SUPPORTING INFORMATION

Synthesis of α,ω-bis-mercaptoacyl poly(alkyl oxide)s and development of thioether cross-linked liposome scaffolds for sustained release of drugs

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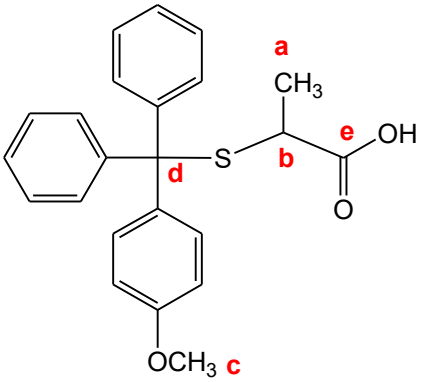
1. NMR spectra, HPLC analysis of *S*-Mmt-mercapto acids

1.1 *S*-Mmt-2-mercaptopropionic acid (thiolactic acid)



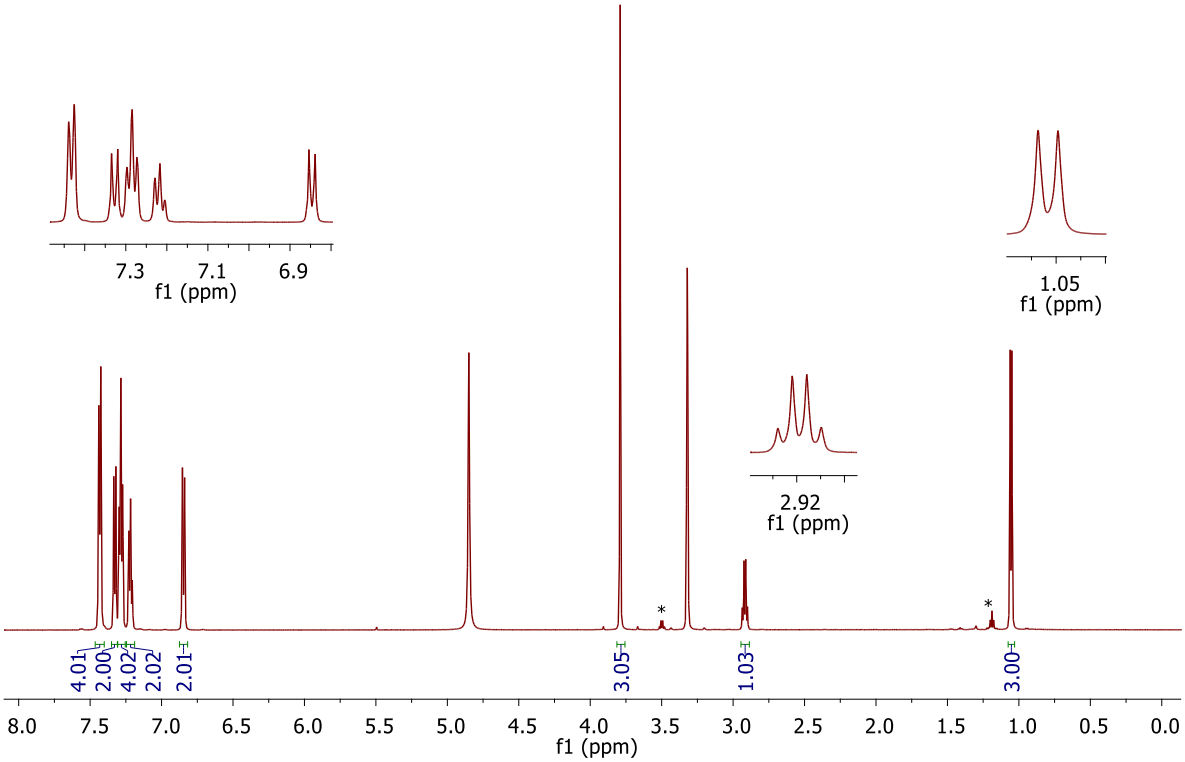


Figure S1. [1]H-NMR of *S*-Mmt-2-mercaptopropionic acid (thiolactic acid) in MeOH-*d*4. *solvent residue

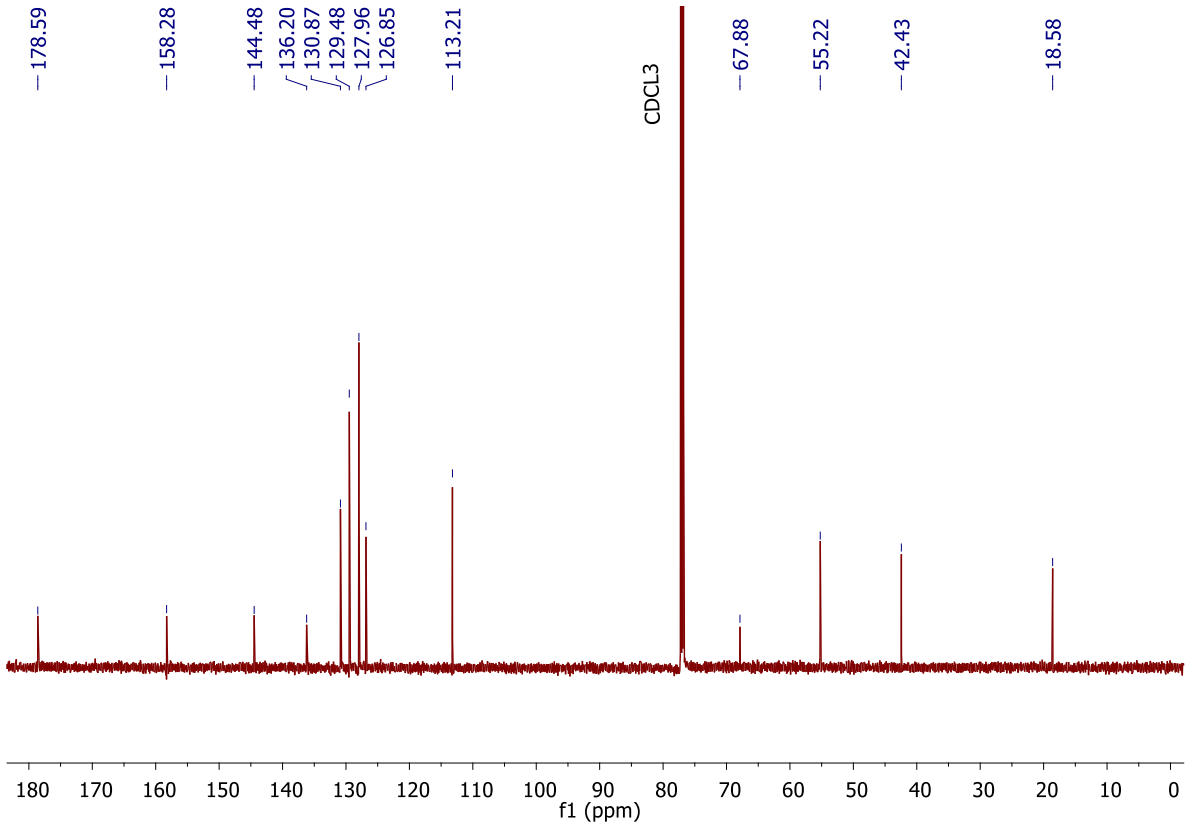


Figure S2. ^{13}C-NMR of *S*-Mmt-2-mercaptopropionic acid (thiolactic acid) in $CDCl_3$

1.2 *S*-Mmt-3-mercaptopropionic acid

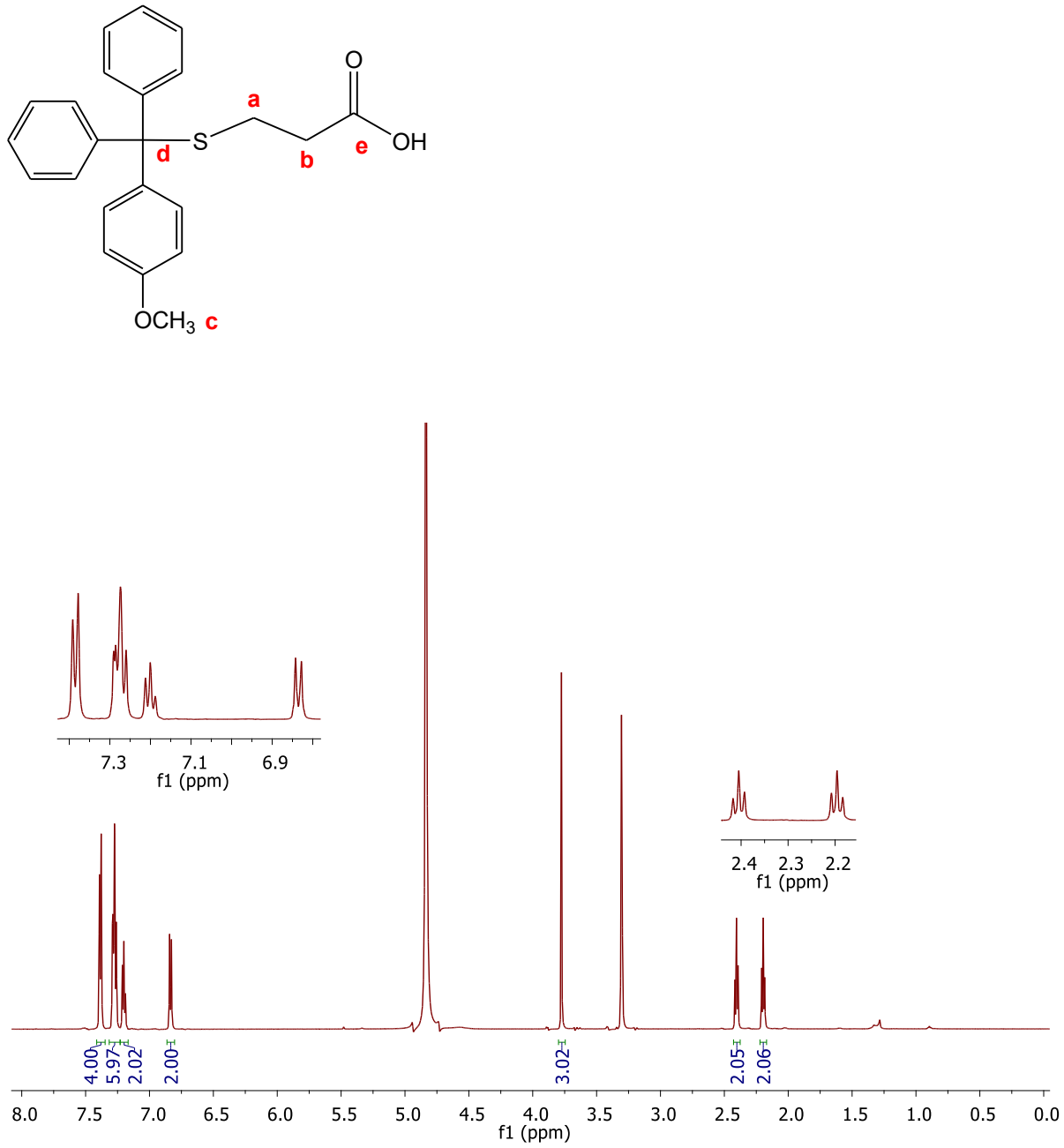


Figure S3. ^{1}H-NMR of *S*-Mmt-3-mercaptopropionic acid in MeOH-*d*4.

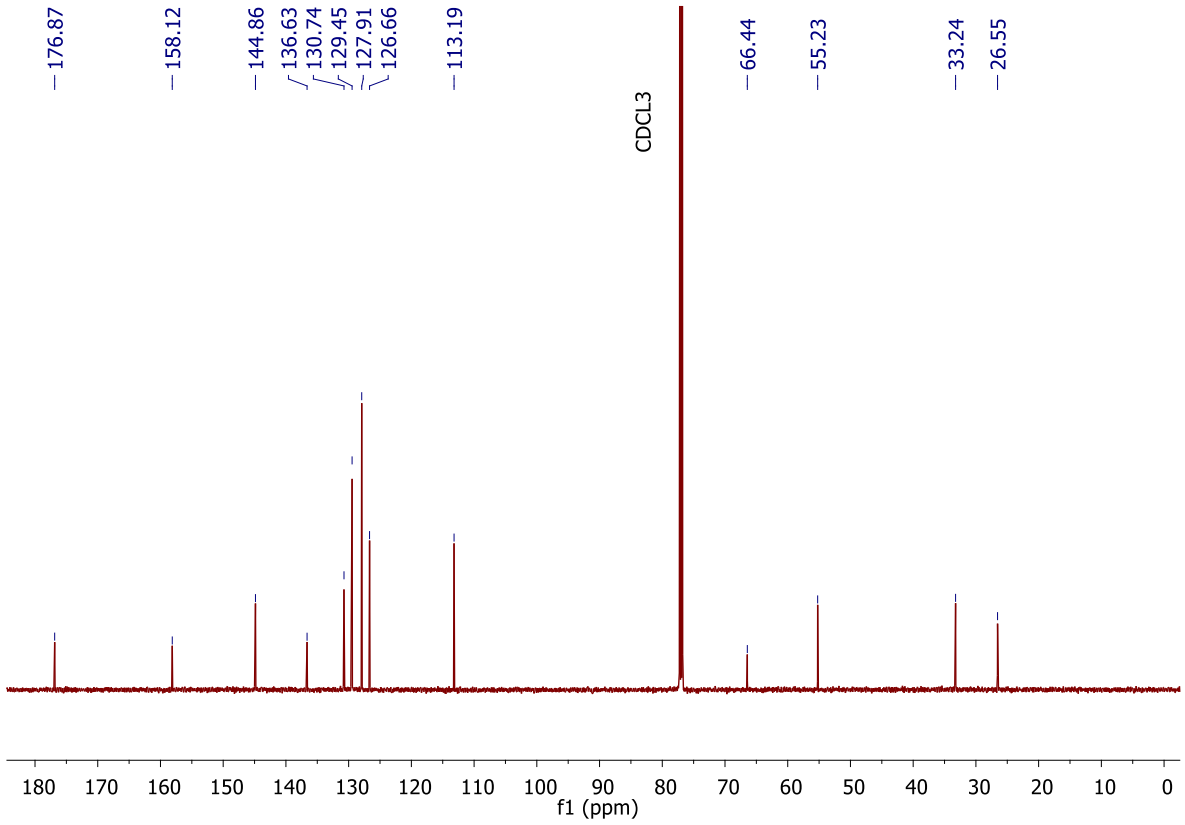


Figure S4. ^{13}C-NMR of *S*-Mmt-3-mercaptopropionic acid in $CDCl_3$.

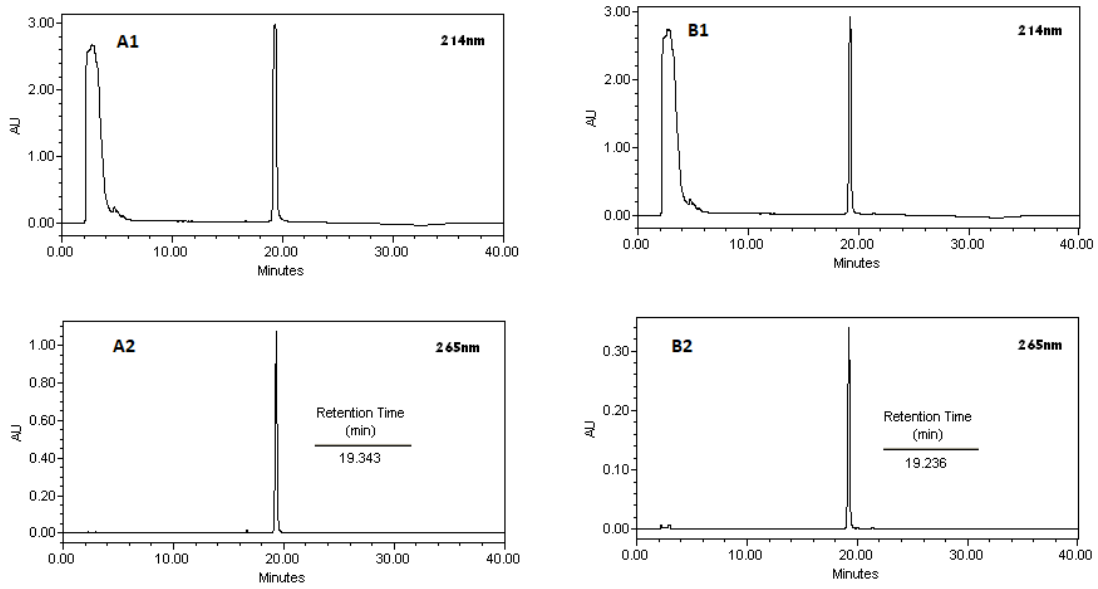


Figure S5. Analytical hplc of *S*-Mmt-3-mercaptopropionic acid (A1, A2) and *S*-Mmt-2-mercaptopropionic acid (thiolactic acid) (B1, B2) at 214 and 265 nm; Column: LiChrospher 100, RP-18, 250-4, 5 µm; Mobile phase solvents: AcCN/water (0.08% TFA); Gradient conditions: 20% to 100% AcCN in 30 min.

2. NMR spectra of α,ω-bis-mercaptoacyl poly(ethylene oxide)s

2.1 di-*S*-Mmt-di-2-mercaptopropionyl PEG10.000

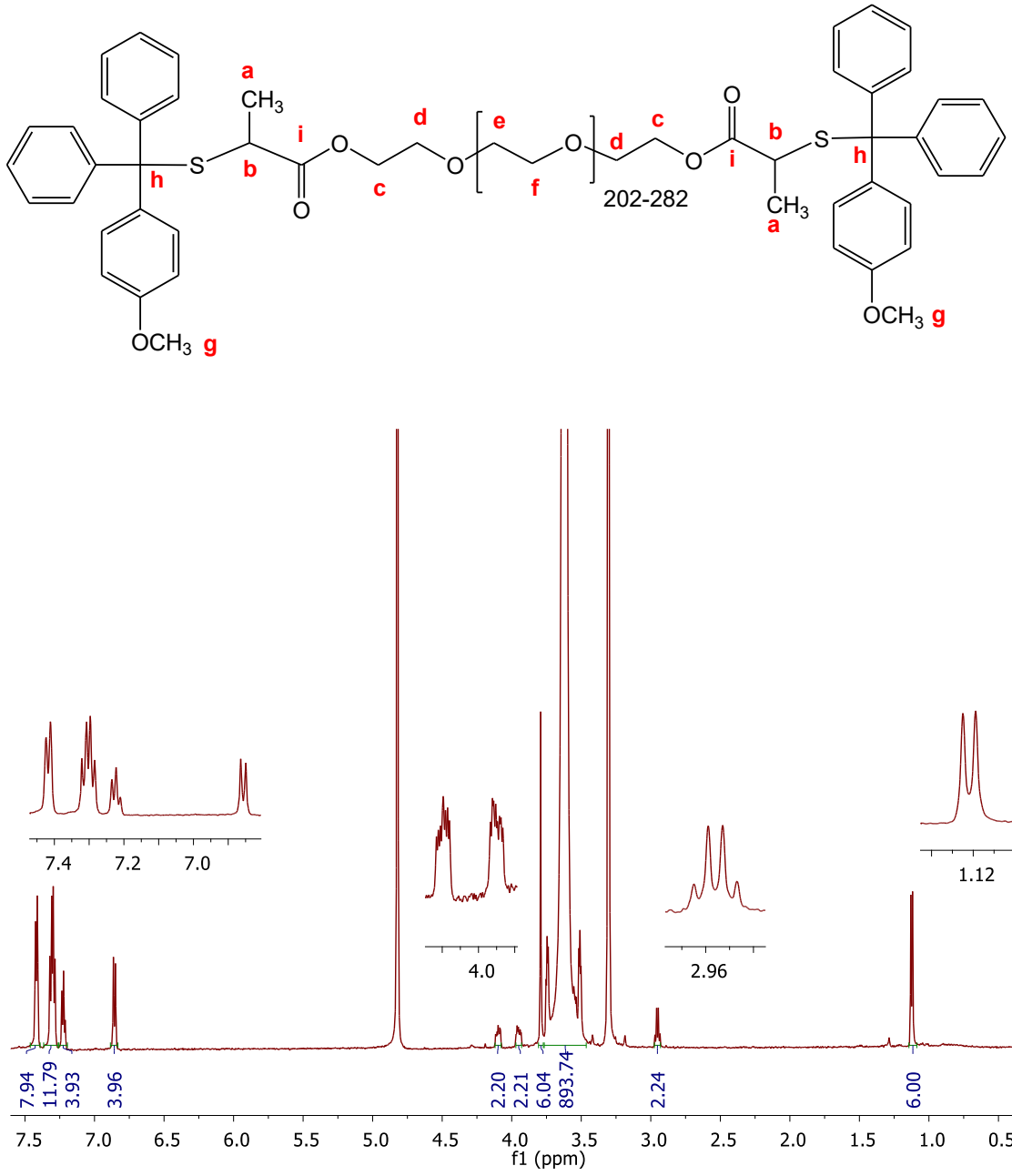


Figure S6. ^{1}H-NMR of di-*S*-Mmt-di-2-mercaptopropionyl PEG10.000 in MeOH-*d*4.

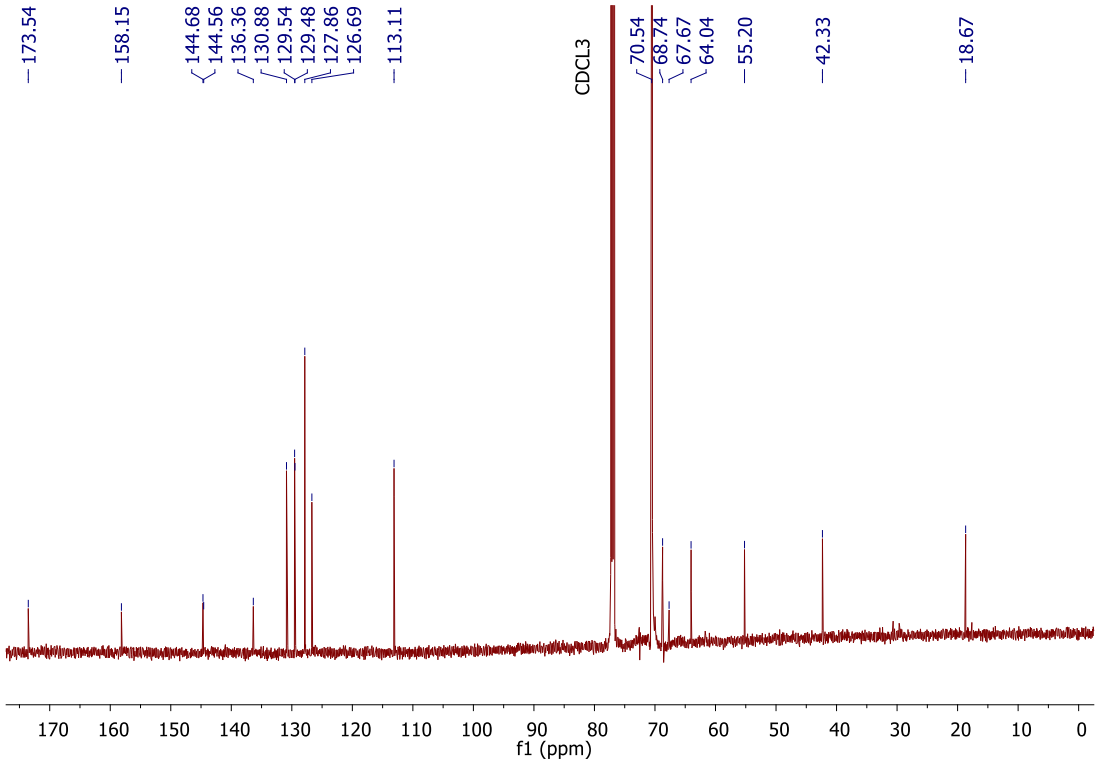


Figure S7. ^{13}C-NMR of di-*S*-Mmt-di-2-mercaptopropionyl PEG10.000 in $CDCl_3$

2.2 di-2-mercaptopropionyl PEG10.000

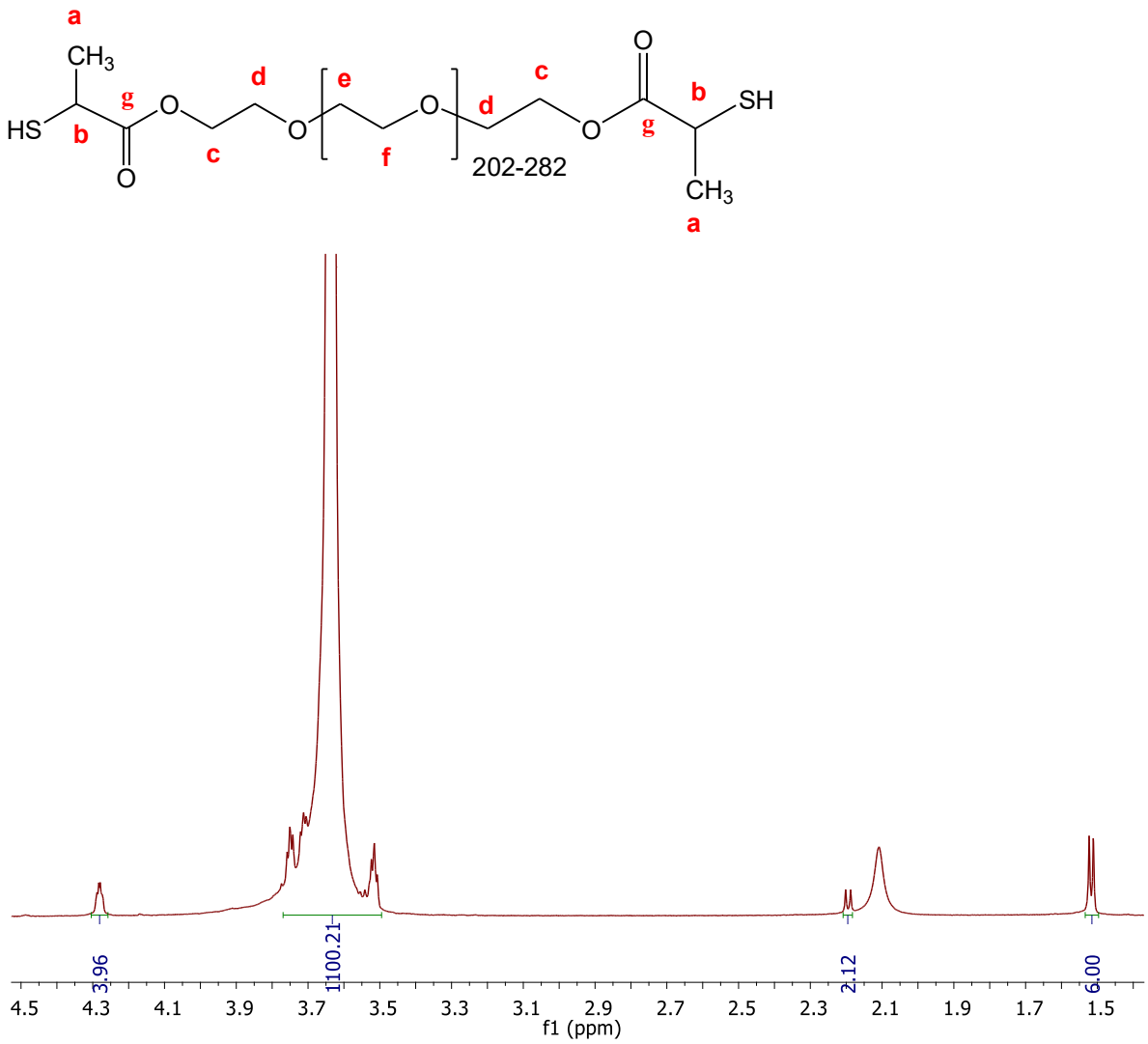


Figure S8. ^{1}H-NMR of di-2-mercaptopropionyl PEG10.000 in $CDCl_3$.

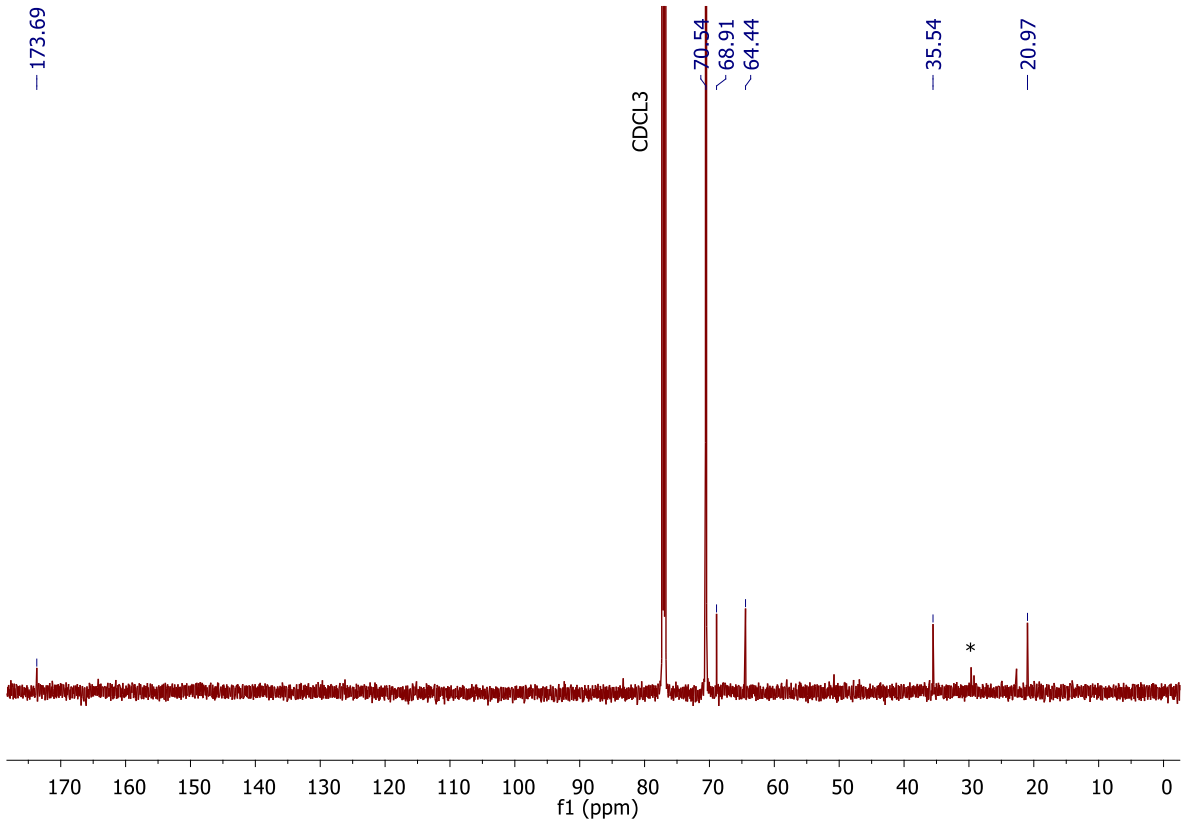
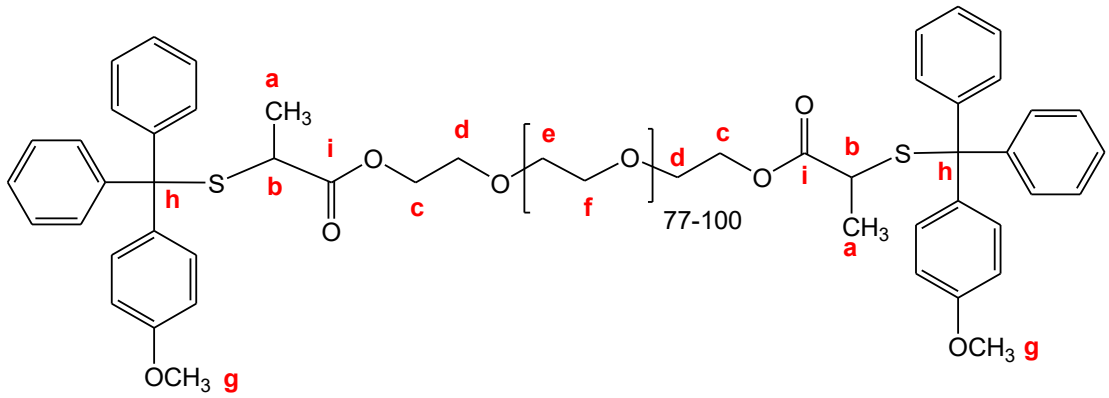


Figure S9. ^{13}C-NMR of di-2-mercaptopropionyl PEG10.000 in $CDCl_3$; *solvent residue

2.3 di-*S*-Mmt-di-2-mercaptopropionyl PEG4.000



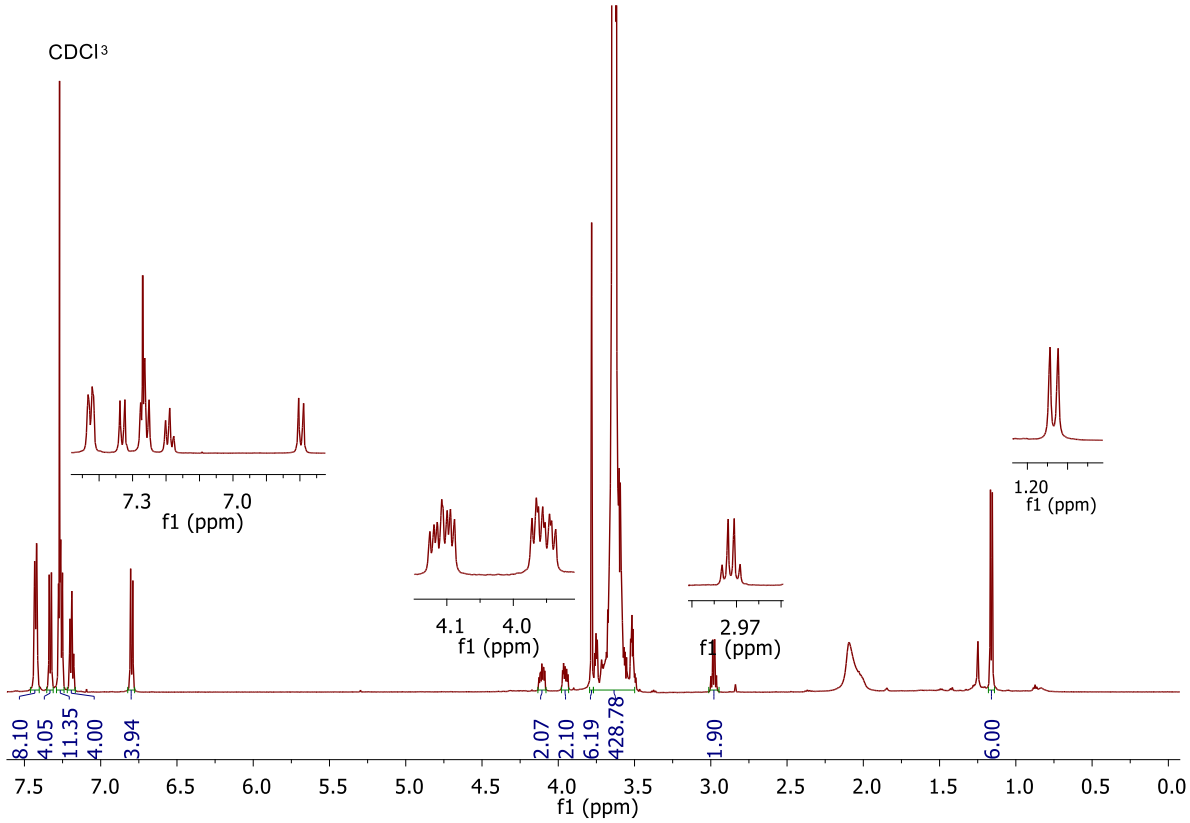


Figure S10. ^{1}H-NMR of di-*S*-Mmt-2-mercaptopropionyl PEG4.000 in $CDCl_3$.

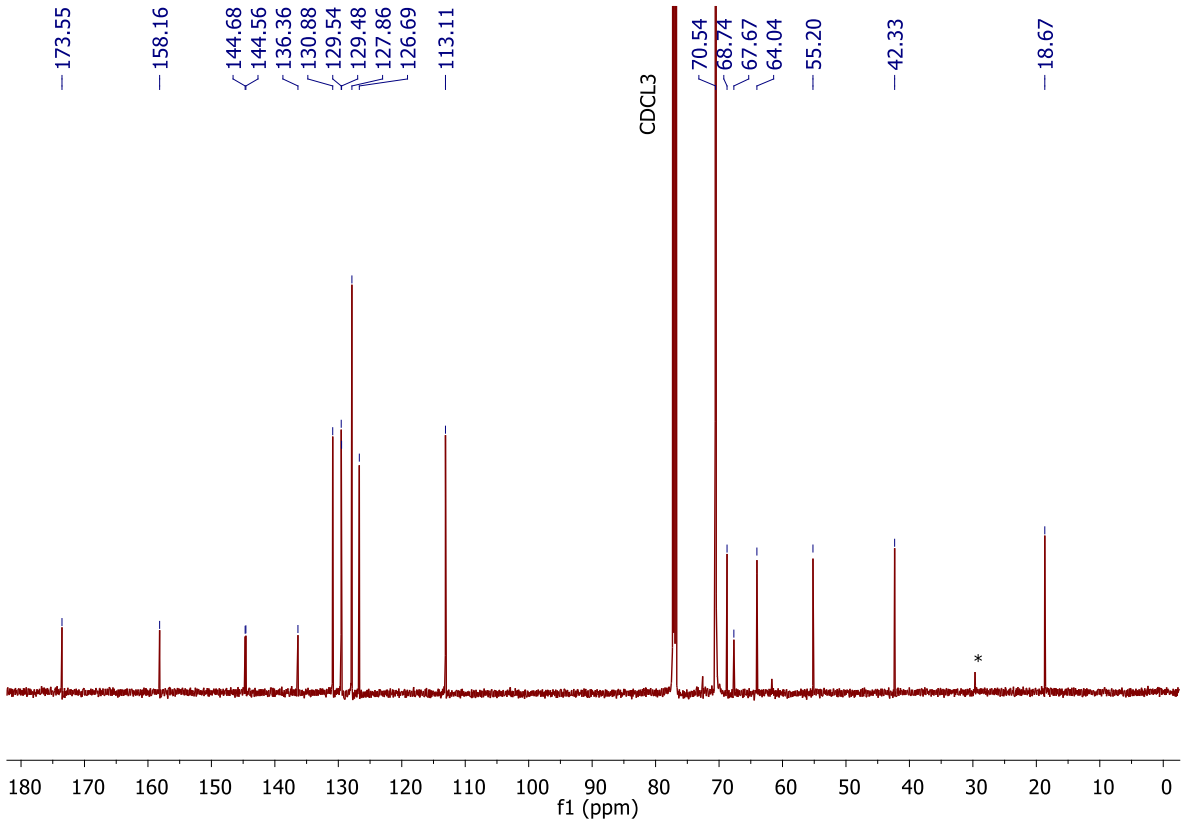
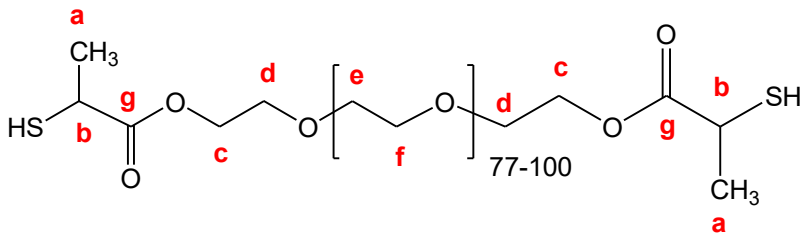


Figure S11. ^{13}C-NMR of di-*S*-Mmt-2-mercaptopropionyl PEG4.000 in $CDCl_3$; *solvent residue

2.4 di-2-mercaptopropionyl PEG4.000



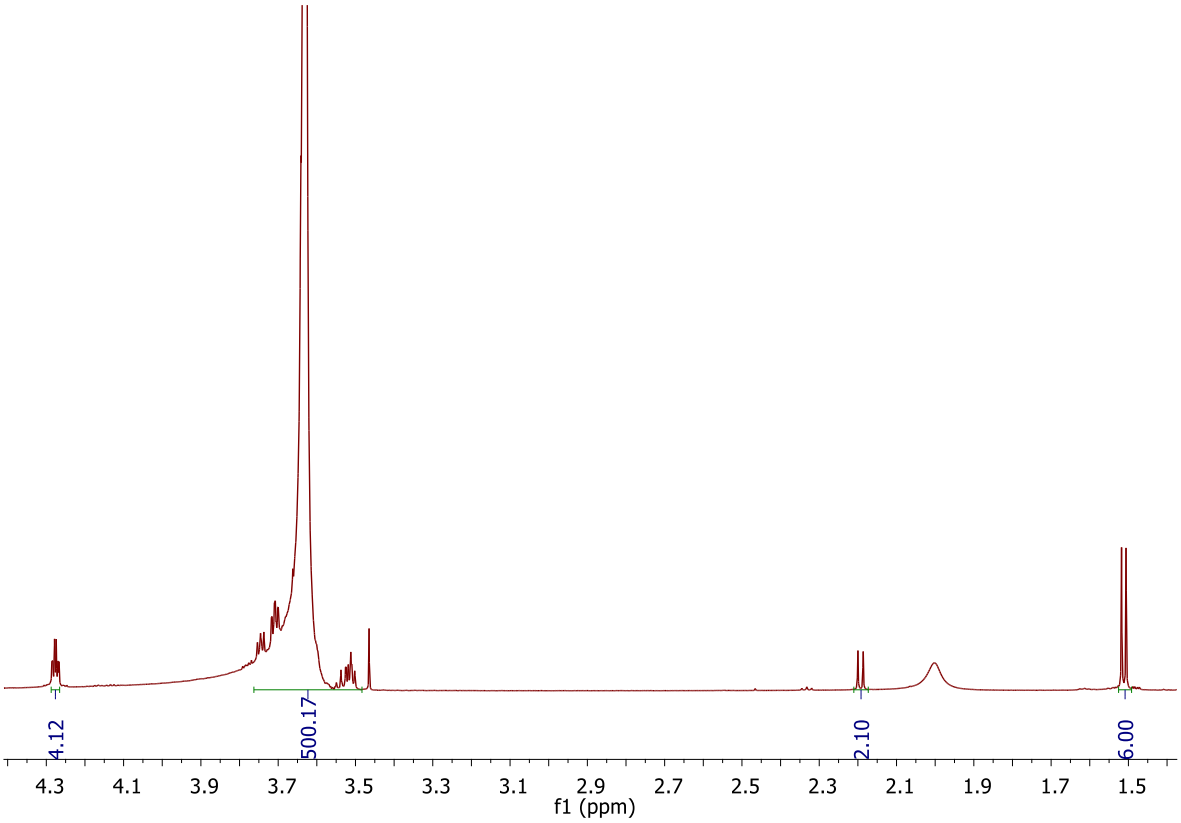


Figure S12. ^{1}H-NMR of di-2-mercaptopropionyl PEG4.000 in $CDCl_3$.

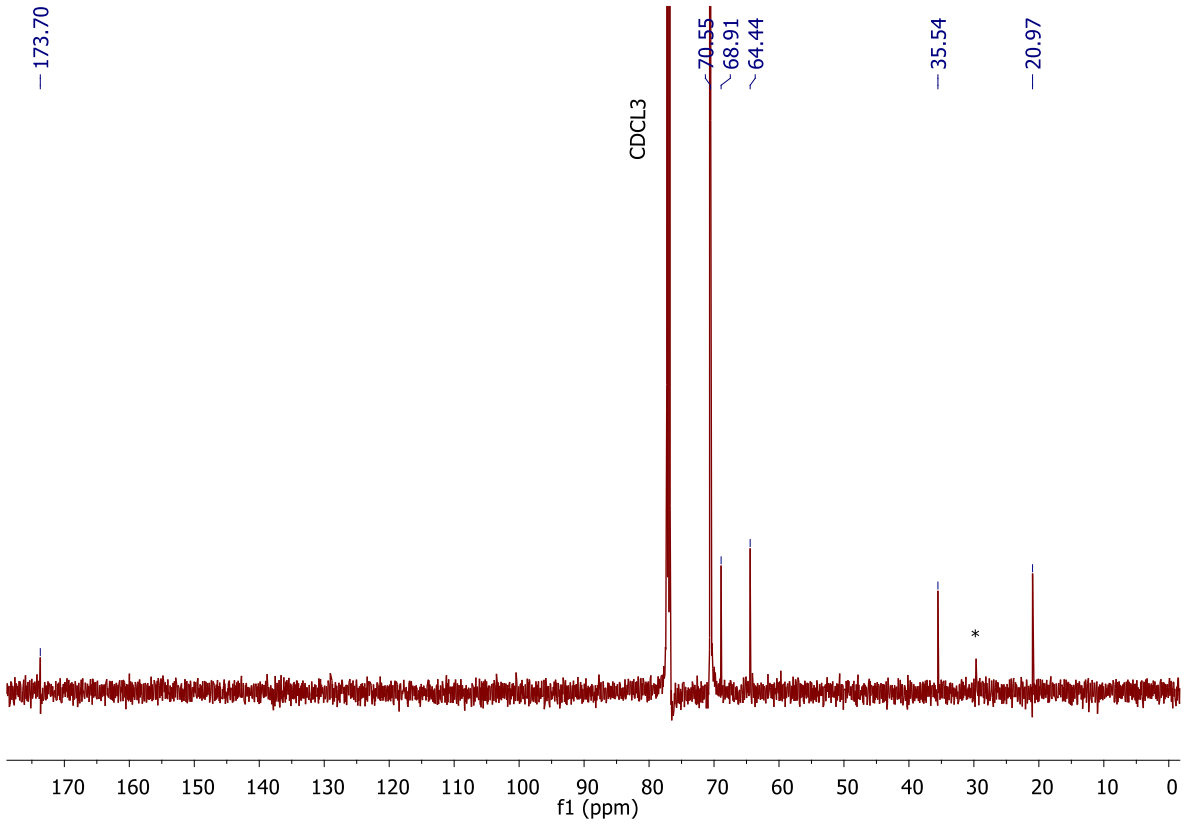


Figure S13. ^{1}H-NMR of di-2-mercaptopropionyl PEG4.000 in $CDCl_3$; *solvent residue

2.5 di-2-mercaptopropionyl PEG1.000

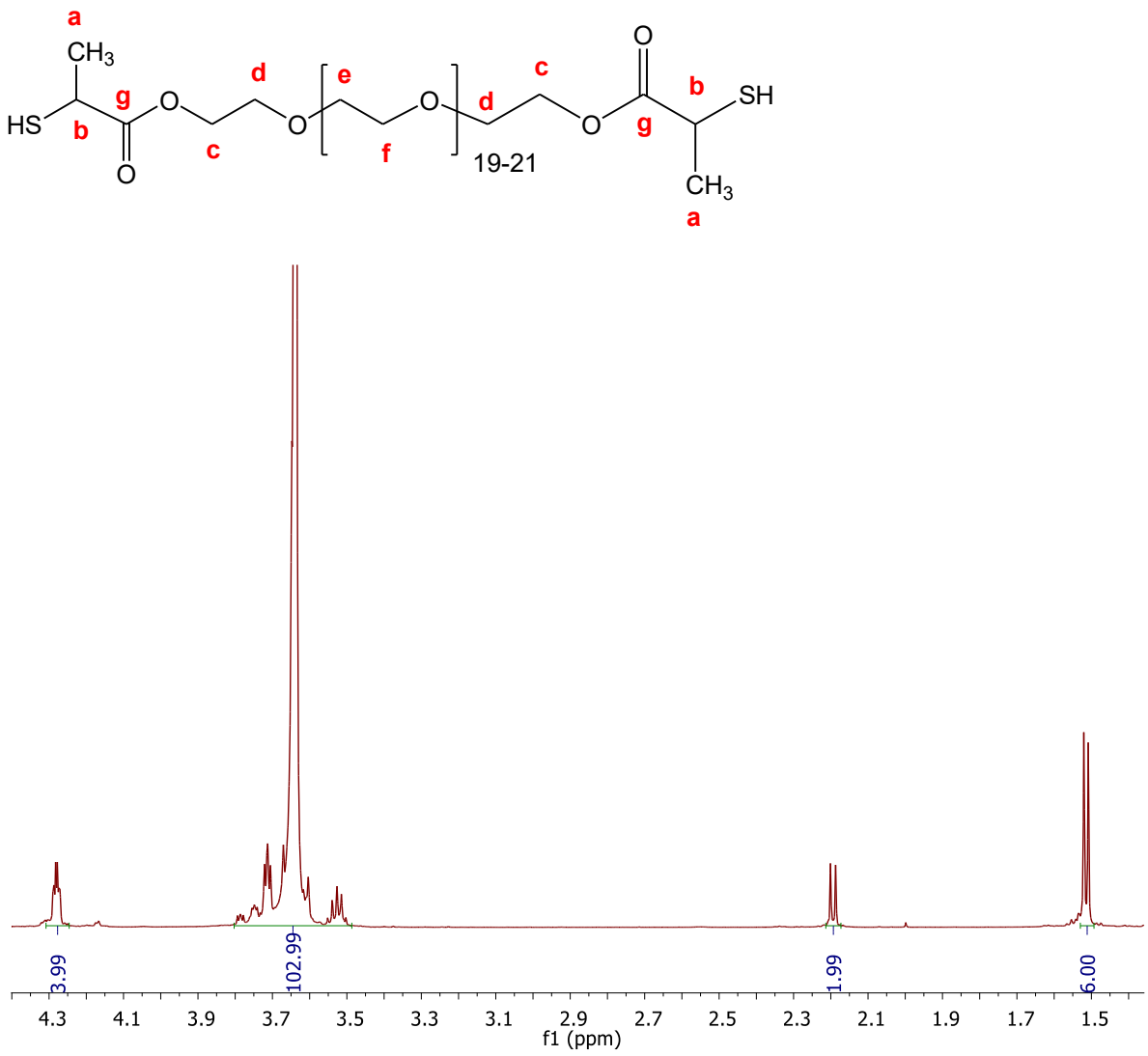


Figure S14. ^{1}H-NMR of di-2-mercaptopropionyl PEG1.000 in $CDCl_3$.

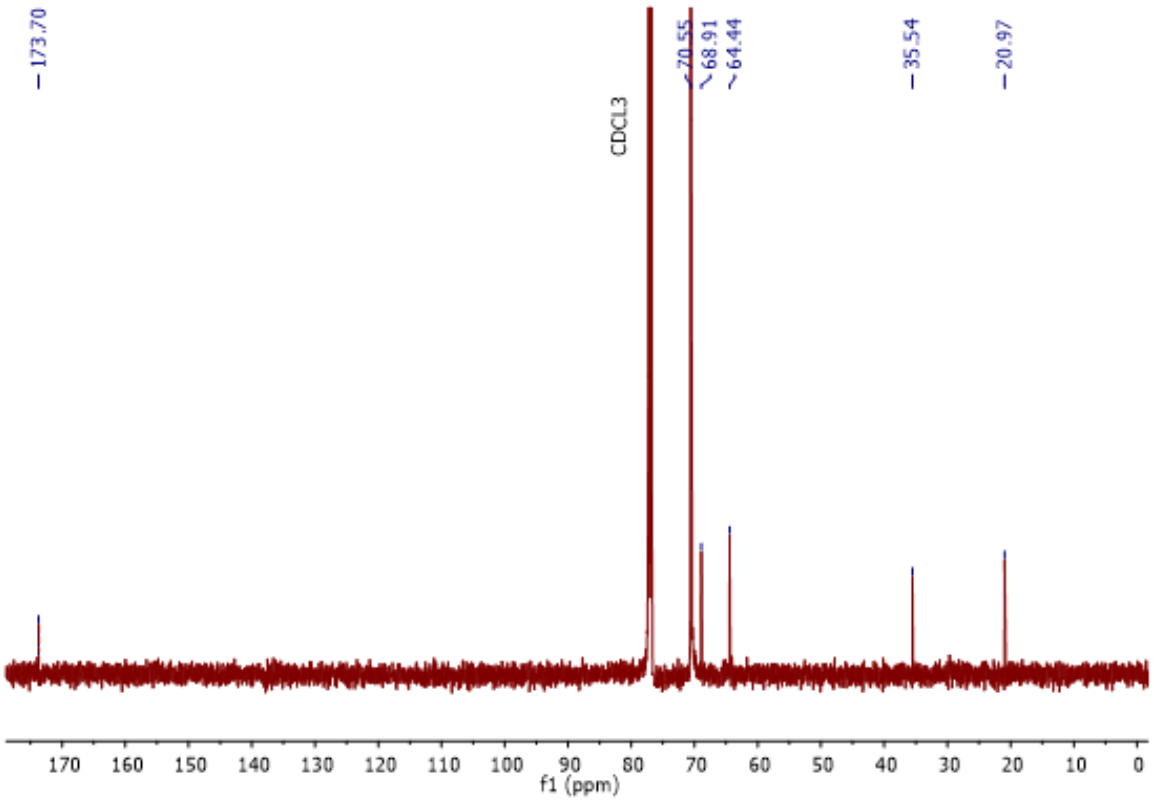


Figure S15. ^{1}H-NMR of di-2-mercaptopropionyl PEG1.000 in $CDCl_3$.

3. ESI-MS spectra of α,ω-bis-mercaptoacyl poly(ethylene oxide)s

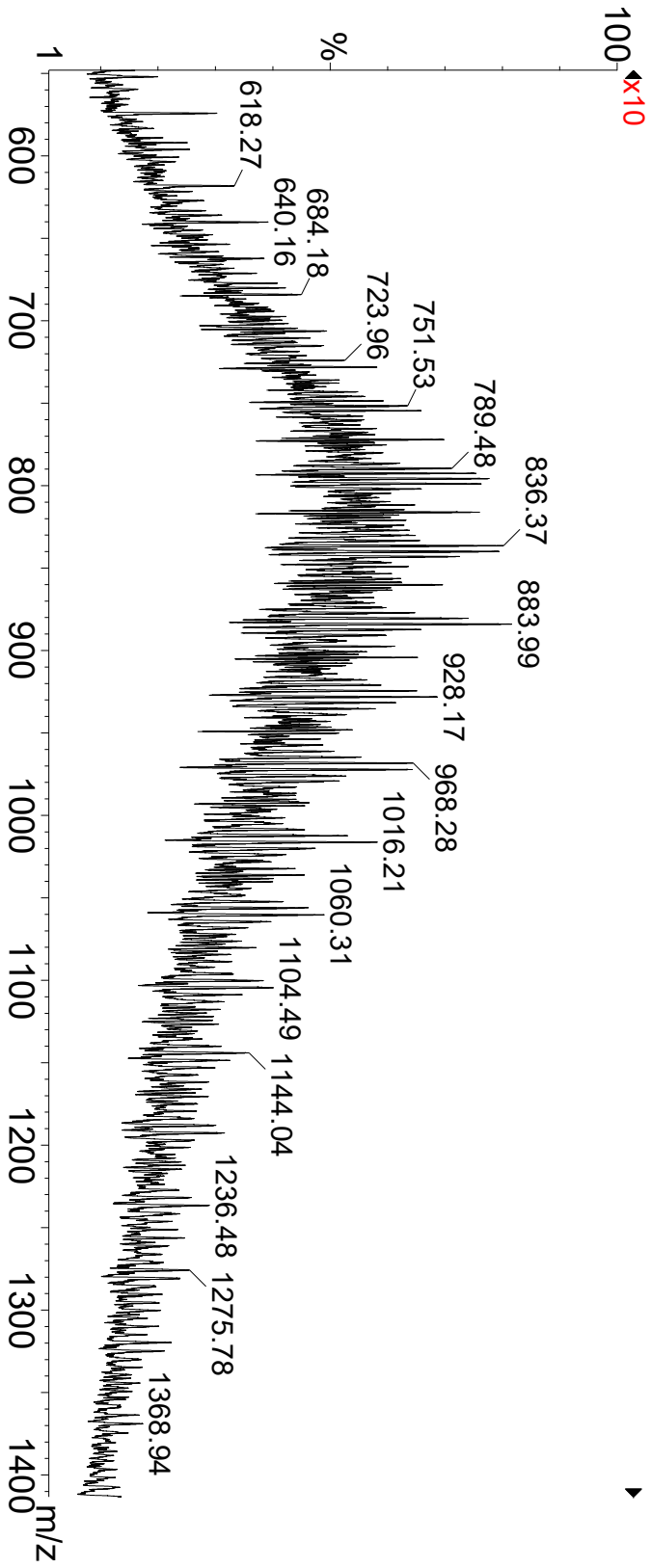


Figure S16. ESI-MS of di-2-mercaptopropionyl PEG10.000; (M+12H)/12

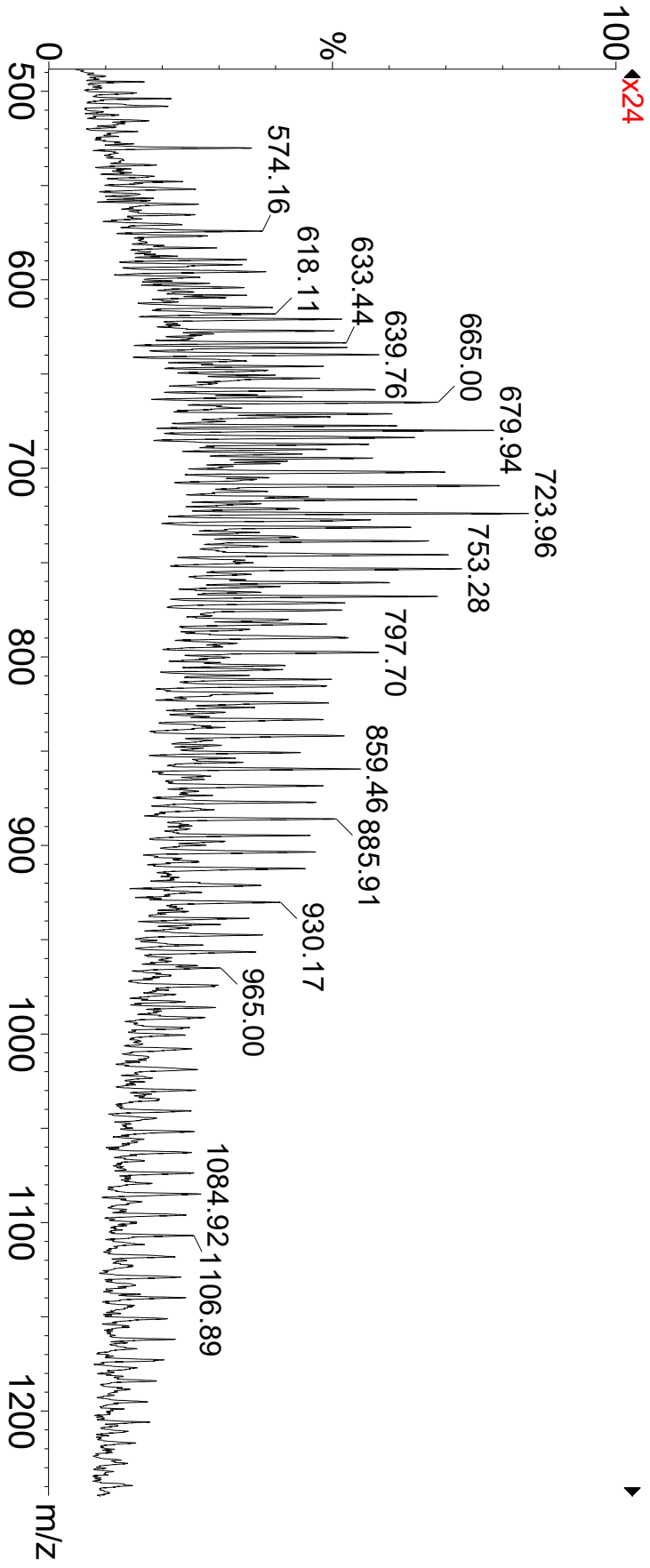


Figure S17. ESI-MS of di-2-mercaptopropionyl PEG4.000; (M+6H)/6

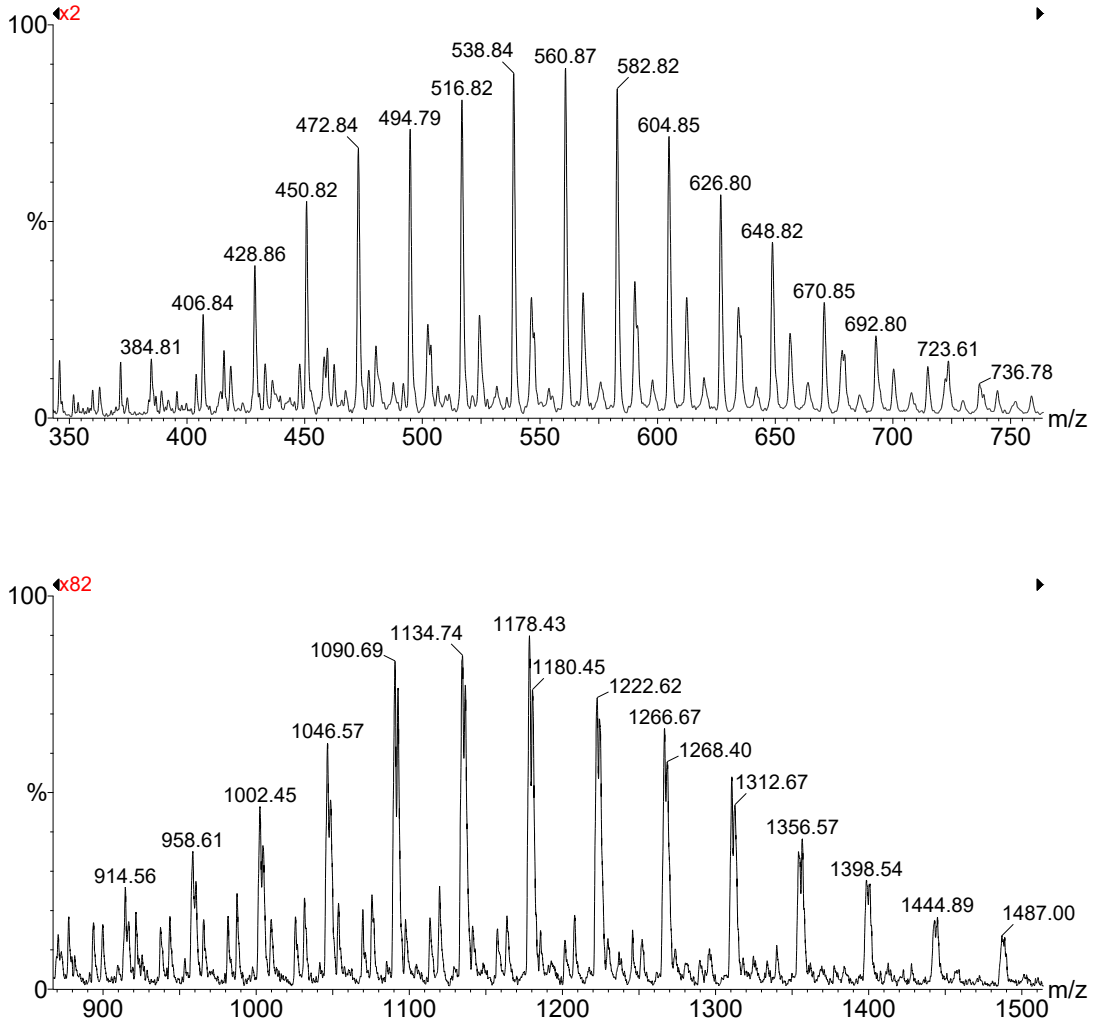


Figure S18. ESI-MS of di-2-mercaptopropionyl PEG1.000; (M+2H)/2, M+H

4. NMR spectra of α,ω-bis-mercaptoacyl pluronic

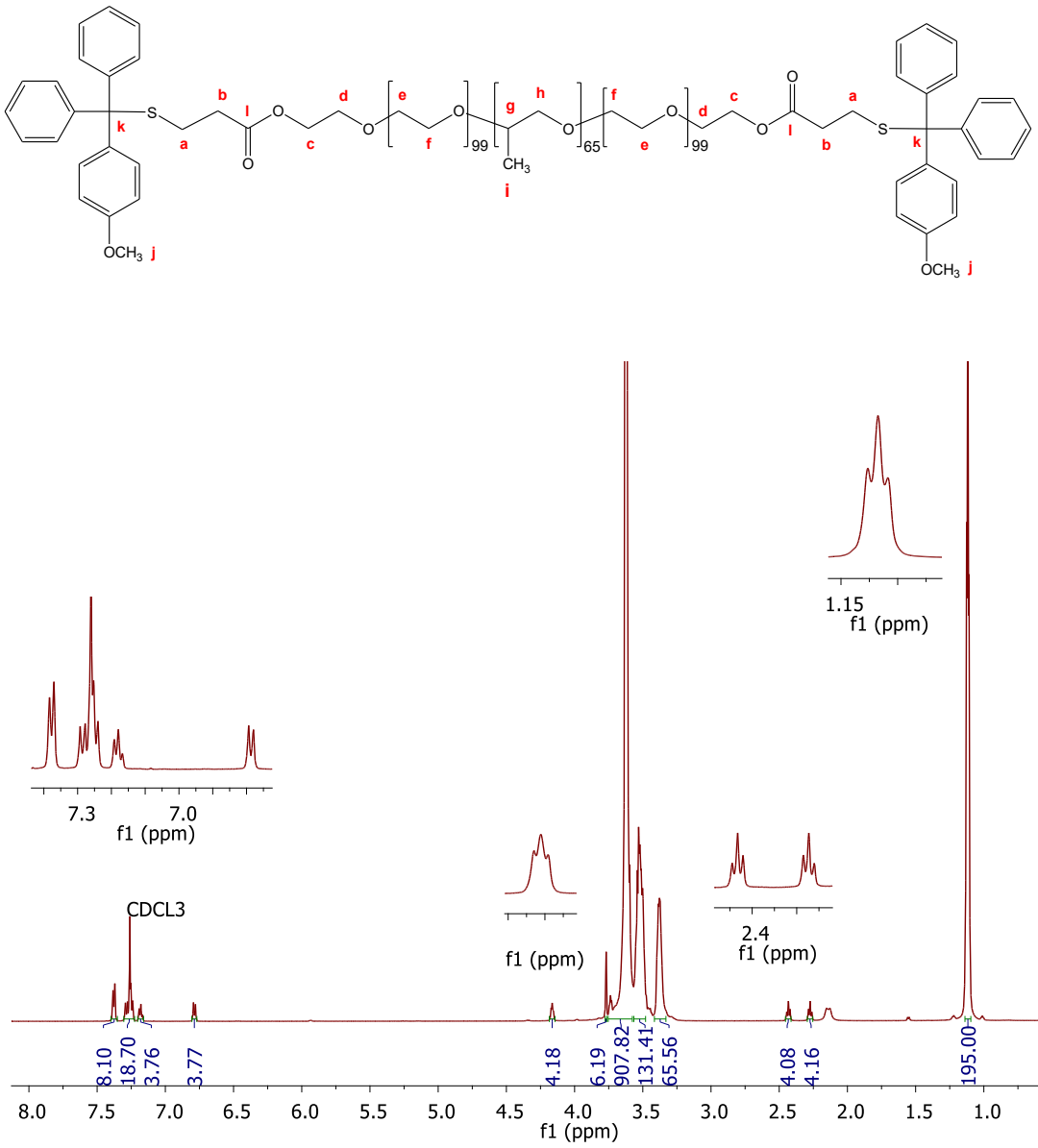


Figure S19. ^{1}H-NMR of di-*S*-Mmt-di-3-mercaptopropionyl pluronic in $CDCl_3$.

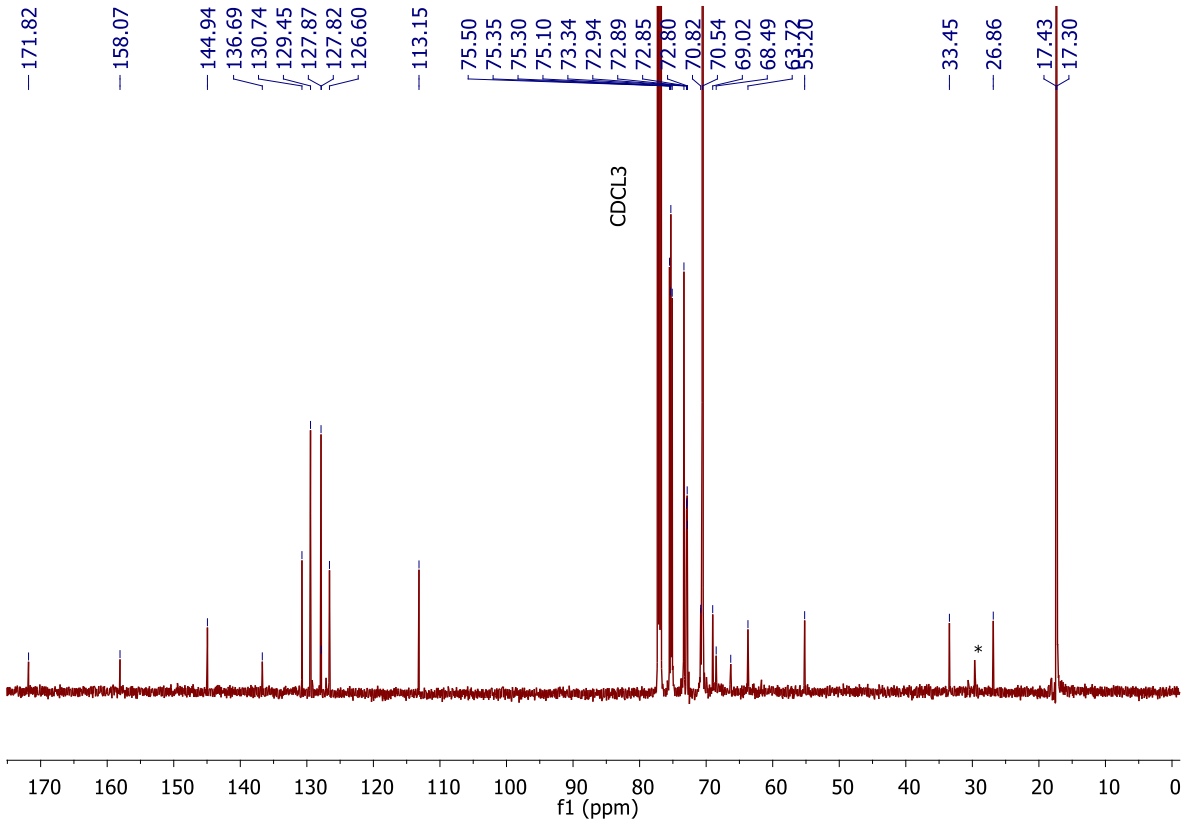


Figure S20. ^{13}C-NMR of di-*S*-Mmt-di-3-mercaptopropionyl pluronic in $CDCl_3$; *solvent residue

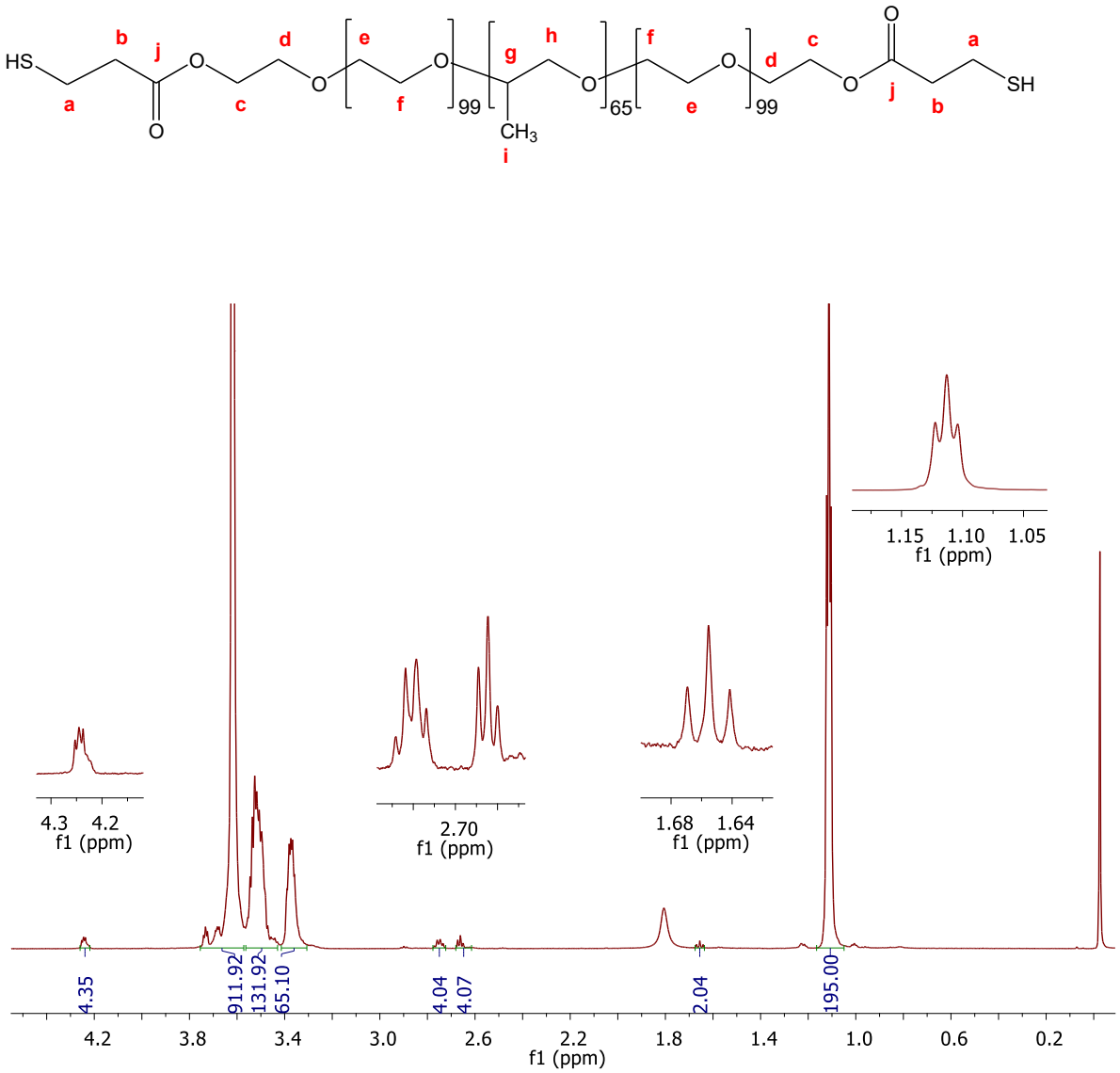


Figure S21. ^{1}H-NMR of di-3-mercaptopropionyl pluronic in $CDCl_3$.

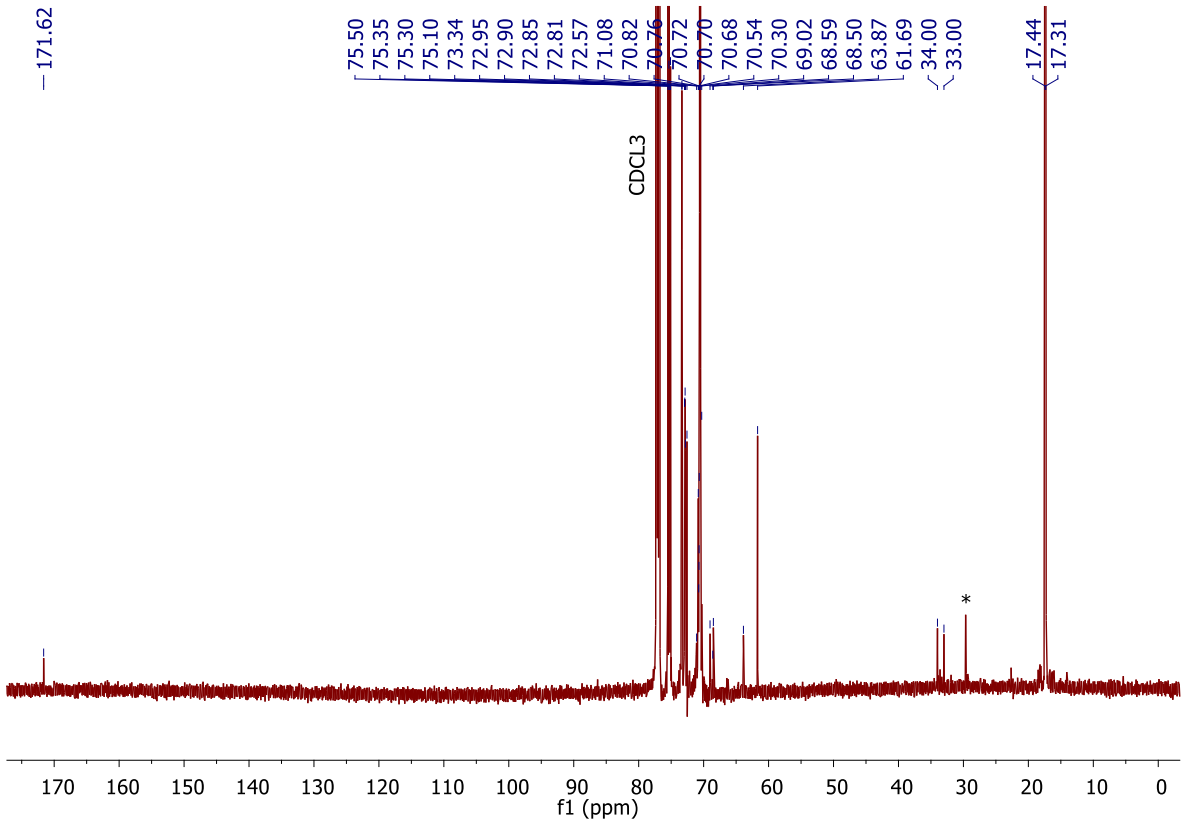


Figure S22. ^{13}C-NMR of di-3-mercaptopropionyl pluronic in $CDCl_3$; *solvent residue

5. ESI-MS spectra of α,ω-bis-mercaptoacyl pluronic

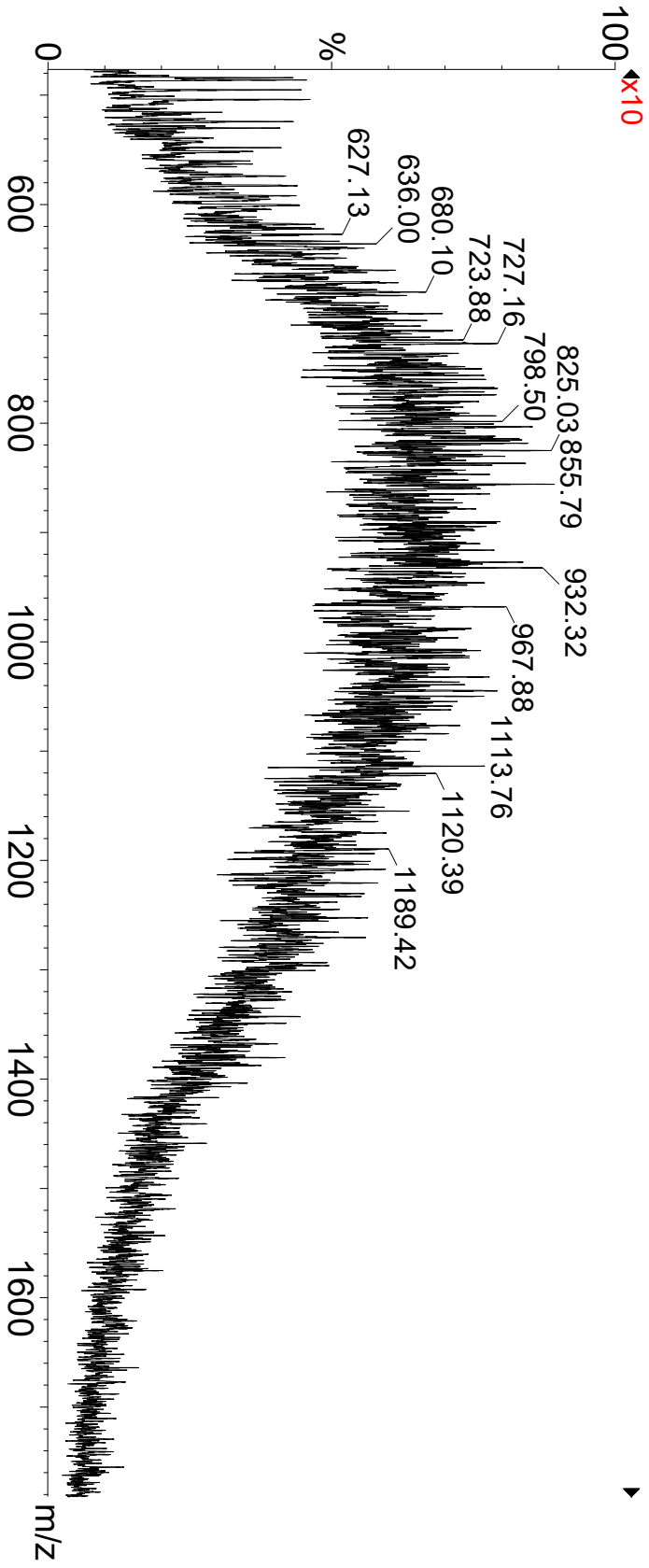


Figure S23. di-3-mercaptopropionyl Pluronic F127; M+14H/14, M+15H/15

6. Liposome physicochemical data before and after cross-linking reaction

6.1 Size distribution graphs for HPC-Lip-Mal before and after their reaction with PEG-di-thiol.

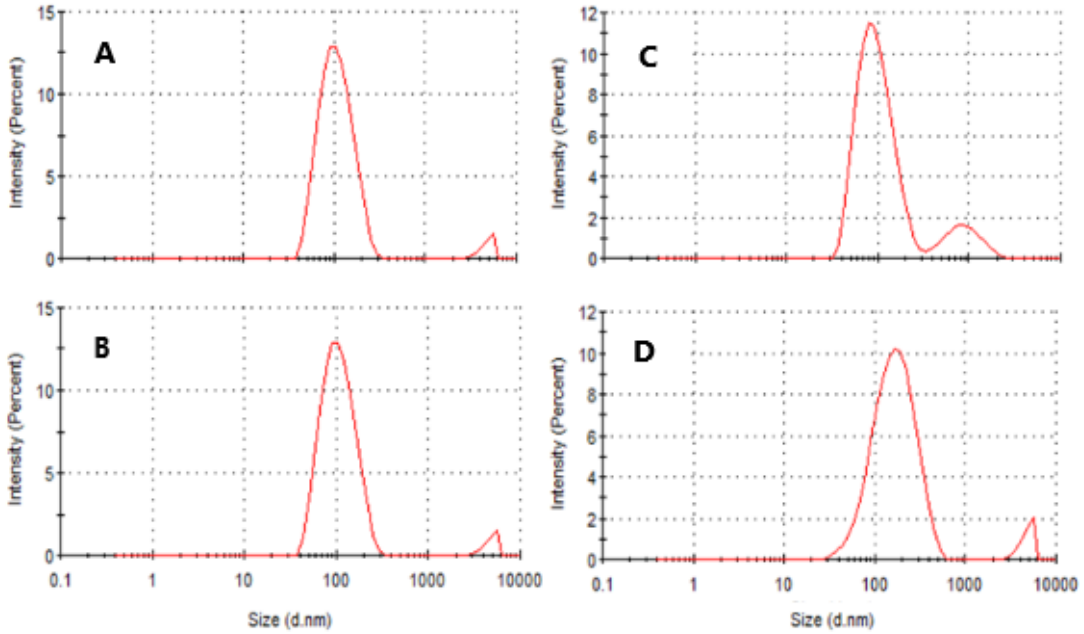
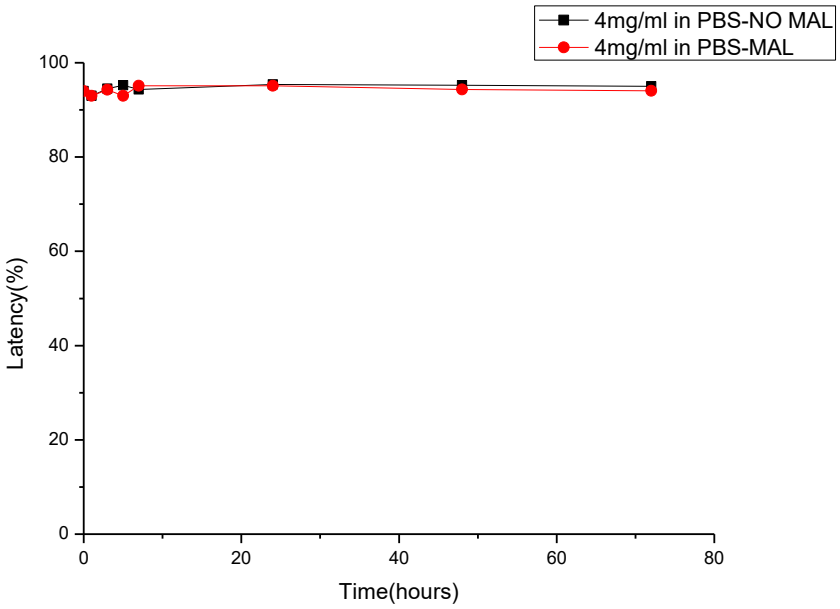
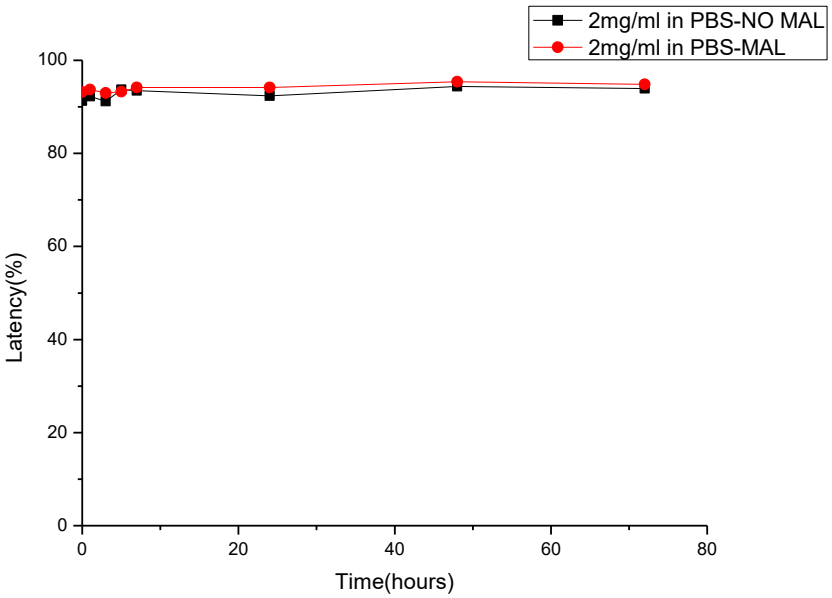
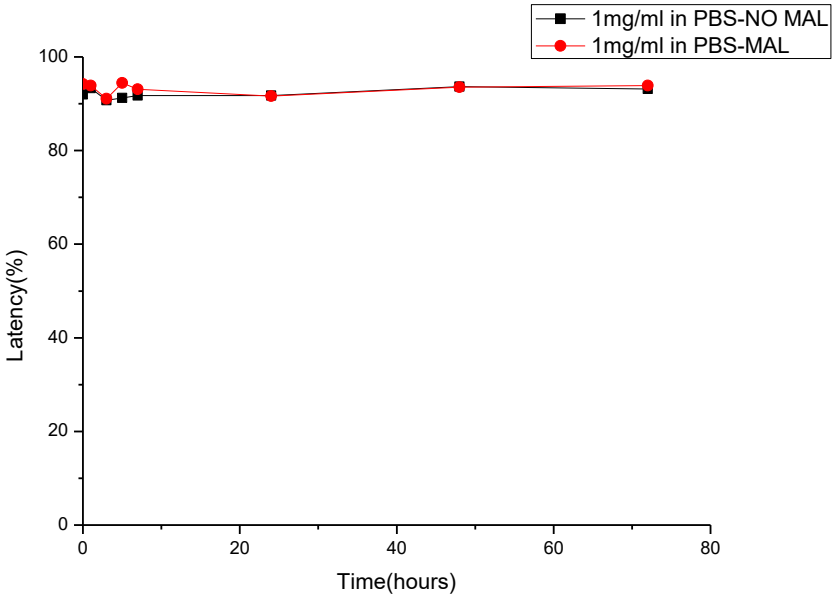


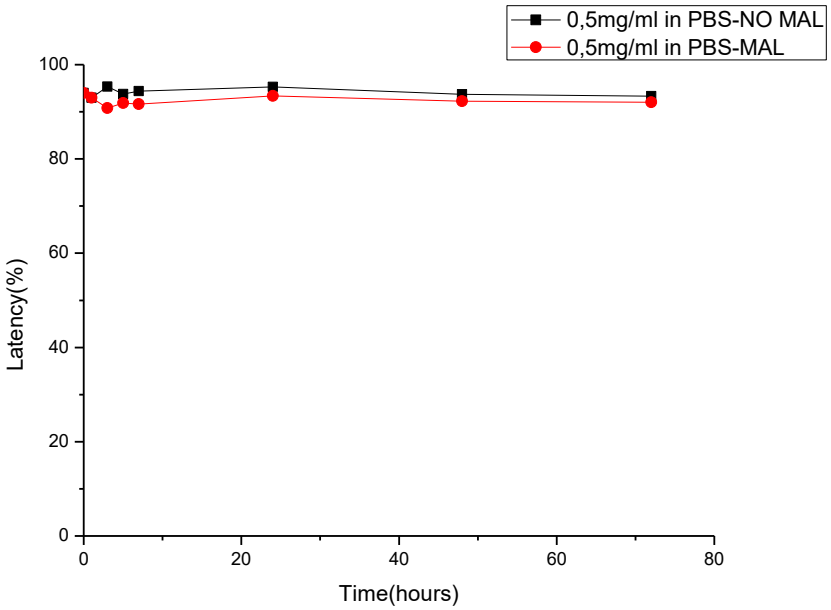
Figure S24. Size distribution before (A) and after reaction (B) for control liposomes. Size distribution before (C) and after reaction (D) for Lips-Mal.

7. Calcein Release from the liposomal structures in PBS






1mg/ml in PBS-NO MAL
1mg/ml in PBS-MAL
Latency(%)
Time(hours)
0
20
40
60
80
100


0,5mg/ml in PBS-NO MAL
0,5mg/ml in PBS-MAL
Latency(%)
Time(hours)
0
20
40
60
80
100

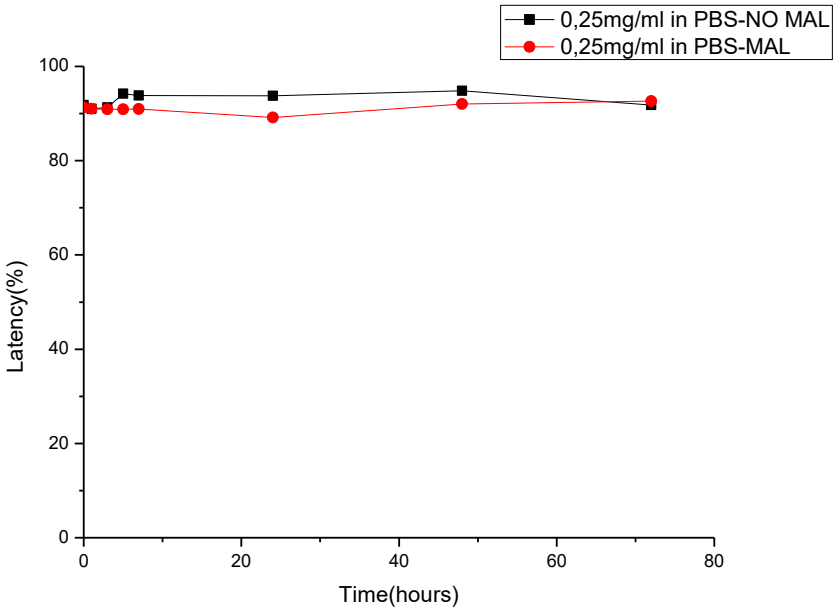


Figure S25. % Latency of calcein by the incubation of liposomes in PBS pH=7.40 at 27 ºC. Control liposomes (HPC-Lip; PBS-NO MAL) and thioether cross-linked liposomes (HPC-LIP-di-thioether-PEG; PBS-MAL) at different concentrations (4 mg/ml, 2 mg/ml, 1 mg/ml, 0.5 mg/ml, 0.25 mg/ml).