System was used to perform flash column chromatography on SiO_2 (SF10-8g, Si-35) or reversed-phase (KP-C18-HS) as the stationary phase.

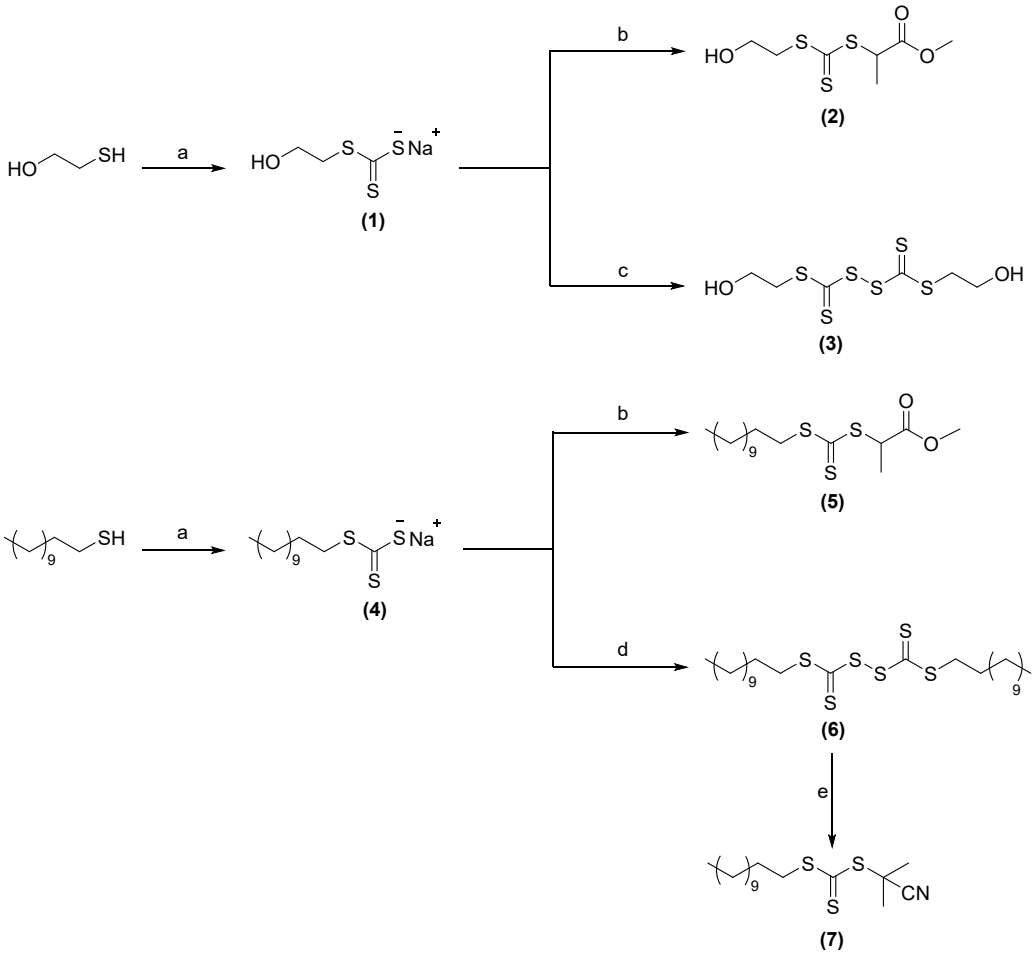
^1H and ^{13}C NMR spectra were recorded on a Bruker DPX400 UltraShield™ Spectrometer and processed with MestReNova 6.0.2© 2009 Mestrelab Research S.L. All chemical shifts are reported in ppm (δ) relative to tetramethylsilane or referenced to the chemical shifts of residual solvent resonances. The following abbreviations were used to explain the multiplicities: s = singlet, bs = broad singlet, d = doublet, t = triplet, q= quartet, m = multiplet, app. t = apparent triplet.

ESI-TOF Mass Spectrometry measurements were carried out using a Bruker MicroTOF spectrometer (LC-TOF instrument equipped with an ESI source).

Polymer molecular weights were determined by size exclusion chromatography (SEC) performed on a Polymer Laboratories GPC 50 system (Polymer Laboratories) equipped with refractive index (RI) detector. Separations were performed on a pair of Agilent PLgel Mixed-D columns (7.5 x 300 mm, 5 µm bead size, Polymer Labs UK), eluting with DMF + 0.1% w/w LiBr at flow rate of 1 $mL \cdot min^{-1}$ and

injection volume of 100 µL. Samples were prepared at 5 mg·mL^{-1} concentration. The molecular weights and dispersities of the polymers were calculated according to a standard calibration method using PMMA narrow standards (500-450,000 g·mol^{-1}). Data were elaborated with Polymer Labs Cirrus 3.0 Software. For n-butyl acrylate polymers, GPC was performed on an Agilent 1200 Infinity Series equipped with a differential refractive index detector. The mobile phase was HPLC grade $CHCl_3$ at 25 °C and a flow rate of 1 mL·min^{-1}. Separations were performed on a pair of PLgel Mixed-D columns (7.8 × 300 mm, 5 µm bead size, Agilent) fitted with a matching guard column (50 × 7.8 mm). The molecular weights and dispersities of the polymers were calculated according to a standard calibration method using PMMA narrow molecular (200-360,000 g·mol^{-1}). Chromatographs were analysed using Astra 6.1 software.

Synthesis of CTA precursors.



Scheme S1. *Reagents and conditions*: (a) i. NaH; ii. CS_2, 0°C; (b) methyl-2-bromopropionate; (c) $K_3Fe(CN)_6$; (d) I_2; (e) AIBN.

Sodium 2-hydroxyethyl carbonotrithioate (1).[1] NaH (60% wt% in mineral oil, 5.55 g, 138 mmol) was dispersed in 150 mL of diethyl ether and cooled to 0°C in an ice bath. Mercaptoethanol (9.00 mL, 128 mmol) was added dropwise under stirring to the organic suspension and the mixture was stirred for 10 minutes, then CS_2 (15.4 mL, 256 mmol) was added dropwise to the suspension and the reaction was stirred at ambient temperature for one hour. The resulting yellow precipitate was obtained and recovered by filtration, washed with diethyl ether, and finally desiccated under reduced pressure, to give the intermediate **(1)** as a yellow solid (20.2 g, 11.5 mmol, 94%), which was used for the next step without further purification.

^{1}H NMR (400 MHz, DMSO-d_6) δ 4.64 (t, *J* = 5.5 Hz, 1H, *H*OCH$_2$CH$_2$SC(S)S), 3.45 (q, *J* = 7.2 Hz, 2H, HOC*H*$_2$CH$_2$SC(S)S), 3.12 (t, *J* = 7.4 Hz, 2H, HOCH$_2$C*H*$_2$SC(S)S).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 239.4 (1C, SC(S)S), 60.0 (1C, HO*C*$H_2$$CH_2$SC(S)S), 42.7 (1C, HO$CH_2$*C*$H_2$SC(S)S).

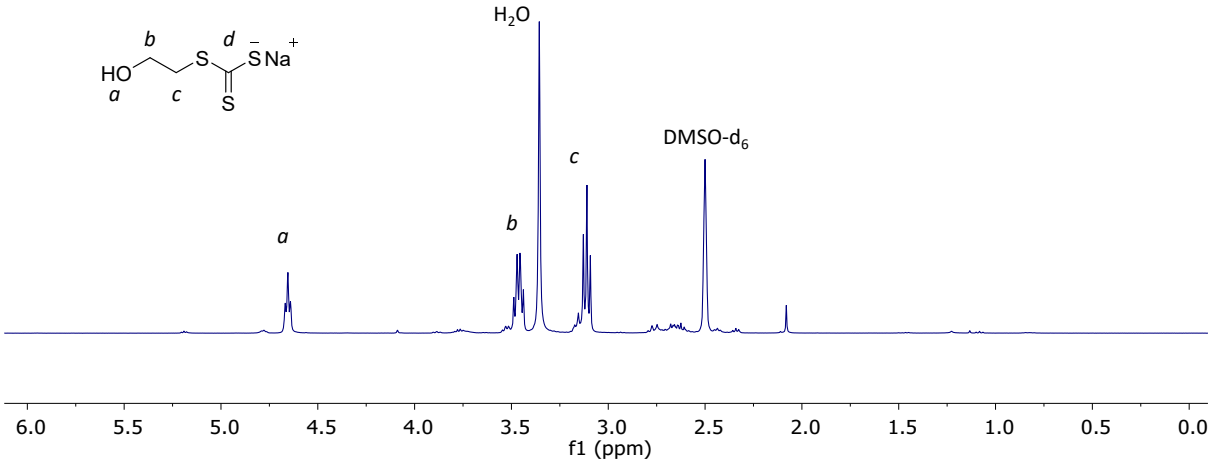


Figure S1. ^{1}H NMR spectrum of sodium 2-hydroxyethyl carbonotrithioate (**1**) in DMSO-d_6.

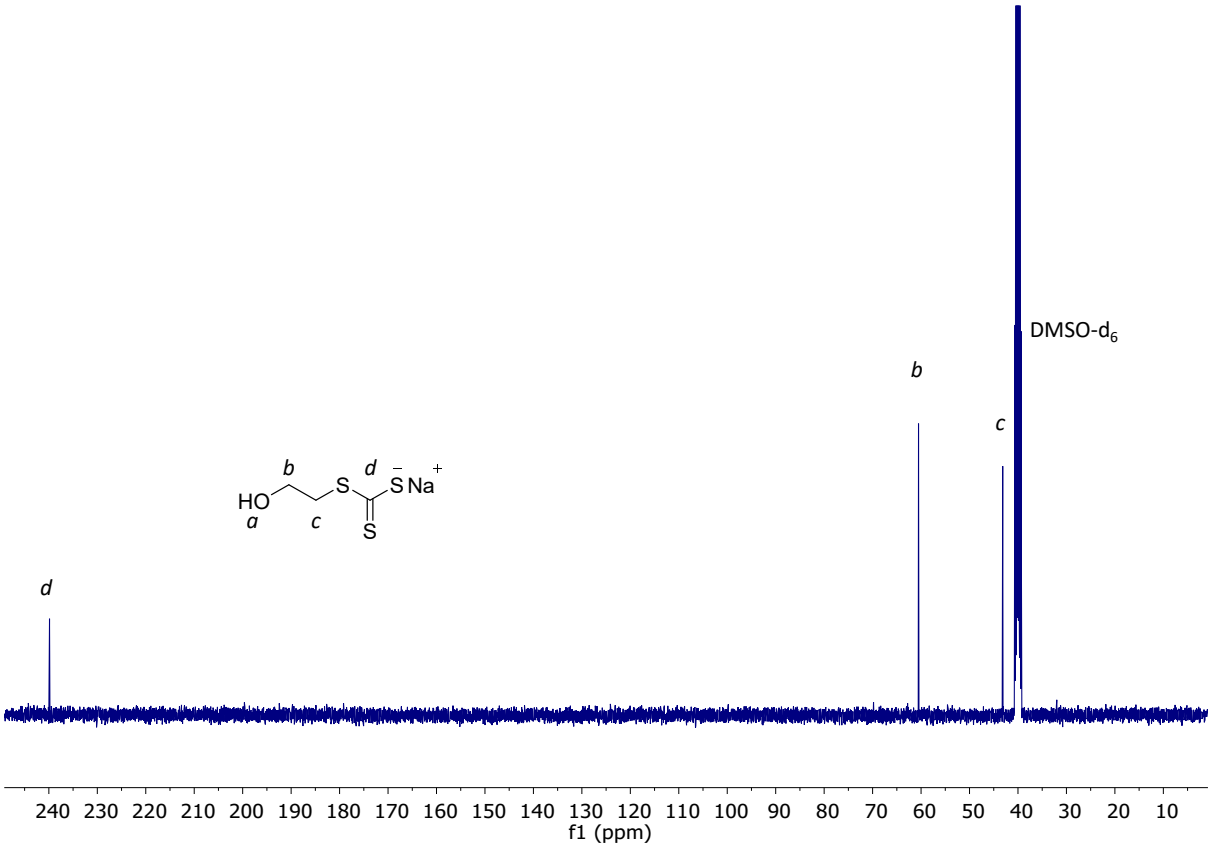


Figure S2. ^{13}C NMR spectrum of sodium 2-hydroxyethyl carbonotrithioate (**1**) in DMSO-d_6.

Methyl 2-((((2-hydroxyethyl)thio)carbonothioyl)thio)propanoate (2). Sodium 2-hydroxyethyl carbonotrithioate intermediate **(1)** (13.26 g, 75.25 mmol) was suspended in acetone (100 mL) and

methyl-2-bromo-propionate (9.2 mL, 82 mmol) was added dropwise under stirring. After 2 hours the solvent was removed under reduced pressure, the product was suspended in 50 mL of Et_2O and washed with water (3 x 100mL). The organic layer was dried over $MgSO_4$, filtered and the solvent evaporated under reduced pressure to give an orange viscous oil which was purified by flash chromatography (silica gel 60, 35-70 um) using petroleum ether/ethyl acetate 8:2 (vol/vol) as the eluent, to give the intermediate **(2)** as a yellow-orange oil (7.20 g, 30.0 mmol, 40%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.9 (q, *J* = 7.4 Hz, 1H, SC*H*(CH_3)), 3.9 (t, *J* = 6.0 Hz, 2H, HOC*H*$_2$$CH_2$S), 3.8 (s, 3H, -C(O)O$CH_3$), 3.6 (t, *J* = 6.1 Hz, 2H, HOCH_2C*H*$_2$S), 1.9 (bs, 1H, *H*OCH_2), 1.6 (d, *J* = 7.4 Hz, 3H, CHC*H*$_3$).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 221.8 (1C, SC(S)S), 171.6 (1C, -*C*(O)OCH_3), 60.3 (1C, HO*C*$H_2$$CH_2$SC(S)S), 52.8 (1C, -SCH), 48.0 (1C, HOCH_2*C*H_2SC(S)S), 39.4 (1C, -OCH_3) 16.8 (1C, -*C*HCH_3).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 262.98, found 262.98 (100%).

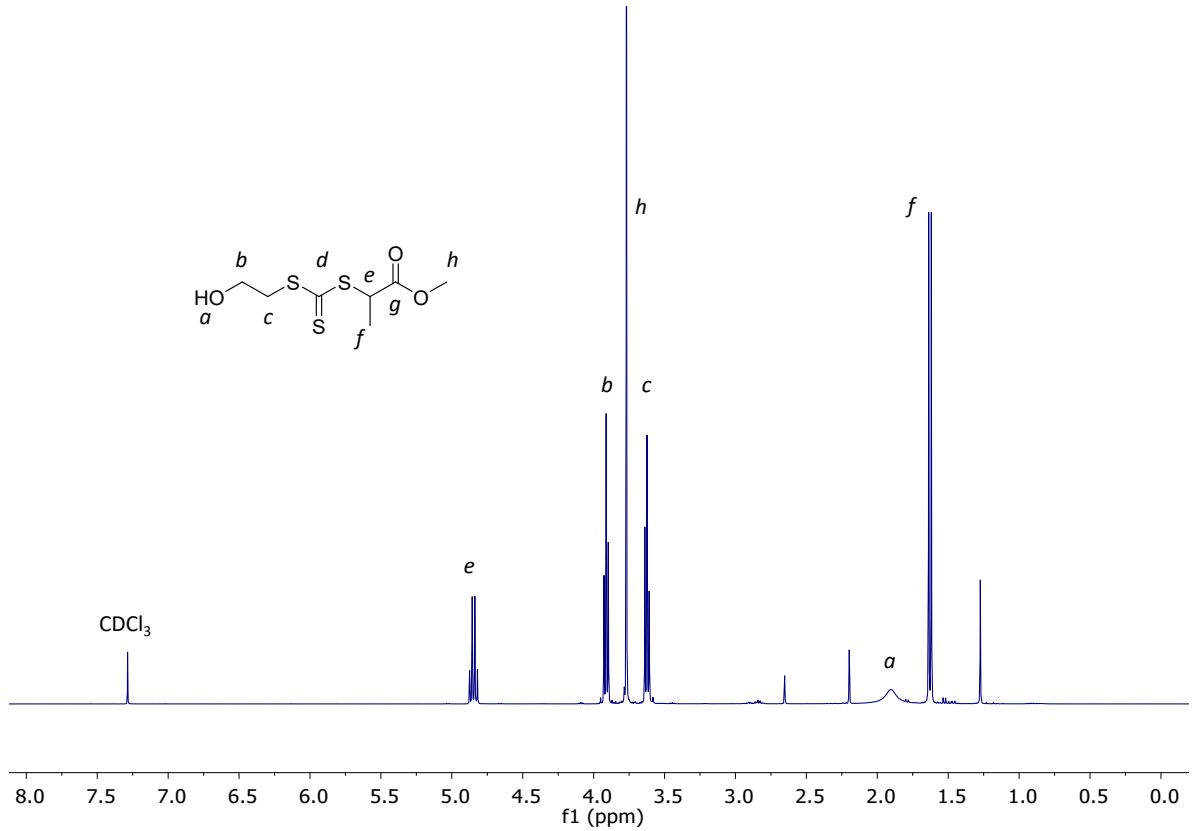


Figure S3. ^{1}H NMR spectrum of methyl 2-((((2-hydroxyethyl)thio)carbonothioyl)thio)propanoate **(2)** in $CDCl_3$.

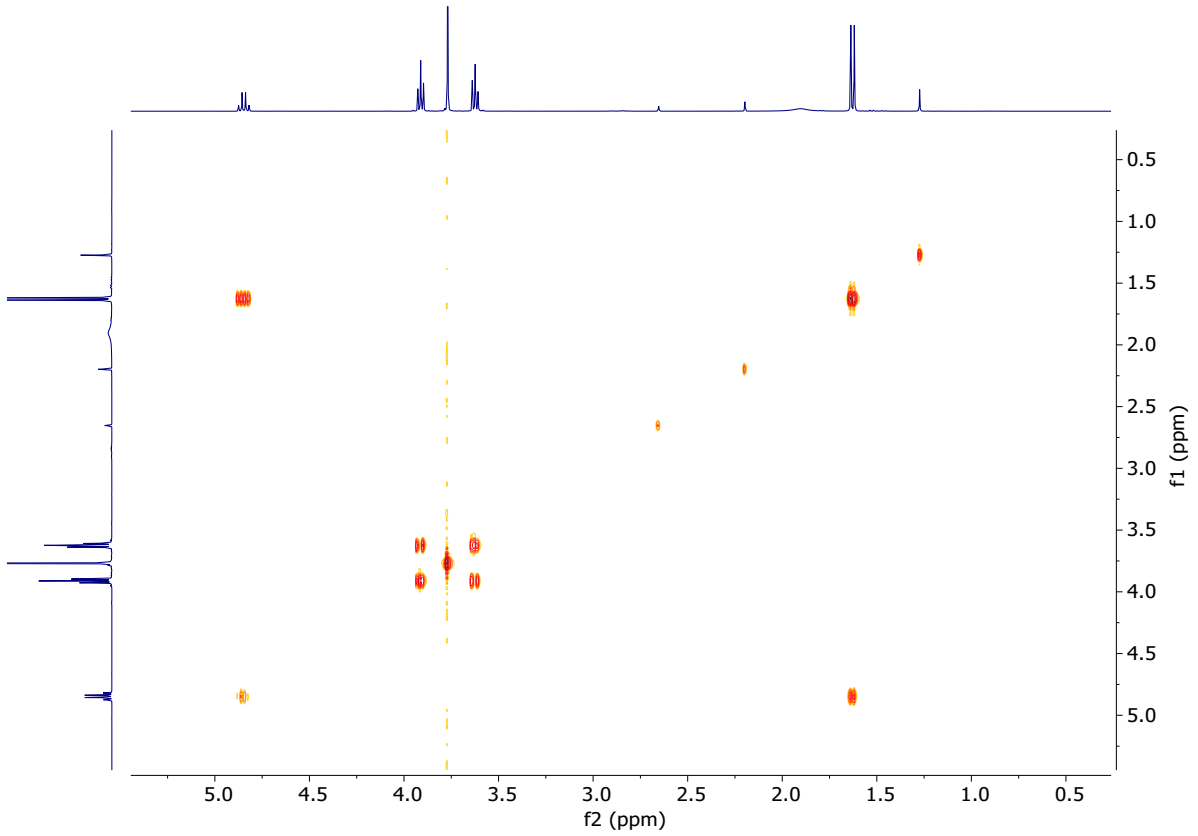


Figure S4. ^{1}H-^{1}H COSY NMR spectrum of methyl 2-((((2-hydroxyethyl)thio)carbonothioyl)thio)propanoate **(2)** in $CDCl_3$.

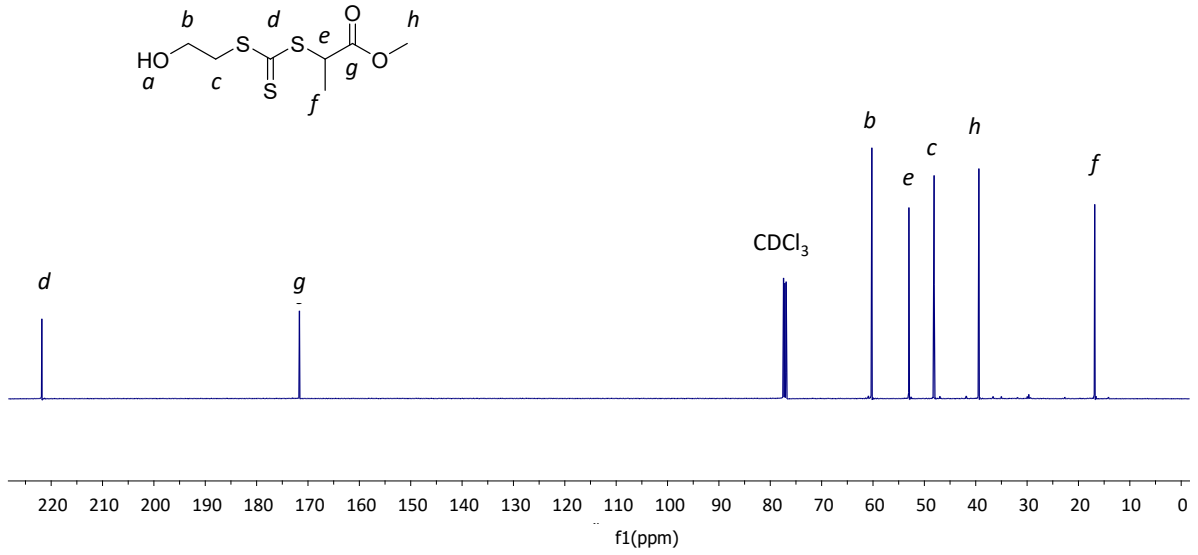


Figure S5. ^{13}C spectrum of methyl 2-((((2-hydroxyethyl)thio)carbonothioyl)thio)propanoate **(2)** in $CDCl_3$.

Dithiobis-2-hydroxyethyl carbonotrithioate disulfide (3). Sodium 2-hydroxyethyl carbonotrithioate intermediate **(1)** (3.07 g, 17.4 mmol) was dissolved in of water (100 mL) and solid $K_3Fe(CN)_6$ (6.31 g,

19.2 mmol) was slowly added. The reaction was stirred at ambient temperature for 30 minutes. The resulting reddish-orange viscous precipitate was extracted from the aqueous mixture with ethyl acetate (100 mL). The extraction process was repeated four times and the organic layers, combined, were dried over $MgSO_4$. The mixture was filtered, and the solvent was evaporated under reduced pressure to give **(3)** (1.14 g, 37.2 mmol, 43 %) as an orange viscous oil which was used for the next step without further purification.

^{1}H NMR (400 MHz, DMSO-d_6) δ 4.64 (t, *J* = 5.5 Hz, 2H, *H*OCH$_2$), 3.46 (q, 4H, HOC*H*$_2$), 3.11 (t, *J* = 7.2 Hz, 4H, CH$_2$C*H*$_2$S).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 221.6 (2C, SC(S)S), 57.7 (2C, HO*C*H$_2$CH$_2$SC(S)S), 41.4 (2C, HOCH$_2$*C*H$_2$SC(S)S).

ESI-TOF Mass spectrometry: expected m/z [M+Na]$^+$ 328.89, found 328.89 (39%).

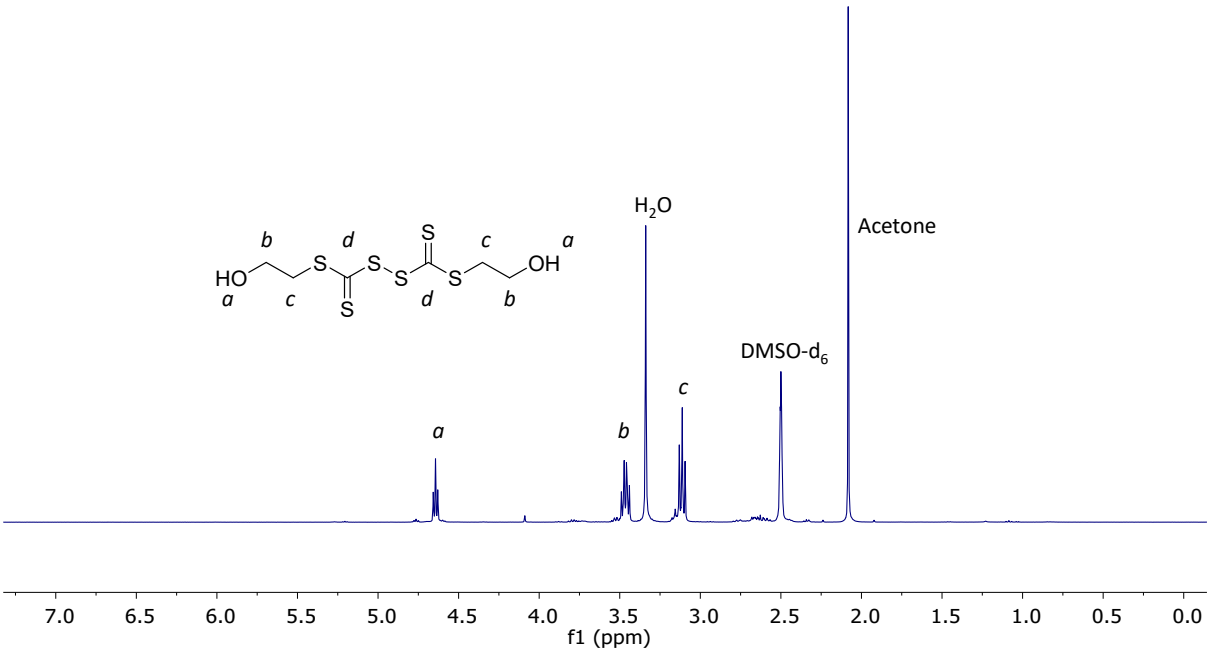


Figure S6. ^{1}H NMR spectrum of dithiobis-2-hydroxyethyl carbonotrithioate disulfide (**3**) in DMSO-d_6.

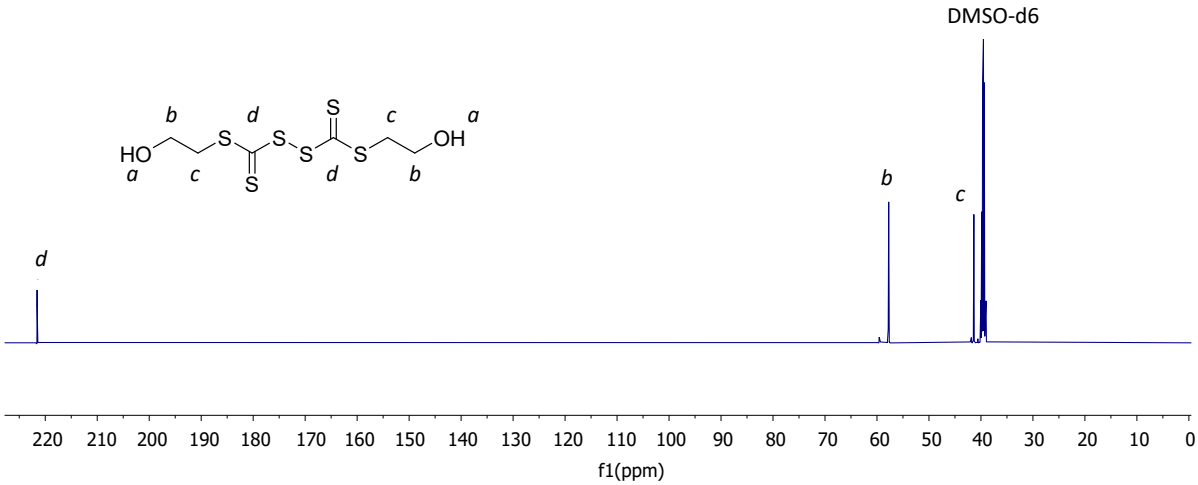


Figure S7. ^{13}C NMR spectrum of dithiobis-2-hydroxyethyl carbonotrithioate disulfide (**3**) in DMSO-d_6.

Sodium dodecyl carbonotrithioate (4). NaH (60% wt% in mineral oil, 3.26 g, 82.5 mmol) was dispersed in diethyl ether (150 mL) and cooled to 0°C in an ice bath. 1-Dodecanethiol (17.7 mL, 74.1 mmol) was added dropwise under stirring to the suspension and the resulting mixture was stirred for 12 hours at ambient temperature. Then CS_2 (13.4 mL, 222 mmol) was added dropwise to the suspension and the reaction was stirred at ambient temperature for further 12 hours. The resulting yellow precipitate was recovered by filtration, washed with diethyl ether, and finally desiccated under reduced pressure, to give the intermediate **(4)** (17.9 g, 59.4 mmol, 80%) which was used for the next step without further purification.

^{1}H NMR (400 MHz, DMSO-d_6) δ 2.98 (t, J = 7.3Hz, 2H, CH_2S), 1.50 (q, 2H, CH_2CH$_2$S), 1.24 (s, 18H, CH_2), 0.85 (t, *J* = 6.8 Hz, 3H, CH_2CH_3).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 239.9 (1C, SC(S)S), 39.5 (1C, CH_2S), 31.3 (1C, *C*H_2CH$_2$S), 29.1 (1C, CH_2), 29.0 (CH_2), 28.8 (1C, CH_2), 28.71 (CH_2), 28.7 (1C, CH_2), 22.1 (1C, CH_2), 14.0 (1C, CH_3).

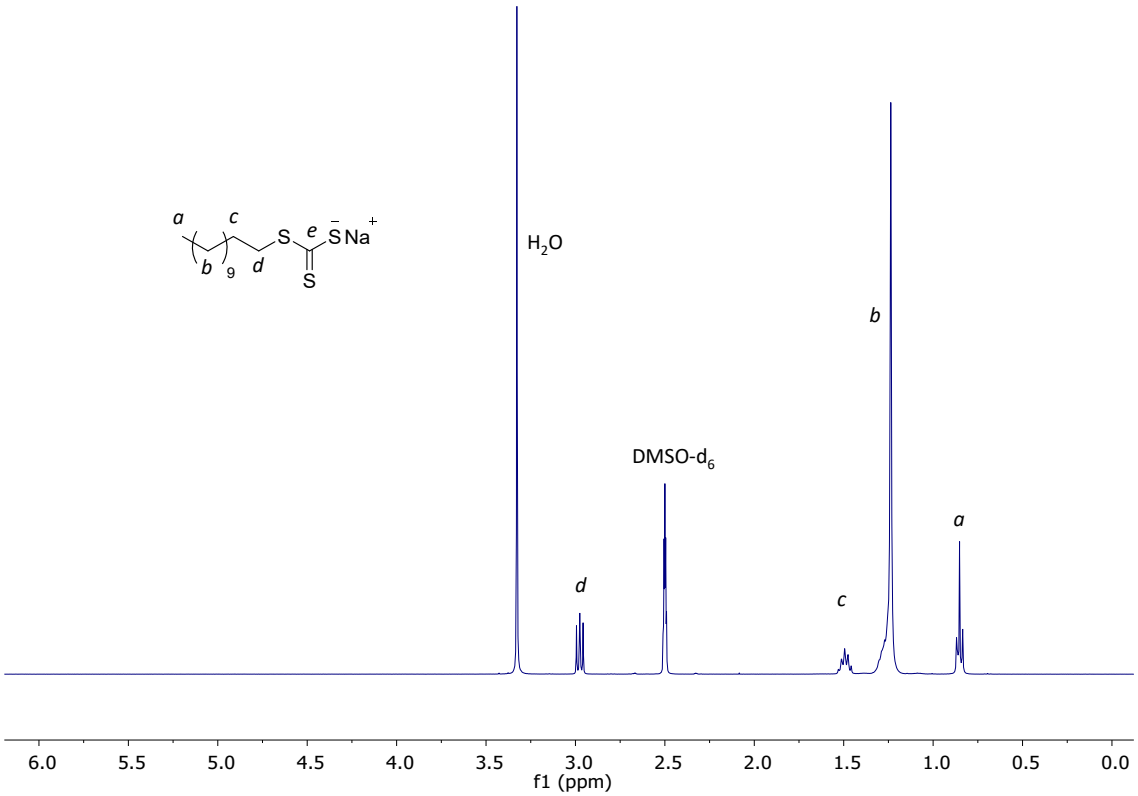


Figure S8. ^{1}H NMR spectrum of sodium dodecyl trithiocarbonate (**4**) in DMSO-d_6.

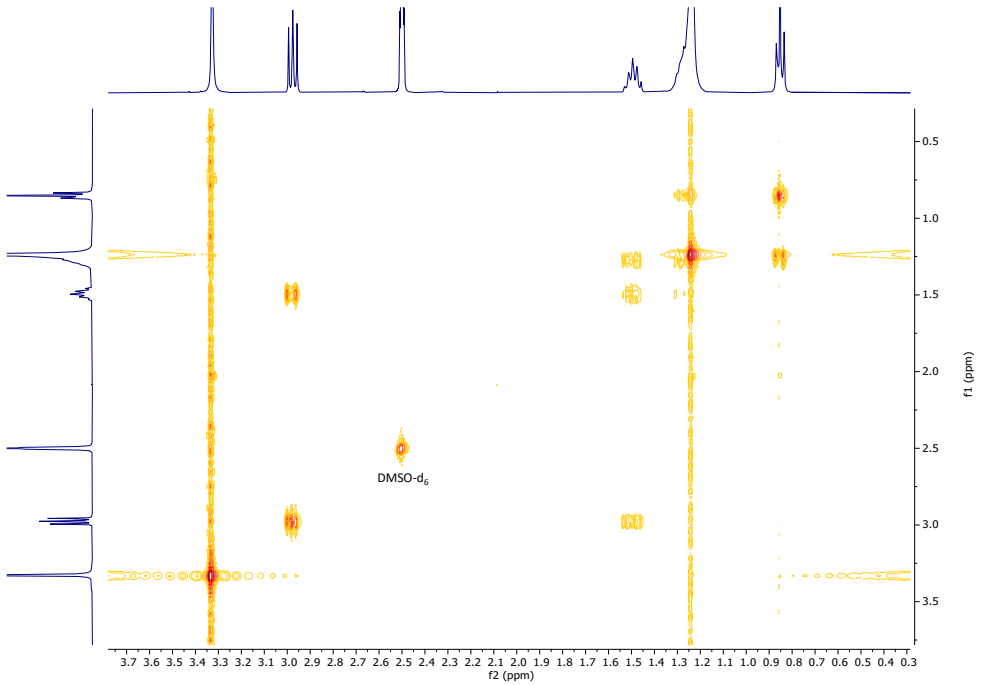


Figure S9. ^{1}H-^{1}H COSY NMR spectrum of sodium dodecyl carbonotrithioate (**4**) in DMSO-d_6.

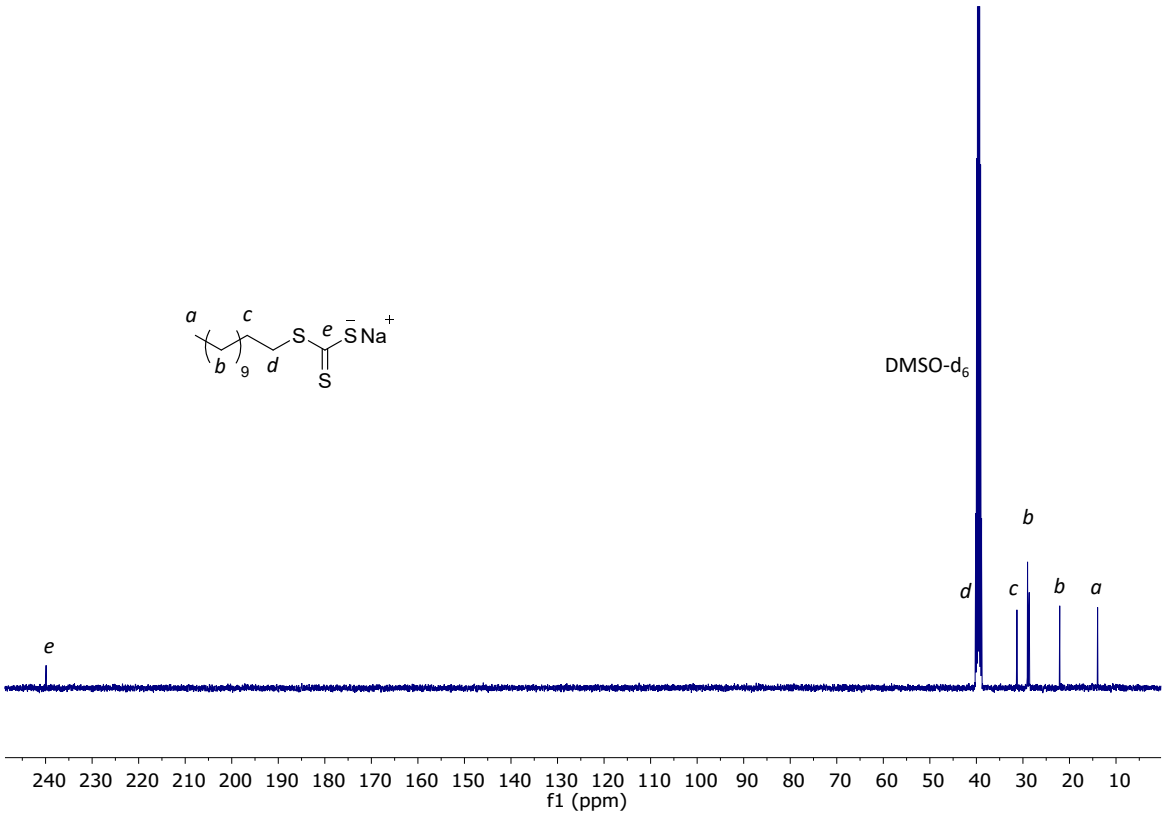


Figure S10. ^{13}C NMR spectrum of sodium dodecyl carbonotrithioate (**4**) in DMSO-d_6.

Methyl 2-(((dodecylthio)carbonothioyl)thio)propanoate (5). Sodium dodecyl trithiocarbonate **(4)** (1.49 g, 4.96 mmol) was dissolved in acetone (30 mL) and methyl-2-bromo-propionate (0.66 mL, 5.9 mmol) was added dropwise under stirring. After 12 hours the precipitated NaBr was filtered off and the solvent was removed under reduced pressure. The resulting residue was solubilised in chloroform (50 mL) and washed with water (3 x 50mL) and, finally with brine (50 mL). The organic layer was dried over $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to give an orange viscous residue which was purified by flash chromatography (silica gel 60, 35-70 um) using petroleum ether as the eluent (71.4 g, 3.85 mmol, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (d, *J* = 7.4 Hz, 1H, C*H*CH_3), 3.75 (s, 3H, OCH_3), 3.35 (t, *J* = 7.4 Hz, 2H, CH_2S), 1.69 (p, *J* = 7.3 Hz, 2H, C$H_2$$CH_2$S), 1.60 (d, *J* = 7.4 Hz, 3H, CHCH_3), 1.39 (m, 2H, CH_2), 1.26 (s, 16H, CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_2CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 222.2 (1C, SC(S)S), 171.8 (1C, CO), 53.0 (1C, OCH_3), 47.9 (1C, SCH), 37.4 (1C, CH_2S), 32.1 (1C, C$H_2$$CH_2$S), 29.7 (1C, CH_2), 29.6 (1C, CH_2), 29.5 (1C, CH_2), 29.2 (1C, CH_2), 29.1 (1C, CH_2), 28.0 (1C, CH_2), 27.5 (1C, CH_2), 23.42 (1C, CH_2), 22.8 (1C, CH_2), 17.1 (CHCH_3), 14.3 (1C, CH_2CH_3).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 387.14, found 387.14 (100%).

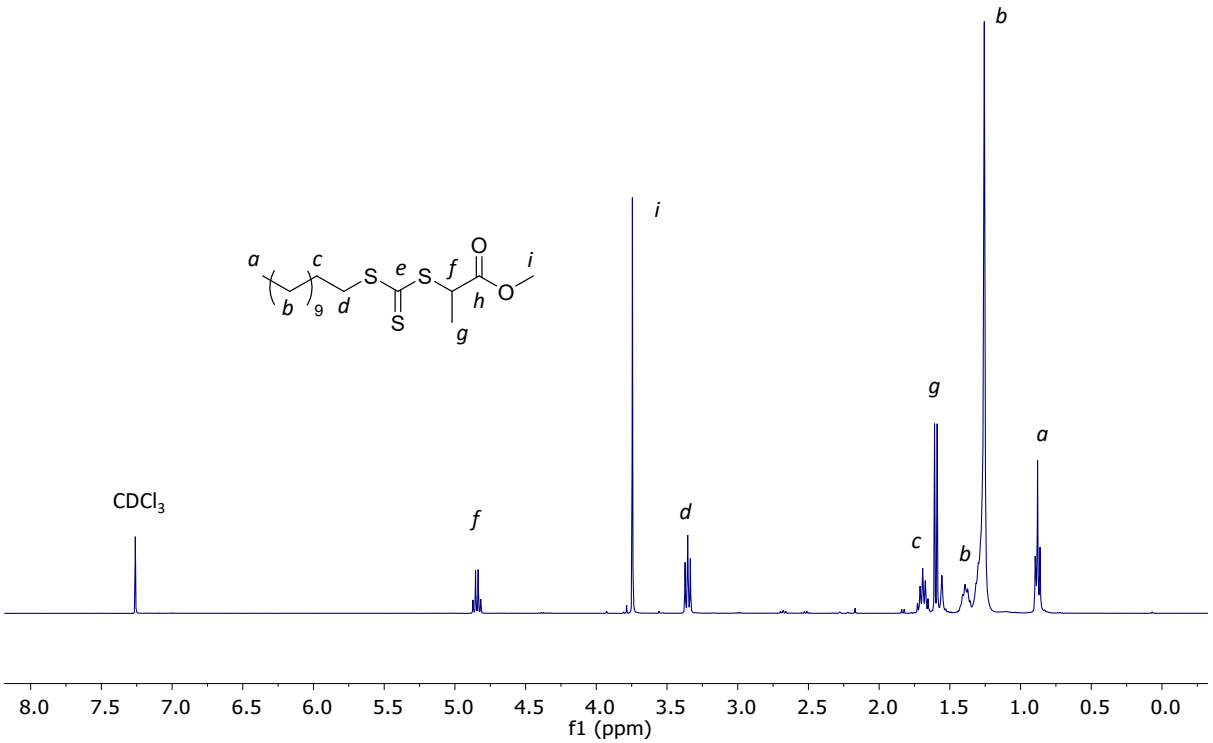


Figure S11. ^{1}H NMR spectrum of methyl 2-(((dodecylthio)carbonothioyl)thio)propanoate **(5)** in $CDCl_3$.

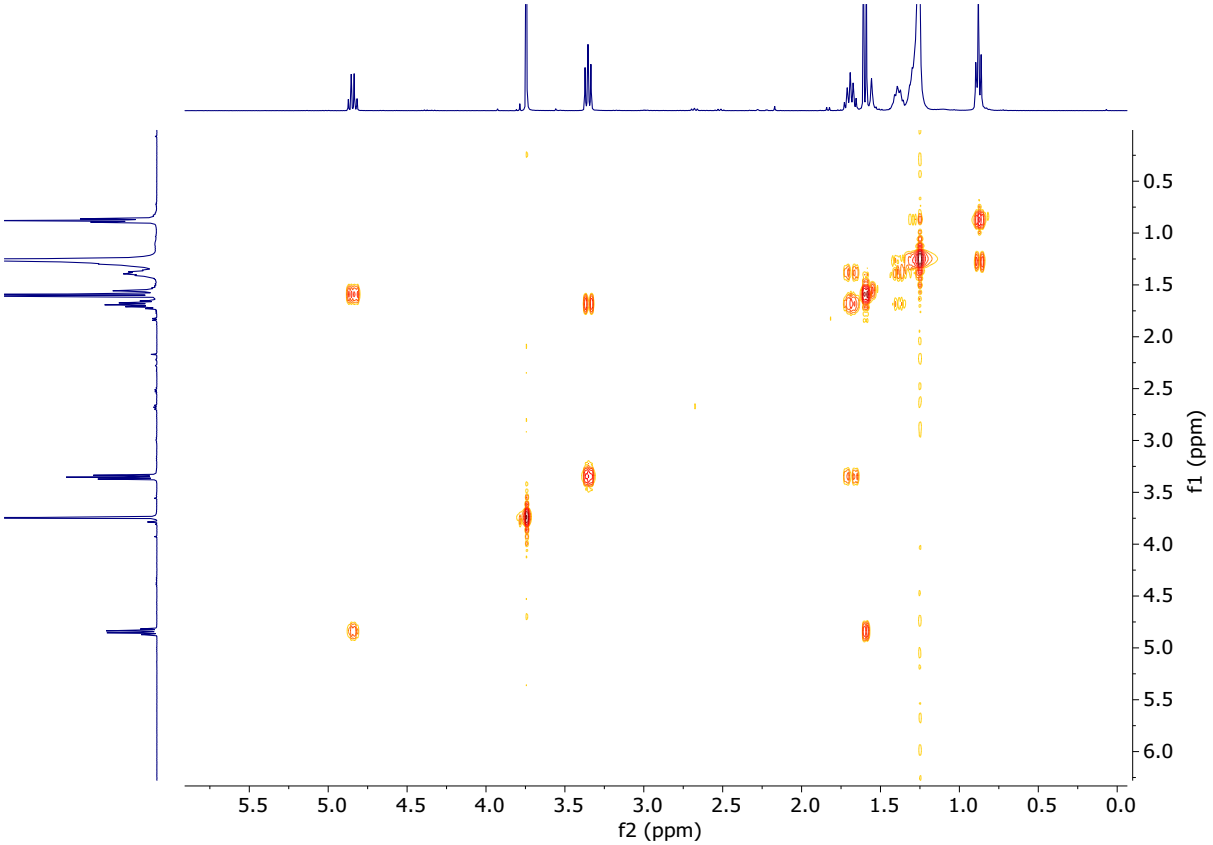


Figure S12. ^{1}H-^{1}H COSY NMR spectrum of methyl 2-(((dodecylthio)carbonothioyl)thio)propanoate **(5)** in $CDCl_3$.

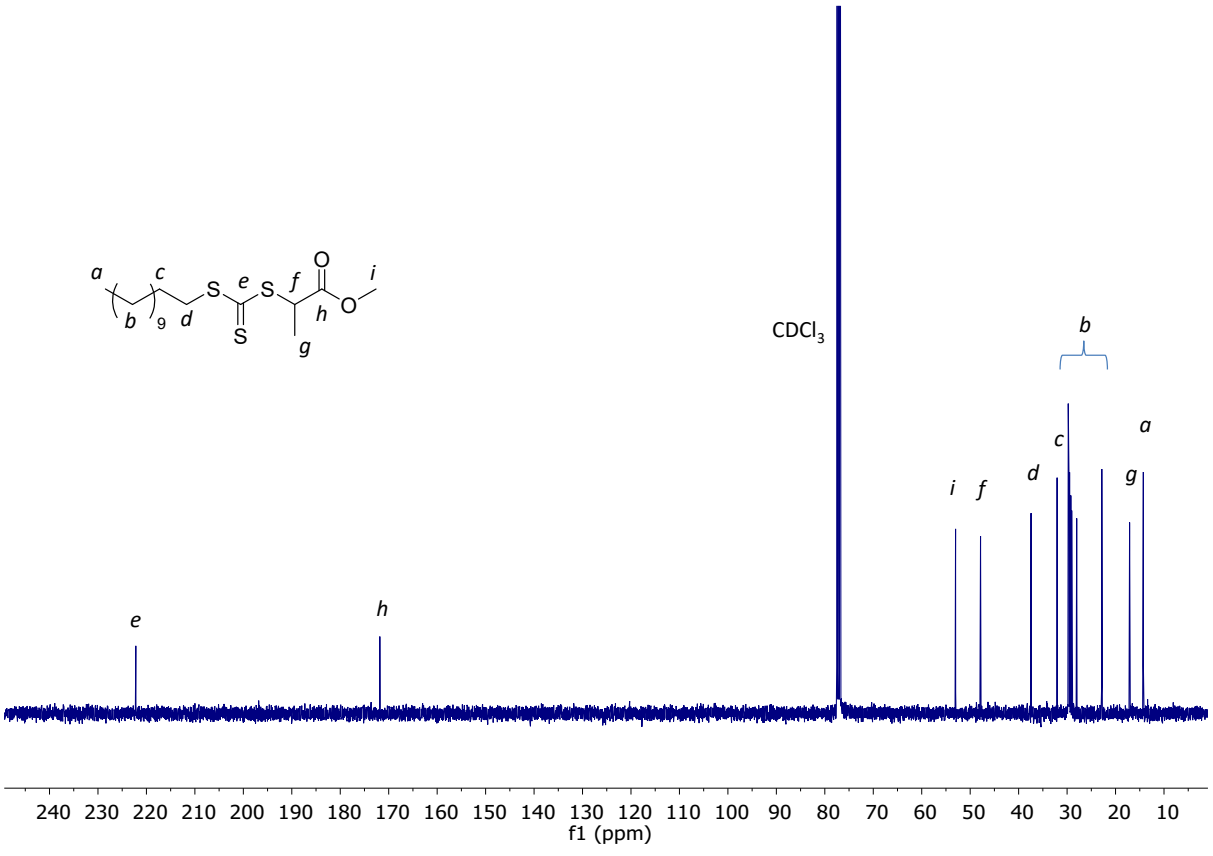


Figure S13. ^{13}C NMR spectrum of methyl 2-(((dodecylthio)carbonothioyl)thio)propanoate **(5)** in $CDCl_3$.

Dithiobis-2-dodecyl carbonotrithioate disulfide (6). Sodium dodecyl trithiocarbonate intermediate **(4)** (17.9 g, 59.4 mmol) was dissolved in diethyl ether (250 mL) and I_2 (8.40 g, 33.1 mmol) was slowly added over 10 minutes. The reaction was stirred at ambient temperature for 12 hours. The resulting dark solution was washed with 5% aqueous $Na_2S_2O_3$ (250 mL), water and finally with brine. The organic layer was dried over $MgSO_4$, filtered and the solvent evaporated under reduced pressure to give **(5)** (14.41 g, 25.95 mmol, 87 %) as an orange viscous oil which was used for the subsequent step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.32 (t, *J* = 7.4 Hz, 4H, C*H*$_2$S), 1.72 (4H, m, C*H*$_2$CH$_2$S), 1.42 (m, 4H, CH_2), 1.28 (s, 32H, CH_2), 0.90 (t, *J* = 6.6 Hz, 6H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 221.7 (2C, SC(S)S), 38.5 (2C, CH_2S), 32.1 (2C, *C*H$_2$CH$_2$S), 29.8 (2C, CH_2), 29,8 (2C, CH_2), 29.7 (2C, CH_2), 29.6 (2C, CH_2), 29.5 (2C, CH_2), 29.2 (2C, CH_2), 29.1 (2C, CH_2), 27.5 (2C, CH_2), 22.0 (2C, CH_2), 14.3 (1C, CH_3).

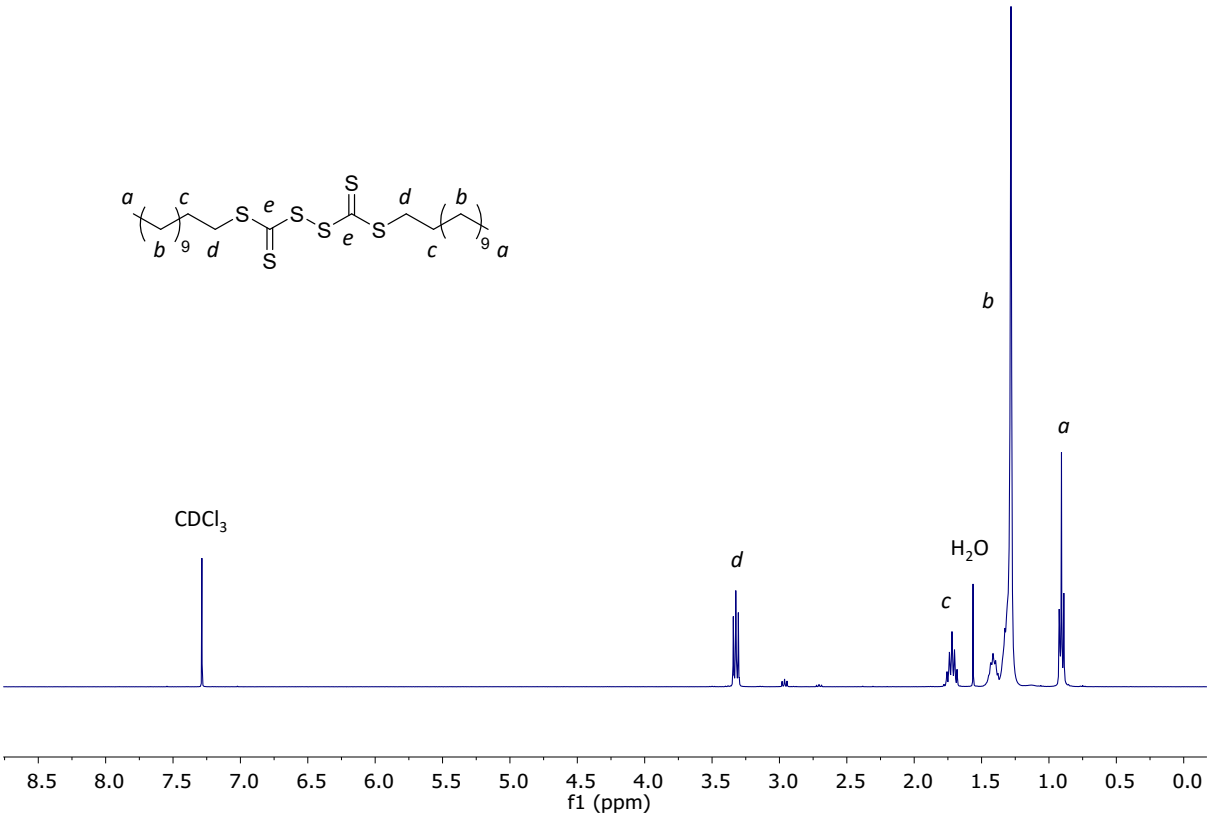


Figure S14. ^{1}H NMR spectrum of dithiobis-2-dodecyl carbonotrithioate disulfide **(6)** in $CDCl_3$.

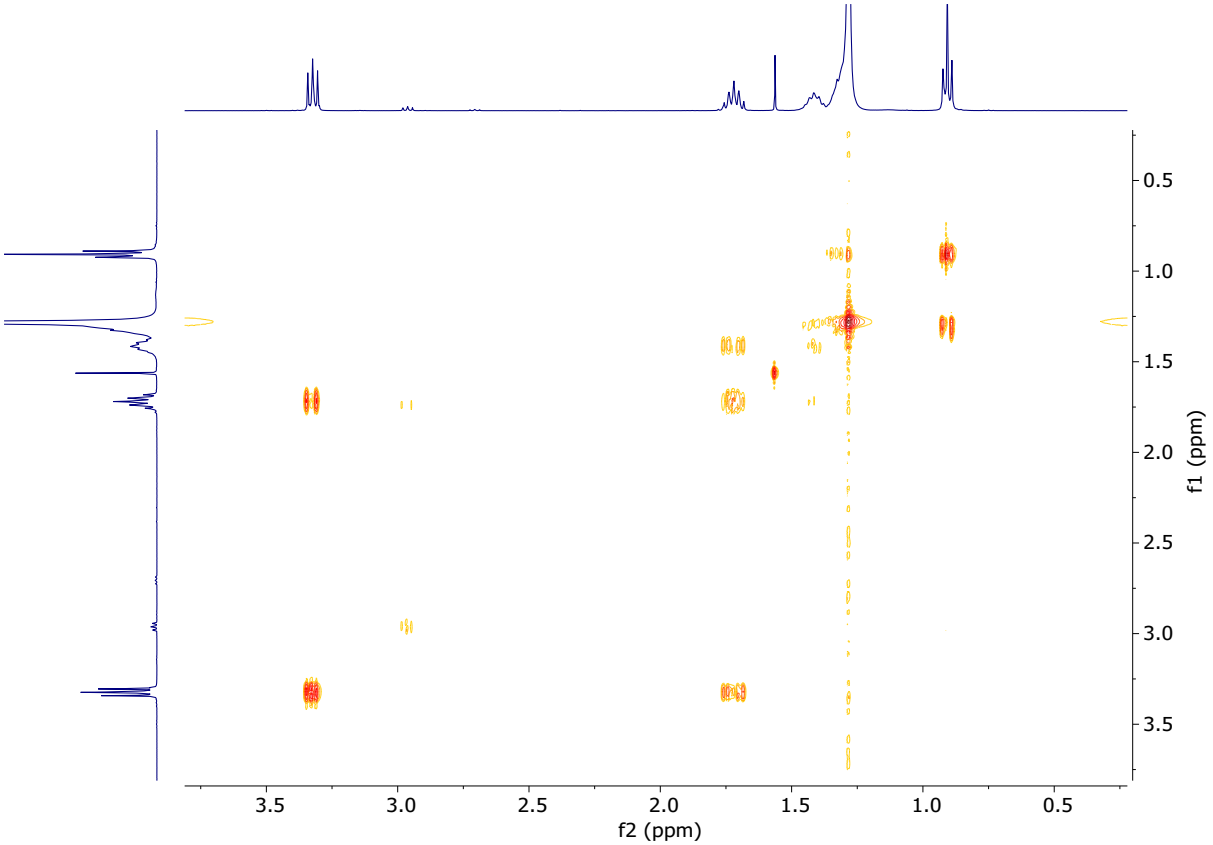


Figure S15. ^{1}H-^{1}H COSY NMR spectrum of dithiobis-2-dodecyl carbonotrithioate disulfide **(6)** in $CDCl_3$.

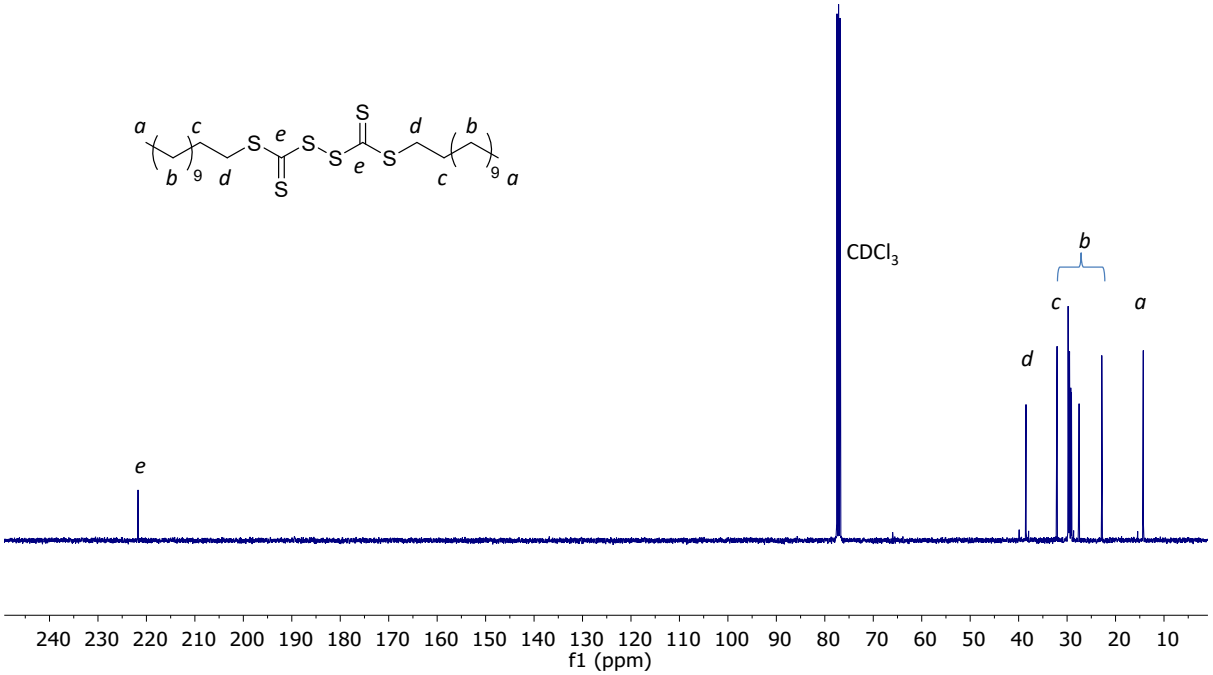


Figure S16. ^{13}C NMR spectrum of dithiobis-2-dodecyl carbonotrithioate disulfide **(6)** in $CDCl_3$.

2-Cyanopropan-2-yl dodecyl carbonotrithioate (7). Dithiobis-2-dodecyl carbonotrithioate disulfide **(6)** (7.60 g, 13.7 mmol) was dissolved in ethyl acetate (50 mL) in a three neck round bottom flask equipped with a condenser. Azobisisobutyronitrile (AIBN) (2.65 g, 16.1 mmol) was added to the reaction mixture. The reactor was sealed, cooled to 0°C in an ice bath and degassed with argon for 40 minutes. The reaction was then heated at 77°C and left to react for 48 hours. The solvent was evaporated under reduced pressure to give an orange viscous oil which was purified by flash chromatography (silica gel 60, 35-70 um) using petroleum ether/ethyl acetate (10:0 to 9.5:0.5 vol/vol) as the eluent (6.24 g, 18.0 mmol, 66%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.33 (t, *J* = 7.4 Hz, 2H, CH_2CH_2S), 1.87 (s, 6H, $C(CH_3)_2$), 1.69 (m, 2H, CH_2CH_2S), 1.40 (m, 2H, CH_2), 1.26 (s, 16H, CH_2), 0.89 (t, *J* = 6.6 Hz, 3H, CH_2CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 218.0 (1C, SC(S)S), 120.6 (1C, CN), 43.0 (1C, $SC(CH_3)_2$, 37.9 (1C, SCH_2CH_2), 32.1 (1C, SCH_2CH_2), 29.8 (1C, CH_2), 29.7 (1C, CH_2), 29.6 (1C, CH_2), 29.5 (1C, CH_2), 29.2 (1C, CH_2), 29.1 (1C, CH_2), 27.9 (1C, CH_2), 27.2 (1C, CH_2), 22.8 (1C, CH_2), 14.3 (1C, CH_2CH_3).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 368.15, found 368.15 (48.2%).

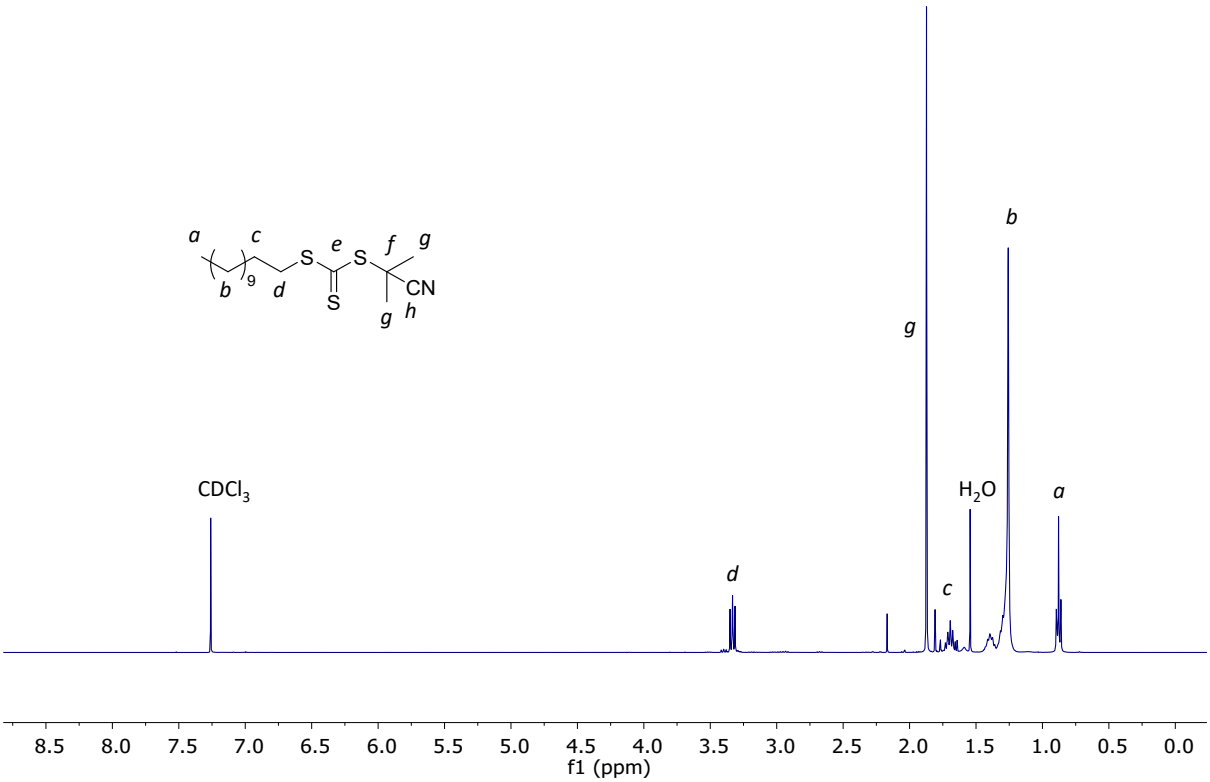


Figure S17. ^{1}H NMR spectrum of 2-cyanopropan-2-yl dodecyl carbonotrithioate **(7)** in $CDCl_3$.

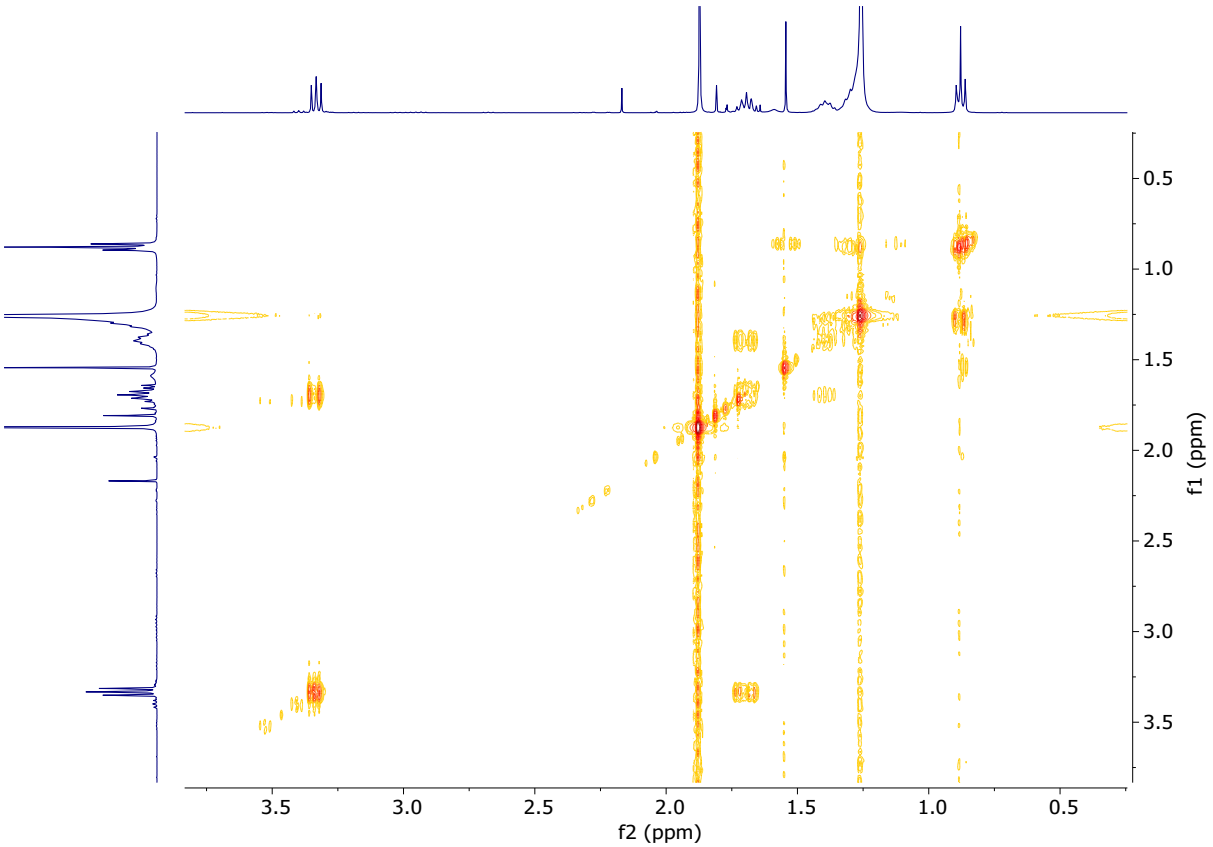


Figure S18. ^{1}H-^{1}H COSY NMR spectrum of 2-cyanopropan-2-yl dodecyl carbonotrithioate **(7)** in $CDCl_3$.

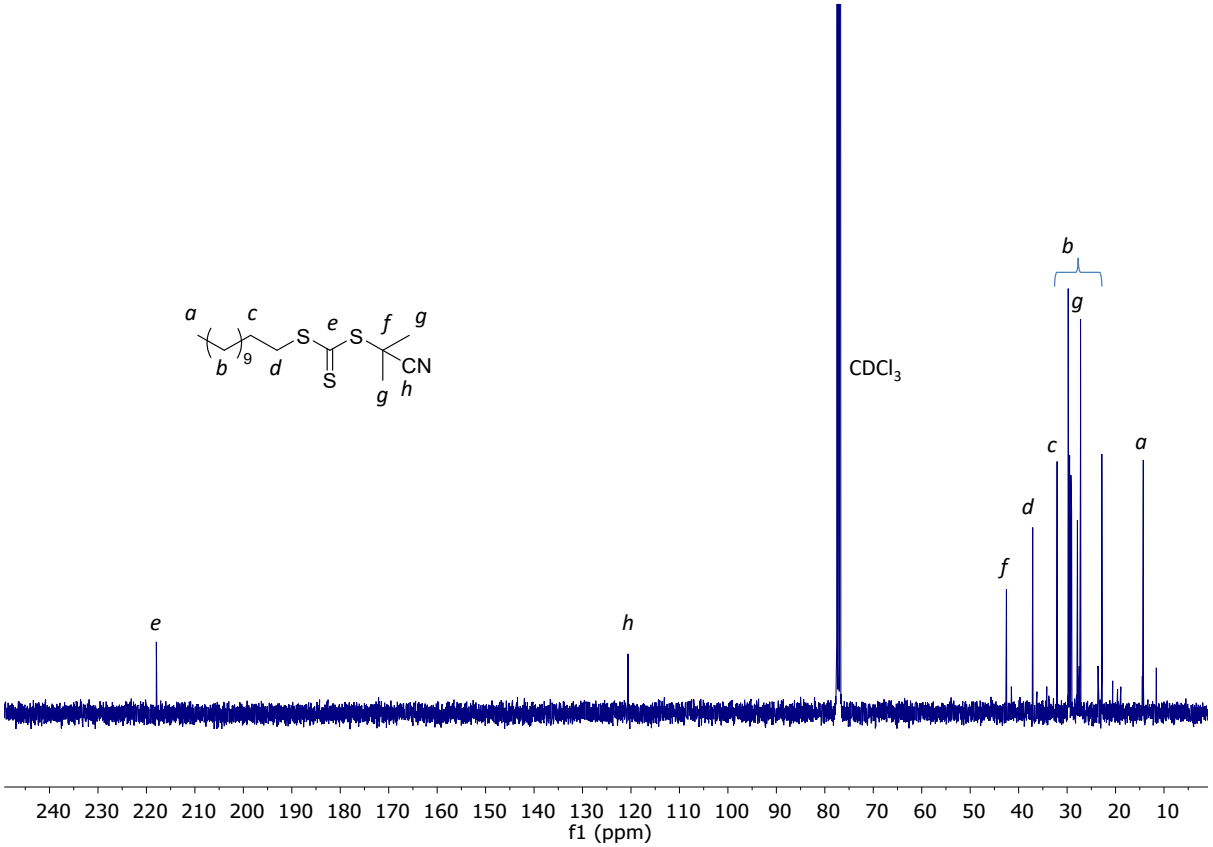
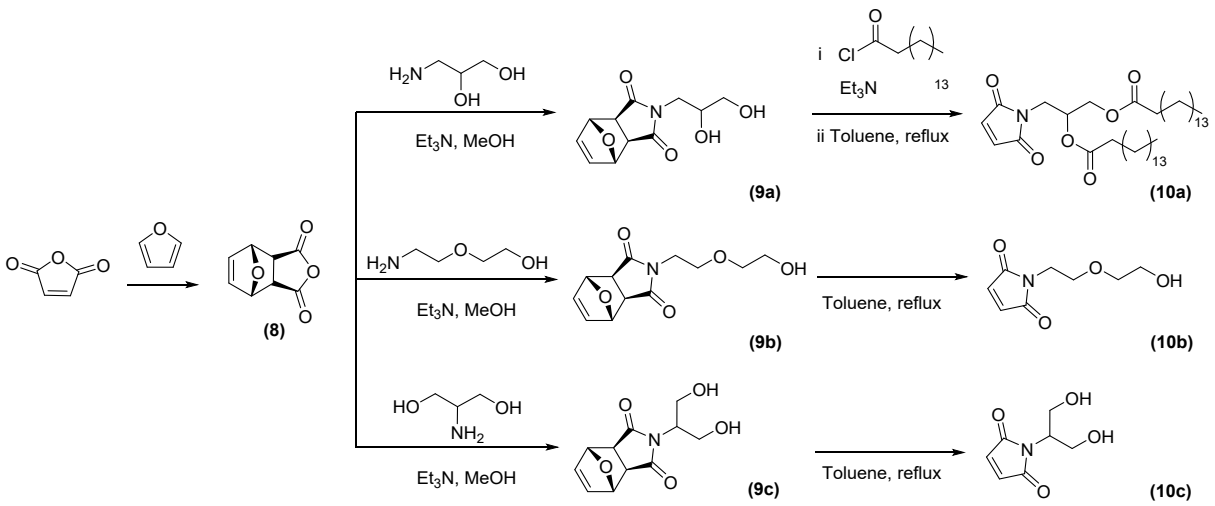


Figure S19. ^{13}C NMR spectrum of 2-cyanopropan-2-yl dodecyl carbonotrithioate (**7**) in $CDCl_3$.

Synthesis of maleimides (B).



Scheme S2. Synthesis of maleimide intermediates **(B)**.

3a,4,7,7a-tetrahydro-4,7-epoxyisobenzofuran-1,3-dione (8). Intermediate **(8)** was synthesised as described by Bolm *et al*.[2] Maleic anhydride (30.0 g, 306 mmol) was suspended in toluene (150 mL) and the suspension was heated at 80°C. Furan (33.5 mL, 459 mmol) was slowly added via syringe and the mixture was left to react under reflux in an oil bath at 80°C for 6 hours. The reaction mixture was then cooled down to ambient temperature and the resulting white crystals were collected by filtration and washed twice with petroleum ether (2 x 60 mL), to give the anhydride **(8)** as a white solid (45.2 g, 272 mmol, 89%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (t, J= 3.4 Hz, 2H, C*H*=C*H*), 5.43-5.54 (m, 2H, CH-O), 3.15 (dd, J=5.3, 2.6 Hz, 2H, CH).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.0 (2C, CO), 137.1 (2C, *C*H=*C*H), 82.2 (2C, CH-O), 48.9 (2C, CH).

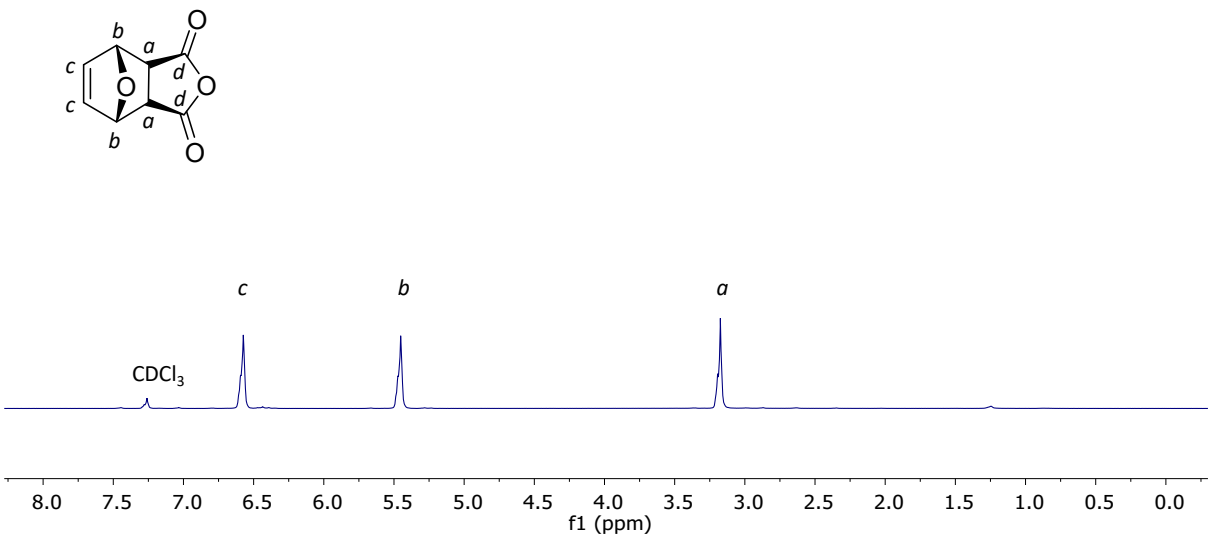


Figure S20. ^{1}H NMR spectrum of 3a,4,7,7a-tetrahydro-4,7-epoxyisobenzofuran-1,3-dione **(8)** in $CDCl_3$.

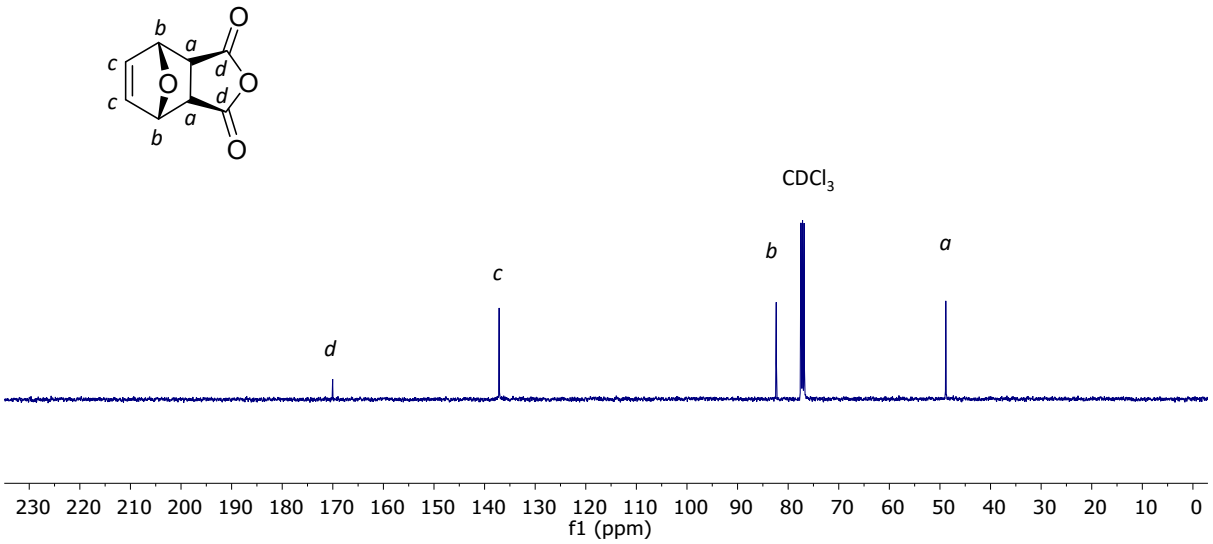


Figure S21. ^{13}C NMR spectrum of 3a,4,7,7a-tetrahydro-4,7-epoxyisobenzofuran-1,3-dione **(8)** in $CDCl_3$.

General procedure for the synthesis of intermediates (9a), (9b) and (9c).

Anhydride **(8)** was suspended in methanol and the mixture cooled at 0°C. A solution of the desired amino-alcohol and triethylamine were added dropwise to the reactor over a period of 30 minutes at a temperature of 0-2°C. After this period, the temperature of the heating block was steadily increased to 70°C and the reaction mixture was stirred at this temperature for 12-18 hours. The reactions mass was then filtered, and the solvent was removed under reduced pressure.

The reaction conditions utilised for the synthesis and purification of each intermediate are described below:

(3aR,4R,7R,7aS)-2-(2,3-dihydroxypropyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (9a). Anhydride **(8)** (10.6 g, 63.8 mmol), methanol (350 mL), 3-amino-1,2-propanediol (6.0 mL, 77 mmol), triethylamine (10.3 mL, 71.9 mmol), 70°C for 12 hours. The reaction mass was then filtered, and the solvent removed under reduced pressure, to give **(9a)** (9.53 g, 39.9 mmol, 62.5% yield).
^{1}H NMR (400 MHz, DMSO-d_6) δ 6.55 (t, *J* = 1.0 Hz, 2H, C*H*C*H*), 5.12 (t, *J* = 1.0 Hz, 2H, CHO), 4.78 (d, *J* = 5.3 Hz, 1H, CHO*H*), 4.57 (t, *J* = 5.7 Hz, 1H, CH_2O*H*), 3.60-3.70 (m, 1H, C*H*OH), 3.35 (d, *J* = 1.9 Hz, 2H, CH_2N), 3.26 (t, *J* = 5.6 Hz, 2H, CH_2OH), 2.91 (q, *J* = 2.6 Hz, 2H, CHCO).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 176.6 (2C, CO), 136.4 (2C, *C*H*C*H), 80.3 (2C, CHO), 68.1 (1C, CHOH), 63.9 (1C, CH_2OH), 47.7 (2C, CHCO), 42.3 (1C, CH_2N).

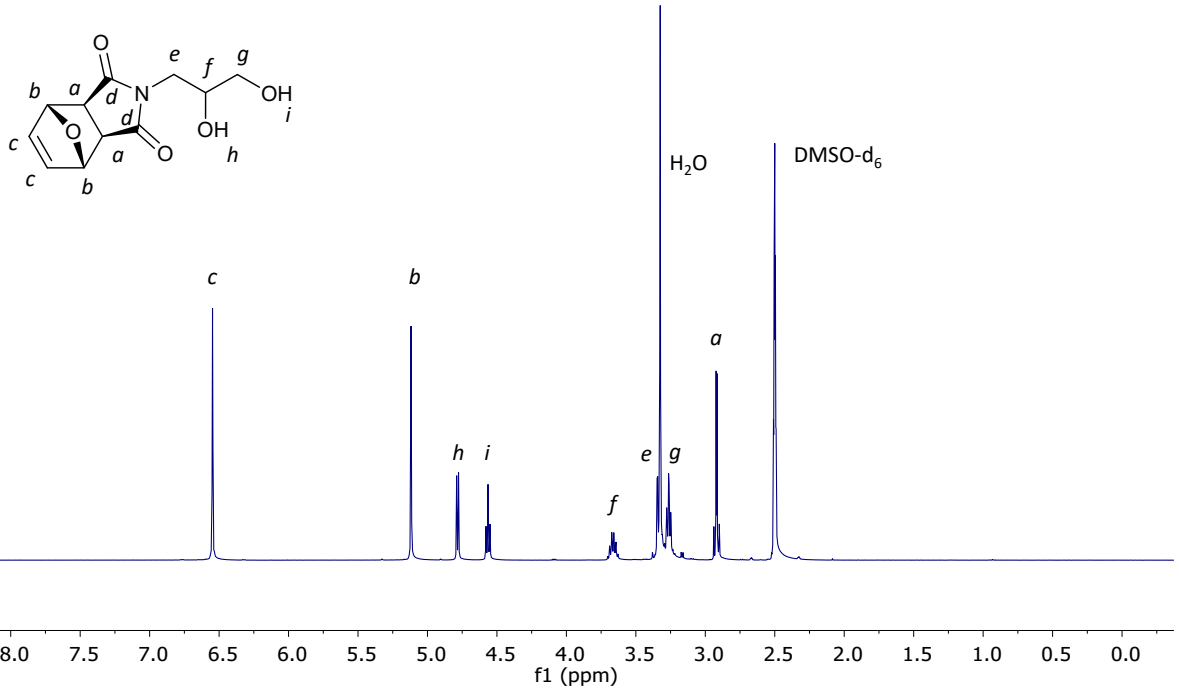


Figure S22. ^{1}H NMR spectrum of (3aR,4R,7R,7aS)-2-(2,3-dihydroxypropyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9a)** in DMSO-d_6.

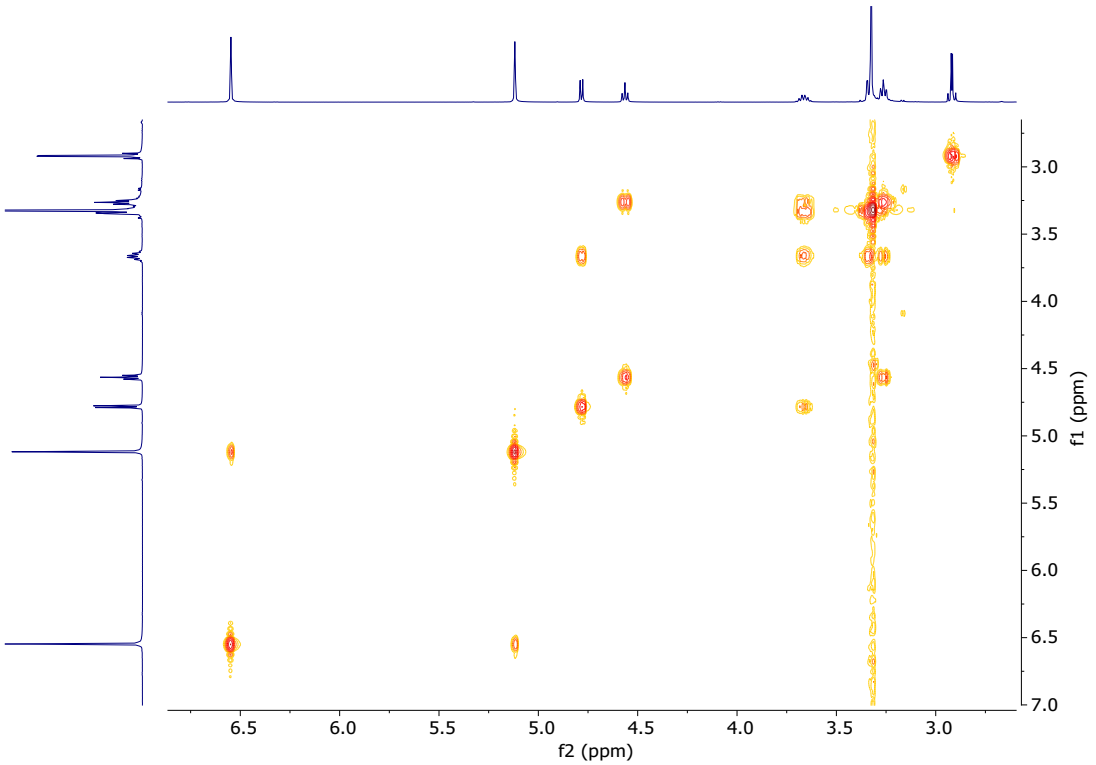


Figure S23. ^{1}H-^{1}H COSY NMR spectrum of (3aR,4R,7R,7aS)-2-(2,3-dihydroxypropyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9a)** in DMSO-d_6.

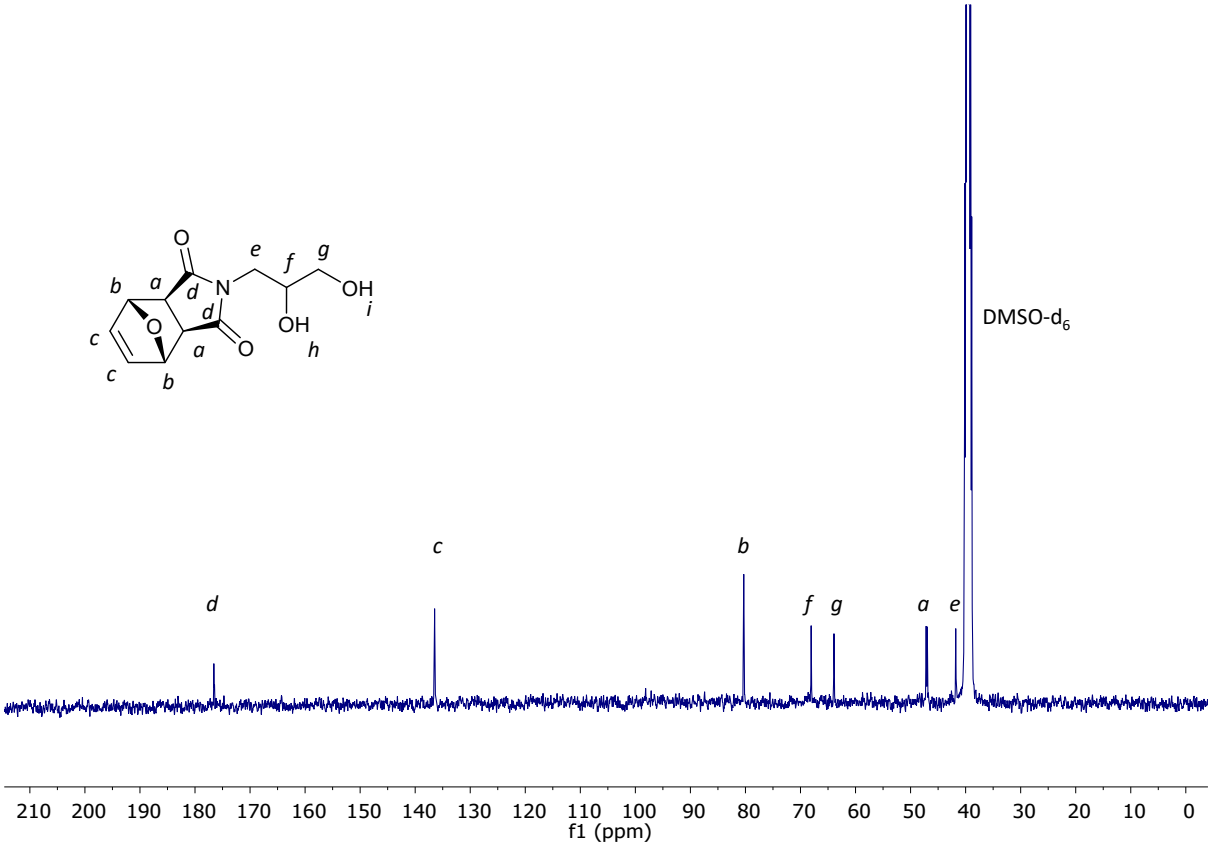


Figure S24. ^{13}C NMR spectrum of (3aR,4R,7R,7aS)-2-(2,3-dihydroxypropyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9a)** in DMSO-d_6.

2-(2-(2-hydroxyethoxy)ethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (9b).

Anhydride **(8)** (23.09 g, 139.0 mmol), methanol (100 mL), 2-(2-aminoethoxy)ethanol (17.54 g, 116.8 mmol), triethylamine (19.4 g, 139 mmol), 70°C for 18 hours. The crude product was purified via flash chromatography (silica gel 60, 35–70 µm, eluents ethyl acetate /methanol, gradient 9:1 to 1:1, vol/vol) to give **(9b)** as a white solid (20.07 g, 79.31 mmol, 57%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (s, 2H, C*H*=C*H*), 5.20 (s, 2H, C*H*OC*H*), 3.63 (t, *J* = 5.5 Hz, 2H, $NCH_2CH_2OCH_2CH_2OH$), 3.56 (t, *J* = 5.0 Hz, 4H, $NCH_2CH_2OCH_2CH_2OH$), 3.45 (t, *J* = 4.0 Hz, 2H, $NCH_2CH_2OCH_2CH_2OH$), 2.80 (s, 2H, CHCO), 2.74 (bs, 1H, OH).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 176.4 (2C, CO), 136.5 (2C, *C*H*C*H), 80.3 (2C, CHO), 71.9 (1C, OCH_2CH_2OH), 66.3 (1C, NCH_2CH_2O), 60.1 (1C, OCH_2CH_2OH), 47.1 (2C, CHCH), 37.6 (1C, NCH_2CH_2O).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 276.08, found 276.08 (100%).

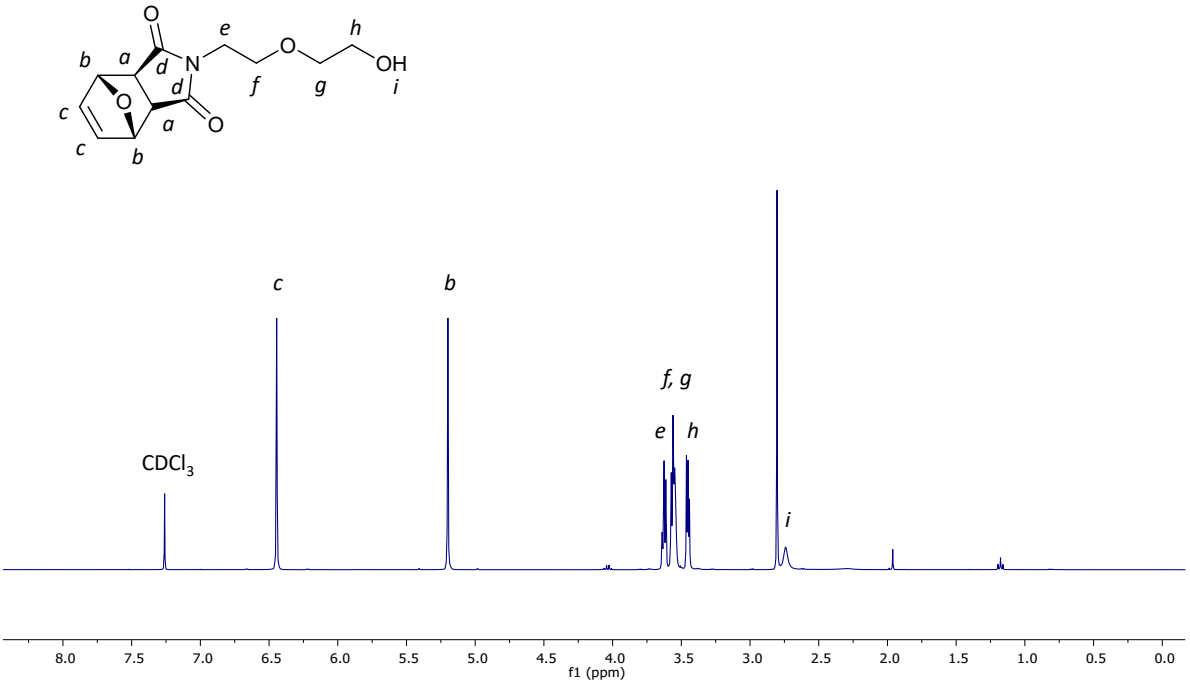


Figure S25. ^{1}H NMR spectrum of 2-(2-(2-hydroxyethoxy)ethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9b)** in $CDCl_3$.

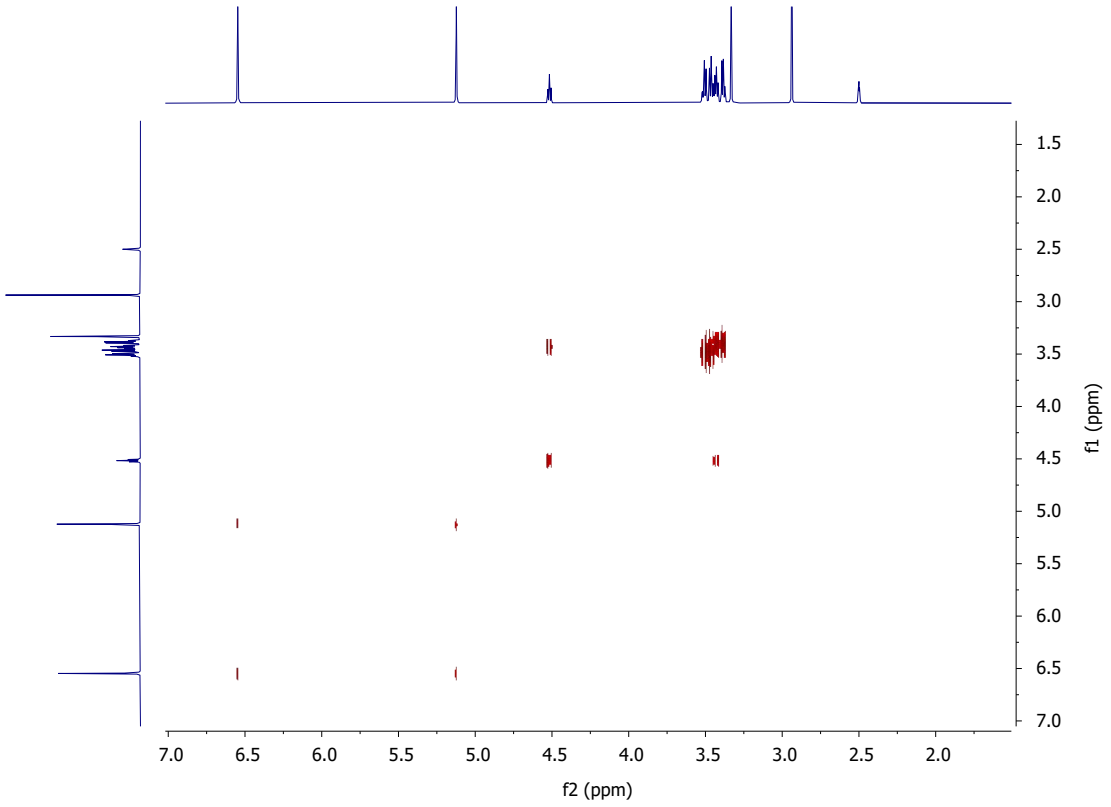


Figure S26. ^{1}H-^{1}H COSY NMR spectrum of 2-(2-(2-hydroxyethoxy)ethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9b)** in DMSO-d_6.

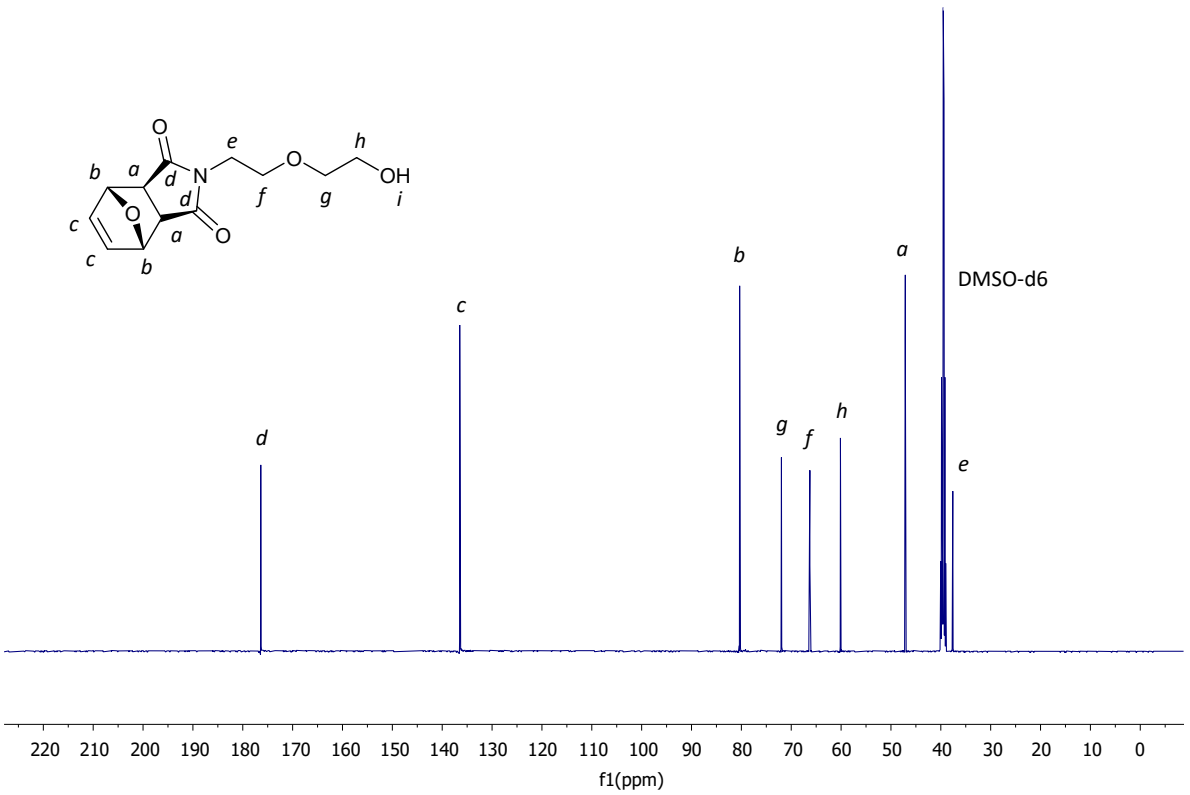


Figure S27. ^{13}C NMR spectrum of 2-(2-(2-hydroxyethoxy)ethyl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione (**9b**) in DMSO-d_6.

2-(1,3-dihydroxypropan-2-yl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9c).** Anhydride **(8)** (11.5 g, 69.3 mmol), methanol (50 mL), 2-amino-1,3-propanediol (6.31 g, 69.3 mmol), triethylamine (7.01 g, 69.3 mmol), 67°C for 18 hours. The crude product was purified by flash chromatography (silica gel 60, 35–70 µm, eluents ethyl acetate /methanol, gradient 9:1 to 1:1, vol/vol) to give **(9c)** as a white solid (10.1 g, 42.2 mmol, 61%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 6.54 (t, *J* = 0.9 Hz, 2H, C*H*C*H*), 5.10 (t, *J* = 0.9 Hz, 2H, CHO), 4.76 (t, *J* = 5.8 Hz, 2H, OH), 4.01 (p, *J* = 7.0 Hz, 1H, CH), 3.60 (t, 4H, *J* = 6.3 Hz, CH_2), 2.87 (s, 2H, C*H*CO).

^{13}C {^{1}H} NMR (101 MHz, DMSO-d_6) δ 176.9 (2C, CO), 136.5 (2C, *C*H*C*H), 80.4 (2C, *C*HO), 58.1 (2C, *C*H_2OH), 56.8 (1C, CHN), 46.9 (2C, *C*HCO).

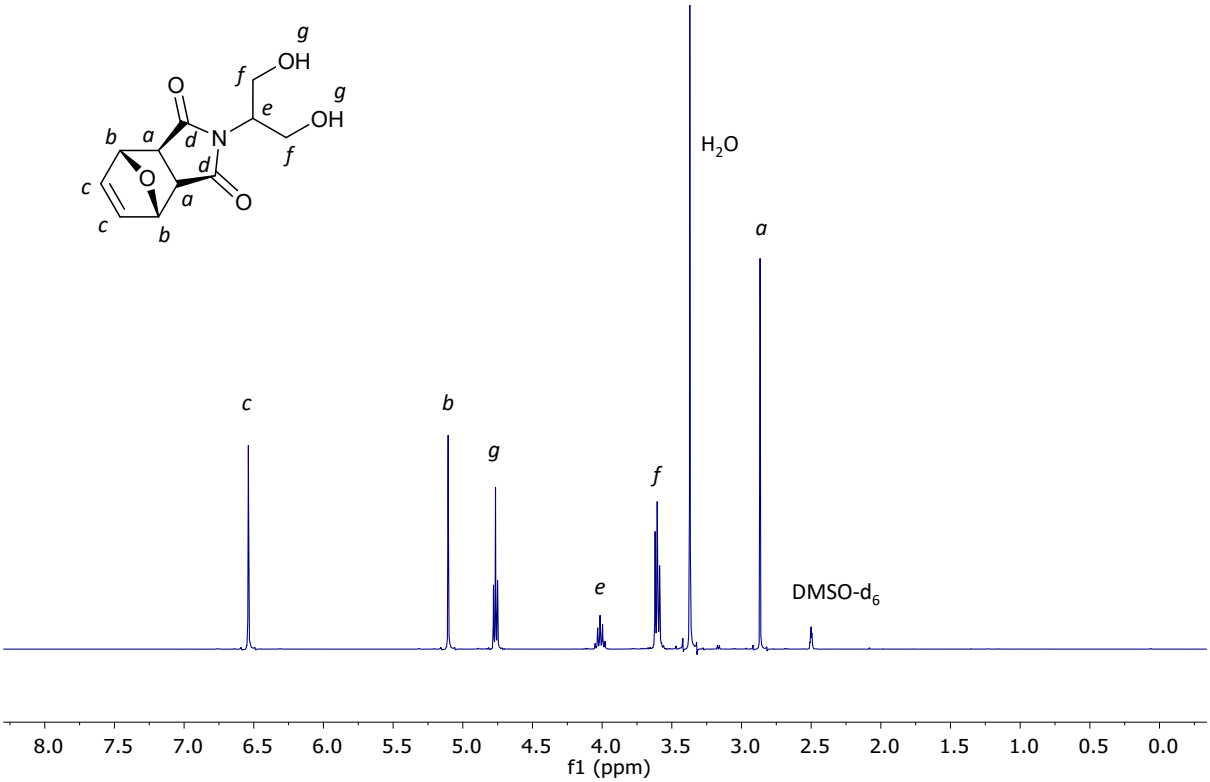


Figure S28. ^{1}H NMR spectrum of 2-(1,3-dihydroxypropan-2-yl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9c)** in DMSO-d_6.

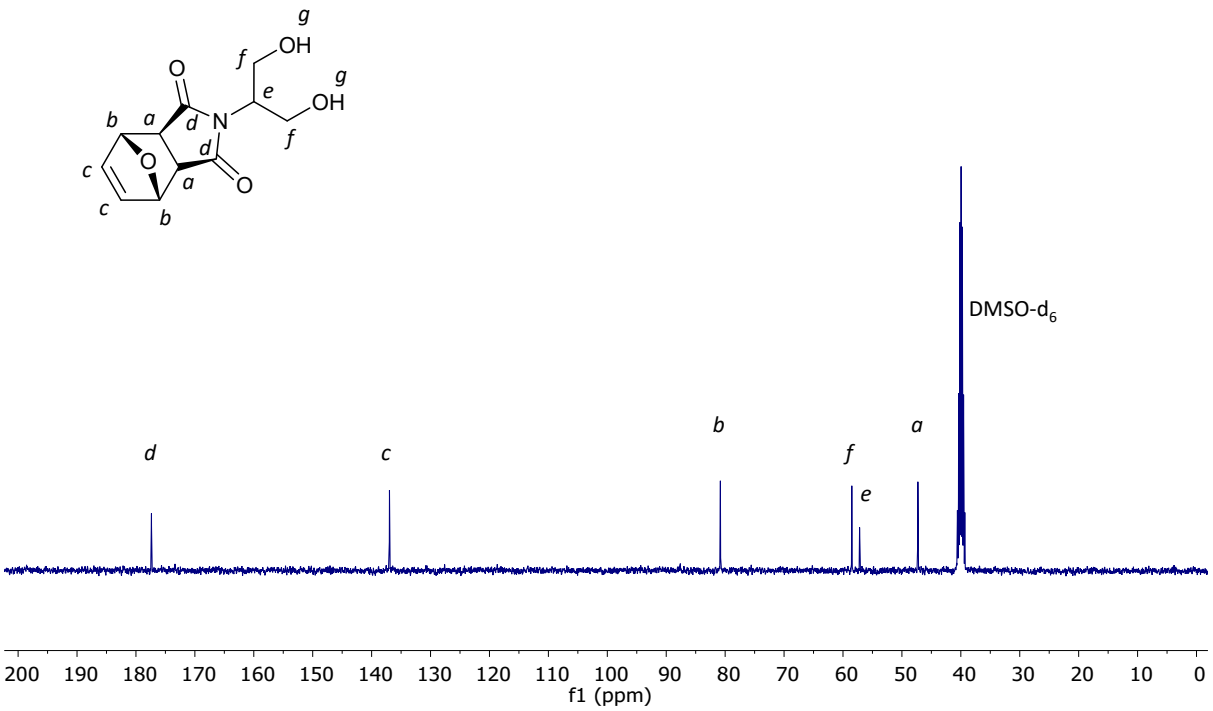


Figure S29. ^{13}C NMR spectrum of 2-(1,3-dihydroxypropan-2-yl)-3a,4,7,7a-tetrahydro-1H-4,7-epoxyisoindole-1,3(2H)-dione **(9c)** in DMSO-d_6.

3-((3aR,4R,7R,7aS)-1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2H-4,7-epoxyisoindol-2-yl) propane-1,2-diyl dipalmitate (10a1). Compound **(9a)** (4.80 g, 19.9 mmol) was dissolved in dichloromethane (25 mL). A solution of palmitoyl chloride (15.1 mL, 49.8 mmol) in dichloromethane (20 mL) was added to the reactor. The resulting solution was cooled to 0°C and triethylamine (8.3 mL, 60 mmol) was then added dropwise at to the stirred solution and left overnight at room temperature. NMR analysis of an aliquot taken from the reaction mixture showed that the reaction was not complete. To push the reaction to higher conversion, (dimethyl-amino)pyridine (DMAP) (4.00 g, 39.9 mmol) organocatalyst was then added, along with more palmitoyl chloride (6.04 mL, 19.9 mmol), and the reaction stirred overnight at room temperature. Methanol (20 mL) was added dropwise at 0°C to convert the excess of acid chloride into the corresponding methyl ester and facilitate its subsequent removal. The volume of the reaction mixture was reduced under reduced pressure and the resulting semi-solid mass added of diethyl ether (500 mL). The resulting slurry was filtered and washed with more diethyl ether (60 mL), and the solvent was removed from the combined diethyl ether solutions under reduced pressure, and the solid residue was purified by silica column chromatography (gradient of diethyl ether: petroleum ether from 40:60 to 60:40 vol/vol). **(10a1)** was isolated as a white solid (6.6 g, 9.2 mmol, 46% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (t, *J* = 1.0 Hz, 2H, C*H*C*H*), 5.22 (m, 1H, NCH_2CH), 5.18 (m, 2H, C*H*OC*H*), 4.10 (m, 2H, NCH_2CHCH_2O), 3.72 (m, 2H, NCH_2), 2.78 (dd, *J* = 17.3, 6.5 Hz, 2H, CHCO), 2.22 (dt, *J* = 23.8, 6.5 Hz, 4H, CH_2CO), 1.51 (m, 4H, CH_2), 1.22 (m, 48H, CH_2), 0.80 (t, *J* = 7.0 Hz, 6H, CH_3),

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) 175.9 (2C, CO). 173.3 (2C, CO_{ester}), 136.6 (2C, *C*HC*H*), 81.0 (2C, CHO), 68.3 (1C, CHO), 62.7 (1C, CH_2O), 47.4 (2C, *C*HCO), 39.1 (1C, CH_2N), 31.9 (1C, CH_2CO), 34.1 (1C, *C*H_2CO), 22.71-29.7 (26C, CH_2), 14.1 (2C, CH_3).

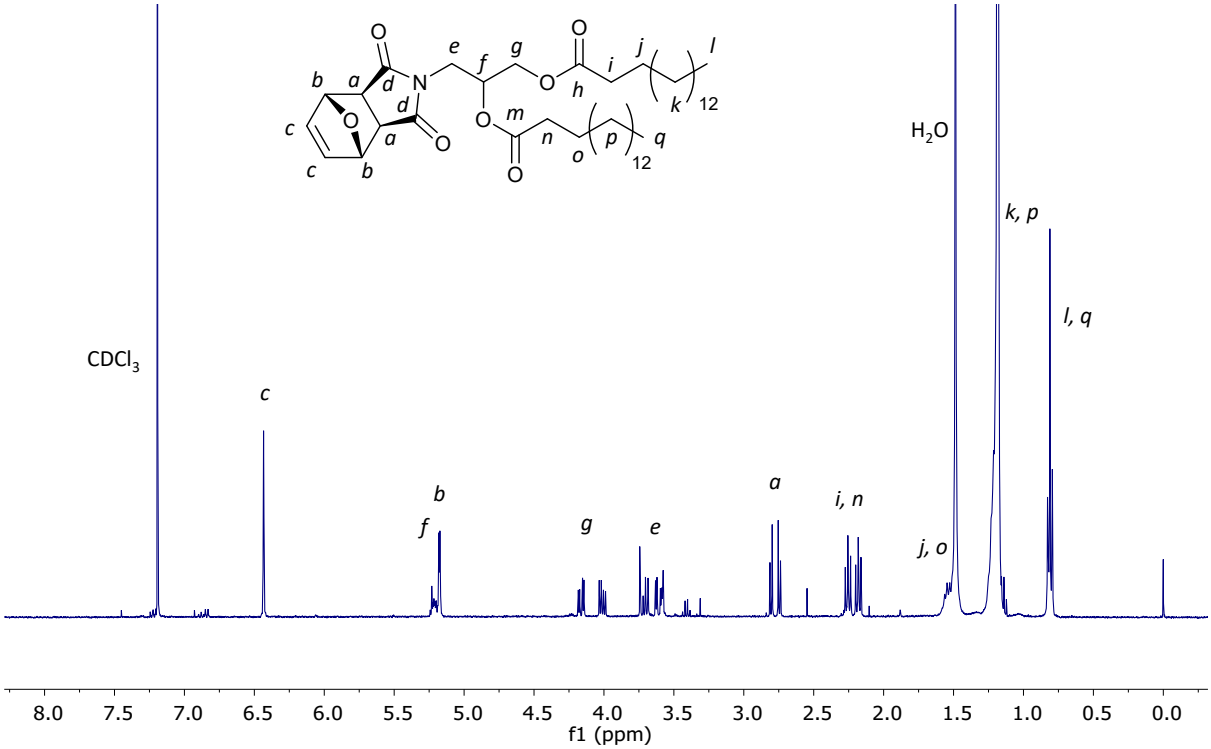


Figure S30. ^{1}H NMR spectrum 3-((3aR,4R,7R,7aS)-1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2H-4,7-epoxyisoindol-2-yl) propane-1,2-diyl dipalmitate (**10a1**) in $CDCl_3$.

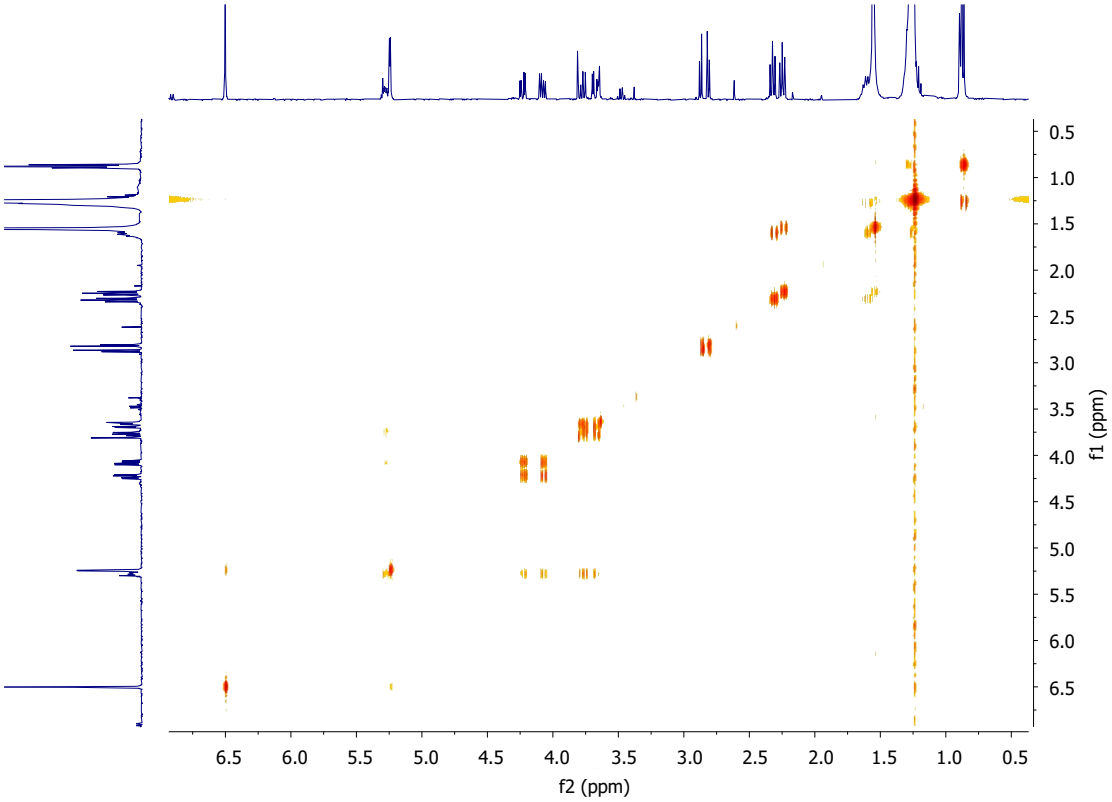


Figure S31. ^{1}H-^{1}H COSY NMR spectrum 3-((3aR,4R,7R,7aS)-1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2H-4,7-epoxyisoindol-2-yl) propane-1,2-diyl dipalmitate (**10a1**) in $CDCl_3$.

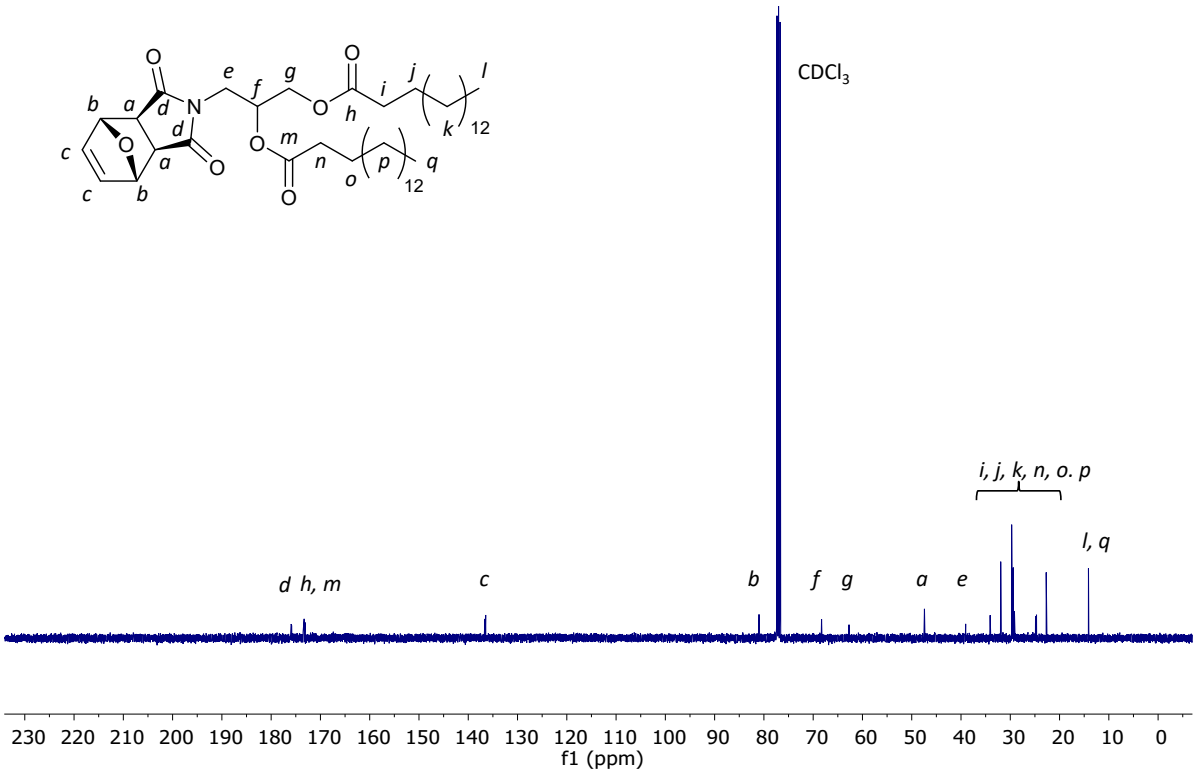


Figure S32. ^{13}C NMR spectrum 3-((3aR,4R,7R,7aS)-1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2H-4,7-epoxyisoindol-2-yl) propane-1,2-diyl dipalmitate (**10a1**) in $CDCl_3$.

3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propane-1,2-diyl dipalmitate (10a). Intermediate **(10a1)** (6.6 g, 9.2 mmol) was suspended in toluene (150 mL) and the mixture heated to reflux (heating block at 130°C) for 6 hours. The solvent was then removed under reduced pressure to give **(10a)** as a white solid (5.03 g, 7.76 mmol; 84.7% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (s, 2H, C*H*C*H*), 5.24 (m, 1H, CHO), 3.99-4.20 (m, 2H, CH_2O), 3.57-3.76 (m, 2H, CH_2N), 2.23 (dt, *J* = 26.7, 7.6 Hz, 4H, CH_2CO), 1.38-1.85 (m, 4H, CH_2), 1.16-1.25 (m, 48H, CH_2), 0.81 (t, *J* = 6.6 Hz, 6H, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 173.27 (2C, COO), 170.25 (2C, CO), 134.25 (2C, *C*H*C*H), 68.94 (1C, CHO), 62.74 (1C, CH_2O), 38.17 (1C, CH_2N), 34.10 (1C, CH_2CO), 31.94 (1C, CH_2CO), 22.71-29.72 (26C, CH_2), 14.13 (2C, CH_3).

Mass spectrometry (MALDI TOF) m/z (%): expected for [M+Na^{+}] 670.50, found 670.70 (100).

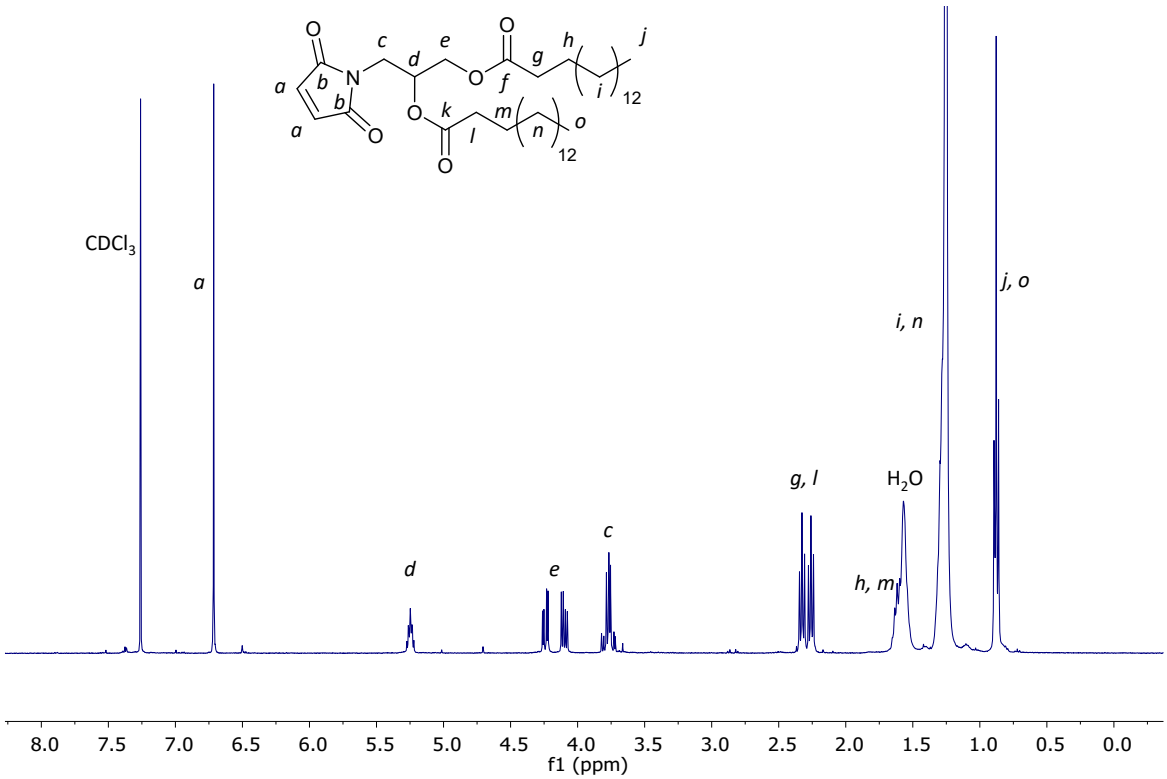


Figure S33. ^{1}H NMR spectrum 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propane-1,2-diyl dipalmitate (**10a**) in $CDCl_3$.

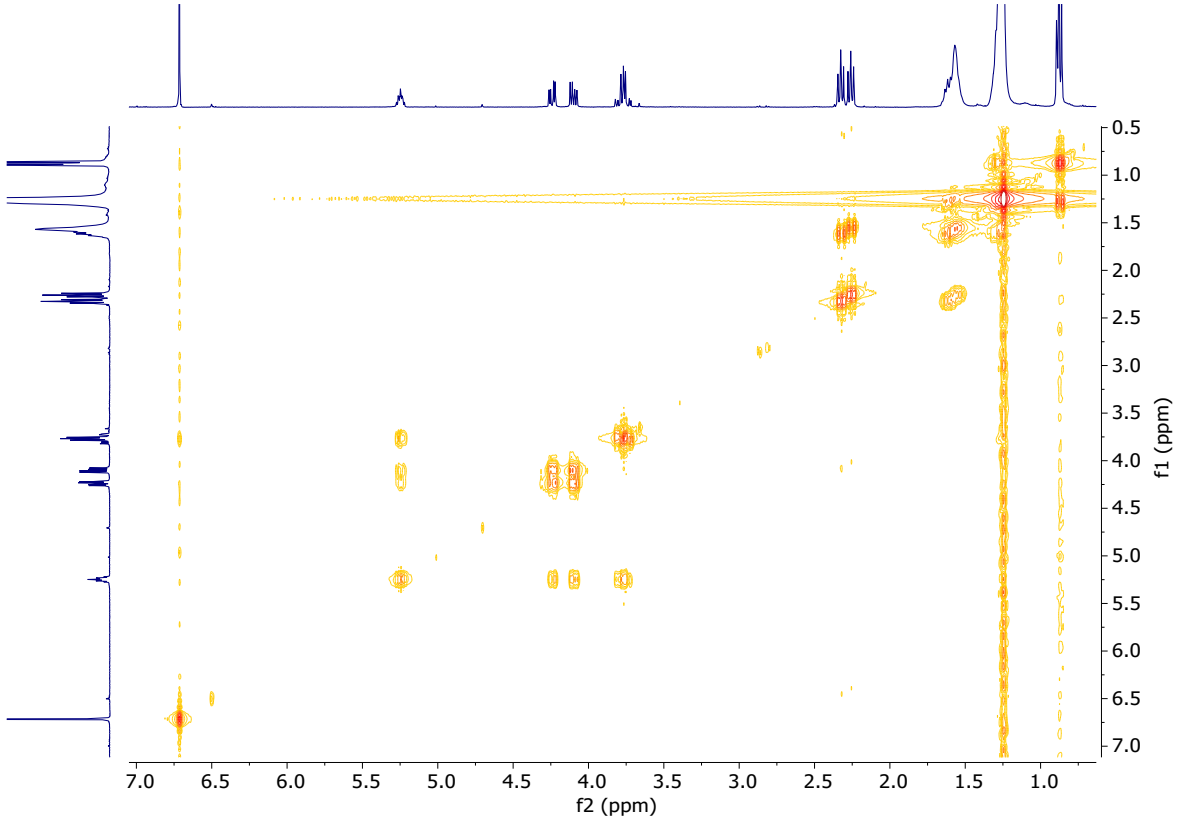


Figure S34. ^{1}H-^{1}H COSY NMR spectrum 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propane-1,2-diyl dipalmitate (**10a**) in $CDCl_3$.

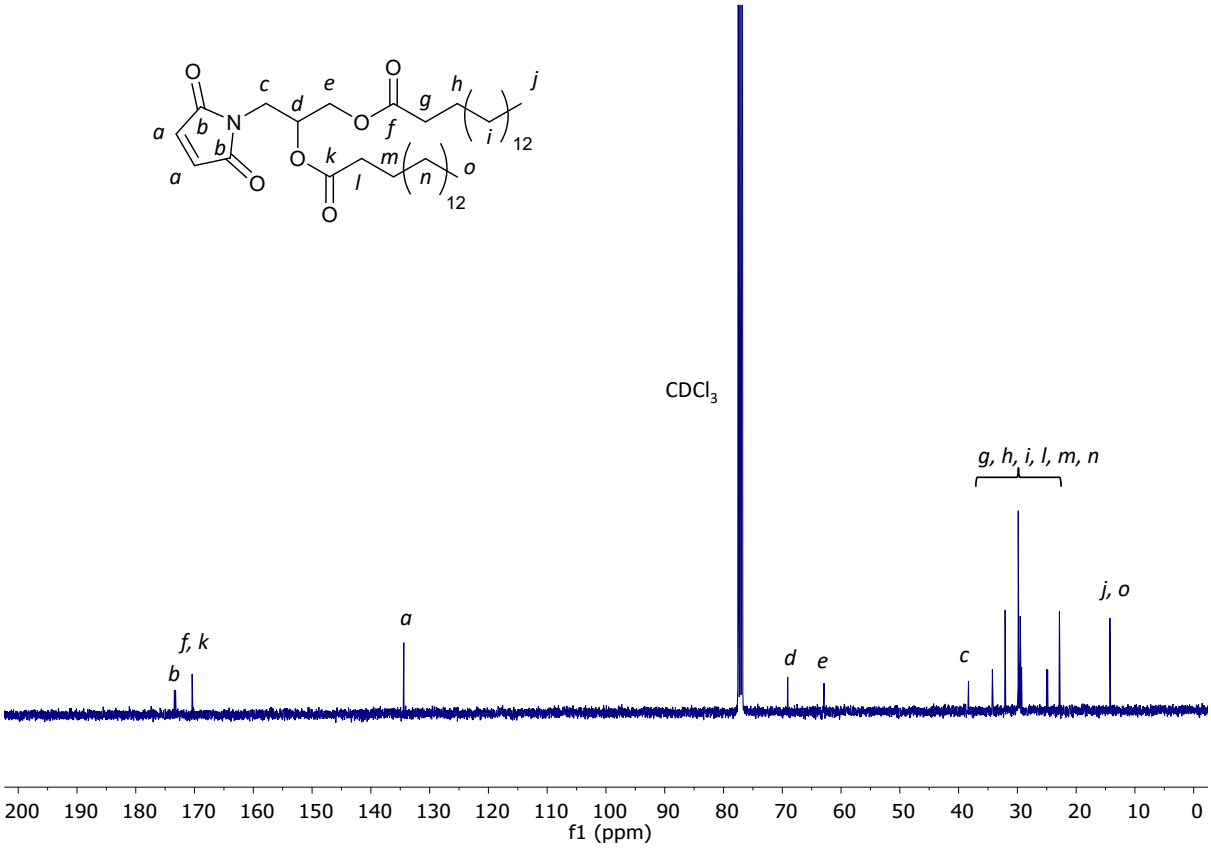


Figure S35. ^{13}C NMR spectrum of 3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propane-1,2-diyl dipalmitate (**10a**) in $CDCl_3$.

1-(2-(2-hydroxyethoxy)ethyl)-1H-pyrrole-2,5-dione (10b).

Intermediate **(9b)** (6.00 g, 23.7 mmol) was suspended in toluene (150 mL) and the mixture heated to reflux (heating mantle kept at 120°C) for 16 hours. Subsequently, the solvent was removed under reduced pressure to give **(10b)** as an off-white solid (3.82 g, 20.6 mmol; 87.1% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (2H, s, C*H*C*H*), 3.73 (t, *J* = 5.2 Hz, 2H, $NCH_2CH_2OCH_2CH_2OH$), 3.68-3.63 (m, 4H, $NCH_2CH_2OCH_2CH_2OH$), 3.56 (t, *J* = 5.1 Hz, 2H, $NCH_2CH_2OCH_2CH_2OH$), 2.63 (bs, 1H, CH_2OH).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.80 (2C, CO), 134.18 (2C, *C*H*C*H), 72.11 (1C, $NCH_2CH_2OCH_2$), 68.07 (1C, NCH_2CH_2O) 61.55 (1C, CH_2OH), 37.33 (NCH_2).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 208.06, found 208.06 (100%).

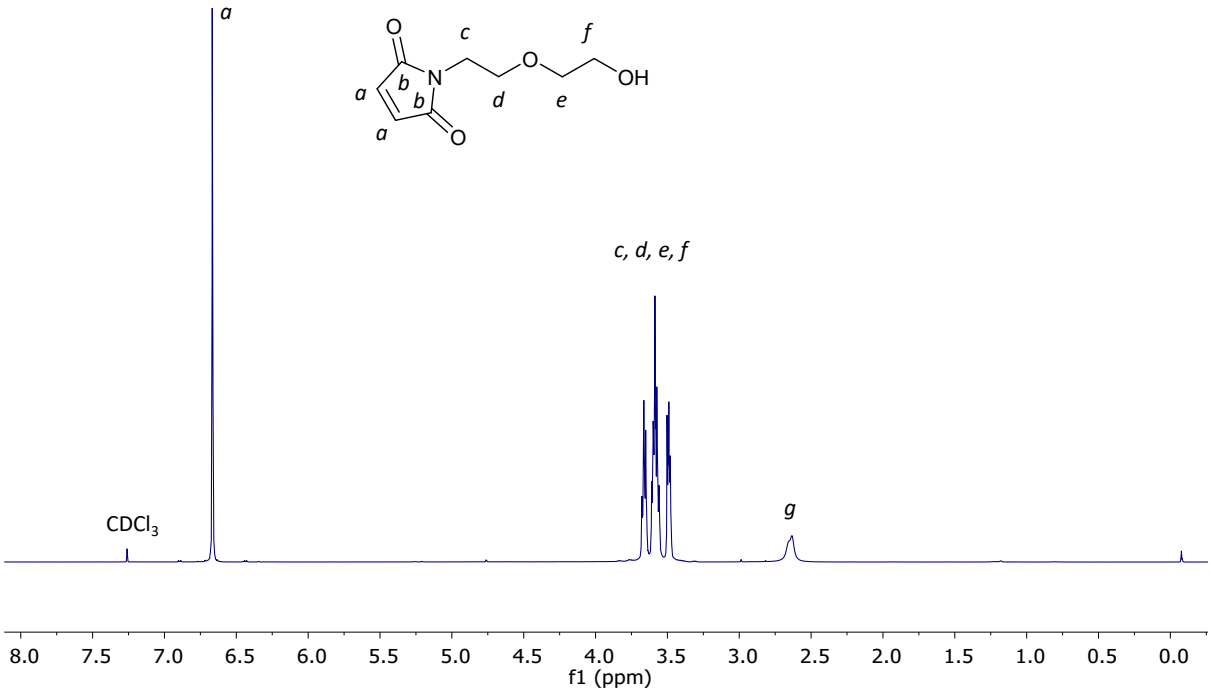


Figure S36. ^{1}H NMR spectrum of 1-(2-(2-hydroxyethoxy)ethyl)-1H-pyrrole-2,5-dione **(10b)** in $CDCl_3$.

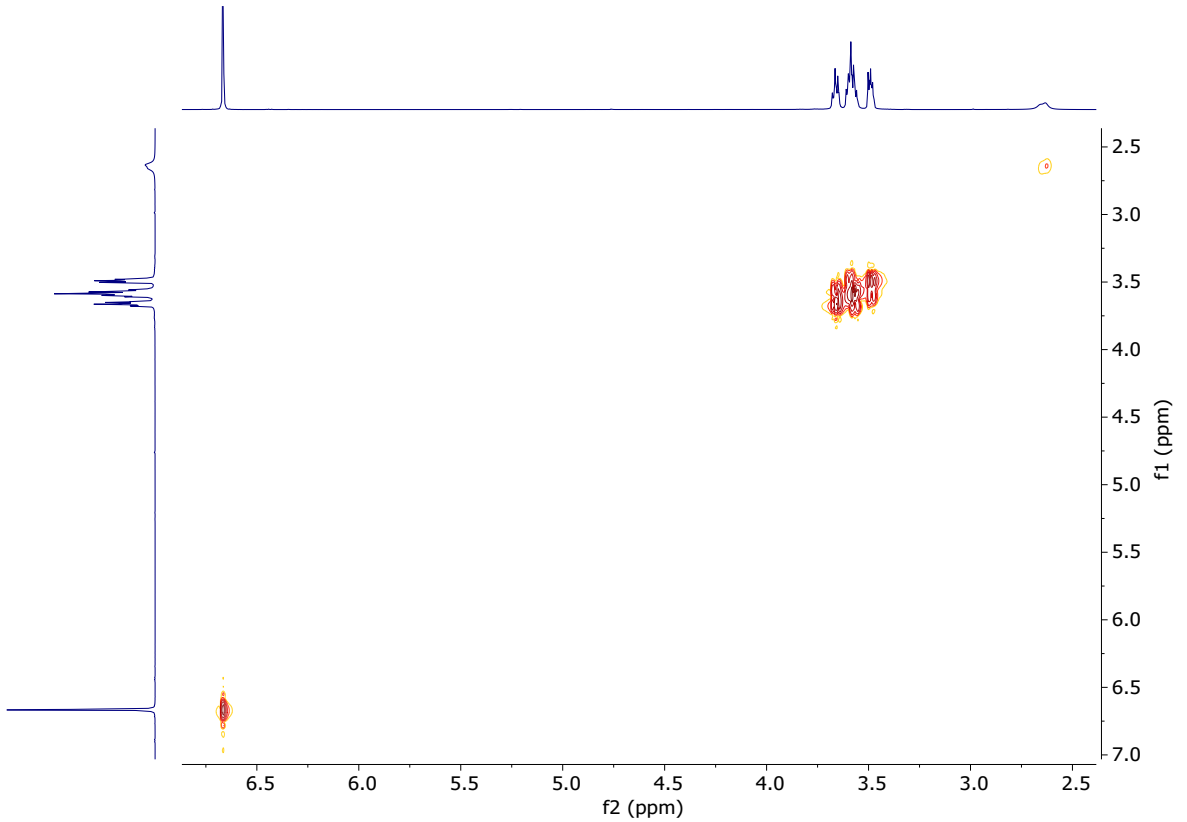


Figure S37. ^{1}H-^{1}H COSY NMR spectrum of 1-(2-(2-hydroxyethoxy)ethyl)-1H-pyrrole-2,5-dione **(10b)** in $CDCl_3$.

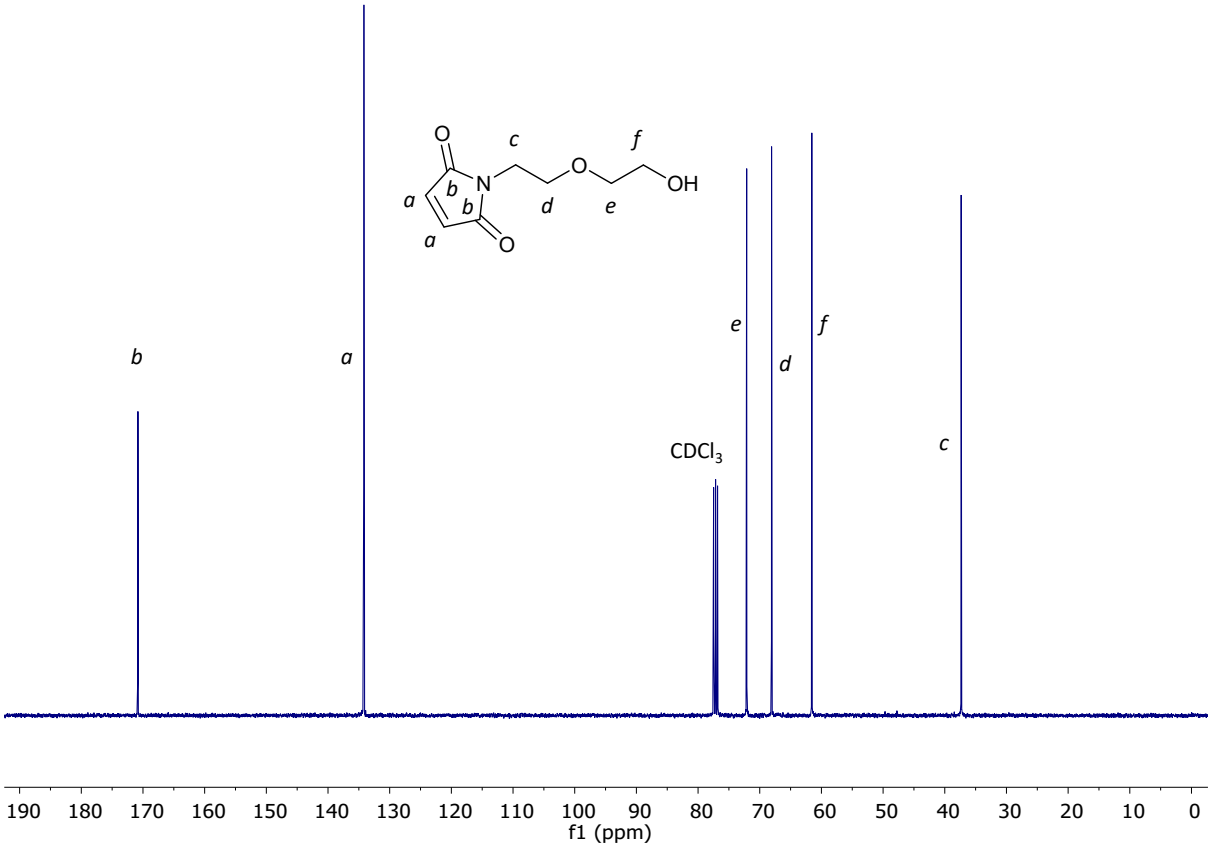


Figure S38. ^{13}C NMR spectrum of 1-(2-(2-hydroxyethoxy)ethyl)-1H-pyrrole-2,5-dione **(10b)** in $CDCl_3$.

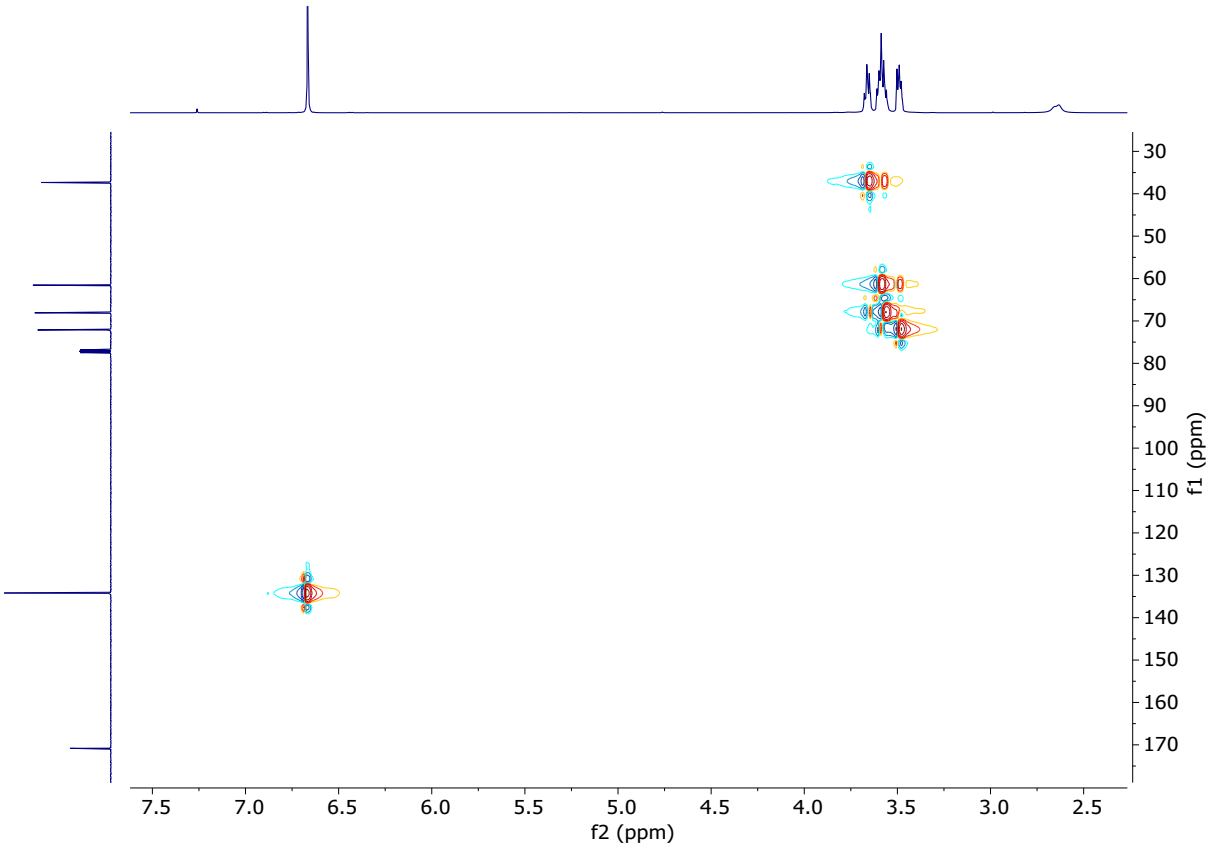


Figure S39. ^{1}H-^{13}C HSQC NMR spectrum of 1-(2-(2-hydroxyethoxy)ethyl)-1H-pyrrole-2,5-dione **(10b)** in $CDCl_3$.

1-(1,3-dihydroxypropan-2-yl)-1H-pyrrole-2,5-dione (10c). Intermediate **(9c)** (1.0 g, 4.2 mmol) was suspended in toluene (150 mL) and the mixture heated to reflux (heating mantle kept at 120°C) for 16 hours. Subsequently, the solvent was removed under reduced pressure to give **(10b)** as a solid (0.58 g, 3.39 mmol; 80.7% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (2H, s, C*H*=C*H*), 4.81 (t, 2H, OH), 4.01 (m, 1H, NCH), 3.68-3.54 (m, 4H, CH_2).

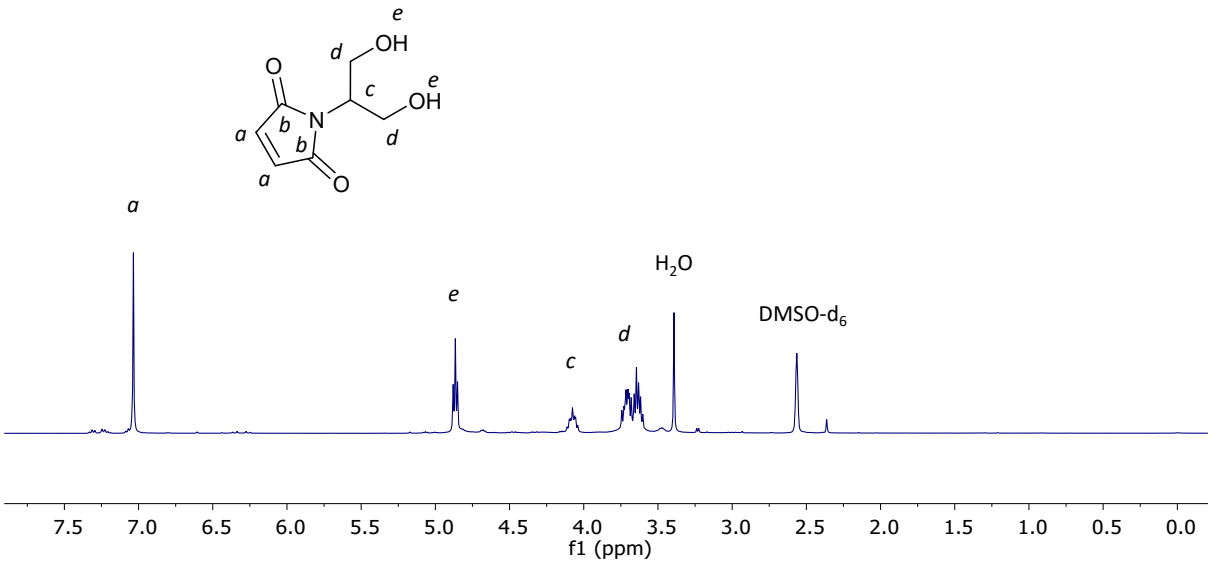


Figure S40. ^{1}H NMR spectrum of 1-(1,3-dihydroxypropan-2-yl)-1H-pyrrole-2,5-dione **(10c)** in DMSO-d_6.

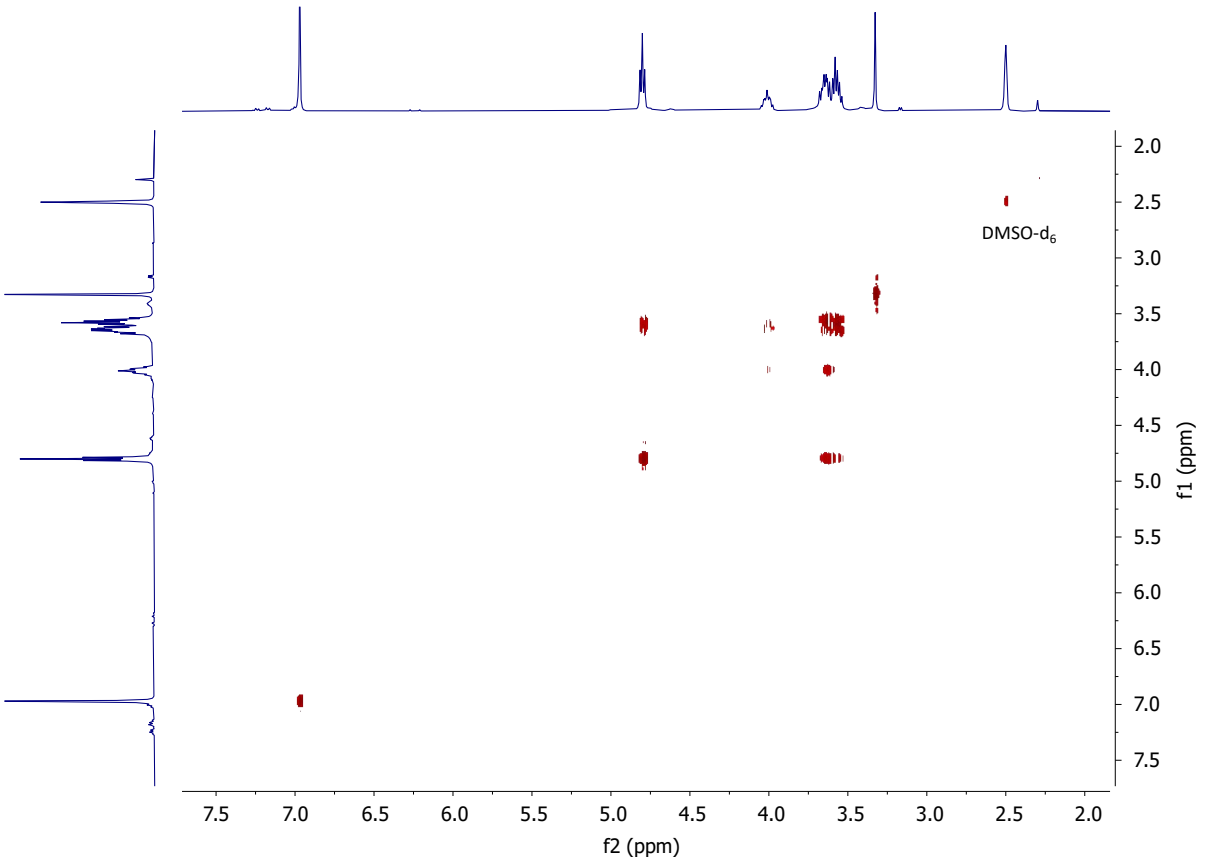


Figure S41. ^{1}H-^{1}H COSY NMR spectrum of 1-(1,3-dihydroxypropan-2-yl)-1H-pyrrole-2,5-dione **(10c)** in DMSO-d_6.

General procedure for the synthesis of Maleimide based RAFT agents (Mal-CTA). Maleimide and CTA starting materials were dissolved in the required solvent in a Schlenk tube containing a magnetic stirrer, and their molar ratio in the reaction feed was confirmed by ^{1}H NMR. The radical initiator was added as an aliquot taken from a stock solution and the tube sealed with a rubber septum. The mixture was cooled with an ice bath and was deoxygenated by argon bubbling for 15 minutes. The reaction was started by placing the Schlenk tube in a thermostated oil bath at the desired temperature.

Synthesis of Maleimide based RAFT agents

Table S1. Synthesis of maleimide-RAFT agents (**Mal-CTAs**) via route 1: reaction conditions.

	Route 1a		Route 1b	
	(13b)	**(14b)**	**(13a)**	**(13b)**
Maleimide	10b	10b	10a	10b
$m_{maleimide\ added}$ (mg)	71.3	69.9	118	60.5
mmol	0.385	0.378	0.182	0.327
CTA	-	-	**(7)**	**(7)**
bis(thioacyl) disulfide	**(6)**	**(3)**	-	-
$m_{CTA\ added}$ (mg)	230.3	123.7	69	124
mmol	0.4155	0.4042	0.20	0.360
Initiator	AIBN	AIBN	AIBN	AIBN
$m_{initiator\ added}$ (mg)	122.9	122.8	1.65	2.95
mmol	0.7484	0.7478	0.0100	0.0180
Solvent 1	Toluene	EtOAc	Toluene	Toluene
$V_{solvent\ 1\ added}$ (mL)	1	1	0.183	0.327
[monomer] (mol·L^{-1})	0.4	0.4	1	1
[CTA or bis(thioacyl) disulfide] / [initiator]	0.5	0.5	20	20
Temperature (°C)	70	70	75	75
Time (h)	16	16	48	48
$m_{product}$ (mg)	108.9	96.8	132.3	72.0
mmol	0.21	0.24	0.13	0.14
Yield (%)	55	63	73	42

Table S2. Synthesis of maleimide-RAFT agents (**Mal-CTAs**) via route 2: reaction conditions.

	11a	**11b**	**11c**	**12a**	**12b**
Maleimide	10a	10b	10c	10a	10b
$m_{maleimide\ added}$ (mg)	131	824.9	200	124	57.8
mmol	0.183	4.454	1.17	0.174	0.284
CTA	**(2)**	**(2)**	**(2)**	**(5)**	**(5)**
$m_{CTA\ added}$ (mg)	48.5	1176	309.6	70.0	114
mmol	0.202	4.900	1.288	0.192	0.312
Initiator	AIBN	VA-044	VA-044	AIBN	VA-044
$m_{initiator\ added}$ (mg)	0.301	15.8	3.79	1.43	1.01
mmol	$1.83 \cdot 10^{-3}$	0.0489	0.117	$8.71 \cdot 10^{-3}$	$3.12 \cdot 10^{-3}$
Solvent 1	Toluene	DMSO	DMSO	Toluene	DMSO
$V_{solvent\ 1\ added}$ (mL)	0.183	1.485	0.390	0.174	0.95
Solvent 2	-	H_2O	H_2O	-	H_2O
$V_{solvent\ 2\ added}$ (mL)	-	0.742	0.195	-	0.47
[monomer] ($mol \cdot L^{-1}$)	1	2	2	1	2
[CTA]/[initiator]	100	100	100	20	100
Temperature (°C)	75	100	65	75	90
Time (h)r	24	4	24	48	12
$m_{product}$ (mg)	48.0	0.60	223	43.6	37.4
mmol	0.05	1.41	0.544	0.04	0.07
Yield (%)	30	32	46	26	22

At the end of each reaction, the reaction mixture was purified *via* flash column chromatography (Agilent 971-FP Flash Purification System) according to the following condition. Compounds **11b** and **11c** were purified on reversed-phase (KP-C18-HS) as the stationary phase, and acetonitrile (from 5% to 20% and from 5% to 15%, respectively) in water as mobile phase.

All the other compounds were purified on SiO_2 as the stationary phase, mobile phases were as follow: petroleum ether/diethyl ether 1:1 (vol/vol) for **11a**; diethyl ether/petroleum ether 3:7 (vol/vol) for **12a**; diethyl ether/petroleum ether 2:8 (vol/vol) for **13a**; diethyl ether for **12b** and **13b**; ethyl acetate for **14b**.

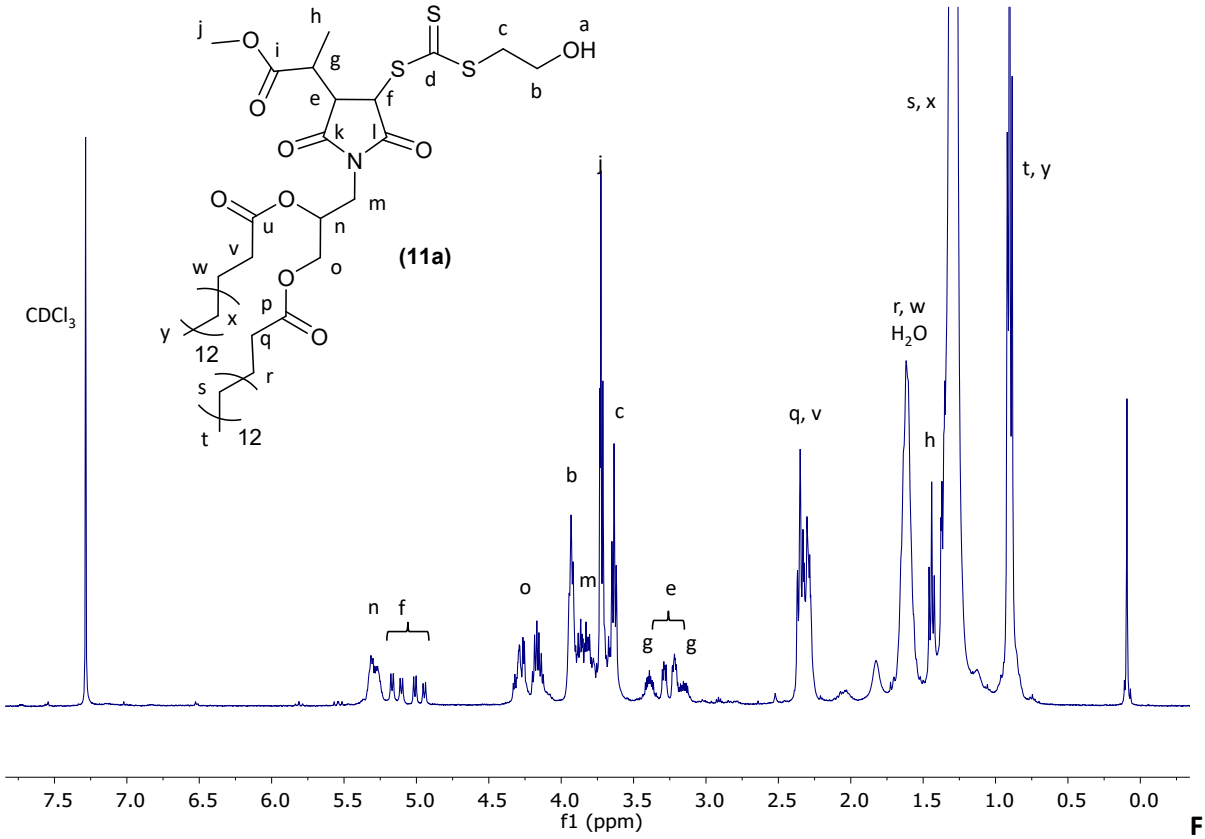
Characterisation:

Mal-CTA **(11a)**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31-5.22 (m, 1H, NCH_2CHCH_2O), 5.15-5.09-4.99-4.93 (d, 1H, SC(S)SC*H*) , 4.31-4.10 (m, 2H, NCH_2CHCH_2O), 3.91 (t, 2H, $HOCH_2CH_2$), 3.86-3.74 (m, 2H, NCH_2CHCH_2O), 3.71 -3.70 - 3.69 (s, 3H, OCH_3), 3.61 (t, 2H, $HOCH_2CH_2$), 3.39-3.34 and 3.16-3.10 (1H, $CHCHCH_3$) 3.28-3.18 (1H, $CHCHCH_3$), 2.34-2.26 (m, 4H, $C(O)CH_2(CH_2)_{13}CH_3$), 1.59 (m, 4H, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 1.42-1.25 (m, 58H, $(CH_2)_{12}CH_3$, and $CHCHCH_3$), 0.88 (t, 6H, $(CH_2)_nCH_3$).

^{13}C NMR (101 MHz, $CDCl_3$) δ 221.06-220.63 (1C, SC(S)S), 175.70-175.25 (1C, $C(O)OCH_3$), 173.92-172.30 (2C, CO_{Mal} and 2C, CO_{ester}), 68.77 (1C, NCH_2CHCH_2O), 62.91 (1C, NCH_2CHCH_2O), 60.30 (1C, $HOCH_2CH_2$), 52.56 (1C, OCH_3), 49.20 (1C, SC(S)SCH), 48.76 (1C, $CHCHCH_3$), 40.30 (1C, $HOCH_2CH_2$), 39.32-38.35 (1C, NCH_2CHCH_2O), 34.21 (2C, $CHOC(O)CH_2(CH_2)_{13}CH_3$), 32.07, 29.85-29.29 (24C, $(CH_2)_{12}CH_3$), 25.08-24.81 (2C, $CH_2CH_2(CH_2)_{12}CH_3$), 22.84 (1C, $CHCHCH_3$), 14.26 (2C, $(CH_2)_nCH_3$).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 910.50, found 910.50 (100%).



F igure S42. ^{1}H NMR spectrum of Mal-CTA **(11a)** in $CDCl_3$.

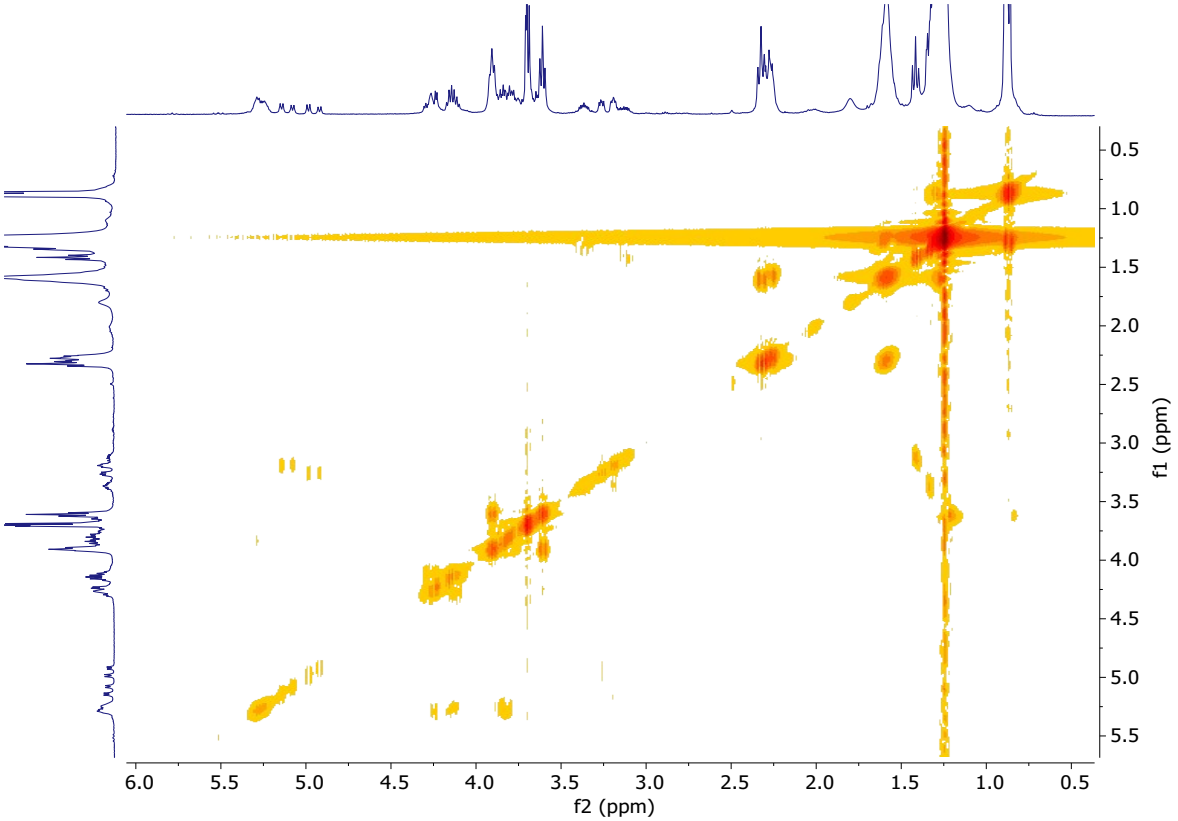


Figure S43. ^{1}H-^{1}H COSY NMR spectrum of Mal-CTA **(11a)** in $CDCl_3$.

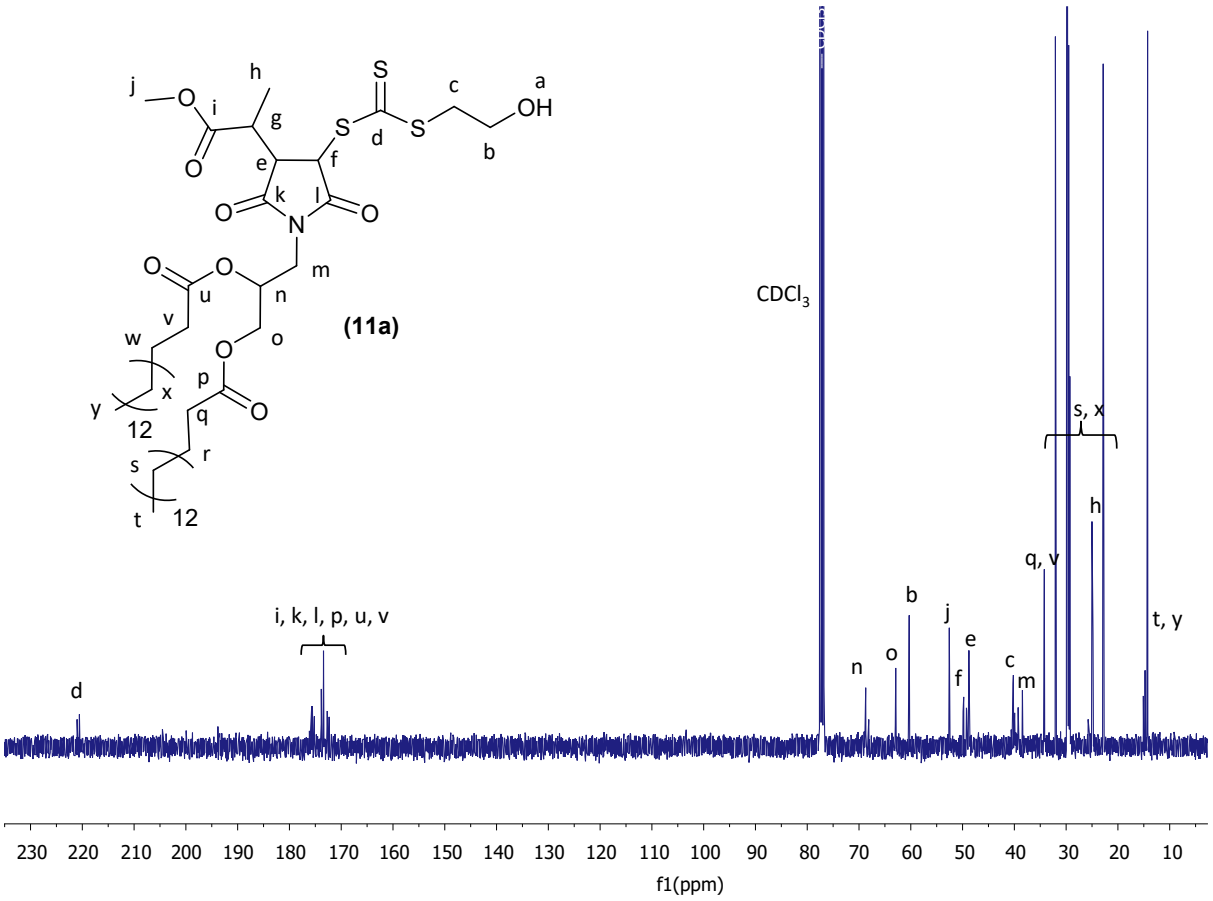


Figure S44. ^{13}C NMR spectrum of Mal-CTA **(11a)** in $CDCl_3$.

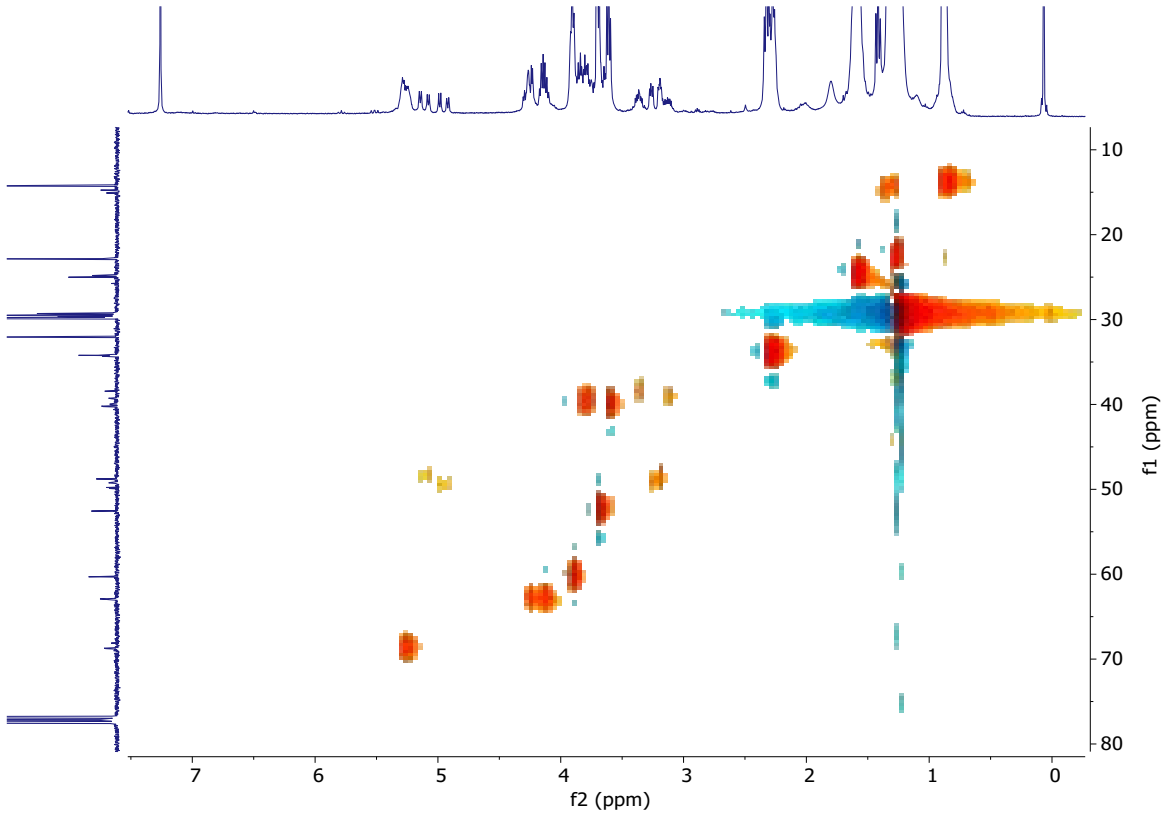


Figure S45. ^{1}H-^{13}C HSQC NMR spectrum of Mal-CTA **(11a)** in $CDCl_3$.

Mal-CTA **(11b)**. *Anti*:*Syn* molar ratio: 95:5

^{1}H NMR (400 MHz, $CDCl_3$, anti adduct) δ 5.02 (d, 1H, *J* = 6.6 Hz, SC(S)SC*H*), 4.90 (d, 1H, , *J* = 6.6 Hz, SC(S)SC*H*), 3.89 (q, 2H, *J* = 5.9 Hz, HOC*H*$_2$CH$_2$S), 3.83-3.75 (m, 2H, NCH$_2$CH$_2$OC*H*$_2$), 3.71 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 3.70-3.65 (m, 4H, NCH$_2$C*H*$_2$OCH$_2$C*H*$_2$OH), 3.61-3.56 (m, 4H, HOCH$_2$C*H*$_2$S and NC*H*$_2$), 3.45-3.38 and 3.16-3.11 (m, 1H, CHC*H*CH$_3$, respectively *J* = 7.6, 3.9 Hz and *J* = 7.4, 3.7 Hz), 3.28-3.22 (td, 1H, *J* = 6.6, 3.7 Hz, C*H*CHCH$_3$), 2.85 (t, 1H, *J* = 6.2 Hz, OCH$_2$CH$_2$O*H*), 2.74 (t, 1H, *J* = 6.2 Hz, OCH$_2$CH$_2$O*H*), 2.31 (t, 1H, *J* = 5.7 Hz, *H*OCH$_2$CH$_2$S), 1.46 (d, 3H, *J* = 7.4 Hz, CHCHC*H*$_3$), 1.36 (d, 3H, *J* = 7.6 Hz, CHCHC*H*$_3$).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, anti adduct) δ 221.0 (1C, SC(S)S), 220.5 (1C, SC(S)S), 176.1 (1C,CO_{Mal}), 175.6 (1C,CO_{Mal}), 174.3 (1C,CO_{ester}), 174.2 (1C,CO_{ester}), 173.0 (1C,CO_{Mal}), 172.6 (1C,CO_{Mal}), 72.5 (1C, N*C*H$_2$CH$_2$OCH$_2$CH$_2$OH), 67.2 (1C, NCH$_2$CH$_2$OCH$_2$*C*H$_2$OH), 61.8 (1C, NCH$_2$*C*H$_2$O), 60.2 (1C, HO*C*H$_2$CH$_2$S), 52.7 (1C, OCH_3), 52.7 (1C, OCH_3), 50.2 (1C, SC(S)S*C*H), 49.3 (1C, SC(S)S*C*H), 48.8 (1C, *C*HCHCH$_3$), 48.7 (1C, *C*HCHCH$_3$), 40.3 (1C, HOCH$_2$*C*H$_2$S), 40.2 (1C, HOCH$_2$*C*H$_2$S), 39.5 (1C, NCH$_2$CH$_2$O*C*H$_2$CH$_2$OH), 39.3 (1C, CH*C*HCH$_3$), 38.5 (1C, CH*C*HCH$_3$), 15.2 (1C, CHCH*C*H$_3$), 14.9 (1C, CHCH*C*H$_3$).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 448.05, found 448.05 (100%).

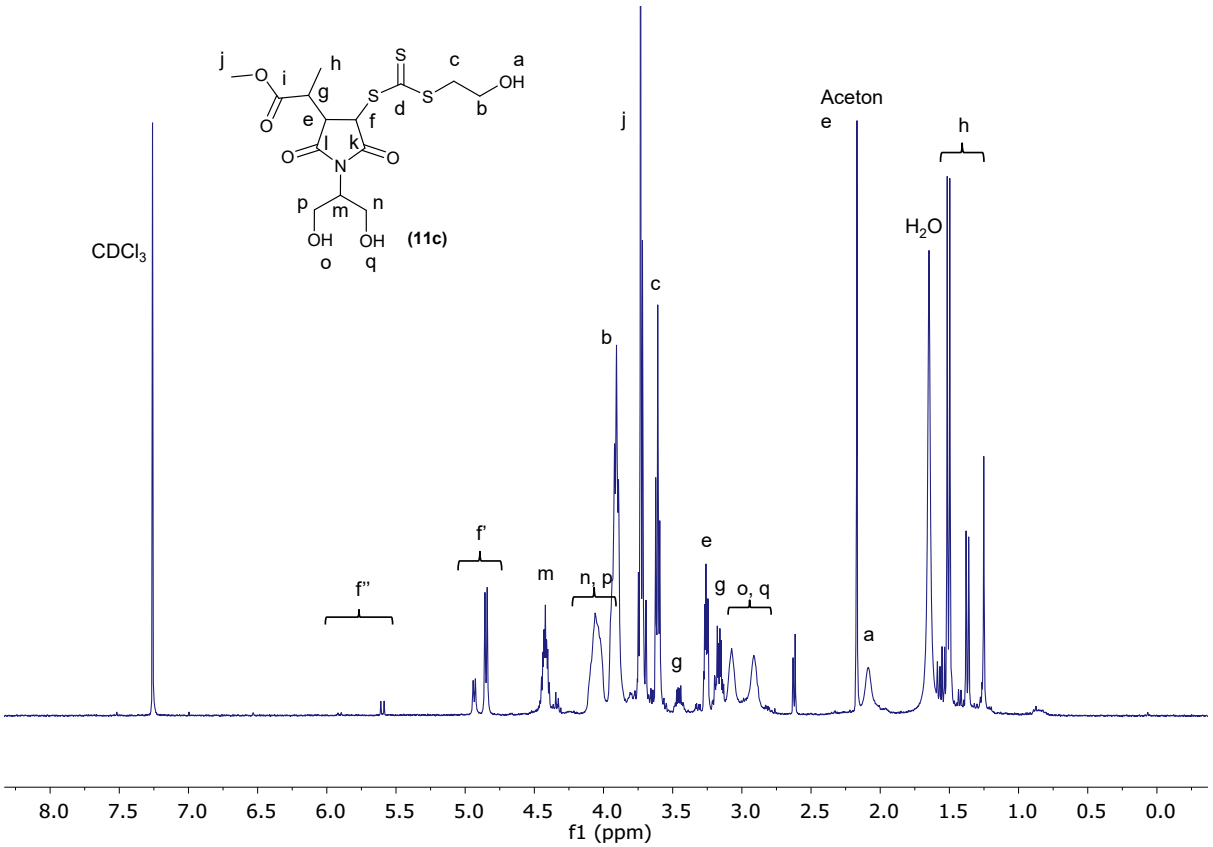


Figure S46. ^{1}H NMR spectrum of Mal-CTA **(11b)** in $CDCl_3$. f' and f'' refer to the-CHSC(S)SZ proton of the trans (anti) and cis (syn) adducts, respectively.

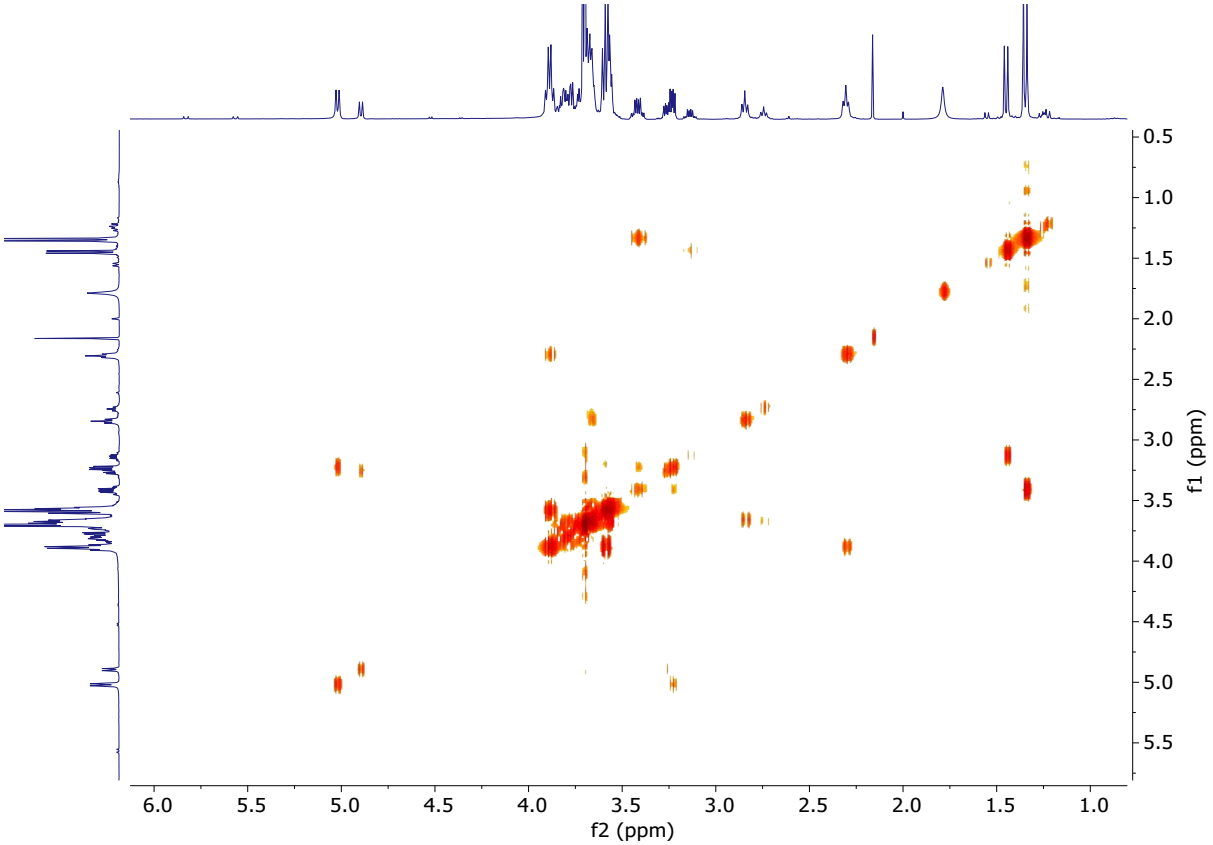


Figure S47. ^{1}H-^{1}H COSY NMR spectrum of Mal-CTA **(11b)** in $CDCl_3$.

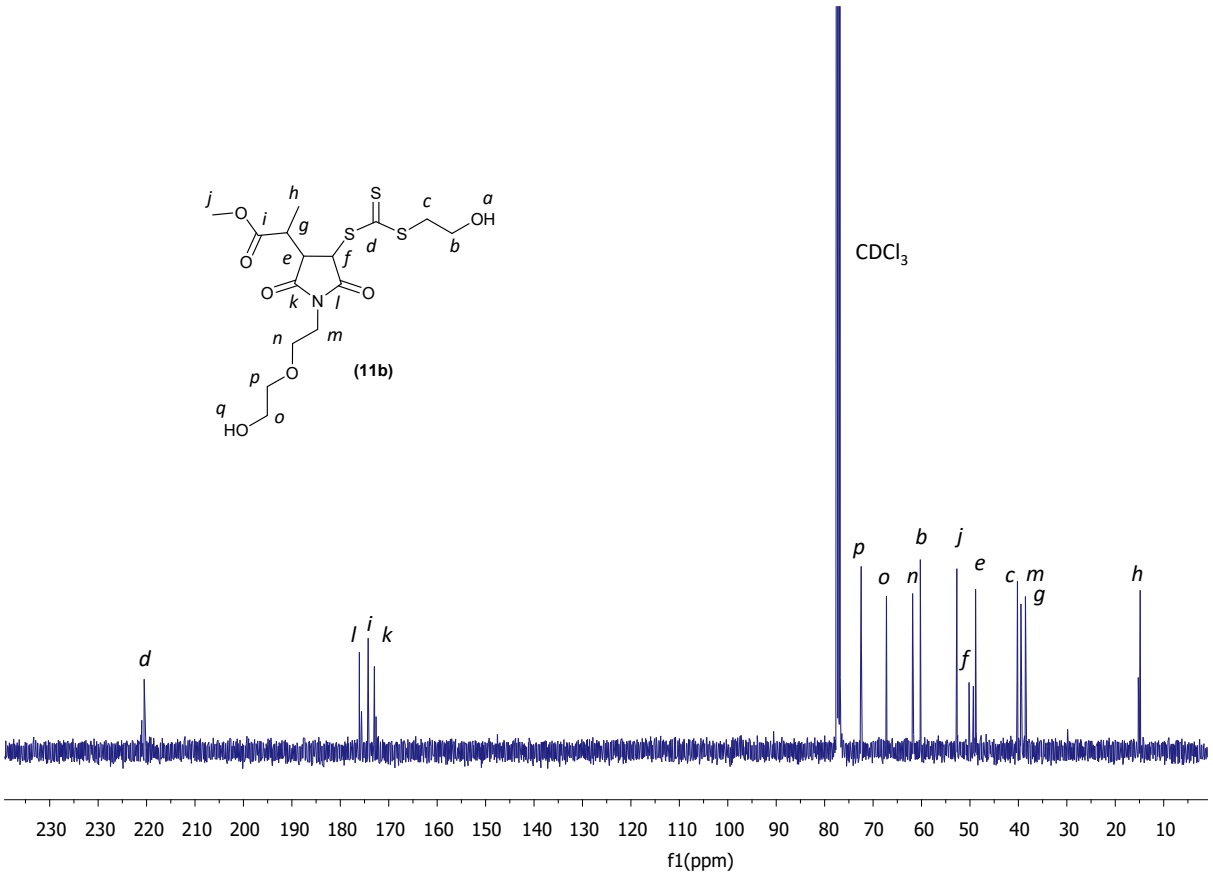


Figure S48. ^{13}C NMR spectrum of Mal-CTA **(11b)** in $CDCl_3$.

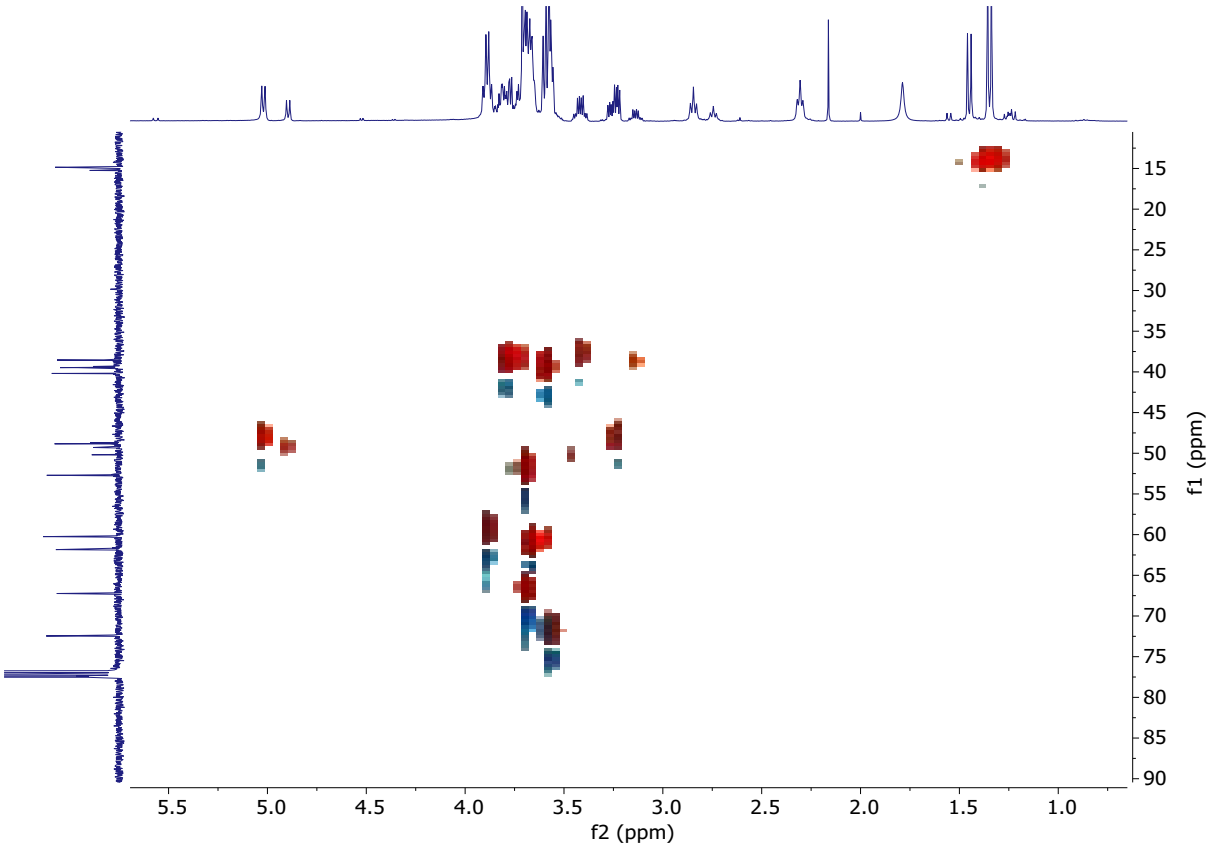


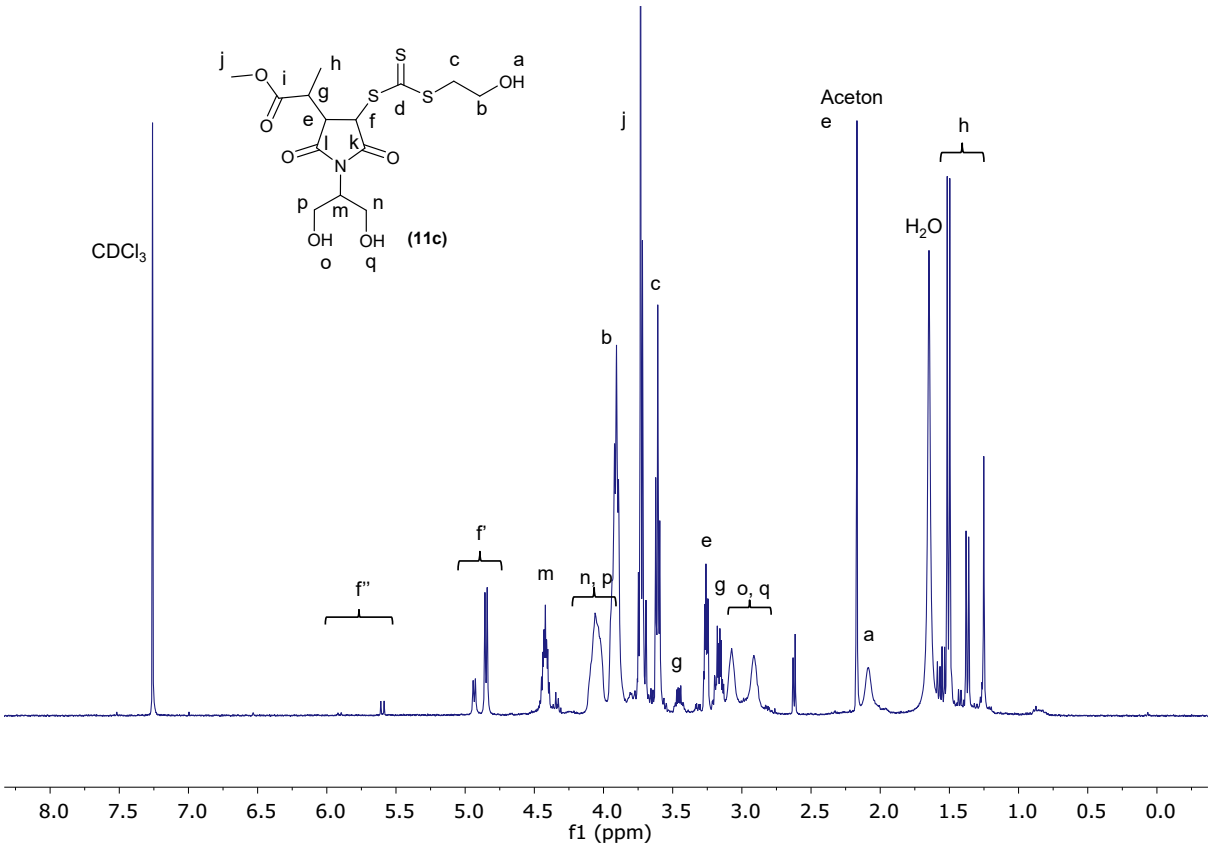
Figure S49. ^{1}H-^{13}C HSQC NMR spectrum of Mal-CTA **(11b)** in $CDCl_3$.

Mal-CTA **(11c).** *Anti*:*Syn* molar ratio: 94:6

^{1}H NMR (400 MHz, $CDCl_3$, anti adducts) δ $_{H}$ (400 MHz, $CDCl_3$) 4.94 (d, *J* = 6.4 Hz, 1H, SC(S)SC*H*), 4.86 (d, *J* = 6.5 Hz, 1H, SC(S)SC*H*), 4.42 (m, 1H, NCH), 4.06 (m, 2H, NCHC*H*$_2$OH) 3.91 (m, 2H,NCHC*H*$_2$OH overlapping t, *J* = 6.0 Hz, 4H, HOC*H*$_2$CH$_2$S), 3.75, 3.73, 3.72, 3.69 (4s, 3H, OCH_3), 3.61 (t, *J* = 6.0 Hz, 2H, HOCH$_2$C*H*$_2$S), 3.48-3.43 and 3.20- 3.13 (m, 1H, CHC*H*CH$_3$), 3.28-3.24 (m, 1H, C*H*CHCH$_3$) , 3.07 (bs, 1H, NCHCH$_2$O*H*), 2.91 (bs, 1H, NCHCH$_2$O*H*), 2.08 (bs, 1H, *H*OCH$_2$CH$_2$S), 1.51 (d, *J* = 7.4 Hz, 3H, CHCHC*H*$_3$), 1.38 (d, *J* = 7.6 Hz, 3H, CHCHC*H*$_3$).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, anti adducts) δ 221.2 (1C, SC(S)S), 220.6 (1C, SC(S)S), 177.8 (1C,CO_{Mal}), 177.4 (1C,CO_{Mal}), 177.0 (1C,CO_{ester}), 174.5 (1C,CO_{ester}), 174.2 (1C,CO_{Mal}), 173.8 (1C,CO_{Mal}), 60.7 (1C, NCH*C*H$_2$O), 60.5 (1C, NCH*C*H$_2$O), 60.2 (1C, HO*C*H$_2$CH$_2$S), 57.3 (1C, NCH), 53.1 (1C, OCH_3), 52.9 (1C, OCH_3), 50.5 (1C, SC(S)SCH), 49.0 (1C, SC(S)SCH), 48.8 (1C, *C*HCHCH$_3$), 48.5 (1C, *C*HCHCH$_3$), 40.5 (1C, HOCH$_2$*C*H$_2$S), 40.2 (1C, HOCH$_2$*C*H$_2$S), 39.3 (1C, CH*C*HCH$_3$), 38.2 (1C, CH*C*HCH$_3$), 15.7 (1C, CHCH*C*H$_3$), 14.7 (1C, CHCH*C*H$_3$).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 434.04, found 434.04 (100%).



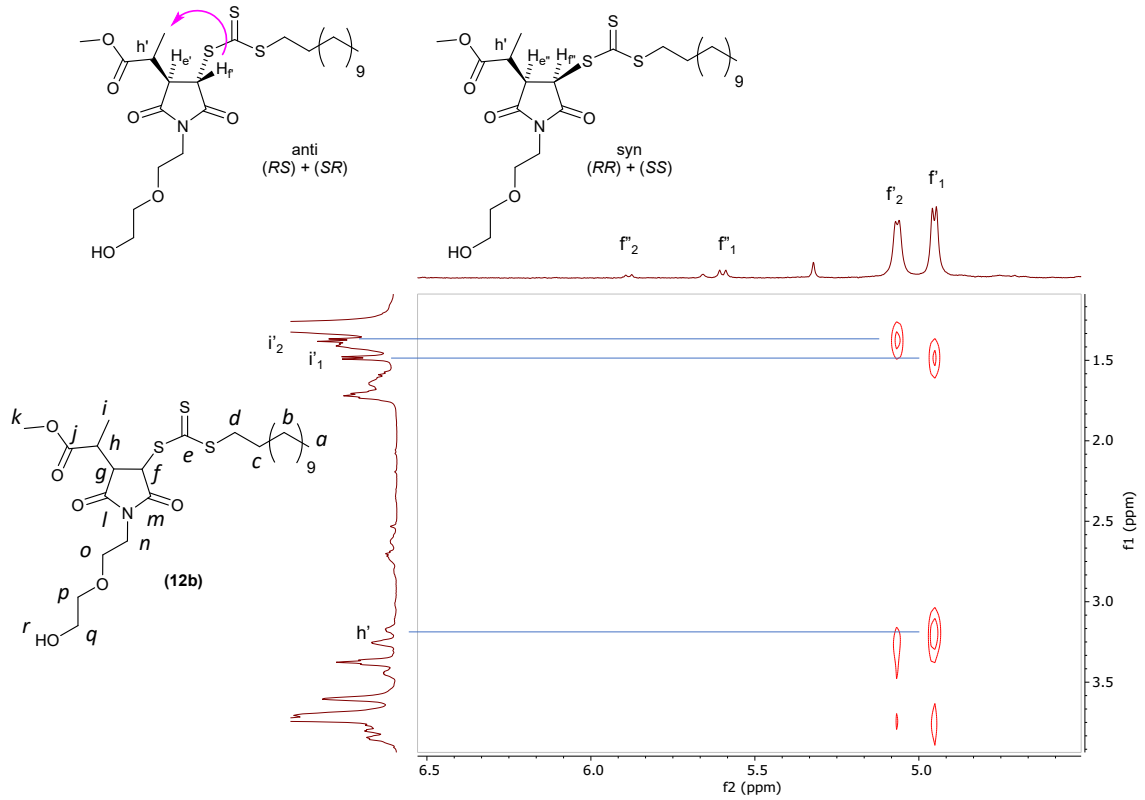


Figure S50. Top: ^{1}H NMR spectrum of Mal-CTA **(11c)** in $CDCl_3$. Bottom: NOESY spectrum showing spatial proximity between protons f'$_1$ and f'$_2$ and the methyl group of the 2-methylpropionate

substituent (h'$_1$ and h'$_2$), confirming the *anti* (trans) structure of the major adduct. Carbon in position g is also chiral, resulting in the observed split of all signals, shown here as f'$_1$ and f'$_2$ for group f'.

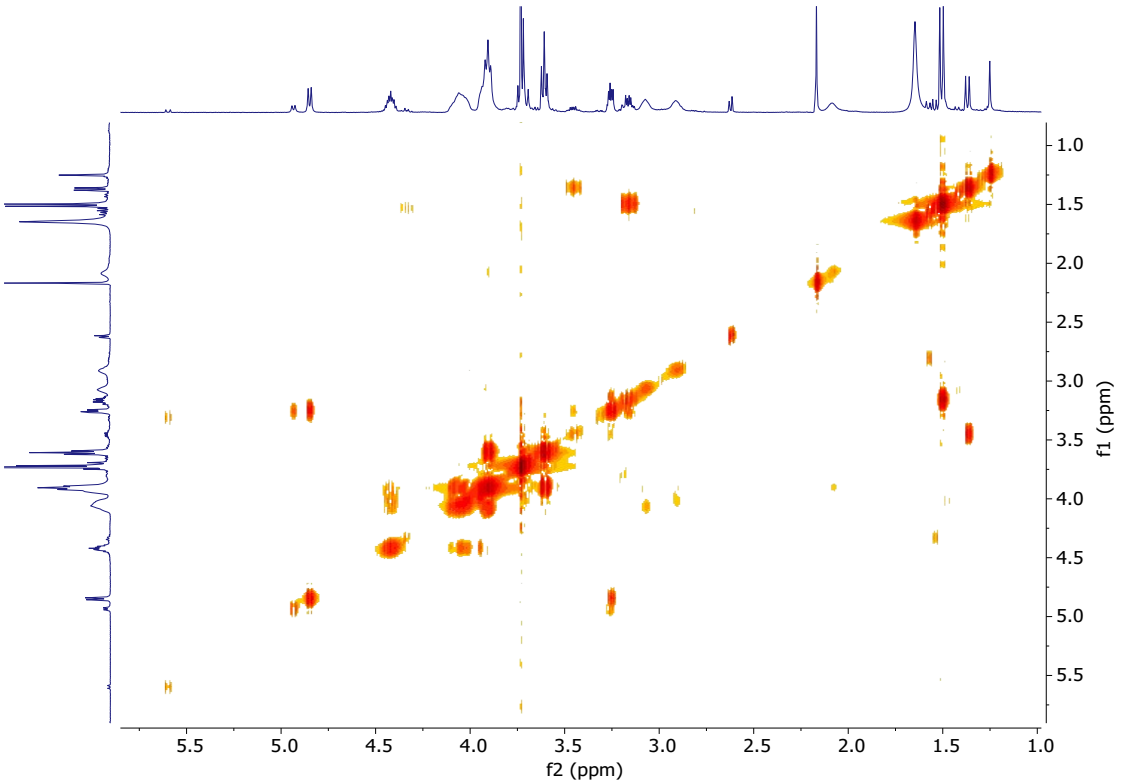


Figure S51. ^{1}H-^{1}H COSY NMR spectrum of Mal-CTA **(11c)** in $CDCl_3$.

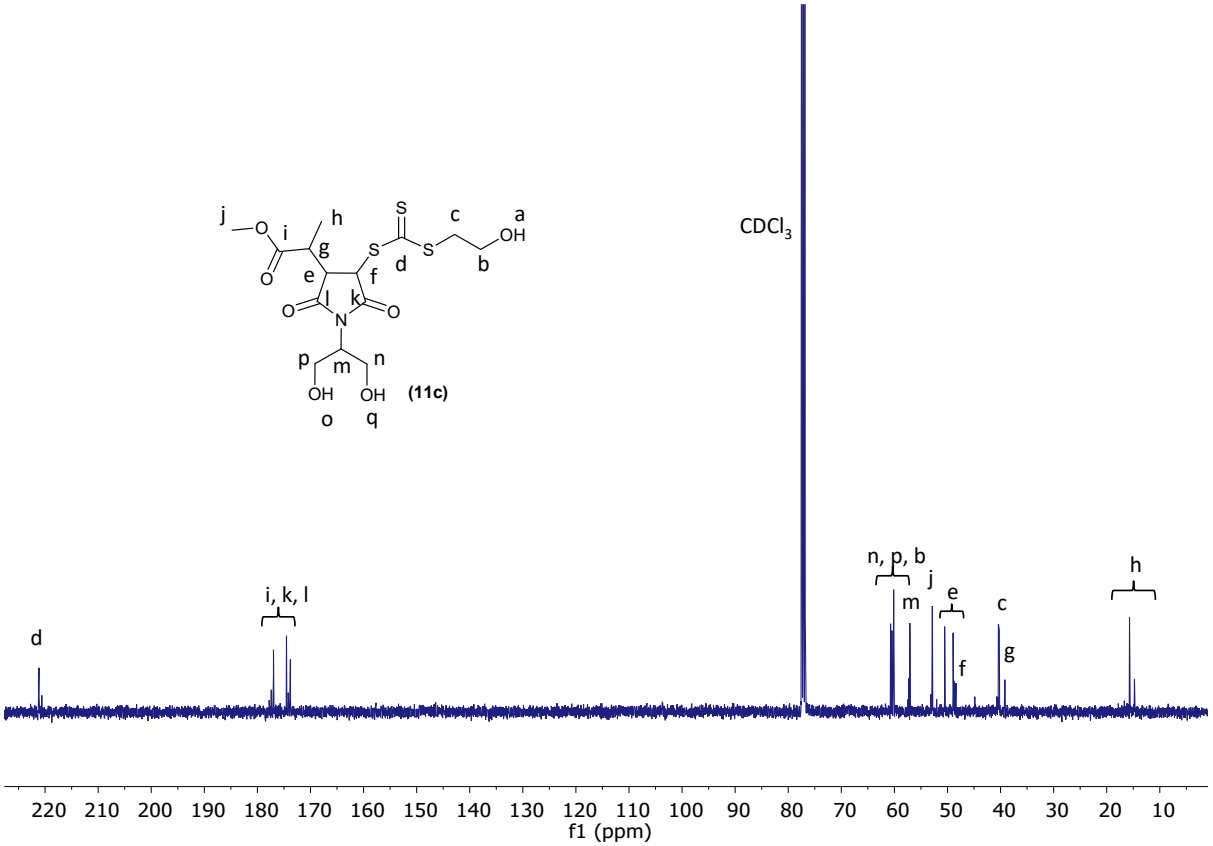


Figure S52. ^{13}C NMR spectrum of Mal-CTA **(11c)** in $CDCl_3$.

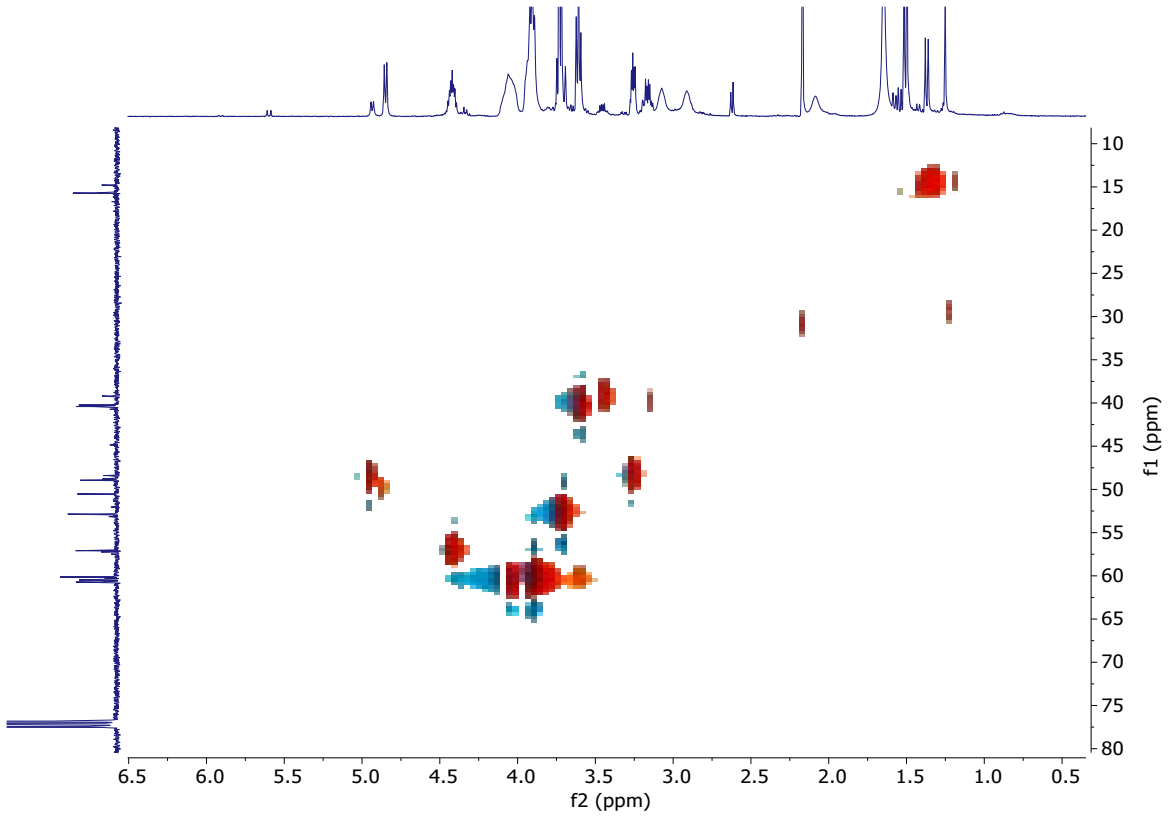


Figure S53. ^{1}H-^{13}C HSQC NMR spectrum of Mal-CTA **(11c)** in $CDCl_3$.

Mal-CTA **(12a)**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31-5.21 (m, 1H, NCH_2CHCH_2O), 5.16 (d, 1H, *J* = 6.6 Hz, SC(S)SC*H*), 5.09 (d, 1H, *J* = 6.6 Hz, SC(S)SC*H*), 5.00 (d, 1H, *J* = 6.6 Hz, SC(S)SC*H*), 4.93 (d, 1H, *J* = 6.6 Hz, SC(S)SC*H*), 4.31 - 4.10 (m, 2H, NCH_2CHCH_2O), 3.89 - 3.73 (m, 2H, NCH_2CHCH_2O), 3.70 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.35 (t, 2H, *J* = 7.4 Hz, $CH_2SC(S)S$), 3.27-3.18 (m, 1H, $CHCHCH_3$), 3.38 and 3.17 (m, 1H, $CHCHCH_3$), 2.34-2.24 (m, 4H, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 1.69 (m, 2H, $CH_2CH_2SC(S)S$), 1.59 (m, 4H, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 1.41-1.25 (bs, 66H, $(CH_2)_{12}CH_3$, $(CH_2)_9CH_3$) overlapping 1.35 (3H, d, *J* = 2.7 Hz, $CHCHCH_3$), 1.32 (3H, d, *J* = 2.7 Hz, $CHCHCH_3$), 0.88 (t, 9H, *J* = 7.0 Hz , $(CH_2)_nCH_3$).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 221.1 (1C, SC(S)S), 220.6 (1C, SC(S)S), 175.8 (1C, $C(O)OCH_3$), 175.3 (1C, $C(O)OCH_3$), 173.9 (1C, CO_{Mal}), 173.4 (2C, CO_{ester}), 172.5 (1C, CO_{Mal}), 68.8 (1C, NCH_2CH), 62.9 (1C, NCH_2CHCH_2O), 52.5 (1C, OCH_3), 52.5 (1C, OCH_3), 49.7 (1C, SC(S)SCH), 49,5 (1C, SC(S)SCH), 49,4 (1C, SC(S)SCH), 49.3 (1C, SC(S)SCH), 48.9 (1C, $CHCHCH_3$), 48.5 (1C, $CHCHCH_3$), 40.1 (1C, NCH_2CHCH_2O), 39.9 (1C, NCH_2CHCH_2O), 39.4 (1C, $CHCH_3$), 39.3 (1C, $CHCH_3$), 38.4 (1C, $CH_2SC(S)S$), 38.1 (1C, $CH_2SC(S)S$), 34.3 (1C, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 34.2 (1C, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 32.1 - 22.8 (33C, $(CH_2)_{12}CH_3$, $(CH_2)_9CH_3$), 27.9 (1C, $CH_2CH_2SC(S)S$), 25.0 (1C, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 24.8 (1C, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 15.1 (1C, $CHCH_3$), 14.8 (1C, $CHCH_3$), 14.7 (1C, $CHCH_3$), 14.3 (3C, $(CH_2)_nCH_3$).

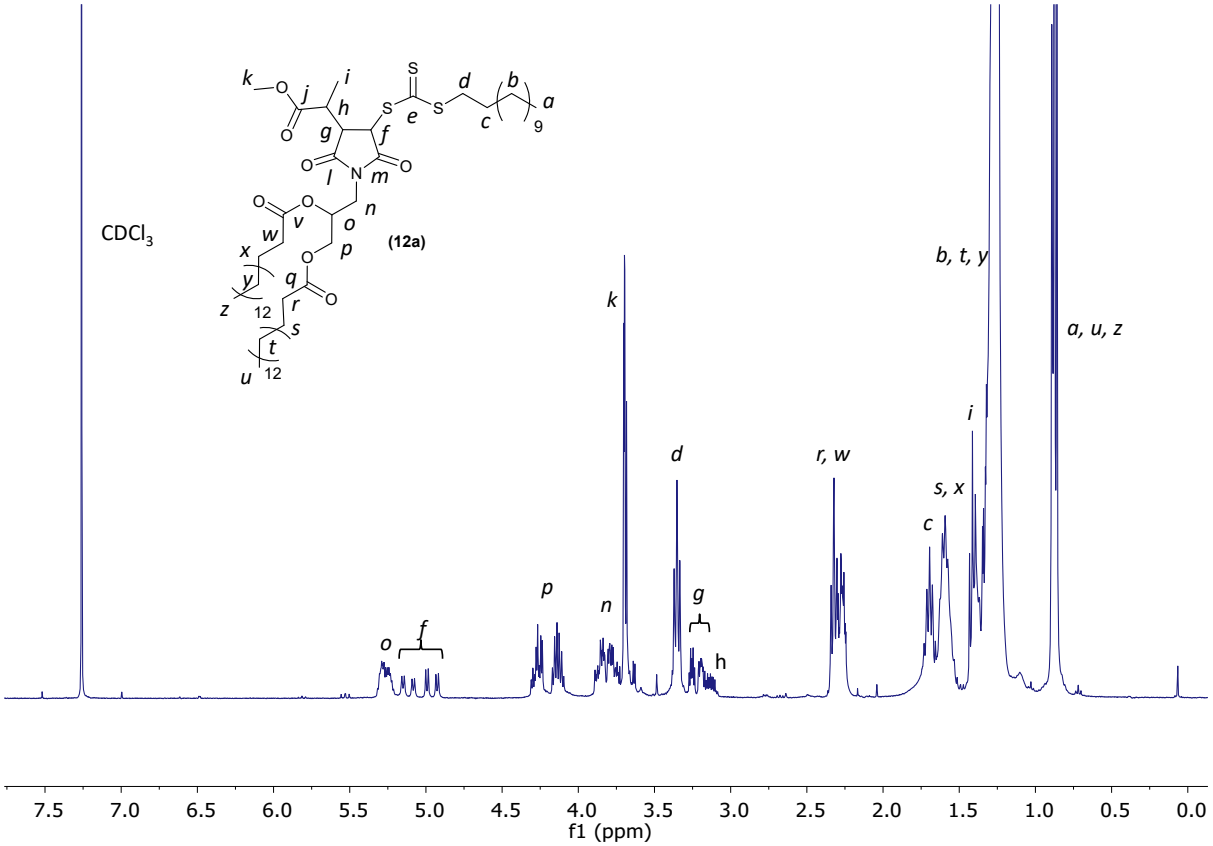


Figure S54. ^{1}H NMR spectrum of Mal-CTA **(12a)** in $CDCl_3$.

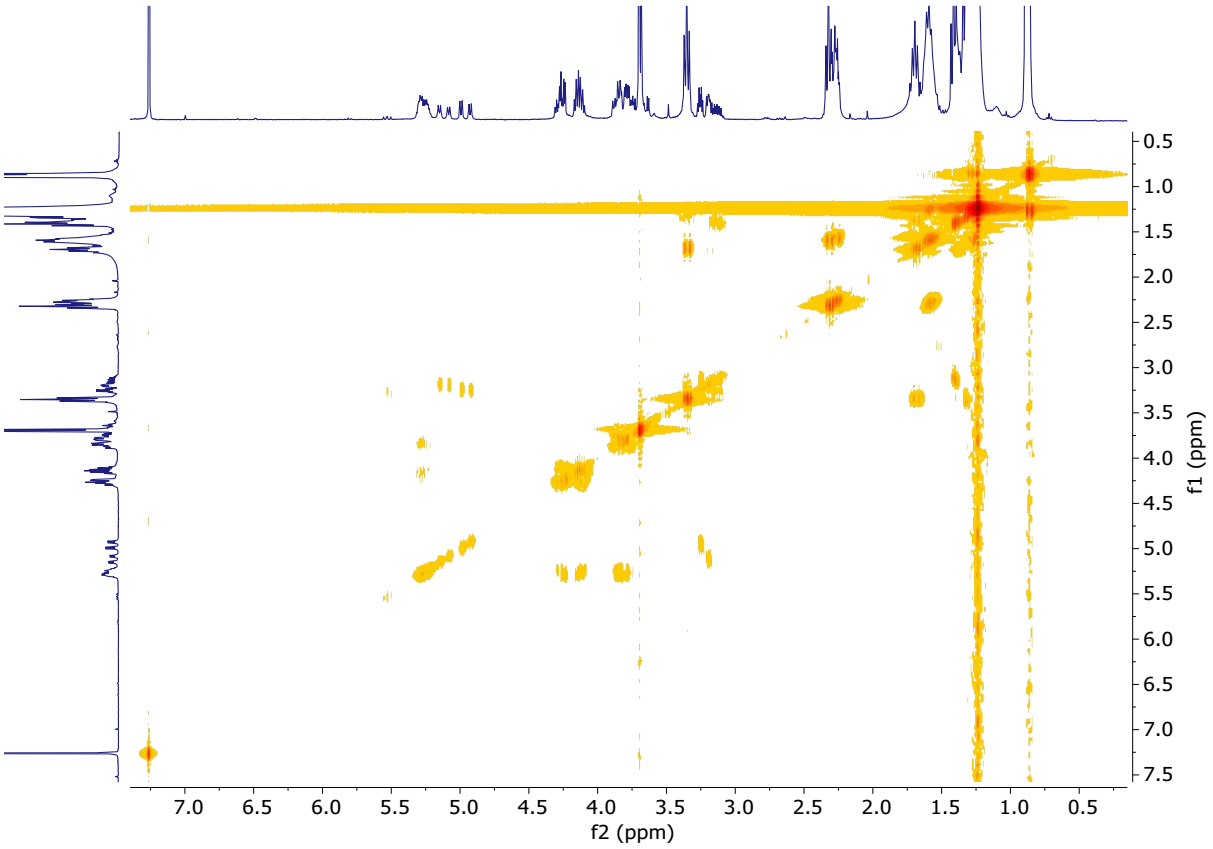


Figure S55. ^{1}H-^{1}H COSY NMR spectrum ($CDCl_3$) of Mal-CTA **(12a)** in $CDCl_3$.

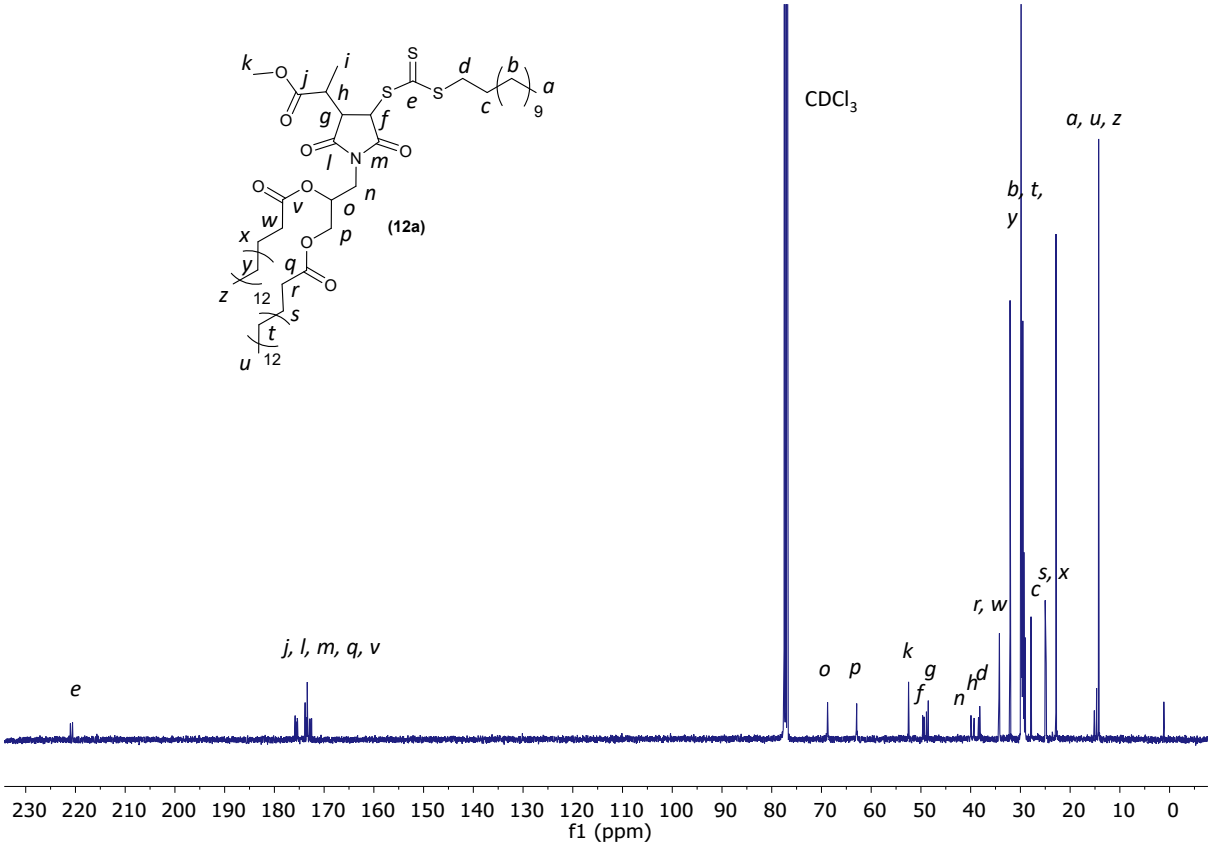


Figure S56. ^{13}C NMR spectrum ($CDCl_3$) of Mal-CTA **(12a)** in $CDCl_3$.

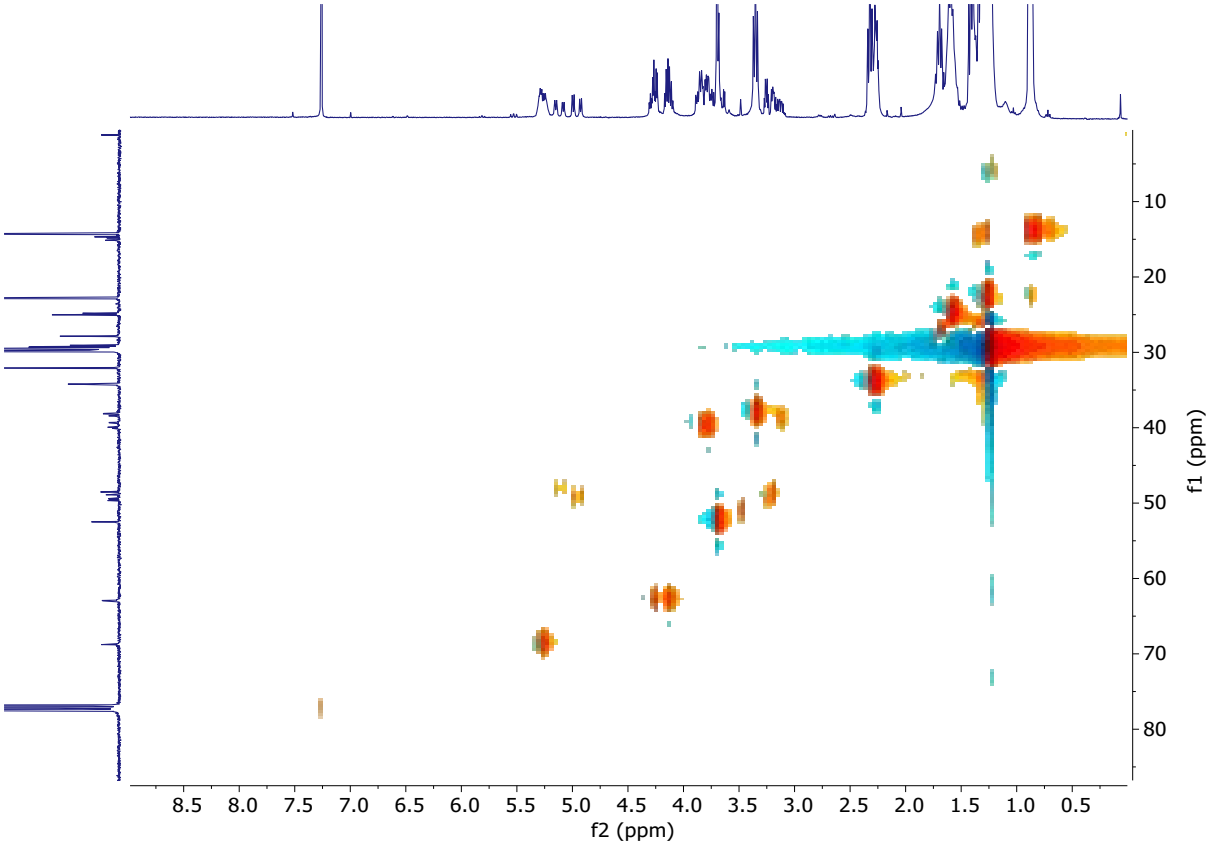


Figure S57. ^{1}H-^{13}C HSQC NMR spectrum of Mal-CTA **(12a)** in $CDCl_3$.

Mal-CTA **(12b)**. *Anti*:*Syn* molar ratio: 92:8

^{1}H NMR (400 MHz, $CDCl_3$, anti isomer) δ 5.05 (d, 1H, *J* = 6.6 Hz, SC(S)SCH), 4.94 (d, 1H, *J* = 6.6 Hz, SC(S)SCH), 3.84-3.65 (m, 2H, NC*H*$_2$CH$_2$OCH$_2$CH$_2$OH and m, 4H, NCH$_2$C*H*$_2$OCH$_2$C*H*$_2$OH) overlapping with 3.71 (s, 3H, OCH$_3$) and 3.70 (s, 3H, OCH$_3$), 3.57 (m, 2H, 2H, NCH$_2$C*H*$_2$O), 3.43-3.41 and 3.16-3.14 (m, 1H, *J* = 7.4, 3.7 Hz, CHC*H*CH$_3$), 3.35 (t, 2H, *J* = 7.4 Hz, C*H*$_2$SC(S)S), 3.25-3.21 (td, 1H, *J* = 6.6, 3.8 Hz, C*H*CHCH$_3$), 1.70 (m, 2H, *J* = 7.2 Hz, C*H*$_2$CH$_2$SC(S)S), 1.47 (d, 3H, *J* = 7.4 Hz CHCHC*H*$_3$), 1.38 (d, 3H, *J* = 7.4 Hz, CHCHC*H*$_3$), 1.42 – 1.21 (m and bs, 2H, 18H, C*H*$_2$CH$_3$), 0.88 (t, 9H, *J* = 6.9 Hz, CH$_3$,).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$, anti isomer) δ 221.0 (1C, SC(S)S), 220.1 (1C, SC(S)S), 176.1 (1C,CO$_{Mal}$), 175.7 (1C,CO$_{Mal}$), 174.2 (1C,CO$_{ester}$), 174.2 (1C,CO$_{ester}$), 173.1 (1C,CO$_{Mal}$), 172.8 (1C,CO$_{Mal}$), 72.5 (1C, OCH$_2$CH$_2$OH), 67.2 (1C, OCH$_2$CH$_2$OH), 61.8 (1C, NCH$_2$CH$_2$), 52.7 (1C, OCH$_3$), 52.6 (1C, OCH$_3$), 49.9 (1C, SC(S)SCH), 49.5 (1C, SC(S)SCH), 48.9 (1C, CHCHCH$_3$), 48.6 (1C, CHCHCH$_3$), 39.5 (1C, NCH$_2$), 39.5 (1C, NCH$_2$CH$_2$OCH$_2$CH$_2$OH), 39.3 (1C, CHCHCH$_3$), 38.5 (1C, CHCHCH$_3$), 38.1 (1C, CH$_2$SC(S)S), 38.0 (1C, CH$_2$SC(S)S),32.0 - 22.8 (9C, (CH$_2$)$_9$CH$_3$), 27.8 (1C, CH$_2$CH$_2$SC(S)S), 15.3 (1C, CHCHCH$_3$), 14.9 (1C, CHCHCH$_3$), 14.3 (3C, (CH$_2$)$_9$CH$_3$).

ESI-TOF Mass spectrometry: expected m/z [M+Na]$^{+}$ 572.22, found 572.21 (92.4%).

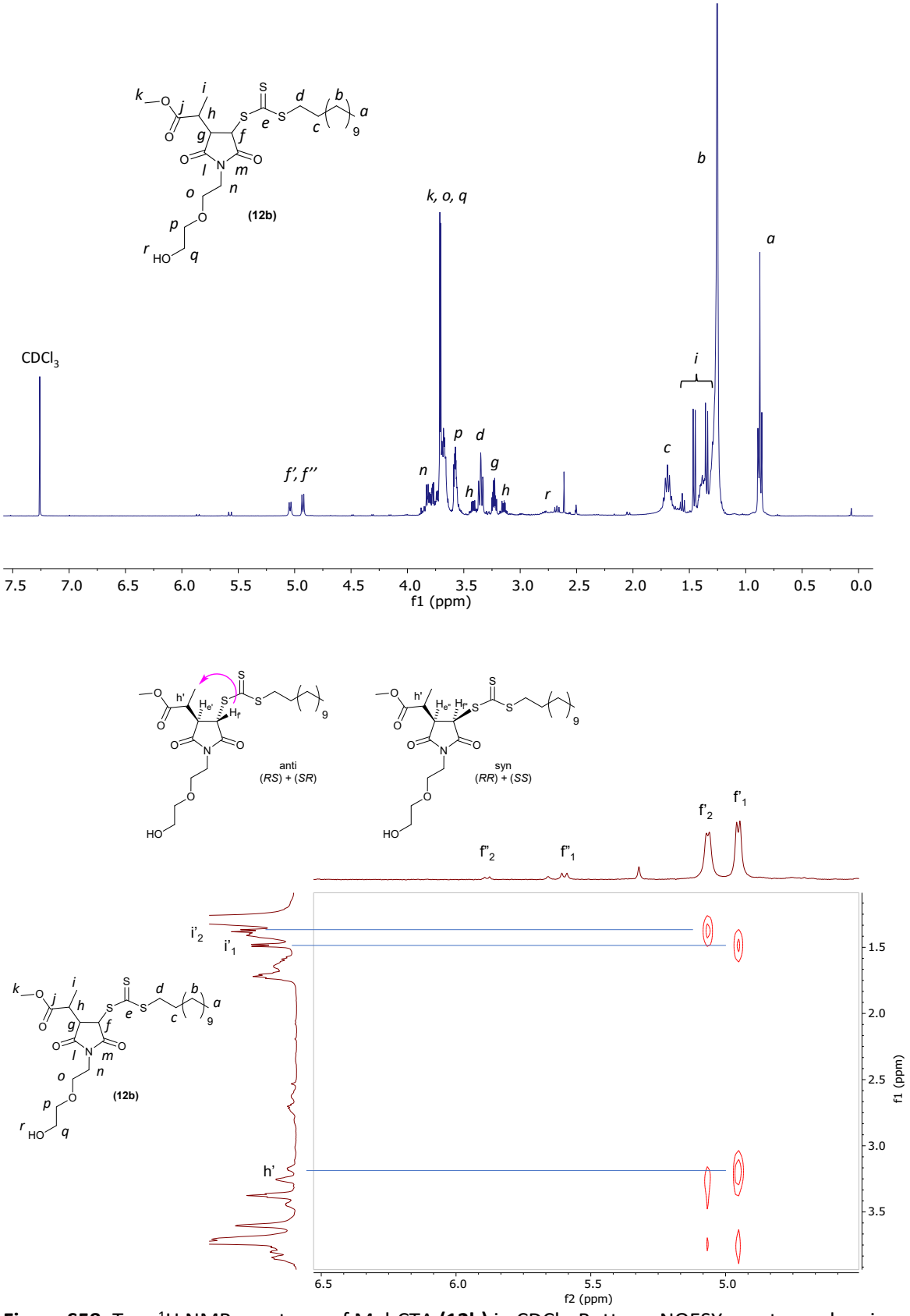


Figure S58. Top: ^{1}H NMR spectrum of Mal-CTA **(12b)** in $CDCl_3$. Bottom: NOESY spectrum showing spatial proximity between protons f'$_1$ and f'$_2$ and the methyl group of the 2-methylpropionate substituent (i'$_1$ and i'$_2$), confirming the *anti* (trans) structure of the major adduct. Carbon in position g is also chiral, resulting in the observed split of all signals, shown here as f'$_1$ and f'$_2$ for group f'.

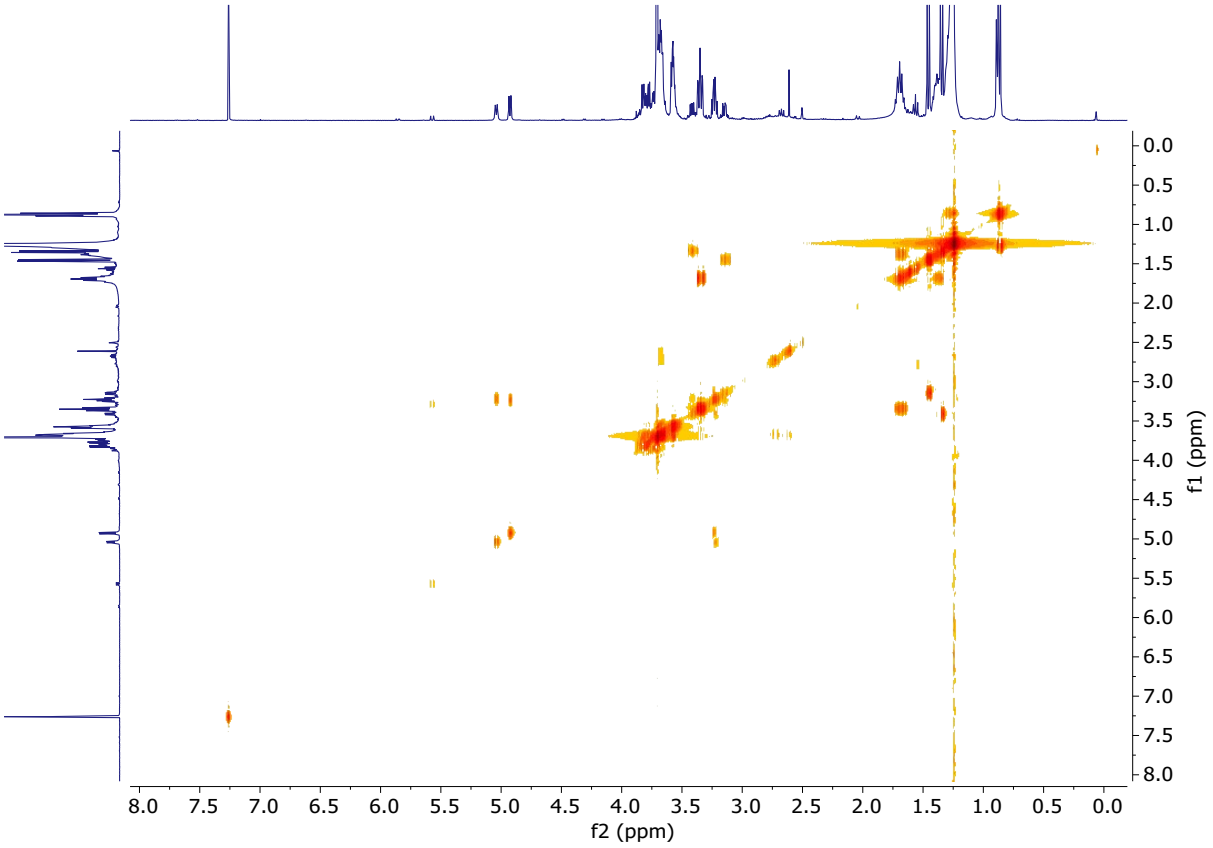


Figure S59. ^{1}H-^{1}H COSY NMR spectrum of Mal-CTA **(12b)** in $CDCl_3$.

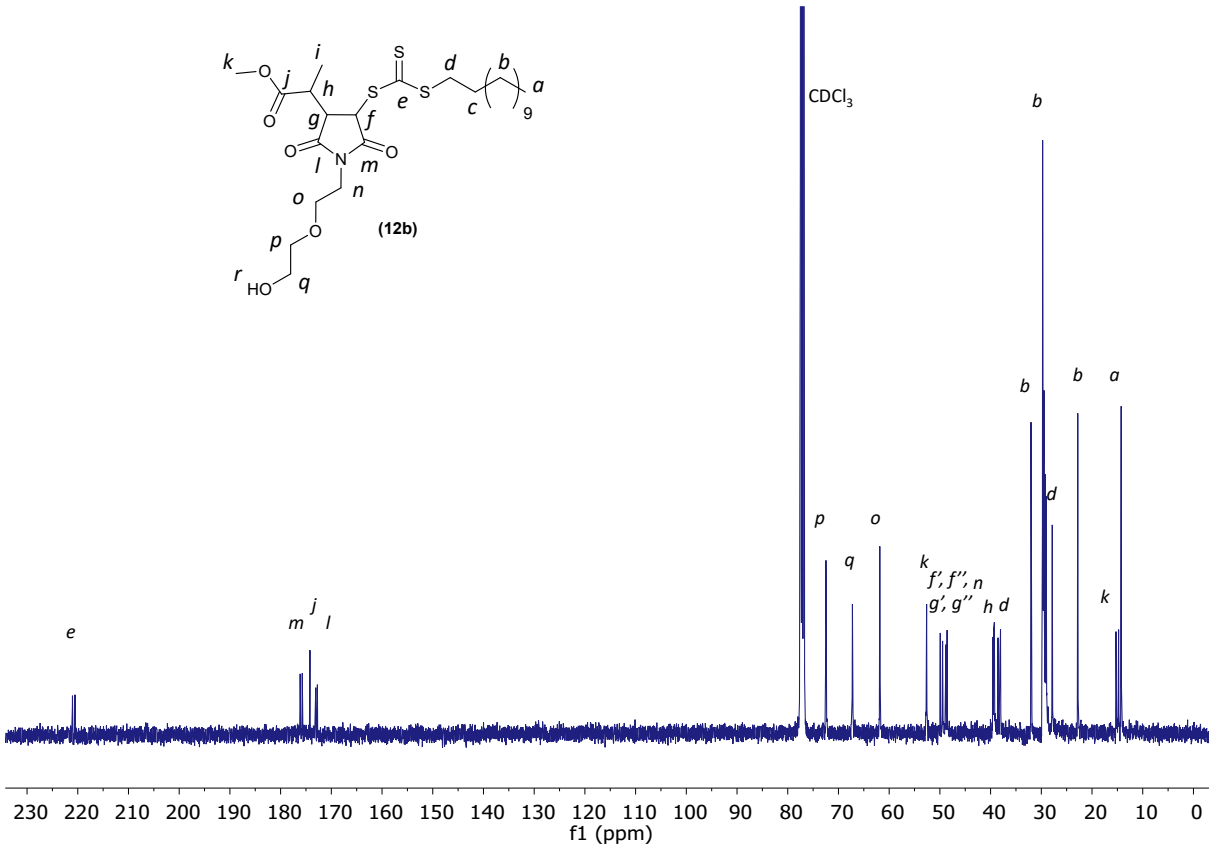


Figure S60. ^{13}C NMR spectrum of Mal-CTA **(12b)** in $CDCl_3$.

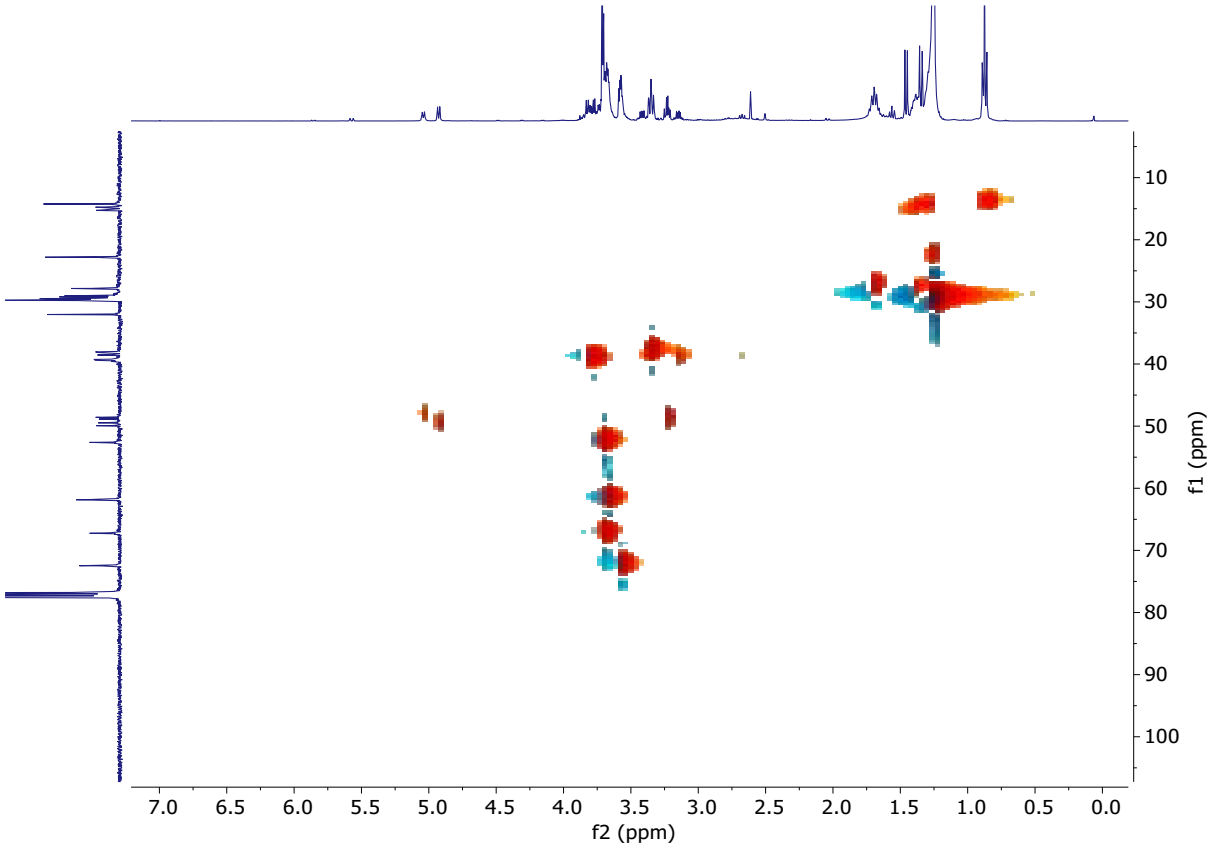


Figure S61. ^{1}H-^{13}C HSQC NMR spectrum of Mal-CTA **(12b)** in $CDCl_3$.

Mal-CTA **(13a)**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.31-5.21 (m, 1H, NCH_2CH), 4.92 (d, 1H, *J* = 6.6 Hz, SC(S)SCH) , 4.77 (d, 1H, *J* = 6.6 Hz, SC(S)SCH), 4.28-4.09 (m, 2H, CH_2O), 3.91-3.71 (m, 2H, NCH_2), 3.38-3.33 (m, 2H, $CH_2SC(S)S$), 3.20 (app. t, 1H, *J* = 6.5 Hz, $CHC(CH_3)_2CN$), 2.32 (t, 2H, *J* = 7.5 Hz, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 2.26 (t, 2H, *J* = 7.5 Hz, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 1.70 (m, 2H, $CH_2CH_2SC(S)S$), 1.63-1.51 (m overlapping with four s, 10H, $C(O)CH_2CH_2(CH_2)_{12}CH_3$, $C(CH_3)_2CN$), 1.39- 1.25 (bs, 66H, $(CH_2)_{12}CH_3$, $(CH_2)_9CH_3$), 0.87 (t, 9H, *J* = 6.8 Hz, CH_3).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 220.2 (1C, SC(S)S), 220.1 (1C, SC(S)S), 173.6 (1C,CO_{Mal}), 172.8 (1C,CO_{Mal}), 171.4 (1C, CO_{ester}), 171.3 (1C, CO_{ester}), 122.0 (1C, CN), 121.9 (1C, CN), 68.8 (1C, NCH_2CHCH_2O), 68.6 (1C, NCH_2CHCH_2O), 62.9 (1C, NCH_2CHCH_2O), 62.8 (1C, NCH_2CHCH_2O), 52.8 (1C, $CHC(CH_3)_2CN$), 52.7 (1C,$CHC(CH_3)_2CN$), 48.4 (1C, SC(S)SCH), 48.4 (1C, SC(S)SCH), 40.4 (1C, NCH_2CHCH_2O), 40.4 (1C, NCH_2CHCH_2O), 38.3 (1C, $CH_2SC(S)S$), 38.3 (1C, $CH_2SC(S)S$), 34.4-34.2 (2C, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 34.0(1C, $C(CH_3)_2CN$), 32.1-22.8 (33C, $(CH_2)_{12}CH_3$, $(CH_2)_9CH_3$), 27.8 (1C, $CH_2CH_2SC(S)S$), 25.5 – 24.5 (2C, $C(CH_3)_2CN$), 25.0 (2C, $C(O)CH_2CH_2(CH_2)_{12}CH_3$), 14.3 (3C, $(CH_2)_nCH_3$).

ESI-TOF Mass spectrometry: expected m/z $[M+Na]^+$ 1015.66, found 1015.73 (33%).

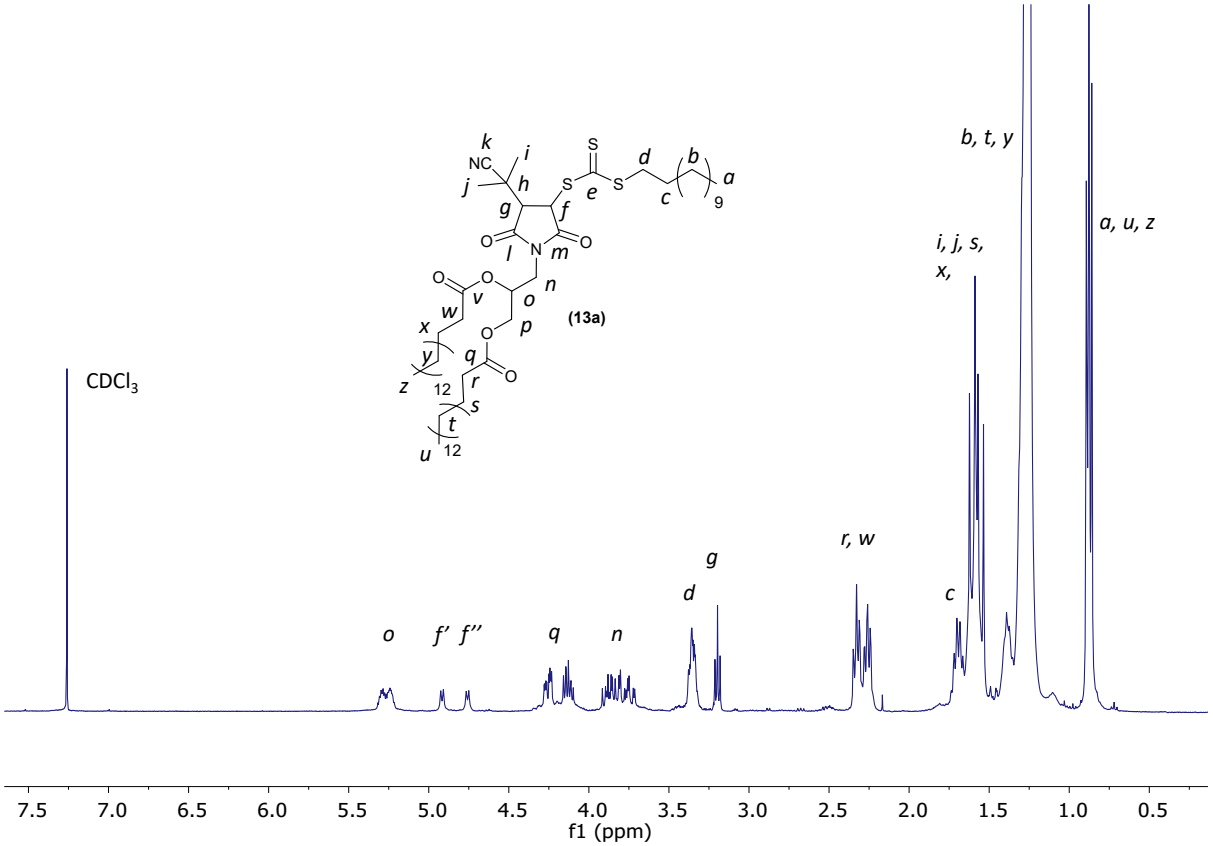


Figure S62. ^{1}H NMR spectrum of Mal-CTA **(13a)** in $CDCl_3$.

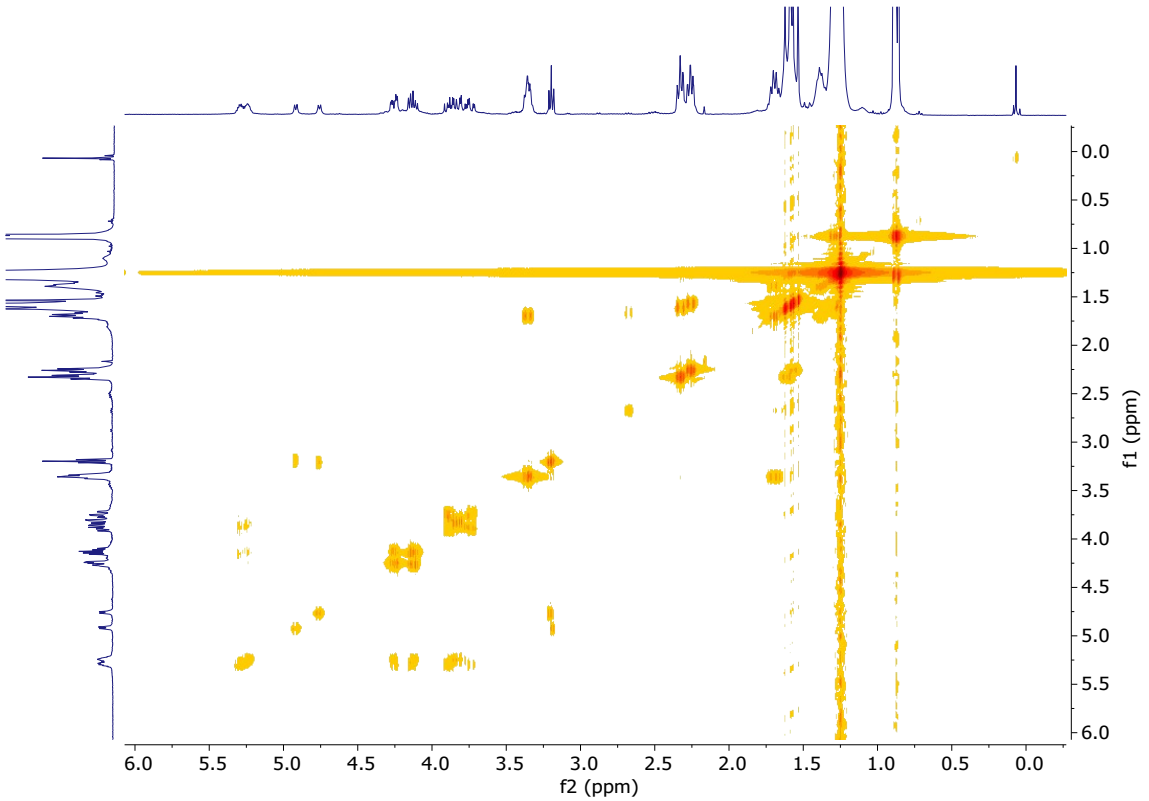


Figure S63. ^{1}H-^{1}H COSY NMR spectrum of Mal-CTA **(13a)** in $CDCl_3$.

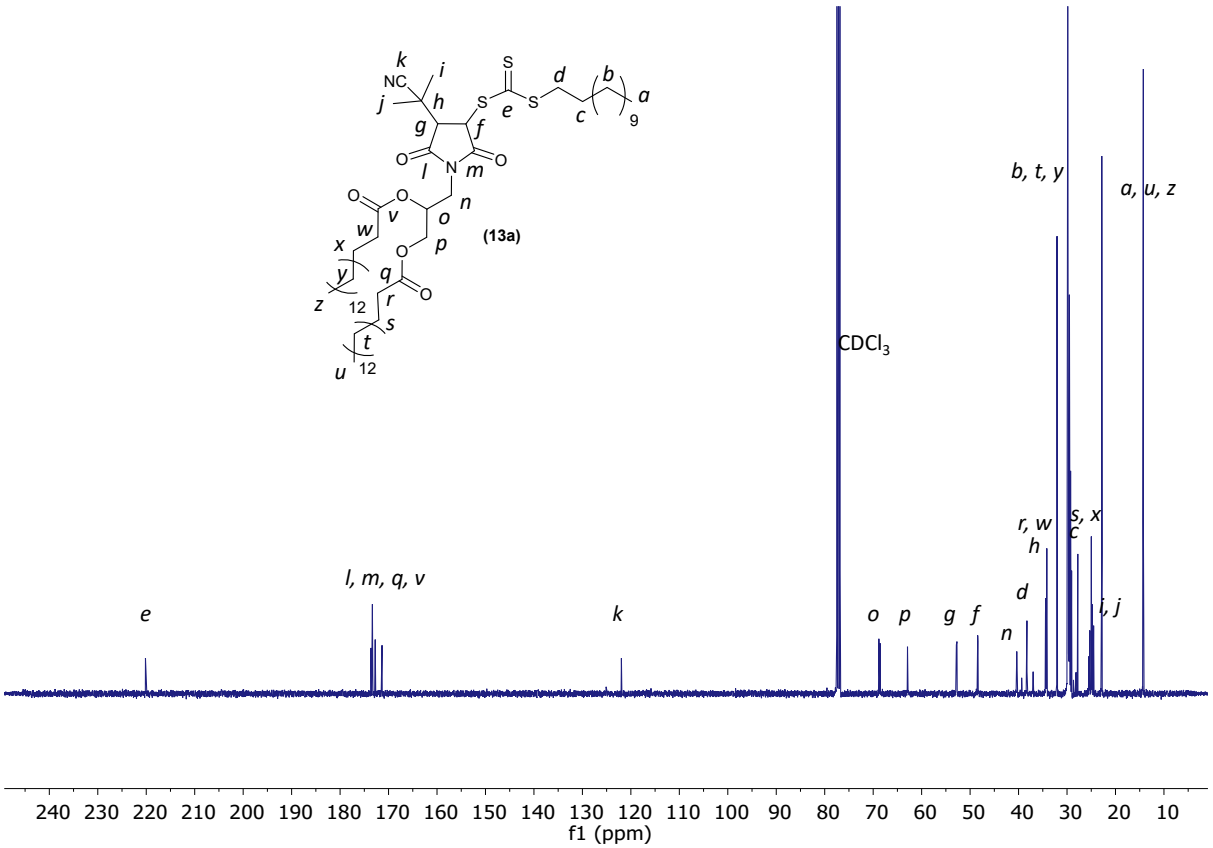


Figure S64. ^{13}C {^{1}H} NMR spectrum of Mal-CTA **(13a)** in $CDCl_3$.

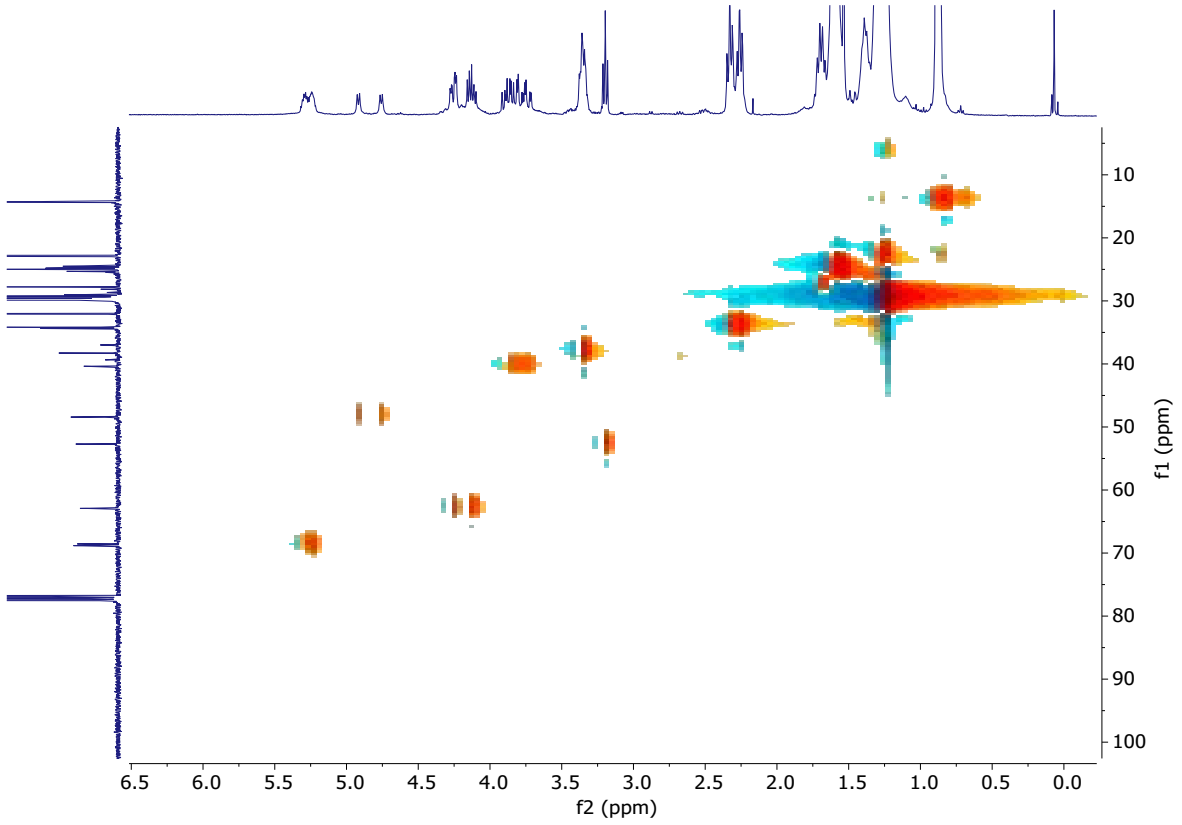


Figure S65. ^{1}H-^{13}C HSQC NMR spectrum of Mal-CTA **(13a)** in $CDCl_3$.

Mal-CTA **(13b)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.72 (d, 1H, *J* = 6.2 Hz, SC(S)SCH), 3.87-3.74 (m, 2H, NC*H*$_2$CH$_2$O), 3.71-3.64 (m, 4H, C*H*$_2$OCH$_2$C*H*$_2$OH), 3.55 (t, 2H, *J* = 4.5 Hz NCH$_2$C*H*$_2$O), 3.35 (t, 2H, *J* = 7.5 Hz, CH$_2$SC(S)S), 3.22 (d, 1H, *J* = 6.2 Hz, C*H*C(CH$_3$)$_2$CN), 2.30 (t, 1H, *J* = 6.4 Hz, OCH$_2$CH$_2$O*H)*, 1.70 (m, 2H, C*H*$_2$CH$_2$SC(S)S), 1.65 (s, 3H, C(CH$_3$)$_2$CN), 1.54 (s, 3H, C(CH$_3$)$_2$CN), 1.39 (m, 2H, C*H*$_2$CH$_2$CH$_2$SC(S)S), 1.25(bs, 16H, (C*H*$_2$)$_8$CH$_3$), 0.87 (t, 9H, *J* = 6.9 Hz, CH$_3$).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 220.0 (1C, SC(S)S), 173.1 (1C,CO), 171.5 (1C,CO), 121.9 (1C, CN), 72.5 (1C, OC*H*$_2$CH$_2$OH), 67.1 (1C, NCH$_2$*C*H$_2$O), 61.9 (1C, NCH$_2$*C*H$_2$O), 53.0 (1C, *C*HC(CH$_3$)$_2$CN), 48.6 (1C, SC(S)S*C*H), 39.5 (1C, NC*H*$_2$CH$_2$O), 38.3 (1C, *C*H$_2$SC(S)S), 34.8 (1C, *C*(CH$_3$)$_2$CN), 32.0-22.8 (9C, (*C*H$_2$)$_9$CH$_3$), 27.8 (1C, *C*H$_2$CH$_2$SC(S)S), 25.6 (1C, C(*C*H$_3$)$_2$CN), 24.9 (1C, (*C*H$_3$)$_2$CN), 14.3 (1C, (CH$_2$)$_9$*C*H$_3$).

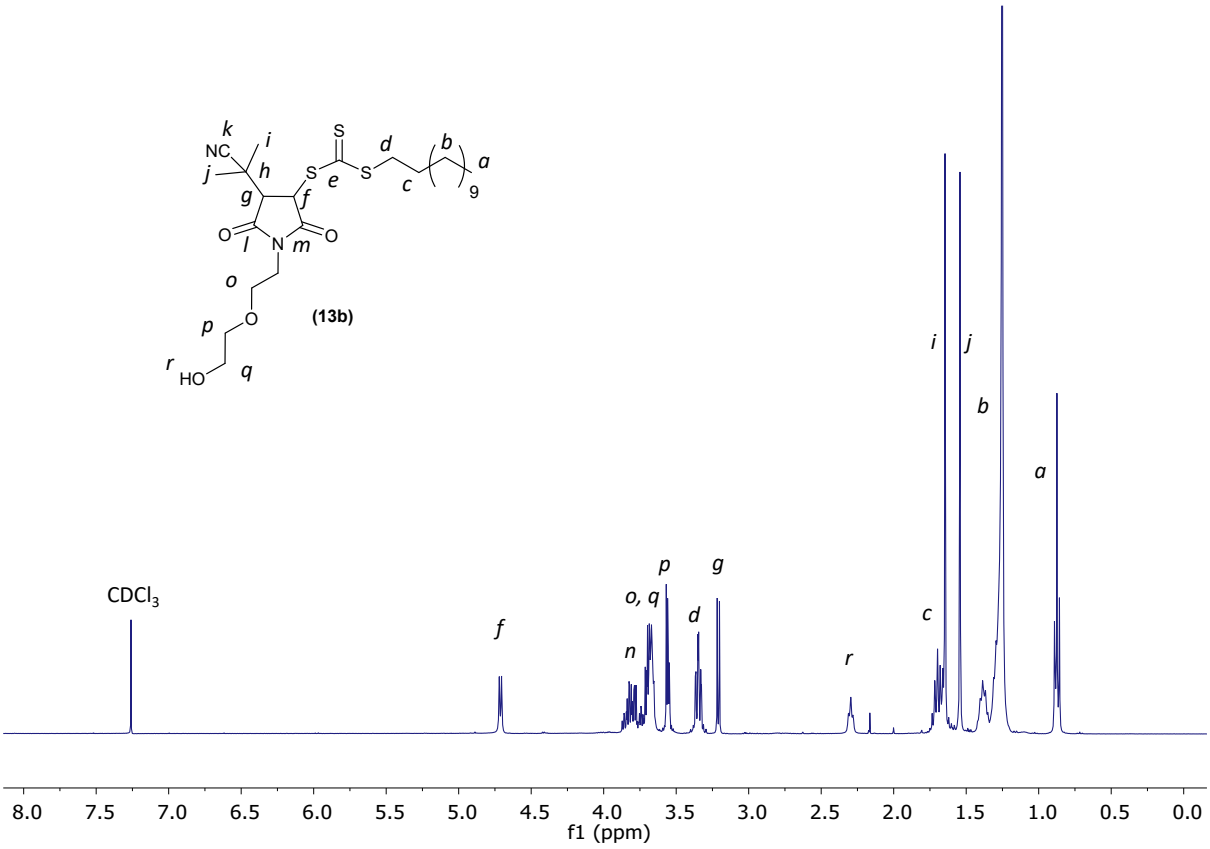


Figure S66. ^{1}H NMR spectrum of Mal-CTA **(13b)** in $CDCl_3$.

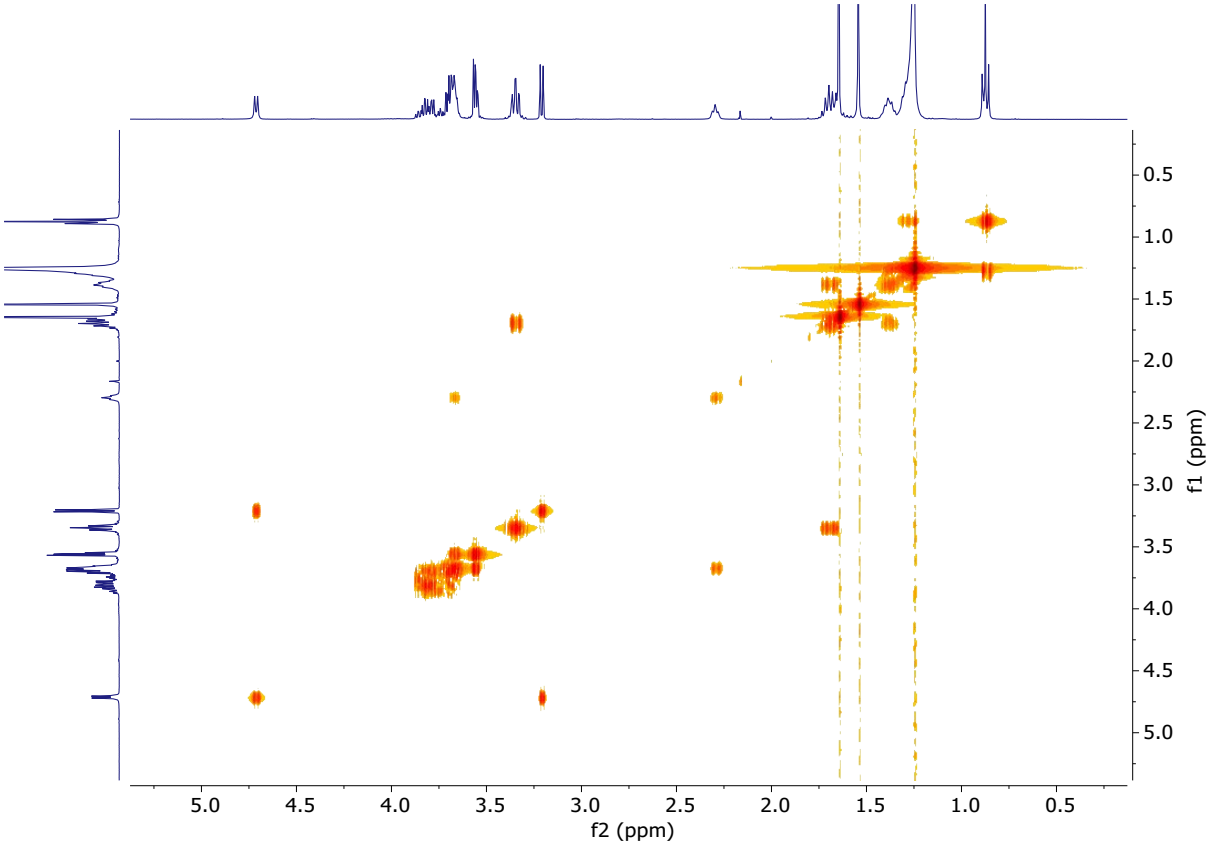


Figure S67. ^{1}H-^{1}H COSY NMR spectrum ($CDCl_3$) of Mal-CTA **(13b)** in $CDCl_3$.

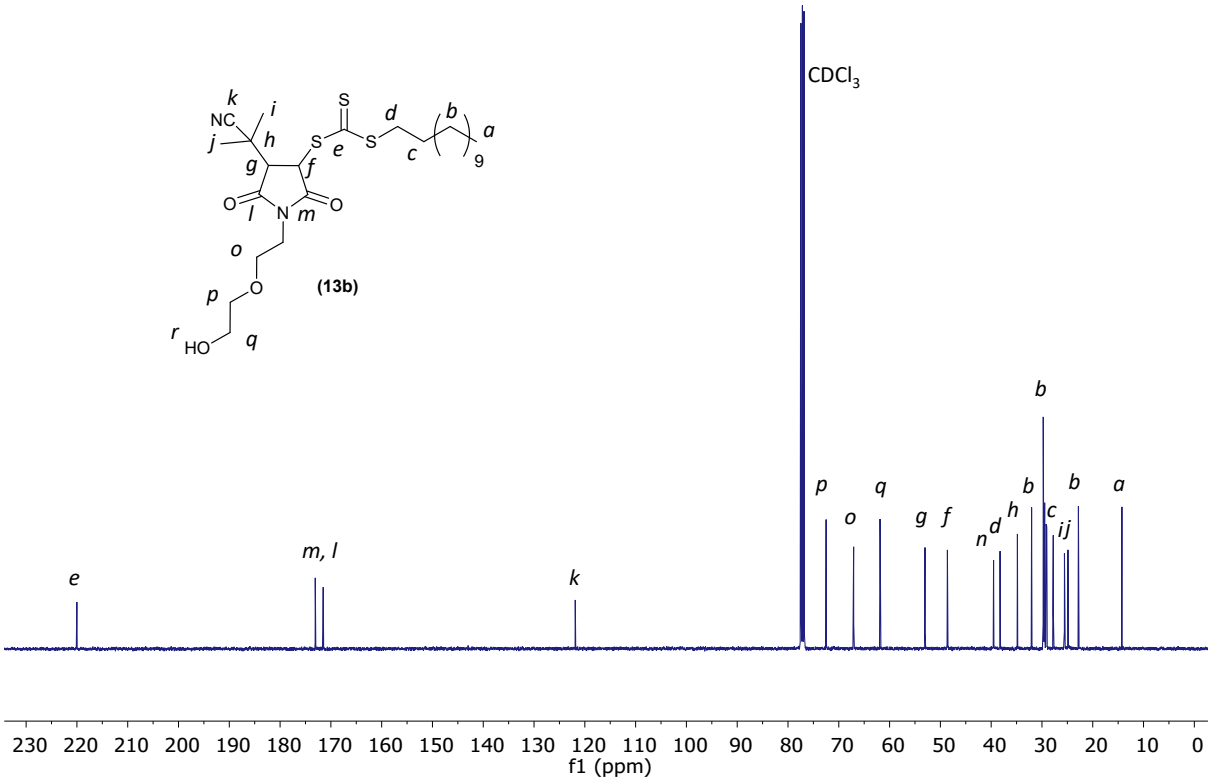


Figure S68. ^{13}C NMR spectrum ($CDCl_3$) of Mal-CTA **(13b)** in $CDCl_3$.

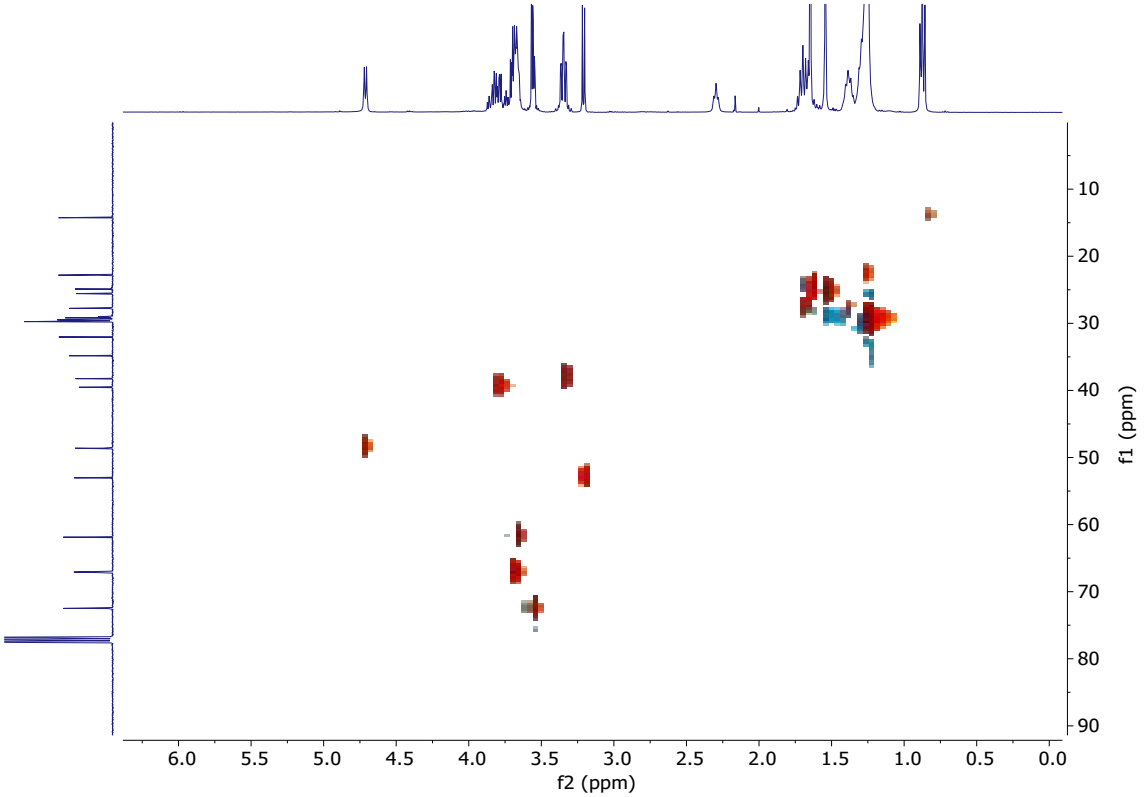


Figure S69. ^{1}H-^{13}C HSQC NMR spectrum ($CDCl_3$) of Mal-CTA **(13b)** in $CDCl_3$.

Mal-CTA **(14b)**

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.71 (d, 1H, *J* = 6.2 Hz, SC(S)SCH), 3.93-3.88 (m, 2H, HOC*H*$_2$CH$_2$S), 3.83-3.75 (m, 2H, NC*H*$_2$CH$_2$O), 3.72-3.66 (m, 4H, C*H*$_2$OCH$_2$C*H*$_2$OH), 3.60 (t, 2H, *J* = 5.9 Hz, HOCH$_2$C*H*$_2$S), 3.56 (m, 2H, OC*H*$_2$CH$_2$OH), 3.22 (d, 1H, *J* = 6.2 Hz, C*H*C(CH$_3$)$_2$CN), 2.8 (bs, 1H, *J* = 6.4 Hz, OCH$_2$CH$_2$O*H)*, 1.91 (bs, 1H, *J* = 5.7 Hz, *H*OCH$_2$CH$_2$S), 1.65 (s, 3H, C(CH$_3$)$_2$CN), 1.54 (s, 3H, C(CH$_3$)$_2$CN).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 220.0 (1C, SC(S)S), 172.9 (1C,CO), 171.4 (1C,CO), 121.8 (1C, CN), 72.5 (1C, OC*H*$_2$CH$_2$OH), 67.1 (1C, OCH$_2$C*H*$_2$OH), 61.9 (1C, NCH$_2$C*H*$_2$O), 59.9 (1C, HOC*H*$_2$CH$_2$S), 52.9 (1C, C*H*C(CH$_3$)$_2$CN), 48.9 (1C, SC(S)S*C*H), 39.9 (1C, C*H*$_2$SC(S)S), 39.5 (1C, NC*H*$_2$CH$_2$O), 35.1 (1C, C(CH$_3$)$_2$CN), 25.6 (1C, C(C*H*$_3$)$_2$CN), 24.9 (1C, (C*H*$_3$)$_2$CN).

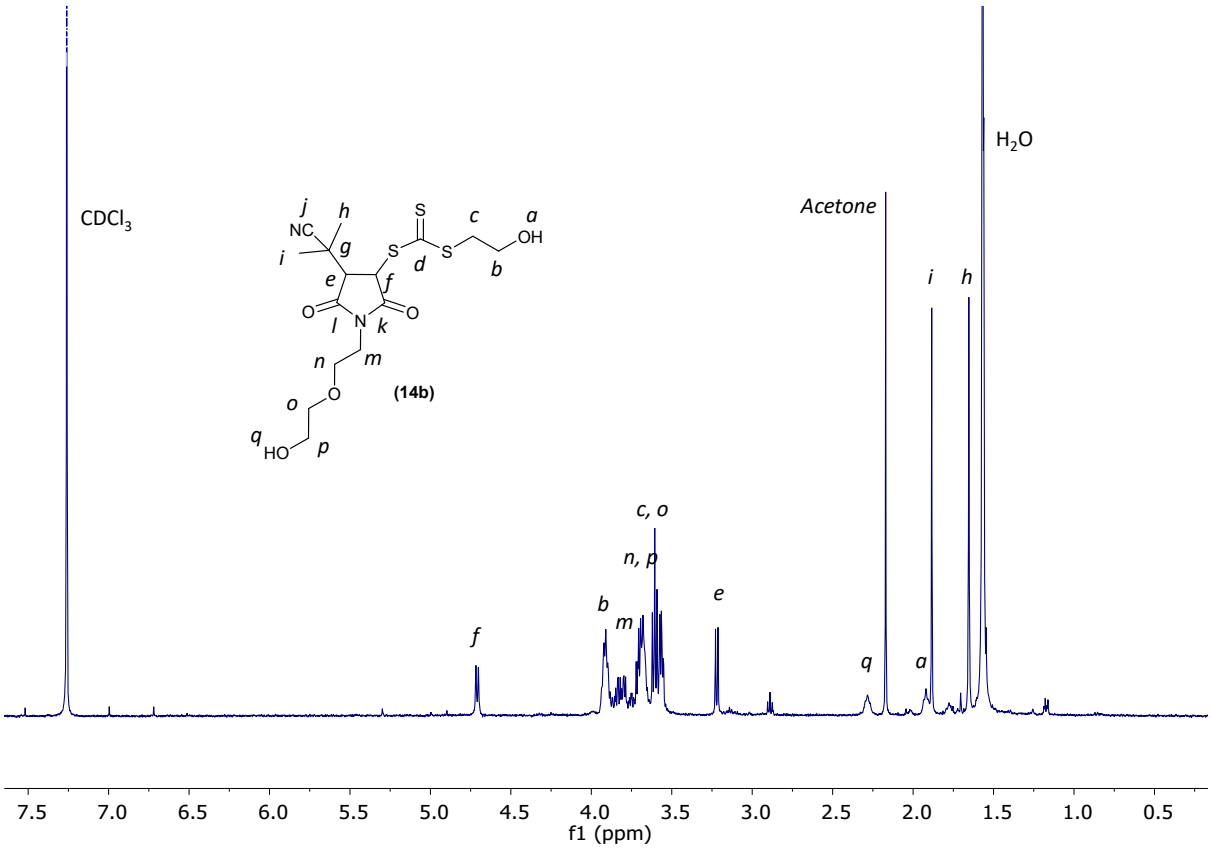


Figure S70. ^{1}H NMR spectrum of Mal-CTA **(14b)** in $CDCl_3$.

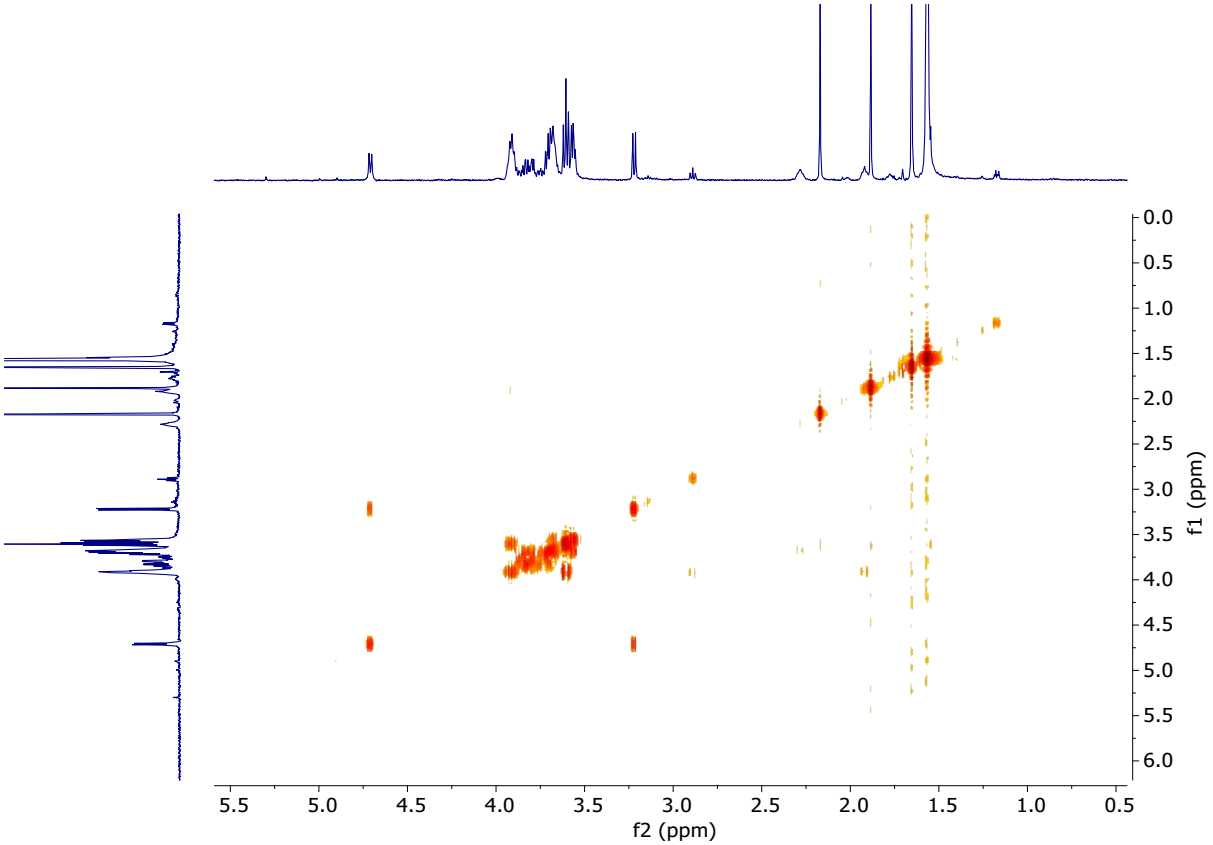


Figure S71. ^{1}H-^{1}H COSY NMR spectrum ($CDCl_3$) of Mal-CTA **(14b)** in $CDCl_3$.

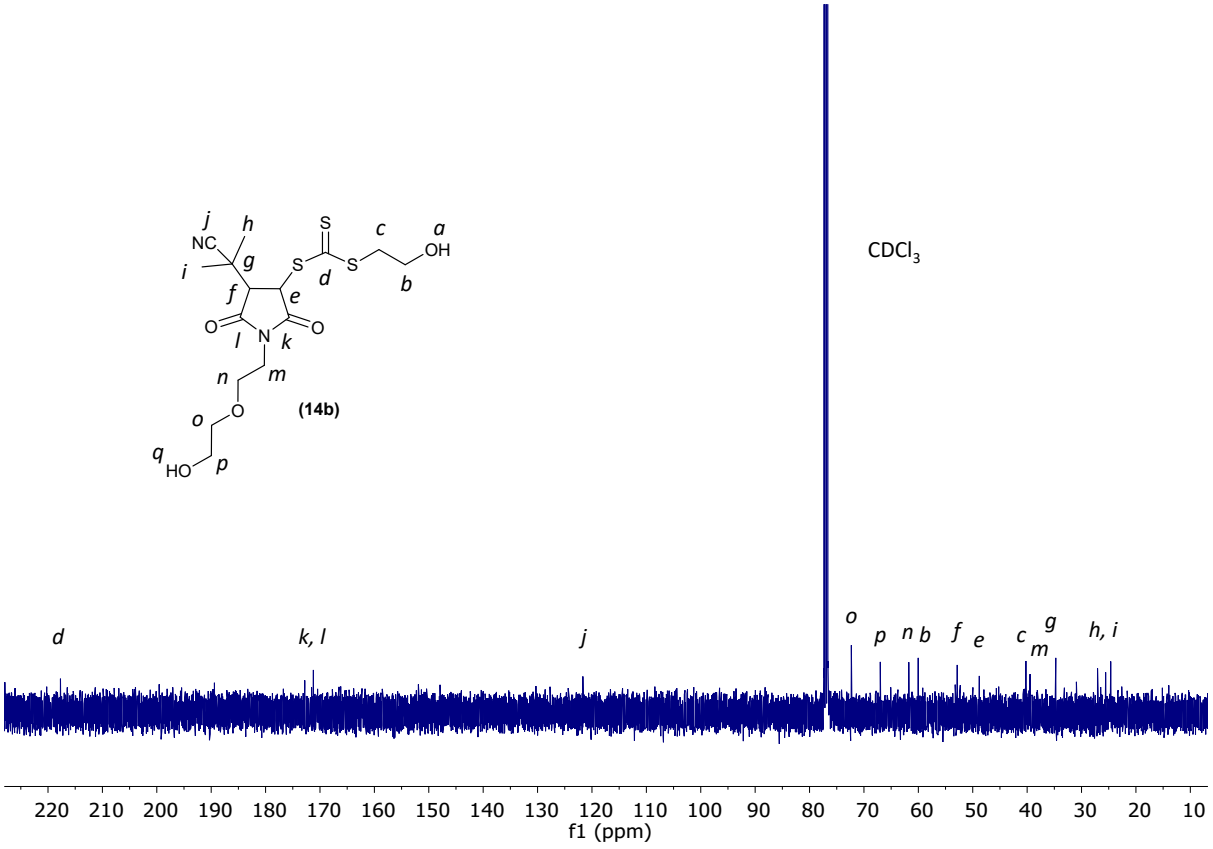


Figure S72. ^{13}C NMR spectrum ($CDCl_3$) of Mal-CTA **(14b)** in $CDCl_3$.

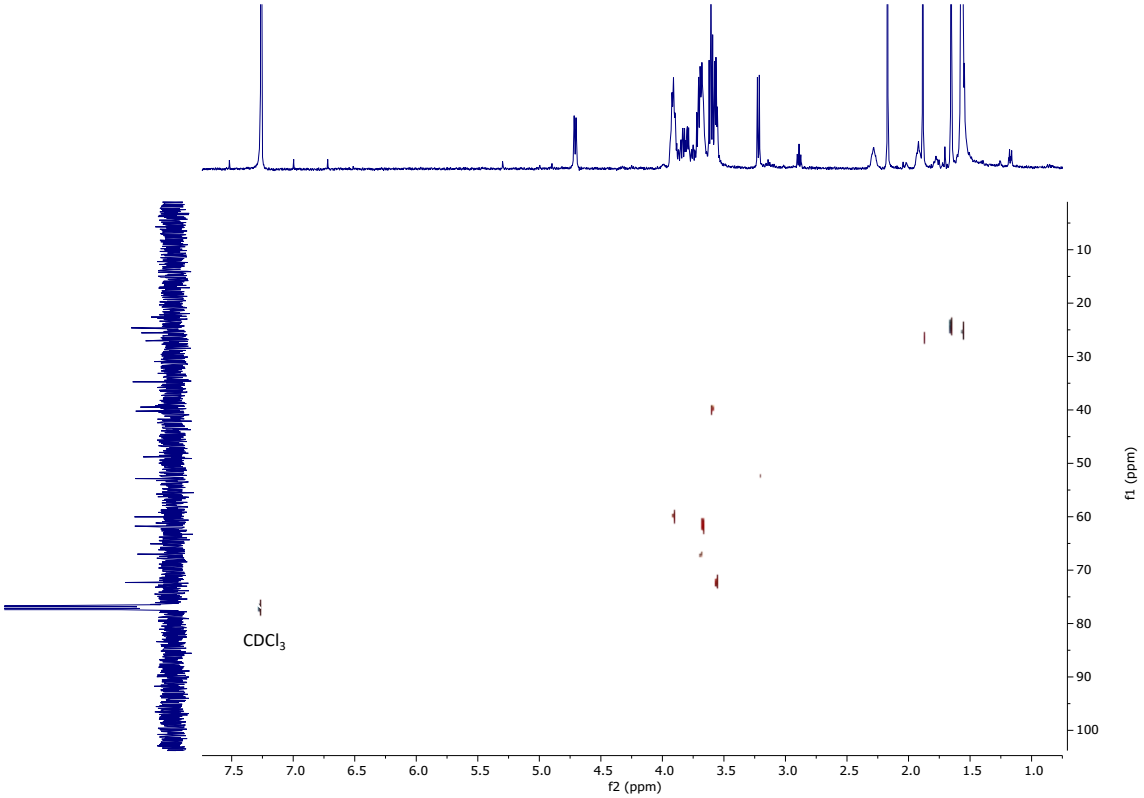


Figure S73. ^{1}H-^{13}C HSQC NMR spectrum ($CDCl_3$) of Mal-CTA **(14b)** in $CDCl_3$.

RAFT polymerisation mediated by Mal-CTAs. General polymerisation procedure: maleimide-based RAFT agent (**Mal-CTA**), monomer, initiator (aliquot from stock solution), and solvent were introduced in a Schlenk tube along with a magnetic stirrer and the tube was sealed with a rubber septum. The mixture was cooled with an ice bath and was degassed by argon bubbling for 15 minutes. The reaction was started by placing the Schlenk tube in a thermostated oil bath at the desired temperature.

Table S3. Synthesis of (**Mal-CTA**)-polymers: reaction conditions.

	Fast		***Ultrafast***					
Polymer	**(11a)**-BA_{48}	**(12a)**-BA_{34}	**(11b)**-HEA_{43}	**(11b)**-NAM_{49}	**(11b)**-DMA_{39}	**(11b)**-DMA_{97}	**(11b)**-DMA_{184}	**(11b)**-DMA_{475}
	15	**16**	**17**	**18**	**19**	**20**	**21**	**22**
Monomer	BA	BA	HEA	NAM	DMA	DMA	DMA	DMA
$DP_{targeted}$	50	50	50	50	50	100	200	500
mg	152.9	134.1	148.8	182.5	128.1	256.3	256.3	640.6
mmol	1.193	1.046	1.293	1.293	1.293	2.585	2.585	6.462
Mal-CTA	**(11a)**	**(12a)**	**(11b)**	**(11b)**	**(11b)**	**(11b)**	**(11b)**	**(11b)**
mg	16.3	16.3	10.0	10.0	10.0	10.0	5.0	5.0
mmol	0.018	0.016	0.024	0.024	0.024	0.024	0.012	0.012
Initiator	AIBN	AIBN	VA-044	VA-044	VA-044	VA-044	VA-044	VA-044
mg	0.30	0.26	0.076	0.076	0.076	0.076	0.038	0.038
mmol	$1.8\cdot10^{-3}$	$1.6\cdot10^{-3}$	$2.4\cdot10^{-4}$	$2.4\cdot10^{-4}$	$2.4\cdot10^{-4}$	$2.4\cdot10^{-4}$	$1.2\cdot10^{-4}$	$1.2\cdot10^{-4}$
V_{total} (mL)	0.596	0.523	0.646	0.646	0.646	1.293	1.293	3.231
Solvent 1	DMF	DMF	H_2O	H_2O	H_2O	H_2O	H_2O	H_2O
$V_{solvent\ 1\ added}$ (mL)	0.425	0.373	0.307	0.290	0.308	0.616	0.616	1.54
Solvent 2	-	-	dioxane	dioxane	dioxane	dioxane	dioxane	dioxane
$V_{solvent\ 2\ added}$ (mL)	-	-	0.205	0.193	0.205	0.410	0.410	1.026
[CTA]/[initiator]	10	10	100	100	100	100	100	100
Temp. (°C)	80	80	100	100	75	75	75	75
Time (min)	90	90	15	15	15	15	15	15

BA = *n*-butyl acrylate, HEA = *N*-hydroxyethylacrylamide, NAM = 4-acryloylmorpholine, DMA = *N,N*-dimethylacrylamide.

At the end of the polymerization, polymers **(11a)**-BA_{48} and **(12a)**-BA_{34} (**14** and **15)** were precipitated in H_2O/MeOH; polymers **(11b)**-HEA_{43}, **(11b)**-NAM_{49}, **(11b)**-DMA_{39}, **(11b)**-DMA_{97}, **(11b)**-DMA_{184}, **(11b)**-DMA_{475} (**16, 17, 18, 19, 20,** and **21**) were purified by dialysis (MWCO: 1 kDa) against water for 24 hours, with three water changes, followed by lyophilisation.

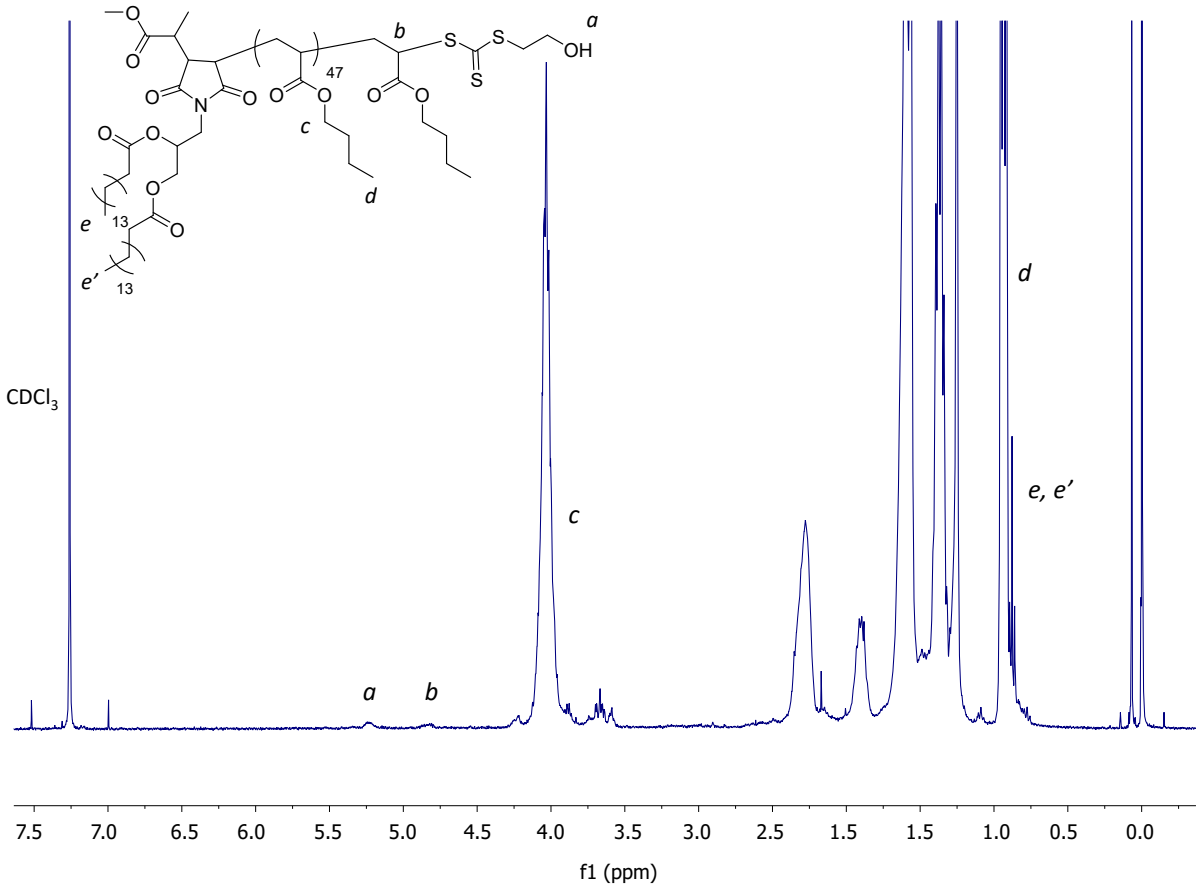


Figure S74. ^{1}H NMR spectrum of polymer **15 (11a)**-BA_{48} in $CDCl_3$.

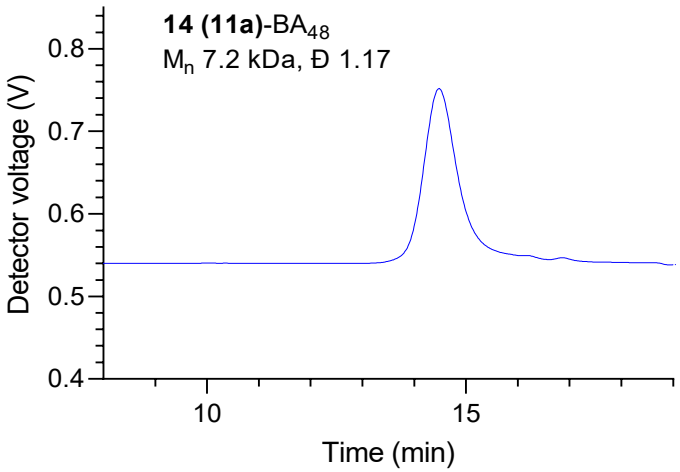


Figure S75. SEC analysis of polymer **15 - (11a)**-BA_{48}, using $CHCl_3$ as the mobile phase.

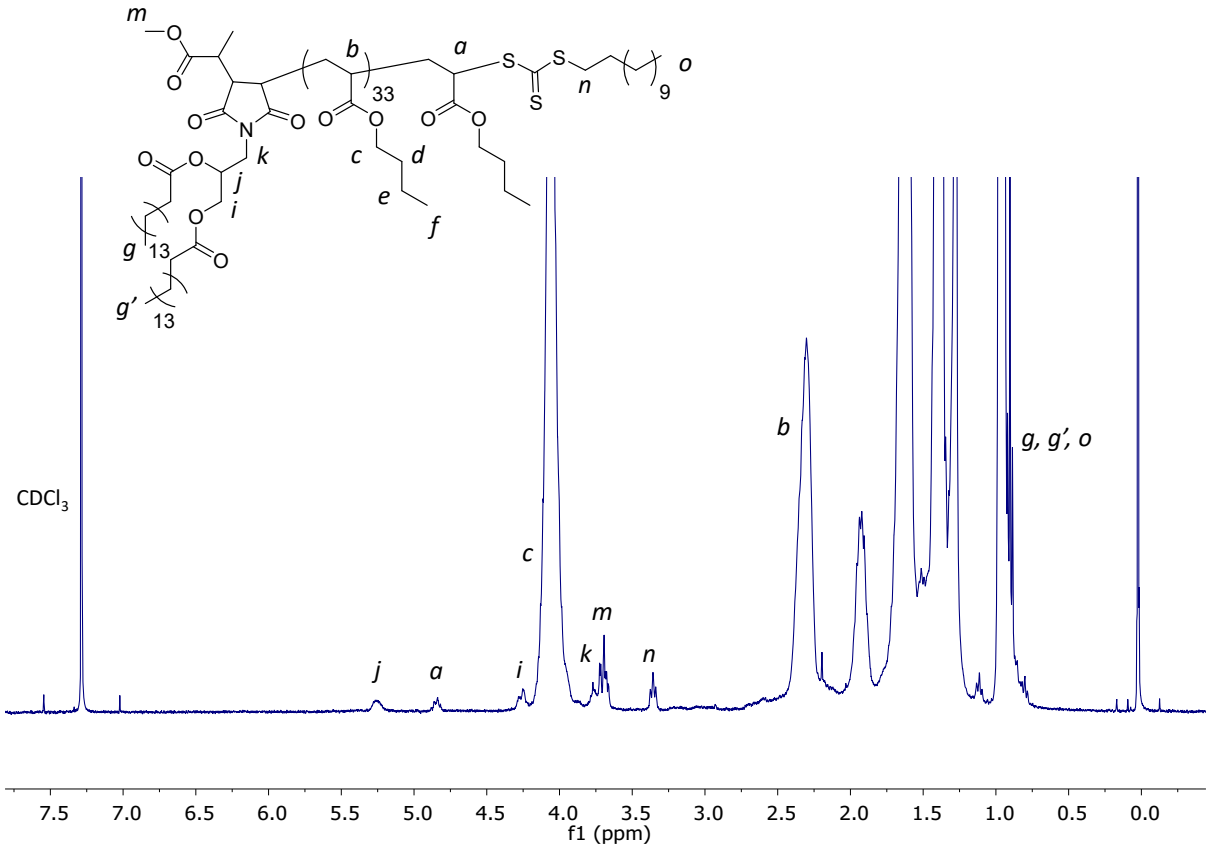


Figure S76. ^{1}H NMR spectrum of polymer **16** - **(12a)**-BA_{34} in $CDCl_3$.

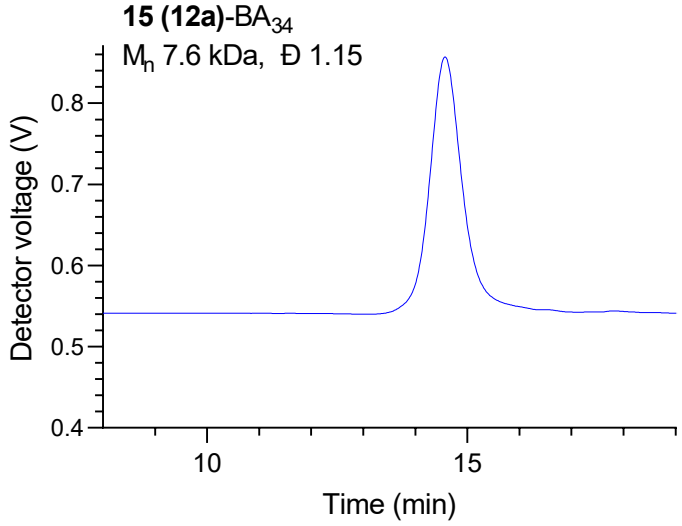


Figure S77. SEC analysis of polymer **16** - **(12a)**-BA_{34}, using $CHCl_3$ as the mobile phase.

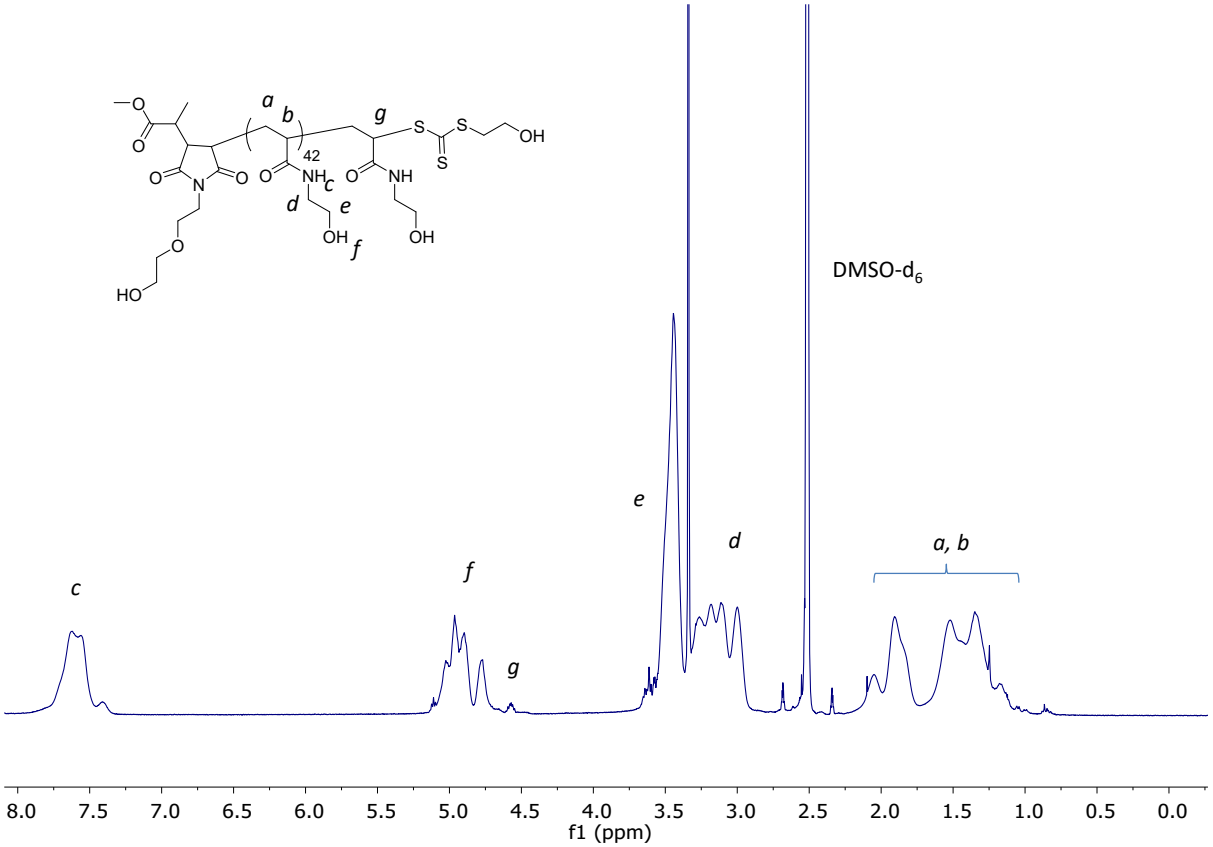


Figure S78. ^{1}H NMR spectrum of polymer **17** - **(11b)**-HEA_{43} in DMSO-d_6.

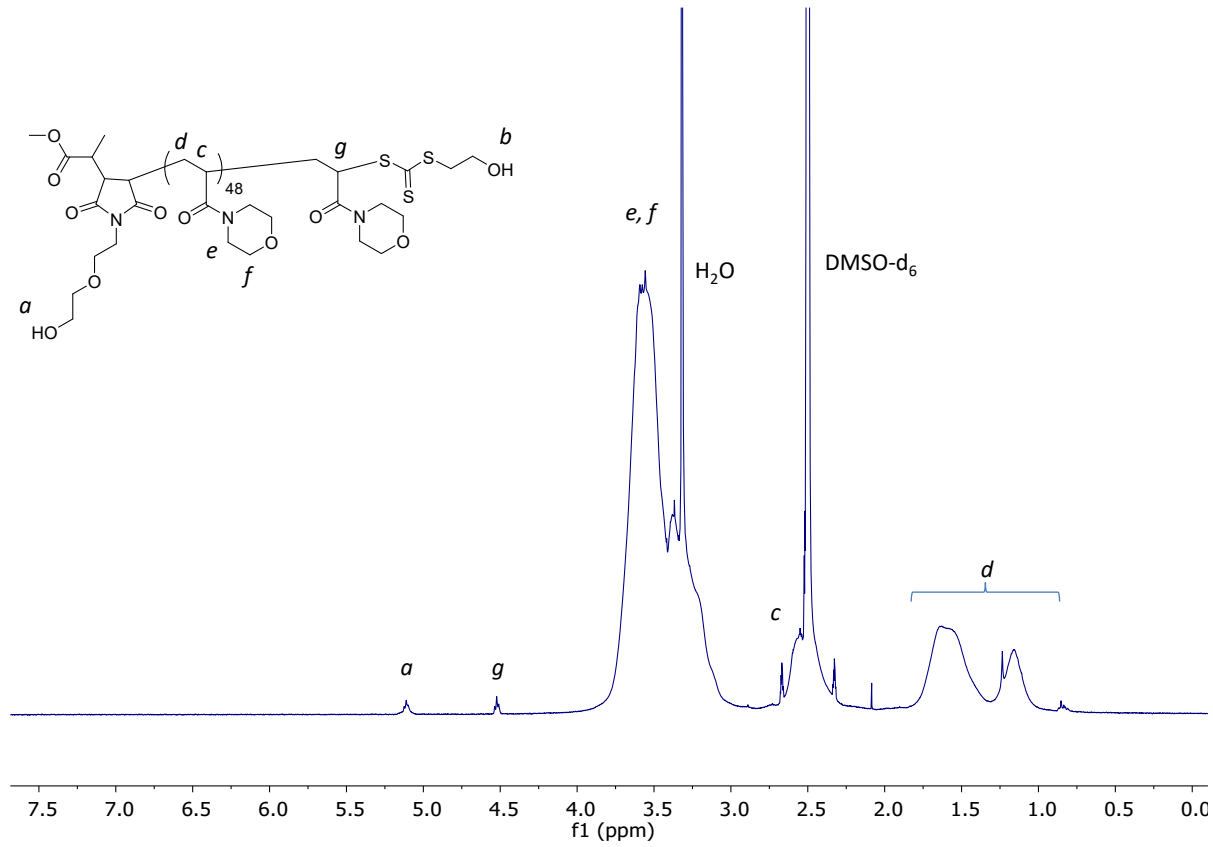


Figure S79. ^{1}H NMR spectrum of polymer **18** - **(11b)**-NAM_{49} in DMSO-d_6.

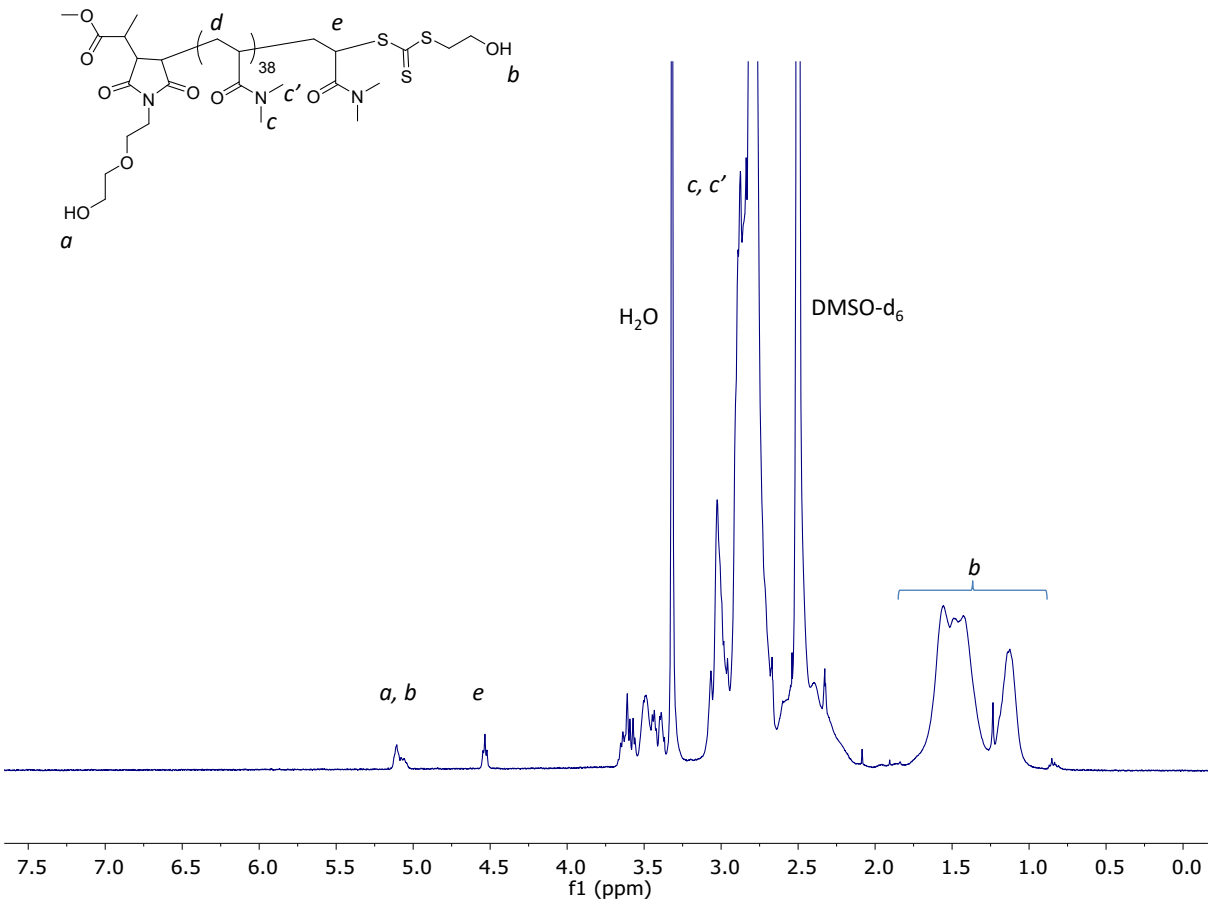


Figure S80. ^{1}H NMR spectrum of polymer **19** - **(11b)**-DMA_{39} in DMSO-d_6.

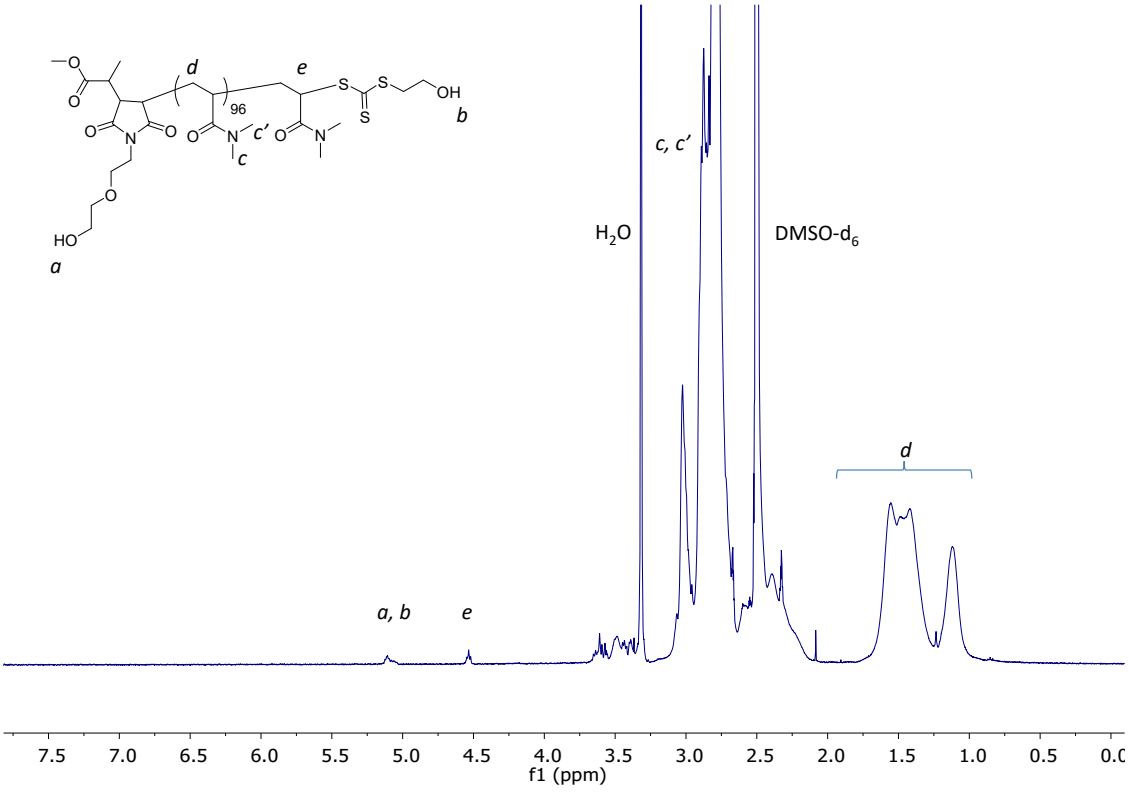


Figure S81. ^{1}H NMR spectrum of polymer **20** - **(11b)**-DMA_{97} in DMSO-d_6.

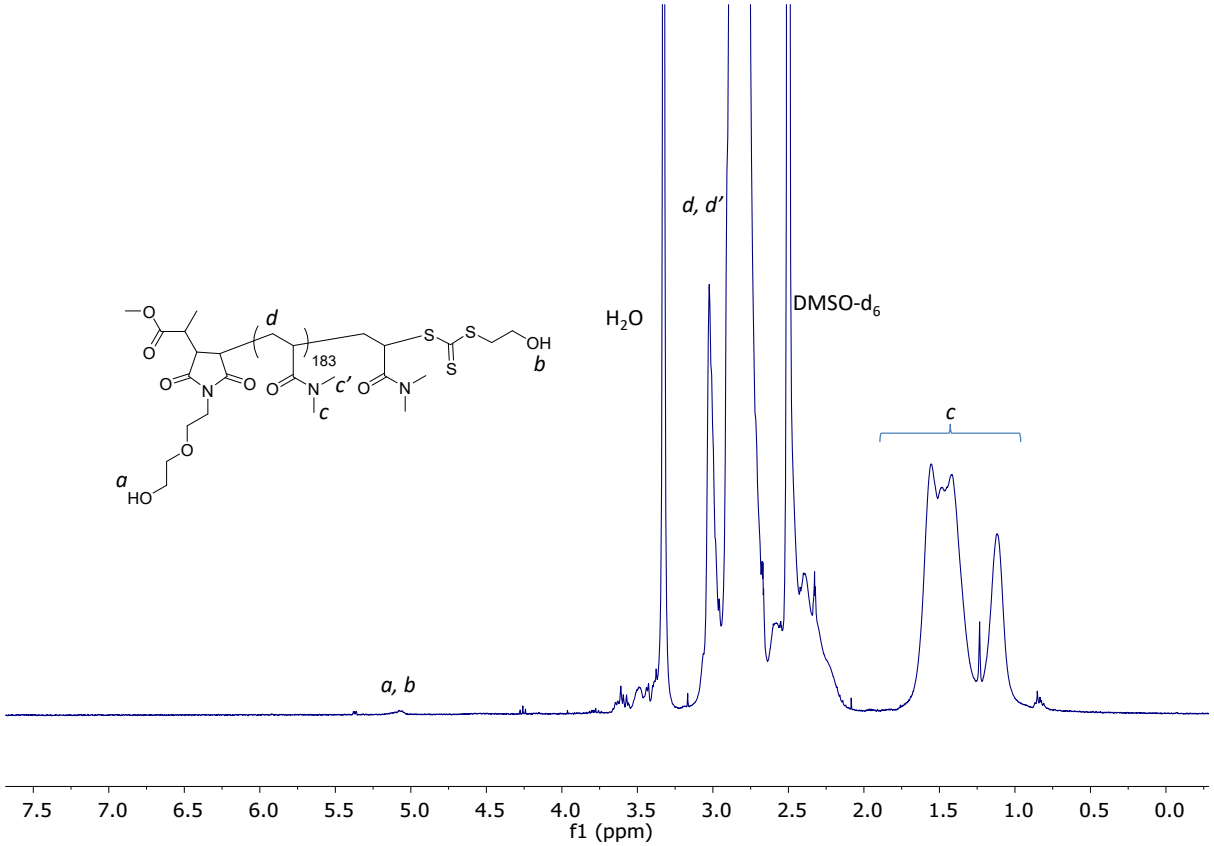


Figure S82. ^{1}H NMR spectrum of polymer **21** - **(11b)**-DMA$_{184}$ in DMSO-d$_6$.

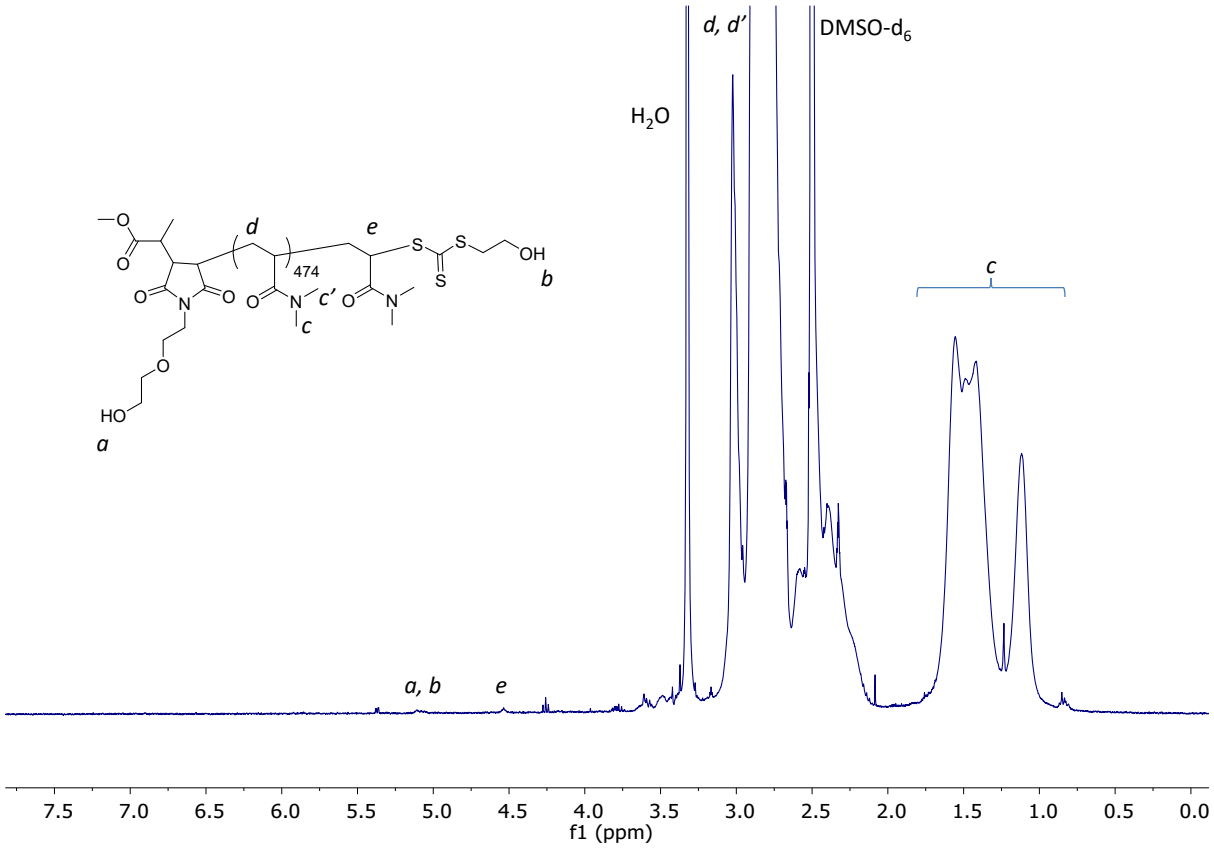


Figure S83. ^{1}H NMR spectrum of polymer **22** - **(11b)**-DMA$_{475}$ in DMSO-d$_6$.

RAFT polymerisation kinetics. The kinetic sampling experiment was performed as with the other polymerisations described in the general procedure. Briefly, a 4 mL test tube was charged with Mal-CTA **(13b)** (13.25 mg, 25 µmol), DMA (0.5 g, 5 mmol), 1,4-dioxane (1.84 mL) and 140 µL of an 4,4'-Azobis(4-cyanovaleric acid) stock solution (5 mg mL^{-1}, 700 µg, 2.5 µmol). A trace amount of 1,3,5-trioxane was added as an internal reference to monitor monomer conversions. The tube was fitted with an appropriate magnetic stir bar, sealed with a rubber septum and purged with N_2 for 15 minutes. The tube was then immersed in a preheated oil bath at 70°C. 100 µL samples were withdrawn using a degassed gas tight syringe at 15, 30, 60, 120 and 360 min.

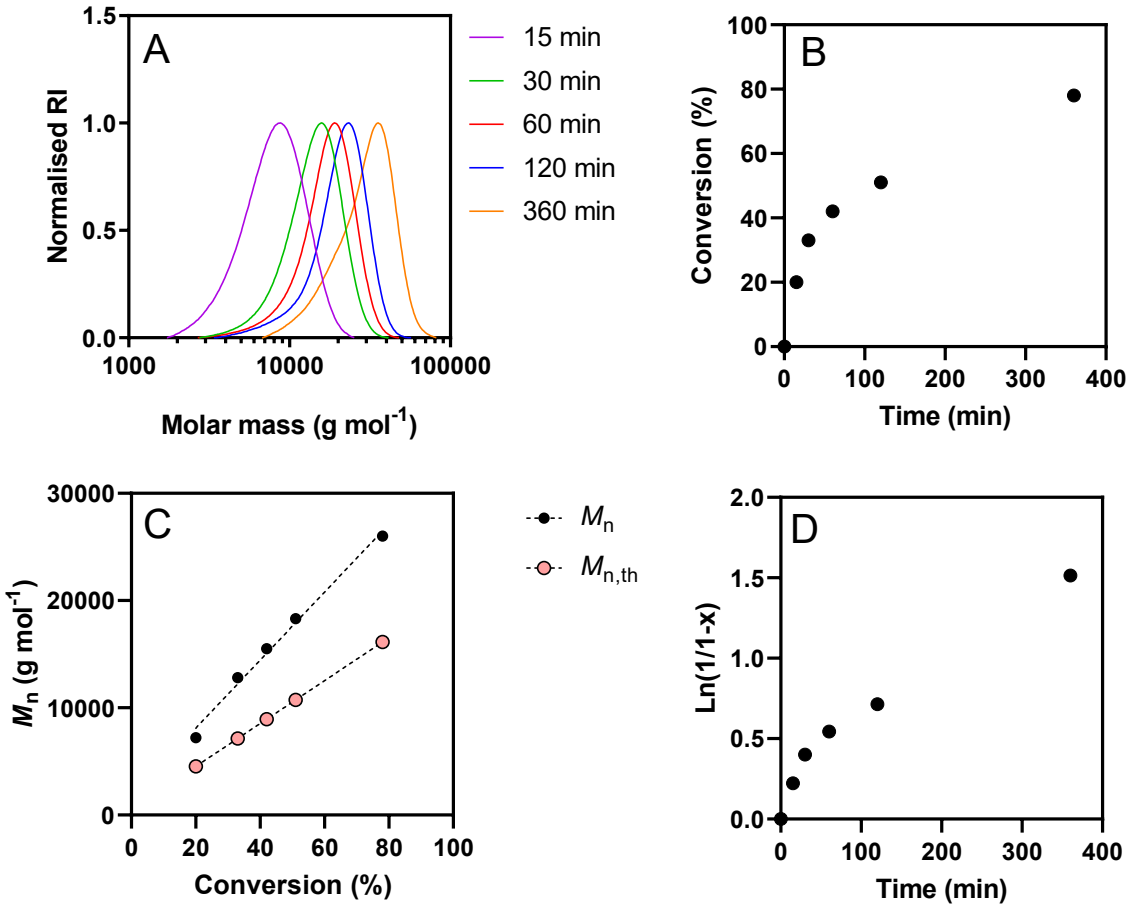


Figure S84 Polymerisation kinetics of DMA monomer mediated by CTA **(13b)**. (A) SEC chromatograms using DMF with 0.1% (wt%) LiBr additive. (B) Evolution of conversion with time. (C) Evolution of $M_{n,SEC}$ with conversion, black filled circles refer to $M_{n,SEC}$ and red filled circles $M_{n,th}$. (D) Pseudo-first order kinetic plot.

Conditions for methacrylate polymerisations. A 4 mL test tube was charged with either Mal-CTA **(13b)** (8.46 mg, 16 µmol) or CTA **(7)** (5.5 mg, (16 µmol), methyl methacrylate (MMA, 0.2 g, 2 mmol), 1,4-dioxane (0.69 mL) and 90 µL of an 4,4'-azobis(4-cyanovaleric acid) stock solution (5 mg mL^{-1}, 440 µg, 1.6 µmol). The tube was fitted with an appropriate magnetic stir bar, sealed with a rubber

septum, and purged with N_2 for 15 minutes. The tube was then immersed in a preheated oil bath at 70°C for 16 h.

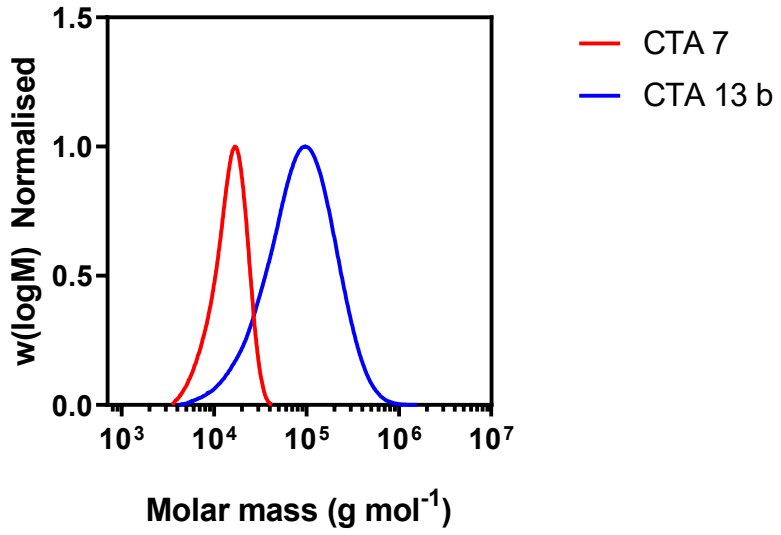


Figure S85 SEC analysis of MMA polymerisations mediated by CTA **(7)** and CTA (**13b**) using DMF with 0.1% (wt%) LiBr additive.

Table S4 $M_{n,SEC}$ and $Đ$ of MMA polymers prepared using CTAs **(7)** and **(13b)**

	$M_{n,SEC}$ (kg mol^{-1})[a]	Monomer conversion (%)[b]	$Đ$[a]
CTA **(7)**	13.2	84%	1.19
CTA **(13b)**	51.0	86%	2.05

[a]Determined by SEC, using DMF with 0.1% (wt%) LiBr as the mobile phase. [b]Determined by ^{1}H NMR spectroscopy.

References

1. F. Mastrotto, S. Salmaso, Y. L. Lee, C. Alexander, P. Caliceti and G. Mantovani, *Polymer Chemistry*, 2013, **4**, 4375-4385.
2. C. Bolm, C. L. Dinter, A. Seger, H. Höcker and J. Brozio, *J. Org. Chem.*, 1999, **64**, 5730-5731.