Supplementary Material (ESI) for RSC Advances

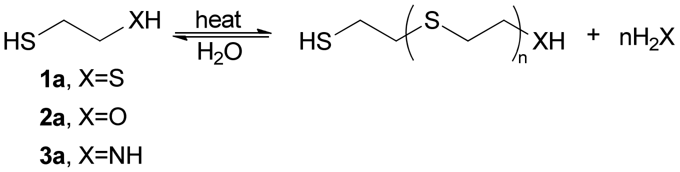
Oligomerisation reactions of beta substituted thiols in water

Efrat Levin,[†] Aviel Anaby,[†] Charles E. Diesendruck,[†] Dvora Berkovich-Berger,[†] Benzion Fuchs,[‡] and N. Gabriel Lemcoff*[,†]

[†]Chemistry Department, Ben-Gurion University of the Negev, Beer-Sheva 84105, Israel

[‡]School of Chemistry, Tel-Aviv University, Tel-Aviv 69978, Israel

Supplementary Information

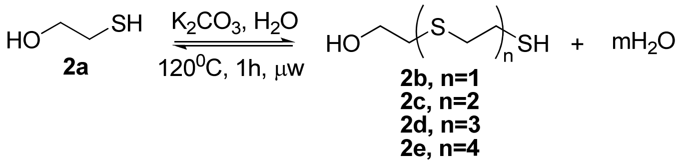


Reaction of **(1a)**/ **(2a)**/ **(3a)** in water

1. General

All reagents were of reagent grade quality, purchased commercially from Sigma, Aldrich or Fluka and used without further purification. Microwave irradiations were performed in a CEM corporation Discover apparatus, equipped with an Explorer robotic arm using Synergy application software. Gas chromatography data was obtained using an Agilent 6850 GC equipped with an Agilent 5973 MSD working under standard conditions and an Agilent HP5-MS column. NMR spectra were recorded on Bruker DPX 400 or DPX 500 instruments; chemical shifts, given in ppm, are relative to the residual solvent peak.[1] A Thermoscientific LTQU XL Orbitrap was used for high resolution mass spectrometry. 1,2-Ethanedithiol oligomer syntheses, purifications and characterisations have been previously reported.[2]

2. Oligomerisation of Mercaptoethanol



2.1. General procedure for oligomerisation of mercaptoethanol 2a: In a 10ml microwave vial, mercaptoethanol **2a** (0.140ml, 2mmol), potassium carbonate (0.834g, 6mmol) and 5.0 ml deionised water were purged with Ar gas for 10 min. The mixture was then stirred and heated by microwave irradiation and kept at 120°C for 1 hour. After cooling, the mixture was neutralised with HCl (32%) and extracted thrice with CH_2Cl_2. The combined organic extracts were dried over magnesium sulphate. The dried organic phase was analyzed by GC-MS.

In order to check mass balance additional experiments starting with 0.63ml **2a** (0.705g, 9.0mmol) were carried out. The reaction yielded 0.504g mixture after workup. GC-MS showed the typical distribution of **2a-2d** and the total yield (of all oligomers) was calculated to be 80.5%, the mass recovery including **2a** is 82%. See below:

<u>Yields calculation of mercaptoethanol oligomers:</u>

General procedure for the oligomerisation of **2a** was used, starting from 705mg **2a** and finished with total weight of 504mg.

Reaction conversion: **2a** 2%, **2b** 39%, **2c** 43%, **2d** 15% (by GC-MS).

$$w(2a) = 0.504gr * 0.02 = 0.0101gr$$
$$w(2b) = 0.504gr * 0.39 = 0.1966gr$$
$$w(2c) = 0.504gr * 0.43 = 0.2167gr$$
$$w(2d) = 0.504gr * 0.15 = 0.0756gr$$

$$mol(2a)=\frac{0.0101gr}{78.13gr/mol}=1.29*10^{-4}mol$$

$$mol(2b)=\frac{0.1966gr}{138.25gr/mol}=1.42*10^{-3}mol$$

$$mol(2c)=\frac{0.2167gr}{198.37gr/mol}=1.09*10^{-3}mol$$

$$mol(2d)=\frac{0.0756gr}{258.49gr/mol}=2.92*10^{-4}mol$$

$$yield=\frac{2mol(2b)+3mol(2c)+4mol(2d)}{mol(2a_i)}$$

$$yield=\frac{1.42*10^{-3}mol*2+1.09*10^{-3}mol*3+2.92*10^{-4}mol*4}{9.02*10^{-3}mol}*100=80.5\%$$

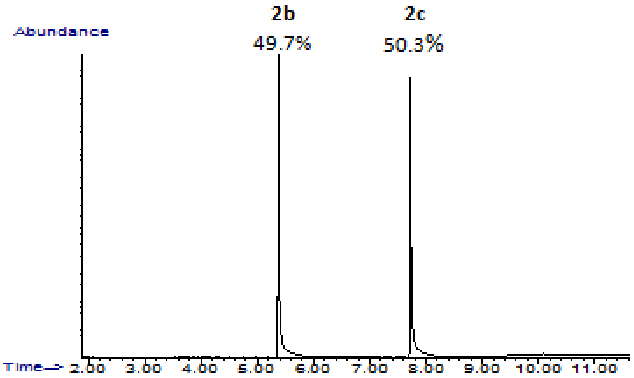
$$yield(2b)=\frac{1.42*10^{-3}mol*2}{9.02*10^{-3}mol}*100=31.5\%$$

$$yield(2c)=\frac{1.09*10^{-3}mol*3}{9.02*10^{-3}mol}*100=36\%$$

$$yield(2d)=\frac{2.92*10^{-4}mol*4}{9.02*10^{-3}mol}*100=13\%$$

The validity of using GC-MS values to calculate the weight distribution was independently checked by injecting weighted samples of **2b** and **2c**.

The GC-MS detector response for oligomeric homologues, reported as % area, may be aproximated in good agreement as % weight. Thus, a weighted sample containing 10.0mg **2b** and 10.0mg **2c** afforded chromatographic signals of equal intensity for both compounds.



For full characterisation of oligomers **2b-2d**, a semipreparative reaction was carried out starting from (2.8ml, 40mmol) mercaptoethanol, applying the general procedure as detailed above. **2b** and **2c** were separated by vacuum fractional distillation at 0.2-0.8 torr (**2b** 70-80°C, **2c** 140-160°C) in a microdistillation apparatus. The heavy residue from the distillation was introduced into a sublimation apparatus to completely remove any remaining **2c** (140-150°C, 0.2 torr). The residual non-volatile solid was pure **2d**. This procedure was used for the full characterisation of the products by GC-MS, ESI-HRMS and NMR analysis as follows. The yields in this case were not calculated because of the high loss of material during the high-vacuum microdistillation and sublimation.

Moreover, a larger preparative run (see text in manuscript) was prepared by joining 13 microwave runs of 0.4M of **2a** (0.56ml, 8mmol) and 2 equivalents of potassium carbonate (2.23g, 16mmol) each, following the general procedure otherwise. After reaction completion, the mixtures were combined and worked up. GC-MS analysis for the mixture afforded **2a** 27%, **2b** 48% and **2c** 25% conversions. Evaporation of solvent and **2a** afforded 4.55g of a mixture of **2b** and **2c**. The relatively larger amount of **2a** and lack of **2d** obtained after the reaction are due to the use of 2 eq. of potassium carbonate and lower concentration of **2a**. This was done in order to facilitate the separation of the dimer and trimer products in large amounts.

The mixture was separated by vacuum fractional microdistillation at 0.08 torr (**2b** 50-64˚C, **2c** 90-110˚C) in a microdistillation apparatus, to give 1.82g (13.2mmol) of **2b** and 1.03g (5.2mmol) of **2c**. Naturally, the yields were decreased due to loss of material in the microdistillation apparatus.

Final isolated yield calculations:

$$yield(2b) = \frac{13.2mmol * 2}{104mmol} * 100 = 25\% \qquad yield(2c) = \frac{5.2mmol * 3}{104mmol} * 100 = 15\%$$

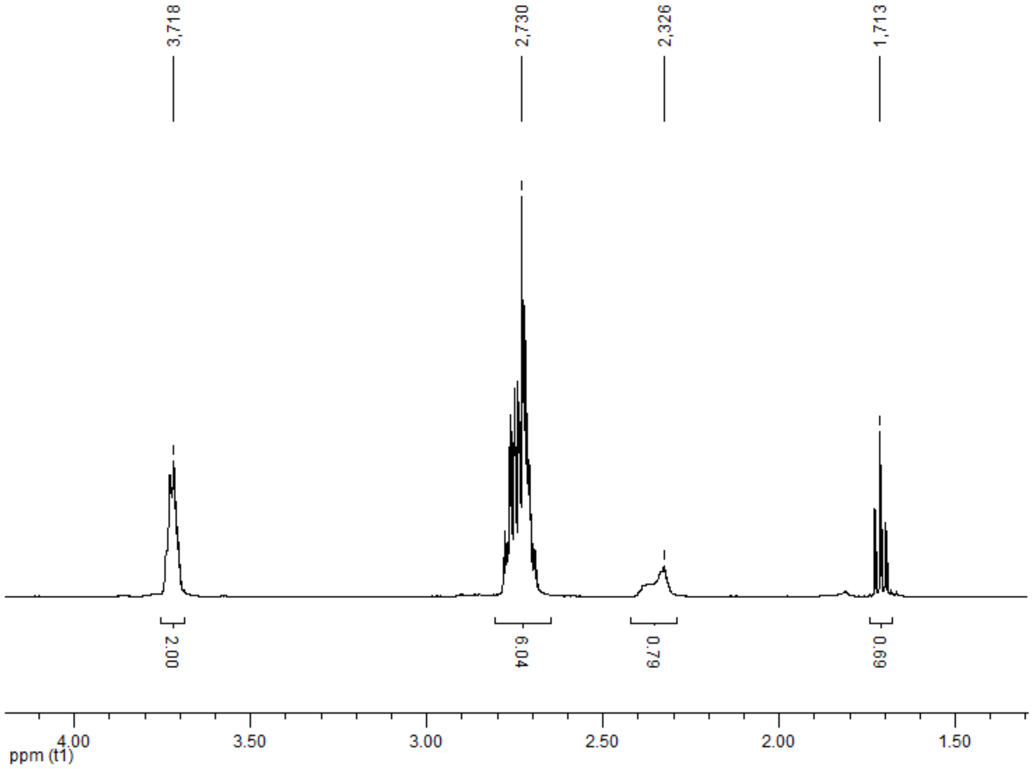
5-mercapto-3-thia-pentanol (2b): ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 1.71 (t, J = 7.9 Hz, 1H, SH), 2.33 (bs, 1H, OH), 2.69-2.78 (m, 6H, S$\underline{\mathrm{CH_2}}$), 3.72 (m, 2H, HO$\underline{\mathrm{CH_2}}$) ppm. ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 24.7, 35.1, 35.7, 60.6 ppm. $C_4H_{10}OS_2$ HR-MS (ESI): m/z $(M + Na)^+$ calculated 161.0065, found 161.0066. GC-MS (EI): m/z M^+ calculated 138.02, found 137.95 peaks (rel. abundance): 137.95 (20%), 119.95 (26%), 104.95 (9%), 91.00 (24%), 61.00 (100%), 44.95 (33%), 31.05 (7%).

8-mercapto-3,6-dithia-octanol (2c): ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 1.73 (t, J = 8.0 Hz, 1H, SH), 2.21 (t, J = 5.9 Hz, 1H, OH), 2.81-2.70 (m, 10H, S$\underline{\mathrm{CH_2}}$) 3.75 (dt, J = 5.9, 11.6 Hz, 2H, HO$\underline{\mathrm{CH_2}}$) ppm. ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 24.7, 31.9, 32.2, 35.4, 36.2, 60.6 ppm. $C_6H_{14}OS_3$ HR-MS (ESI): m/z $(M + Na)^+$ calculated 221.0099, found 221.0098. GC-MS (EI): m/z M^+ calculated 198.02, found 198.00, peaks (rel. abundance): 198.00 (2%), 137.95 (48%), 119.95 (16%), 104.95 (43%), 91.00 (14%), 61.00 (100%), 45.00 (31%), 31.05 (5%).

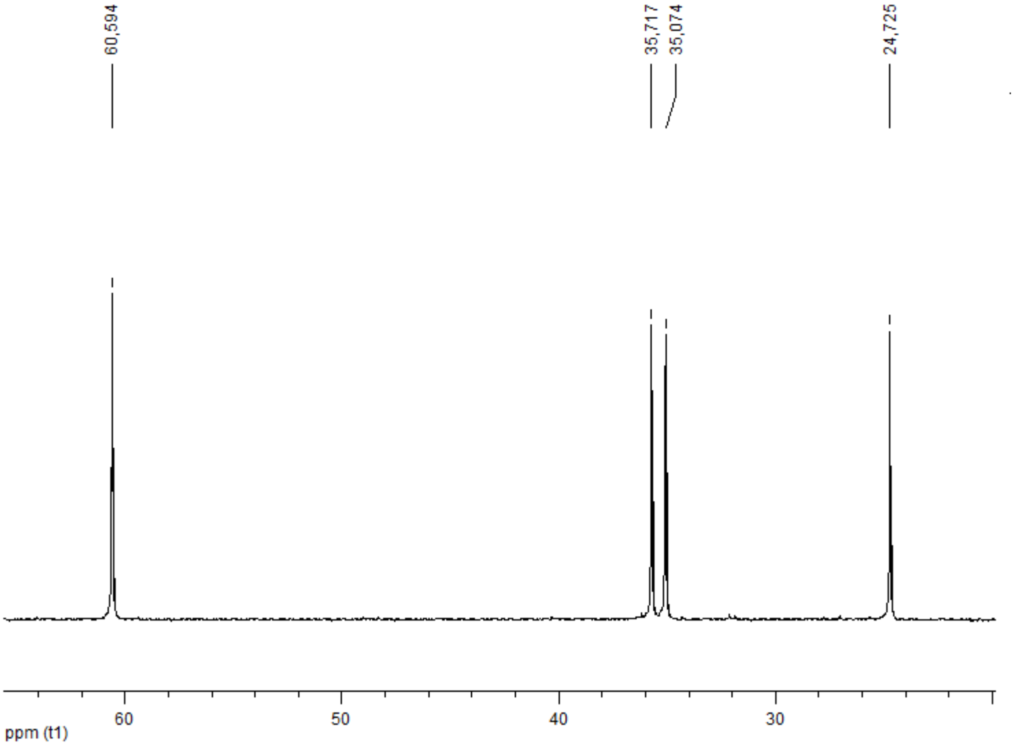
11-mercapto-3,6,9-trithia-undecanol (2d): ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 1.74 (t, J = 8.0 Hz, 1H, SH) , 1.96 (bs, 1H, OH) , 2.81-2.70 (m, 14H, S$\underline{\mathrm{CH_2}}$), 3.75 (t, J = 5.9 Hz, 2H, HO$\underline{\mathrm{CH_2}}$) ppm. ^{13}C-NMR ($CDCl_3$, 125 MHz): δ 24.8, 31.9, 32.2, 32.4, 32.4, 35.4, 36.3, 60.6 ppm. $C_8H_{18}OS_4$ HR-MS (ESI): m/z $(M + Na)^+$ calculated 281.0133, found 281.0134. GC-MS (EI): m/z M^+ calculated 258.02, found 258.00, peaks (rel. abundance): 258.02 (0.3%), 198.00 (4%), 163.95 (13%), 138.00 (33%), 119.95 (39%), 105.00 (67%), 91.00 (10%), 61.00 (100%), 45.00 (30%), 31.05 (3%).

14-mercapto-3,6,9,12 -tetrathia-tetradecanol (2e): (not isolated) $C_{10}H_{22}OS_5$ HR-MS (ESI): m/z $(M + Na)^+$ calculated 341.0166, found 341.0169. GC-MS (EI): m/z M^+ calculated 318.03, found 317.90, peaks (rel. abundance): 317.90 (0.06%) 258.00 (0.3%), 197.95 (14%), 163.95 (20%), 137.95 (13%), 120.00 (25%), 104.95 (76%), 90.95 (9%), 61.00 (100%), 45.00 (28%), 31.05 (2%).

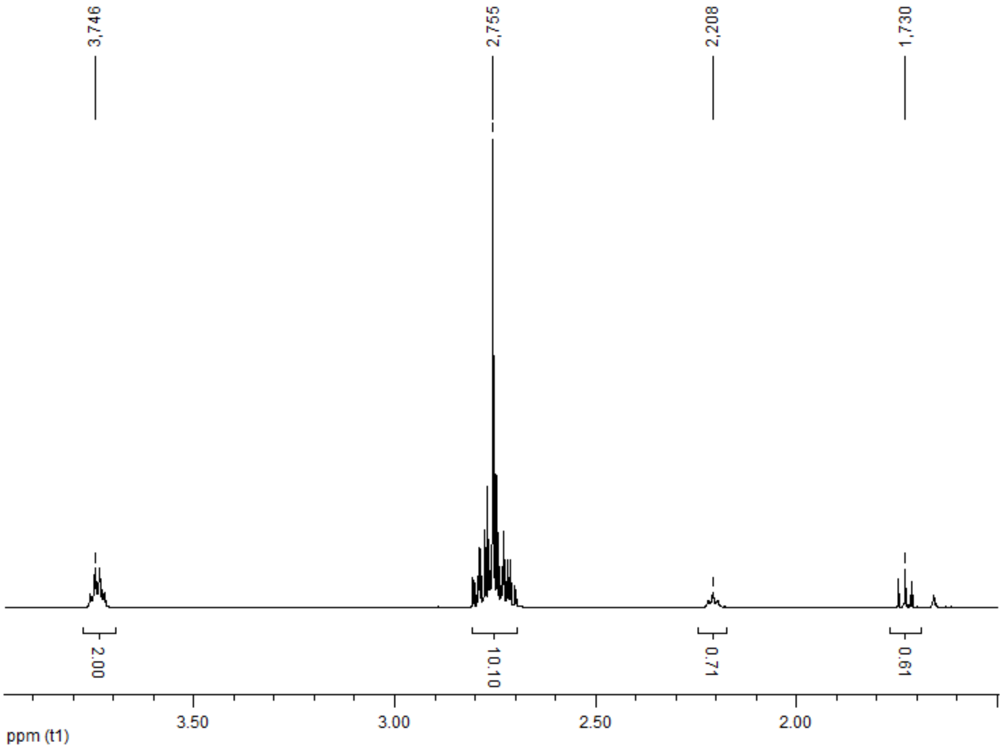
^{1}H-NMR of **2b** (CDCl$_3$, 500 MHz):



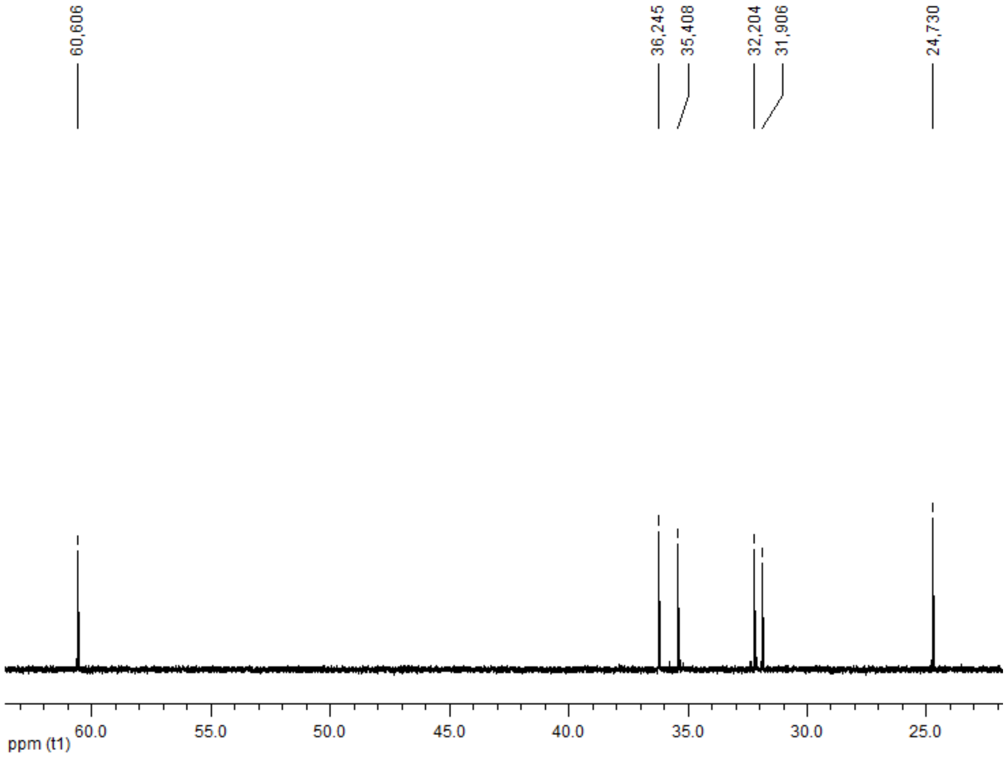
^{13}C-NMR of **2b** (CDCl$_3$, 125 MHz):



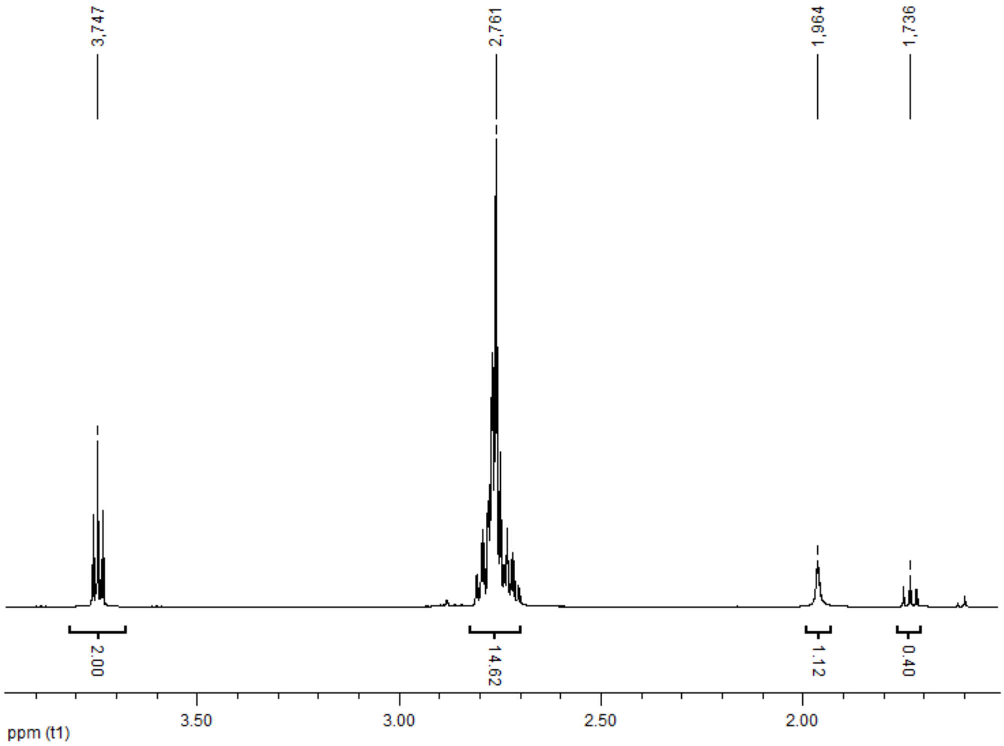
^{1}H-NMR of **2c** (CDCl$_3$, 500 MHz):



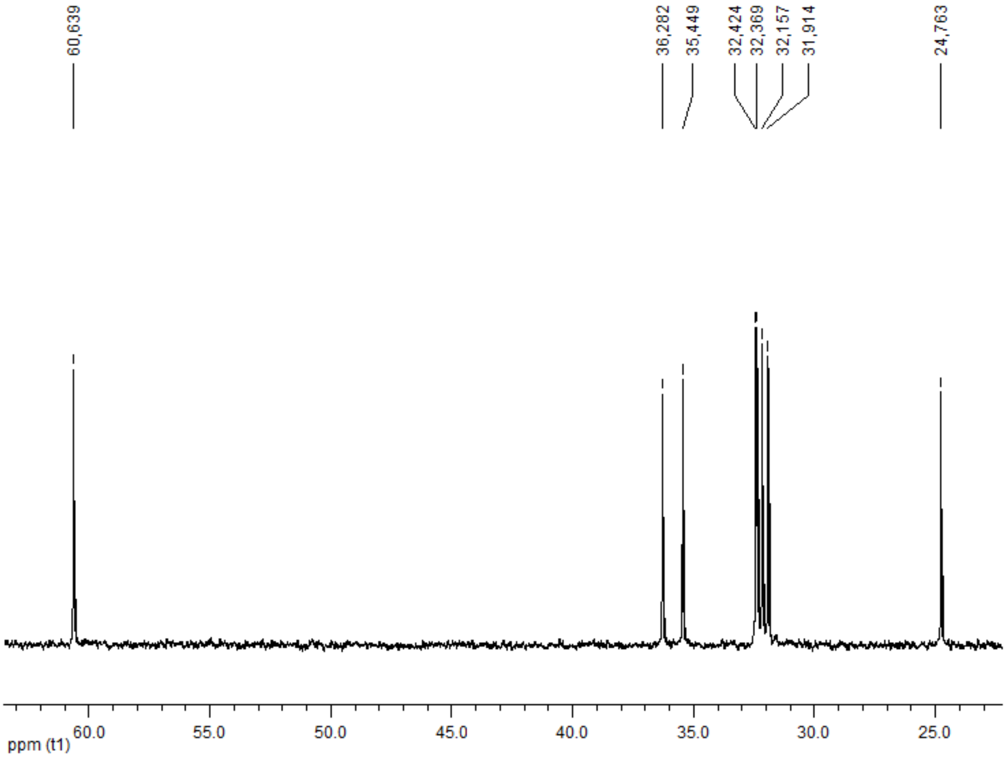
^{13}C-NMR of **2c** (CDCl$_3$, 125 MHz):



^{1}H-NMR of **2d** (CDCl$_3$, 500 MHz):



^{13}C-NMR of **2d** (CDCl$_3$, 125 MHz):



2.2. Oligomerisatinon of 2a with different solvents: The following table summarise the results of oligomerisation of mercaptoethanol in different solvents. Reactions were carried out for 60 minutes in the microwave reactor with 0.4M of **2a** and 3 eq. K_2CO_3.

Entry	Solvent	Temp.	Conversion[a]				
			2a	**2b**	**2c**	**2d**	**2e**
1	Water[b]	120°C	14%	40%	35%	10%	<1%
2	Water[c]	100°C	29%	65%	6%	-	-
3	Acetonitrile[d]	85°C	54%	3%	-	-	-
4	1,4-Dioxane[e]	105°C	85%	None	-	-	-
5	DMF[f]	105°C	N.A.[g]	70%	-	-	-
6	Ethylene glycol	105°C	<1%	16%	45%	39%	-
7	Neat[h,i]	105°C	<1%	25%	53%	22%	-

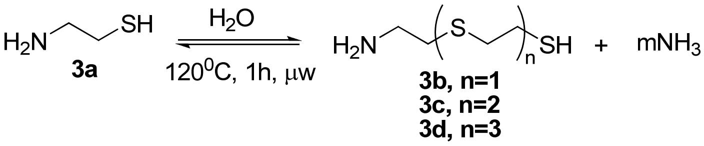
[a] Area % by GC-MS. [b] Similar product distributions are obtained even after 10 min. in the microwave reactor. [c] Conventional heating in oil bath, 2 hours. [d] 2% oxidation products. [e] 15% oxidation products. [f] 30% oxidation products. [g] Not analysed due to solvent signal overlap. [h] 1eq. base. [i] Significant amount of insoluble product, reported percentages are only of the soluble fraction.

2.3. General procedure for the oligomerisation of 2a with different additives: In a 10ml microwave vial, mercaptoethanol **2a** (0.140ml, 2mmol), 3 eq. of chosen reagent and 5.0ml deionised water were purged with Ar gas for 10 min. The mixture was then stirred and heated by microwave irradiation and kept at 120°C for 1 hour. After cooling, the mixture was neutralised with HCl (32%) and extracted thrice with CH_2Cl_2. The combined organic extracts were dried over magnesium sulphate. The dried organic phase was analysed by GC-MS.

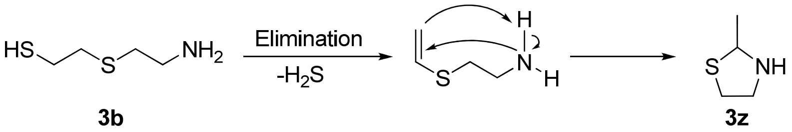
Entry	Reagent	Conversion[a]				
		Mono (**2a**)	Di (**2b**)	Tri (**2c**)	Tetra (**2d**)	Penta (**2e**)
1	No reagent	10%	53%	36%	1%	-
2	K_2CO_3	14%	40%	35%	10%	1%
3	Na_2CO_3	3%	33%	43%	21%	-
4	Cs_2CO_3	15%	41%	34%	9%	1%
5	Na_2SO3[b]	1%	38%	51%	10%	-
6	Na_2SO_4[b]	48%	45%	7%	-	-
7	Na_2S[c]	73%	27%	-	-	-
8	$NaHCO_3$	10%	42%	40%	8%	-
9	NaOH	63%	37%	-	-	-
10	NaOH (pH=13)	70%	30%	-	-	-
11	TEA	63%	37%	-	-	-
12	Triethanolamine[b]	80%	20%	-	-	-
13	Acetic acid (pH=2)[d]	64%	10%	-	-	-
14	KNO_3	11%	58%	31%	-	-
15	KI[e] + TEA	55%	43%	2%	-	-
16	KI[e] + K_2CO_3	16%	43%	30%	11%	-
17	NaCl[e] + Na_2CO_3	14%	41%	34%	11%	-
18	BHT[f] + K_2CO_3	7%	35%	37%	21%	-

[a] Area % by GC-MS. [b] 20 Min. reaction. [c] 2 Eq. of sodium sulfide; trace amounts of dithiol products were also observed. [d] 26% Esterification products. [e] 1 equivalent of salt. [f] 0.1 Equivalent.

3. Oligomerisation of Cysteamine



3.1. General procedure for oligomerisation of cysteamine 3a: In a 10 ml microwave vial, cysteamine **3a** (0.140ml, 2mmol), potassium carbonate (0.8343g, 6 mmol - or without additional base), and 5.0 ml deionised water were purged with Ar gas for 10 min. The mixture was then heated by microwave irradiation to 120°C for 1h. Some experiments were run without the addition of carbonate with very similar results. After cooling, the mixture was extracted with CH_2Cl_2, the aqueous phase was then neutralised with HCl (32%) to pH=7 and repeatedly extracted with CH_2Cl_2, then the aqueous phase was acidified to pH=3, extracted with CH_2Cl_2, and finally sodium bicarbonate was added to the aqueous phase until pH=8 and extracted twice with CH_2Cl_2. An additional minor by-product, observed by GC-MS was 2- methylthiazolidine, **3z** (not isolated). This by-product was also present as a small impurity in the commercial cysteamine purchased, however more of it was produced during the reaction. We hypothesise that additional formation of **3z** may be the result of a parallel mechanism involving intramolecular addition of a terminal amine group to a terminal ene group, formed by elimination reaction in **3b** under basic conditions. The proposed vinyl sulfide intermediate was not observed by NMR or GC analysis.



The combined extracts were dried over magnesium sulphate. The dried organic phase was analyzed by GC–MS. Total yield (of oligomers) after workup was calculated to be 69.3%, and mass recovery was calculated to be 80%.

Yields calculation of cysteamine reaction:

General procedure for the oligomerisation of **3a** was used, starting from 1196mg **3a** and finished with total weight of 800mg. Reaction conversion: **3a** 1%, **3z** 10%, **3b** 25%, **3c** 45%, **3d** 19%.

$$w(3a) = 0.8gr * 0.01 = 0.008gr$$
$$w(3z) = 0.8gr * 0.1 = 0.080gr$$
$$w(3b) = 0.8gr * 0.25 = 0.200gr$$
$$w(3c) = 0.8gr * 0.45 = 0.360gr$$
$$w(3d) = 0.8gr * 0.19 = 0.152gr$$

$$mol(3a) = \frac{0.008gr}{77.15gr/mol} = 1.04 * 10^{-4} mol$$

$$mol(3z) = \frac{0.080gr}{103.19gr/mol} = 7.75 * 10^{-4} mol$$

$$mol(3b) = \frac{0.200gr}{137.27gr/mol} = 1.46 * 10^{-3} mol$$

$$mol(3c) = \frac{0.360gr}{197.38gr/mol} = 1.82 * 10^{-3} mol$$

$$mol(3d) = \frac{0.152gr}{257.50gr/mol} = 5.90 * 10^{-4} mol$$

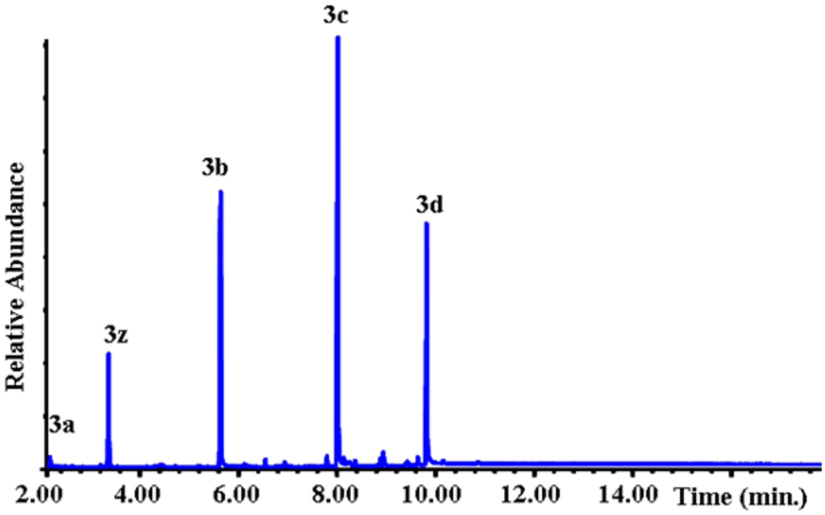
$$yield = \frac{1.46 * 10^{-3} mol * 2 + 1.82 * 10^{-3} mol * 3 + 5.90 * 10^{-4} mol * 4}{0.0155mol} * 100 = 69.3\%$$

$$yield(3z) = \frac{7.75 * 10^{-4} mol \cdot 2}{0.0155mol} * 100 = 10\%$$

$$yield(3b) = \frac{1.46 * 10^{-3} mol \cdot 2}{0.0155mol} * 100 = 19\%$$

$$yield(3c) = \frac{1.82 * 10^{-3} mol \cdot 3}{0.0155mol} * 100 = 35.1\%$$

$$yield(3d) = \frac{5.90 * 10^{-4} mol \cdot 4}{0.0155mol} * 100 = 15.2\%$$



GC-MS of CH_2Cl_2 extract of reaction of 0.4M **3a** and 1.2M K_2CO_3 in water, 60 min., 120°C in a microwave reactor.

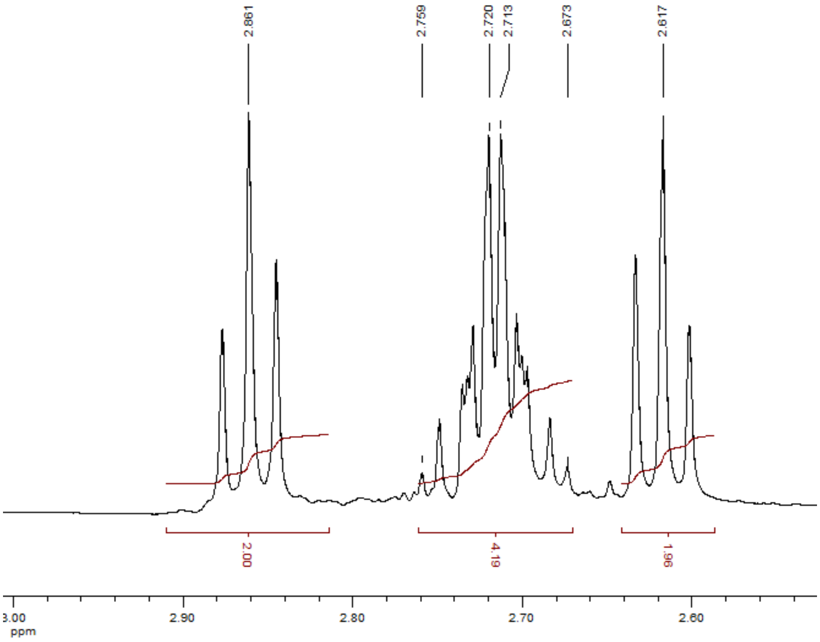
For purification and full characterisation of the oligomers **3b** and **3c**, a preparative scale reaction was carried out starting from (1.00gr, 0.01mol) **3a**, applying the same general procedure as detailed above. **3b** and **3c** were separated by sublimation under vacuum at 0.1-0.2 torr (**3b** 35-45°C, **3c** 55-75°C).

5-mercapto-3-thia-pentanyl amine (3b): ^{1}H-NMR ($CDCl_3$, 400 MHz): δ 2.62 (t, J = 6.4, 2H, HSC$\underline{H_2}$), 2.72 (m, 4H, SC$\underline{H_2}$), 2.86 (t, J = 6.4, 2H, H_2NC$\underline{H_2}$) ppm. ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 24.8, 35.8, 36.0, 41.1 ppm. $C_4H_{11}NS_2$ HR-MS (ESI): m/z $(M + Na)^+$ calculated 160.0225, found 160.0221, m/z $(M + H)^+$ calculated 138.0406, found 138.0402. GC-MS (EI): m/z M^+ calculated 137.03, found 135.00, peaks (rel. abundance): 135.00 (0.1%), 119.95 (32%), 104.05 (100%), 76.95 (3%), 60.95 (43%), 44.95 (16%), 30.10 (95%).

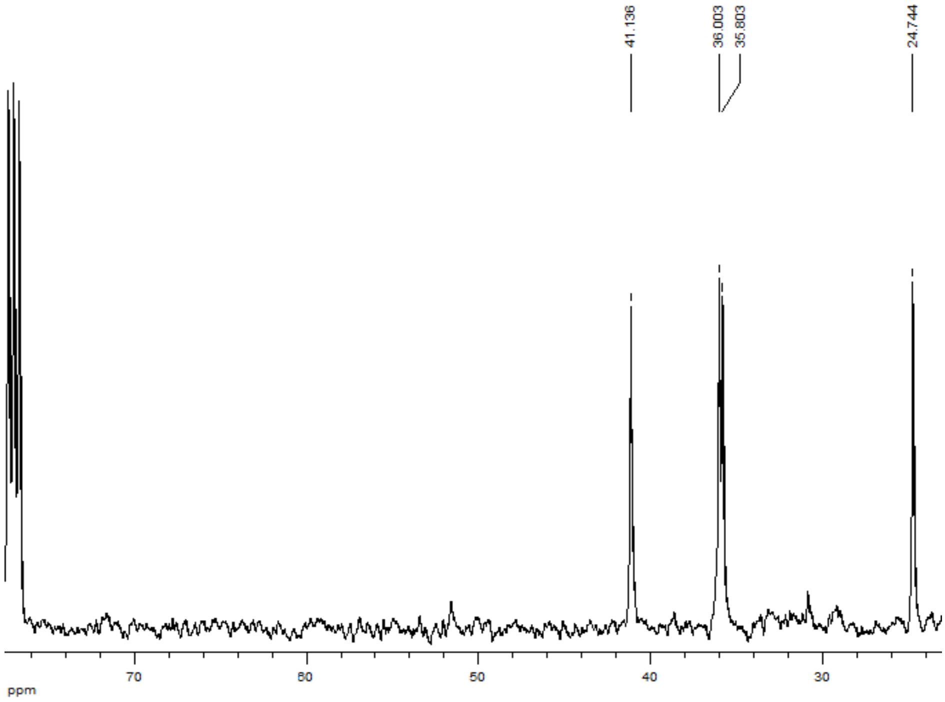
8-mercapto-3,6-dithia-octyl amine (3c): ^{1}H-NMR (CD_3OD, 500 MHz): δ 2.67 (m, 2H, SC$\underline{H_2}$CH_2SH), 2.70 (m, 2H, HSC$\underline{H_2}$), 2.74 (m, 4H, SC$\underline{H_2}$C$\underline{H_2}$S), 2.76 (m, 2H, H_2NC$\underline{H_2}$), 2.80 (m, 2H, H_2NCH_2C$\underline{H_2}$S) ppm. ^{13}C-NMR (CD_3OD, 125 MHz): δ 25.5, 32.9, 33.0, 35.6, 37.2, 41.7 ppm. HMQC NMR correlating ^{1}H NMR and ^{13}C spectra of **3c** is shown below. $C_6H_{15}NS_3$ HR-MS (ESI): m/z $(M + Na)^+$ calculated 220.0259, found 220.0257, $(M + H)^+$ calculated 198.0439, found 198.0437. GC-MS (EI): m/z M^+ calculated 197.04, found 198.00, peaks (rel. abundance): 198.00 (0.5%), 164.05 (24%), 134.00 (5%), 120.00 (11%), 104.00 (94%), 87.00 (31%), 77.00 (87%), 61.00 (93%), 44.00 (30%), 30.10 (100%).

11-mercapto-3,6,9-trithia-undecanyl amine (3d): (not isolated) $C_8H_{19}NS_4$ HR-MS (ESI): m/z $(M + Na)^+$ calculated 280.0293, found 280.0288, $(M + H)^+$ calculated 258.0473, found 258.0470. GC-MS (EI): m/z M^+ calculated 257.04, found 254.90, peaks (rel. abundance): 254.90 (0.06%), 224.00 (2%), 198.00 (2%), 180.00 (14%), 164.00 (30%), 137.00 (27%), 120.00 (41%), 104.00 (53%), 87.00 (31%), 77.00 (37%), 61.00 (100%), 44.00 (34%), 30.10 (72%).

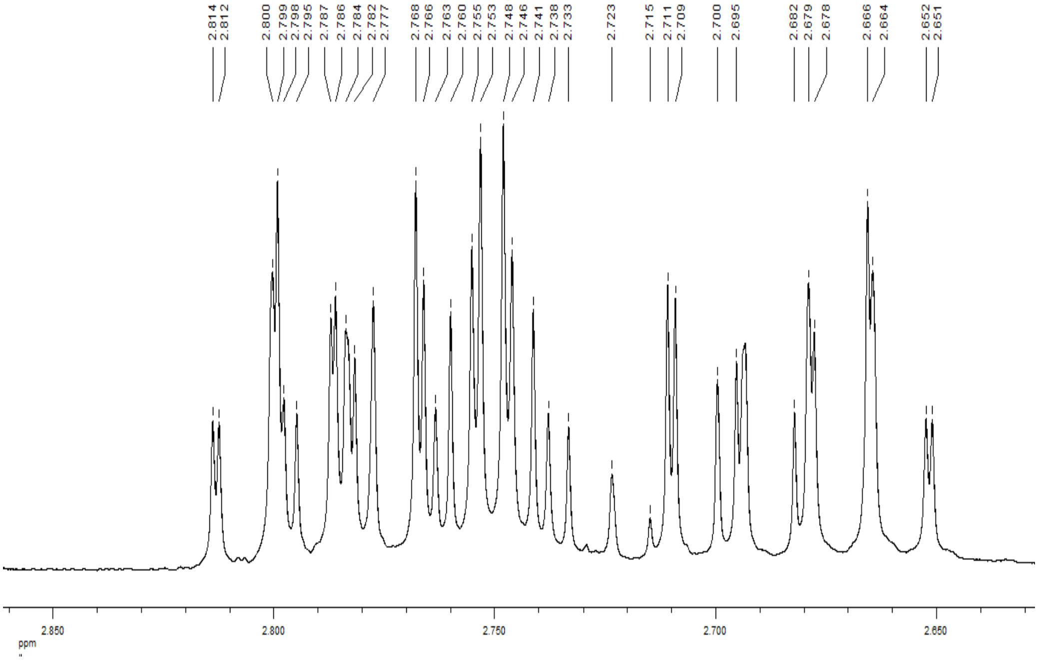
^{1}H-NMR of **3b** (CDCl$_3$, 400 MHz):



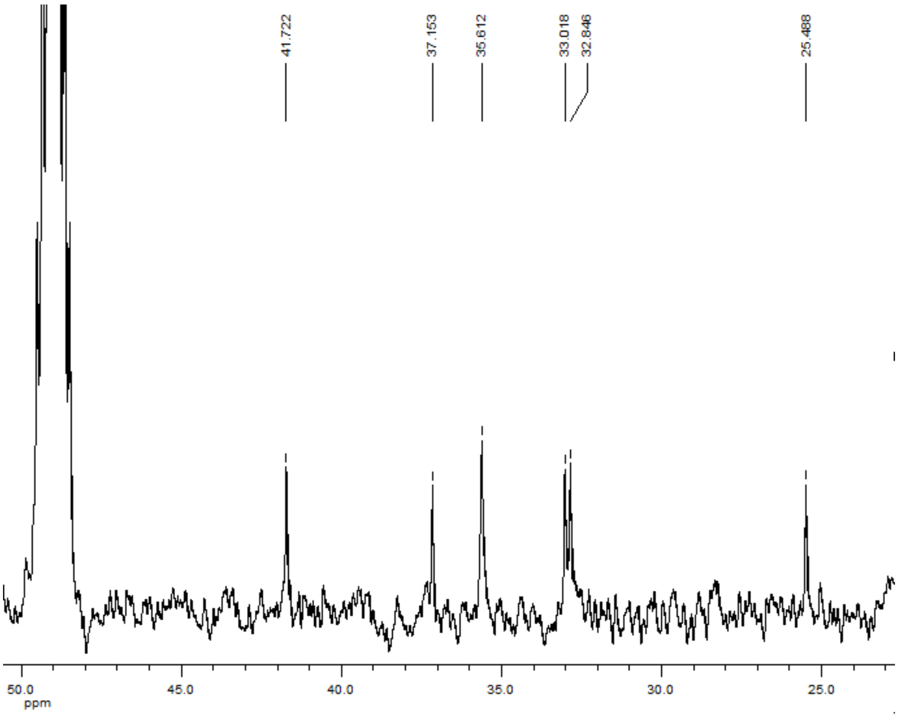
^{13}C-NMR of **3b** (CDCl$_3$, 100 MHz):



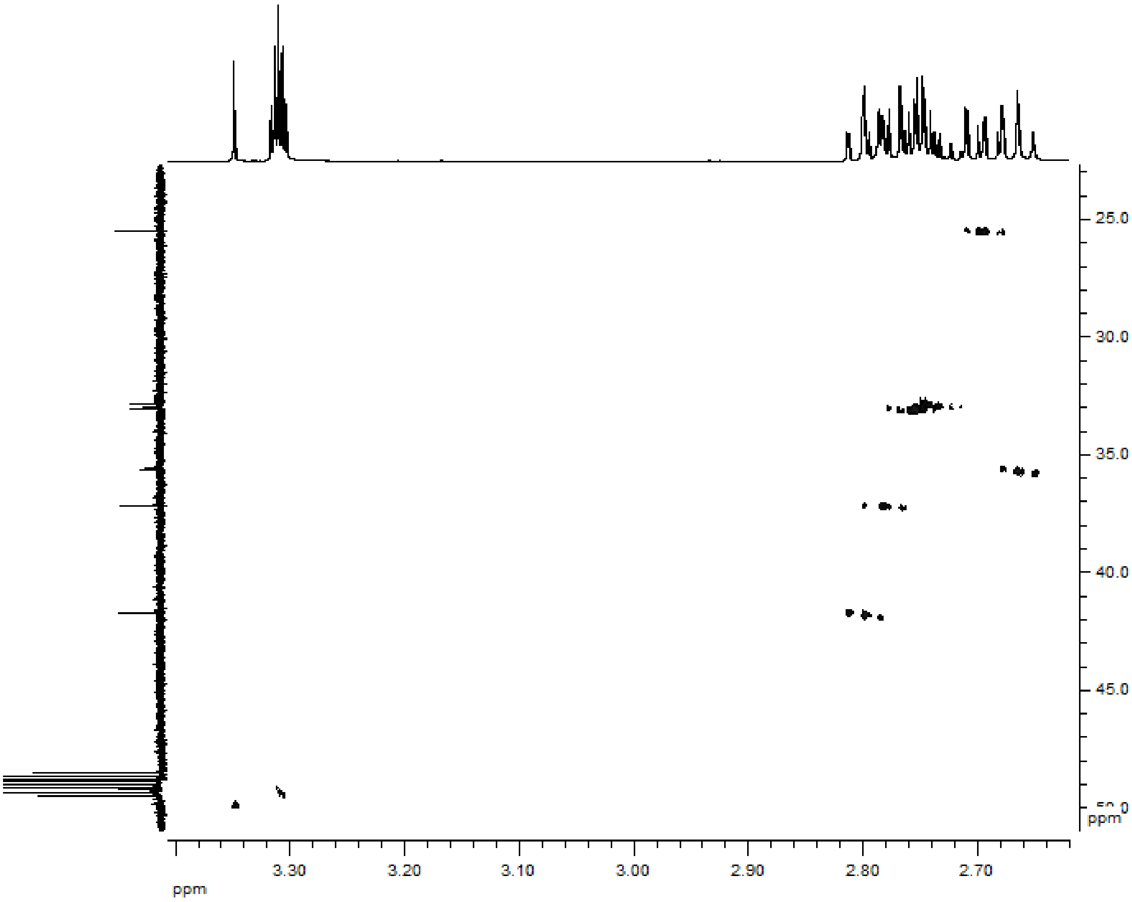
^{1}H-NMR of **3c** (CD$_3$OD, 500 MHz):



^{13}C-NMR of **3c** (CD$_3$OD 125 MHz):



HMQC-NMR of **3c** (CD_3OD 500 / 125 MHz):

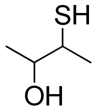
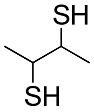
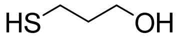
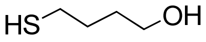
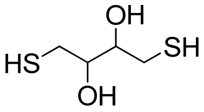


3.2. Oligomerisatinon of 3a with different solvents: The following table summarises the results of oligomerisation of cysteamine in different solvents. Reactions were carried out with 0.4M of **3a** and 3 eq. K_2CO_3.

Solvent	Temp.	Conversion[a]			
		3b	**3c**	**3d**	Disulphides oxidation
Water[b]	120°C	25%	45%	19%	-
Acetonitrile[c]	85°C	2%	-	-	27%
1,4-Dioxane	100°C	-	-	-	68%
Ethylene glycol	105°C	-	-	-	12%

[a] Area % by GC-MS. [b] 10% 2-methylthiazolidine also observed. [c] Using Cs_2CO_3 as a base.

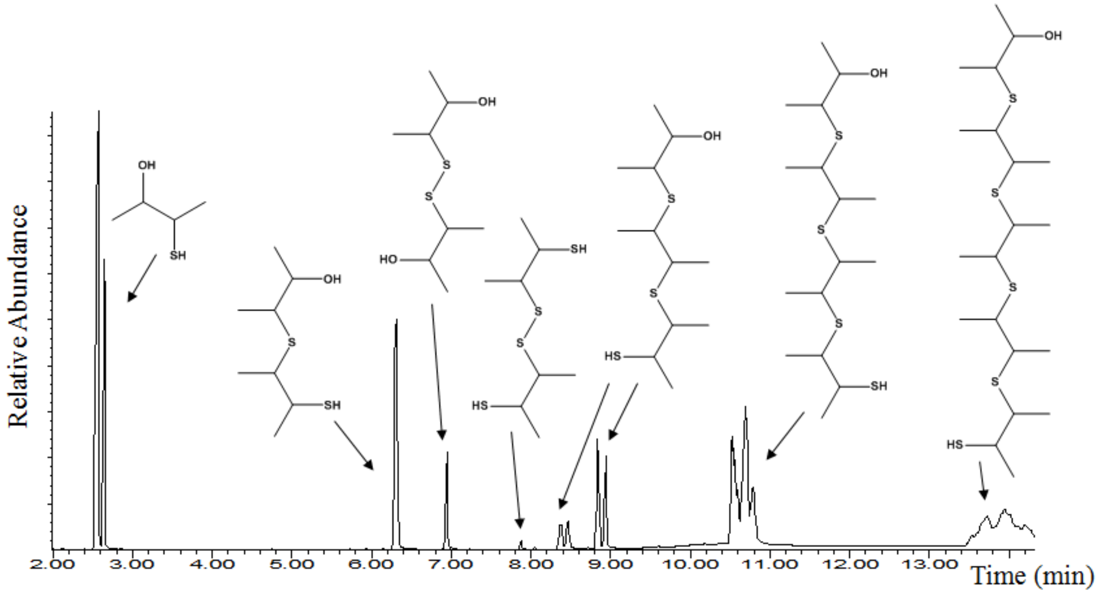
4. Additional Dithiols and Mercaptoalkanols

Substrate[a]	Solvent	Temp.	Base	Conversion[b]			
				Dimer	Trimer	Tetramer	Oxid.
 **4o**[c]	Water	120 ºC	K_2CO_3	11%	10%	24%	3%
 **4s**[d]	Water	120 ºC	K_2CO_3	22%	45%	11%	-
 **5o**	Water	120 ºC	K_2CO_3	1%	-	-	15%
 **5s**	Water	120 ºC	K_2CO_3	-	-	-	5%
			Cs_2CO_3[e]	-	-	-	3%
	Acetonitrile	120 ºC	K_2CO_3	-	-	-	34%
			Cs_2CO_3	13%	-	-	25%
	Pyridine	120 ºC	K_2CO_3[f]	-	-	-	10%
	1,4-Dioxane	105 ºC	Cs_2CO_3	2%	-	-	16%
 **6**	Water	120 ºC	K_2CO_3	-	-	-	-
	Acetonitrile	85 ºC	Cs_2CO_3[g]	-	-	-	15%
	Toluene	115ºC	K_2CO_3+ 18-Crown-6	-	-	-	37%
 **11**	Water	120 ºC	K_2CO_3	-[h]	-	-	8%

[a] Reactions were carried out in a microwave reactor for 60 min., 0.4M substrate and 3 eq. of chosen reagent. [b] Area % by GC-MS. Residual monomer percentages are not shown. [c] 20% higher oligomers. [d] 21% oligomers of **4o** also formed**.** [e] 90 min. reaction. [f] 30 min. reaction. [g] 1% Tetrahydrothiophene is observed as a by-product. [h] 15% 4-mercaptotetrahydrothiophen-3-ol is obtained, a product of an intramolecular ring closing reaction.[3]

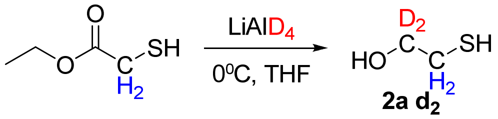
General procedure for the oligomerisation of 2,3-butanedithiol (4s) and 2,3-mercaptobutanol (4o): In a 10ml microwave vial, 0.4M substrate: **4o/4s**, potassium carbonate (0.834g, 6mmol) and 5.0ml deionised water were purged with Ar gas for 10 min. The mixture was then stirred and heated by microwave irradiation and kept at 120°C for 1 hour. After cooling, the mixture was neutralised with HCl (32%) and extracted thrice with CH_2Cl_2. The combined organic extracts were dried over magnesium sulphate. The dried organic phase was analyzed by GC-MS.

GC-MS of oligomerisation reaction of 2,3-mercaptobutanol **4o**:



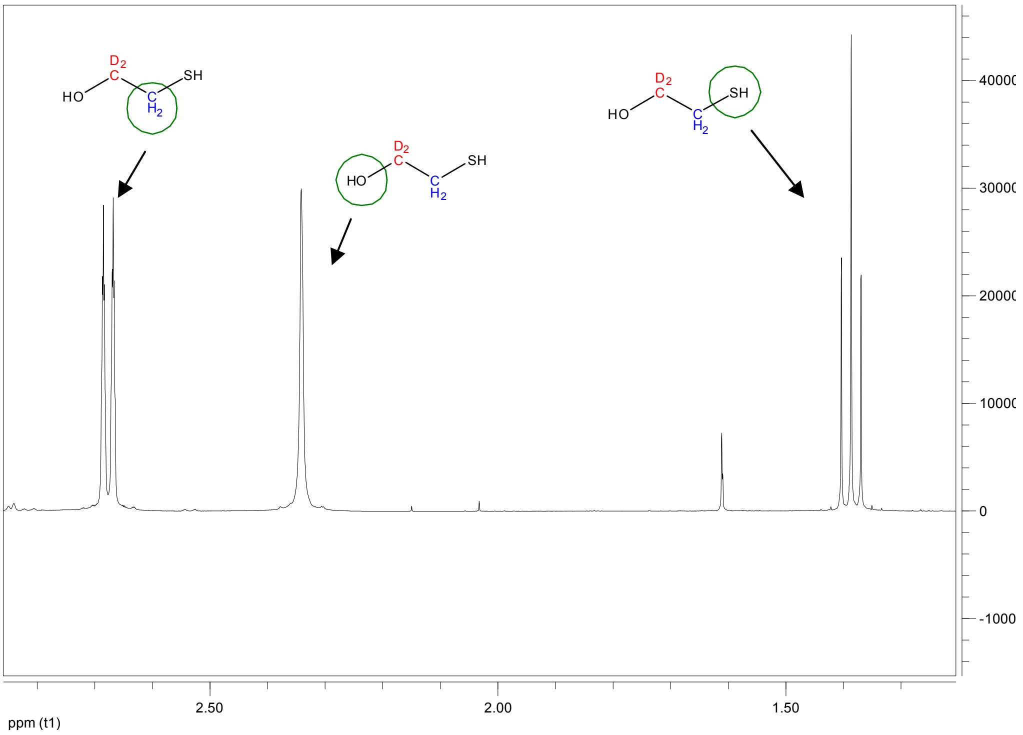
GC-MS of organic extract (CH_2Cl_2) after reaction of **4o**, 3eq K_2CO_3 in water, 60 min., 120°C in a microwave reactor. Multiplicity of the signals is the result of the mixture of diastereoizomers.

5. Deuterium Labeled Mercaptoethanol

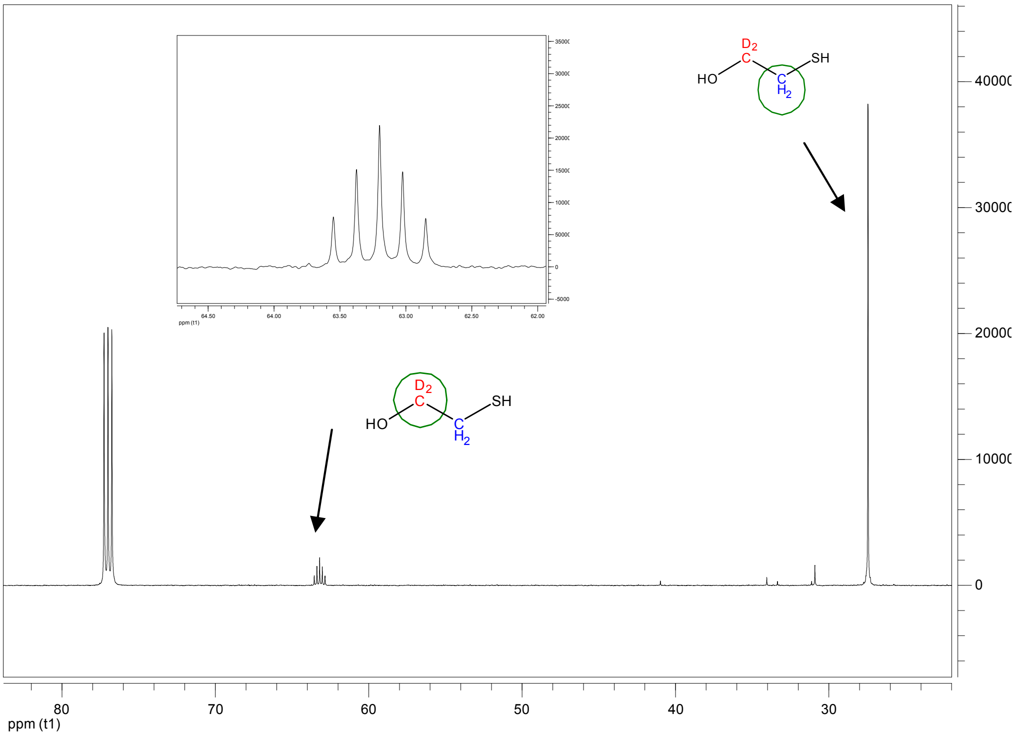

2a d$_2$

Deuterium labeled mercaptoethanol (2a-d$_2$): Lithium aluminium deuteride (0.523g, 0.0125mol) was dissolved in 9.0 ml freshly distilled THF in a 100 ml round-bottom flask in the glove box. To the mixture was added ethyl 2-mercaptoacetate (1.36ml, 0.0125mol) at 0°C and left stirring overnight. The mixture was neutralised with HCl (32%) under dry nitrogen and repeatedly extracted to CH_2Cl_2. The combined extracts were dried over magnesium sulphate to give **2a-d$_2$** (0.421g, 5.3mmol, 42%) as colorless oil. The dried organic phase was analyzed by GC–MS and by ^{1}H,^{13}C-NMR. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 1.39 (t, 1H), 2.34 (s), 2.68 (m, 2H, *J*=8.5, 1.0 Hz) ppm. ^{13}C-NMR ($CDCl_3$, 125 MHz) δ 27.45, 63.20 (m, *J* = 22.0 Hz) ppm.

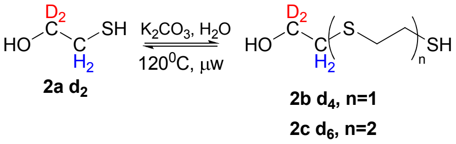
^{1}H-NMR of **2a d$_2$** ($CDCl_3$, 500 MHz):



^{13}C-NMR of **2a d$_2$** (CDCl$_3$, 125 MHz):

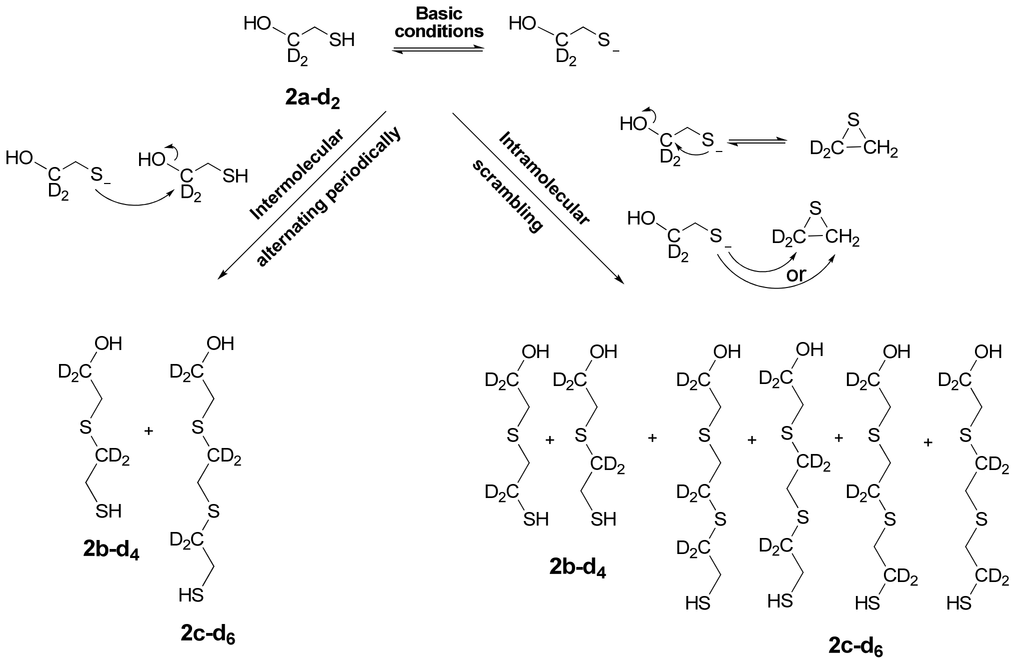


6. Oligomerisation of Deuterium Labeled Mercaptoethanol

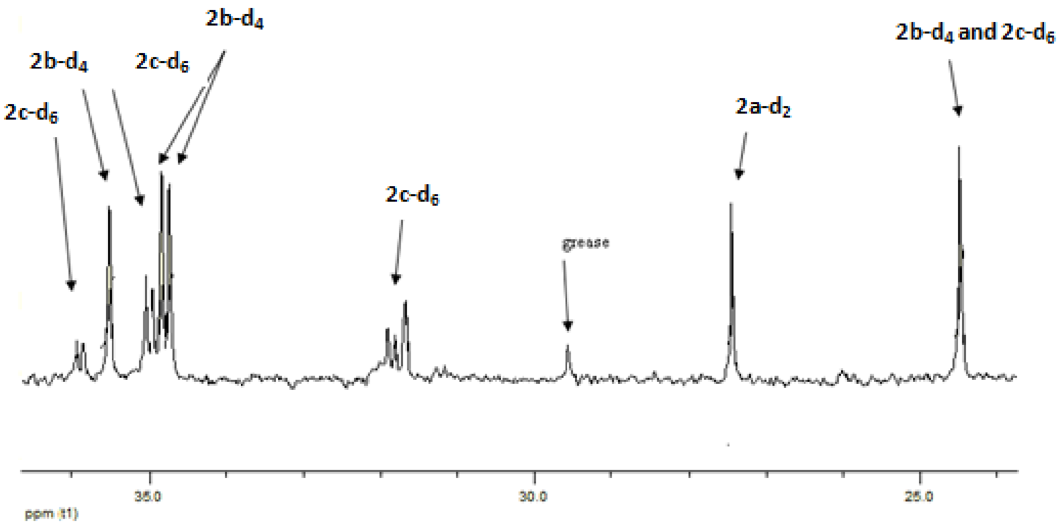


Deuterium labeled mercaptoethanol **2a-d$_2$** (0.149ml, 2.1mmol), potassium carbonate (0.8580 g, 6.2mmol) and 5.0ml deionised water were purged with Ar gas for 10 min. The mixture was then heated by microwave radiation to 120°C for 30min. After cooling, the mixture was neutralised with HCl (32%) and repeatedly extracted with CH_2Cl_2. The combined extracts were dried over magnesium sulphate and analyzed by ^{13}C-NMR 125MHz, $CDCl_3$, the relaxation time D_1 was set to a value of 10 seconds (to allow full relaxation for more reliable peak integration).

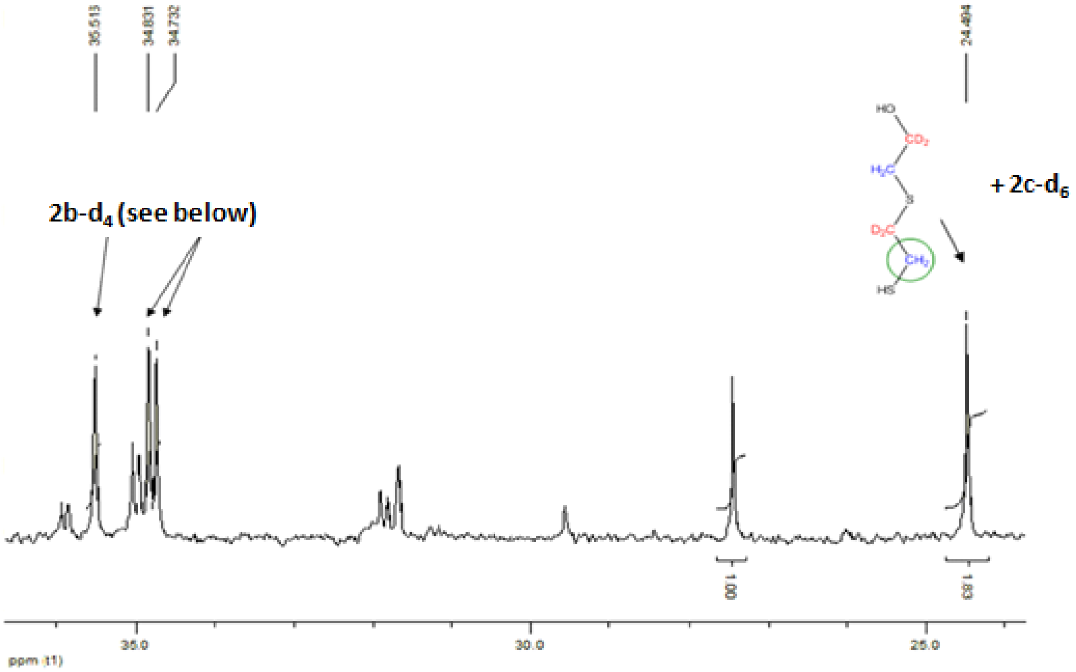
Probing the mechanism through isotopically labeled mercaptoethanol:

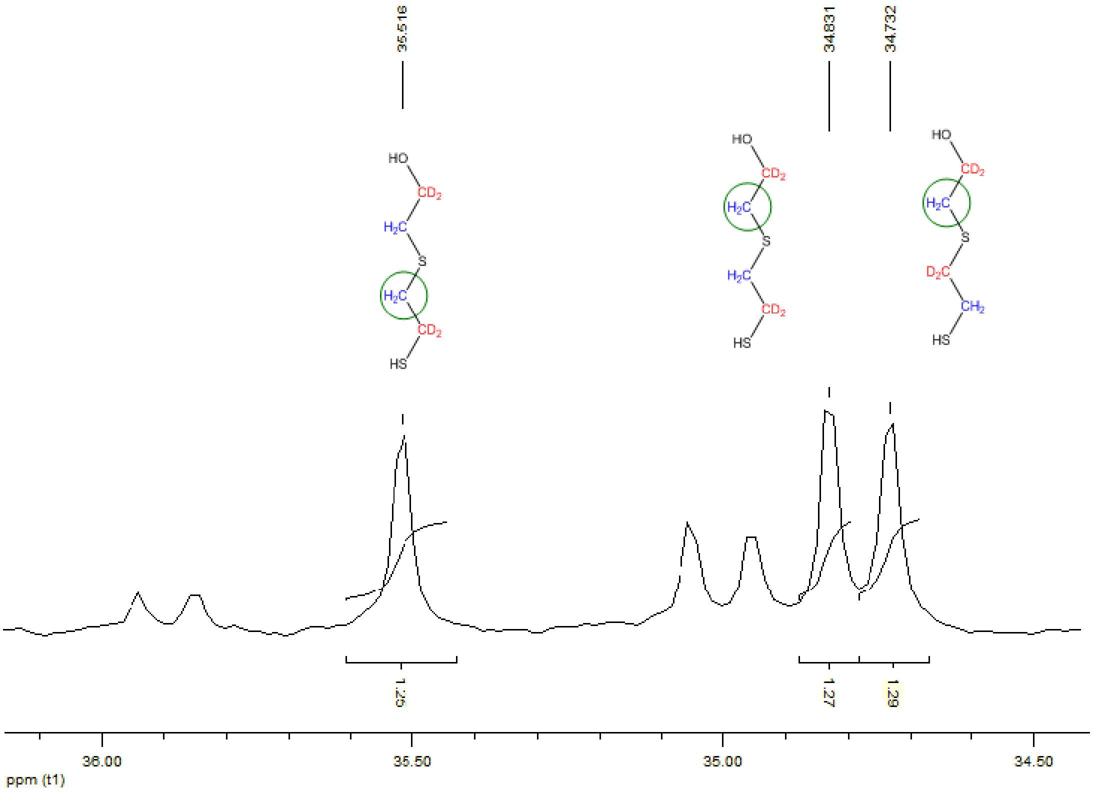


^{13}C-NMR of an oligomerisation reaction of deuterium labeled mercaptoethanol **2a-d$_2$**:

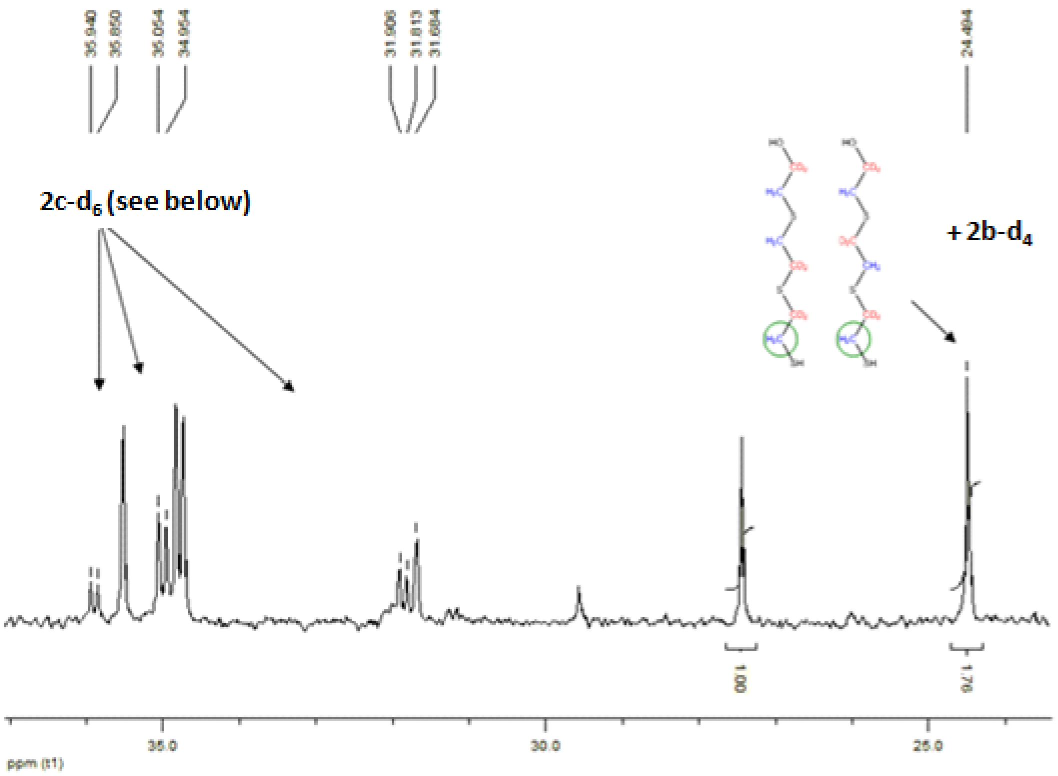


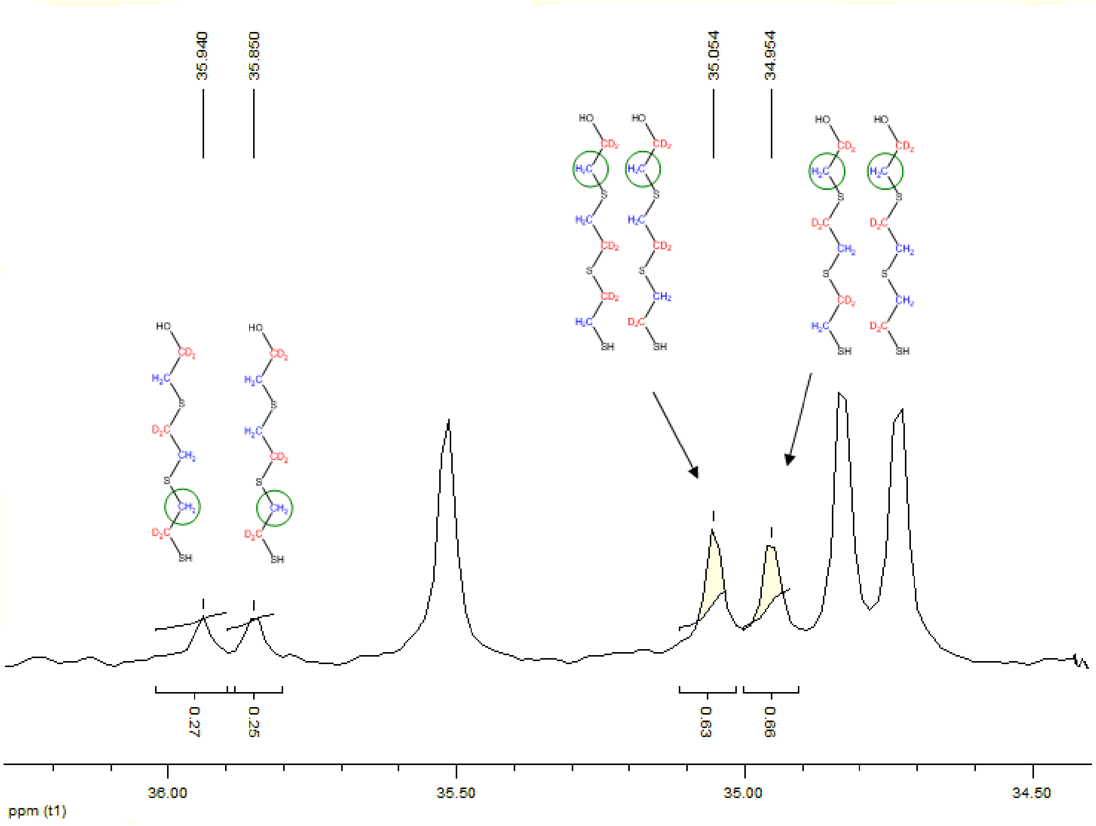
Dimer of deuterium labeled mercaptoethanol **2b-d$_4$**:

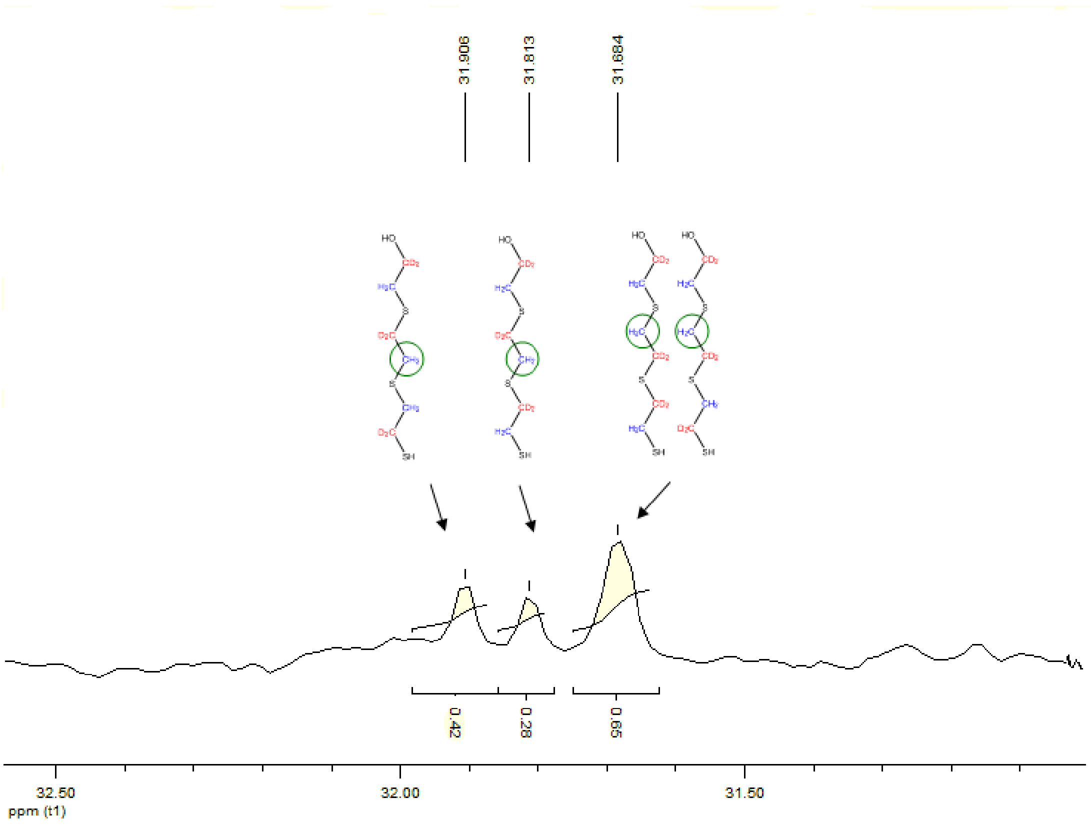




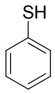
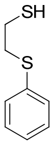
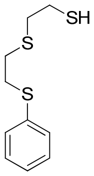
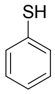
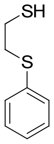
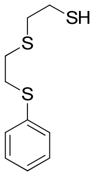
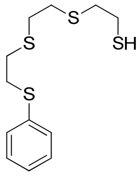
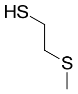
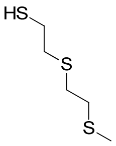
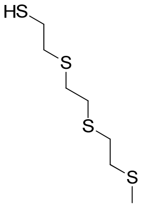
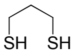
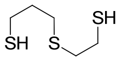
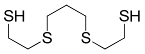
Trimer of deuterium labeled mercaptoethanol **2c-d$_6$**:

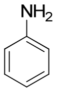
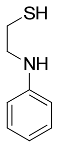
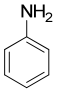
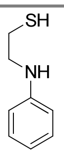
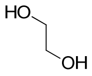
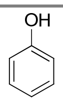
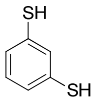
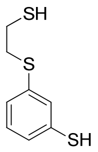
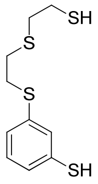
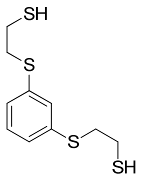
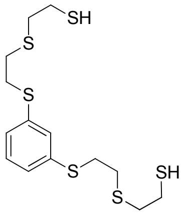


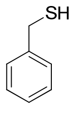
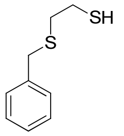
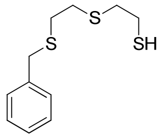
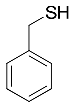
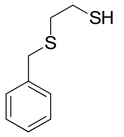
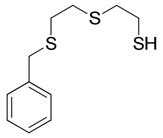
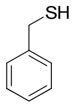
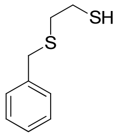
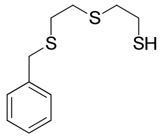
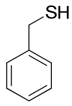
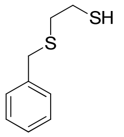



31.906
31.813
31.684
0.42
0.28
0.65
32.50
32.00
31.50
ppm (t1)

7. Cross reactions of various nucleophiles with β-mercaptans

Entry	Nucleophile	Thiol	Observed products and respective yield[b]						
1	 (**8**)	**2a**[c]			**8**	**2a**	**2b**	**2c**	Disulphide products
			11%	<1%	56%	4%	16%	6%	6%
2	 (**8**)	**1a**[d]				**8**	**1a**	**1b**	Disulphide products
			47%	9%	<1%	22%	3%	4%	14%
3	$CH_3S^-Na^+$ (**11**)[g]	**2a**[e]	No cross products			**2a**	**2b**	**2c**	
						10%	61%	29%	
4	$CH_3S^-Na^+$ (**11**)[g]	**2b**[f]				**2a**	**2b**	**2c**	Disulphide products
			7%	3%	<1%	4%	45%	36%	4%
5	 (**5s**)	**2a**[h]			**5s**	**2a**	**2b**	**2c**	Disulphide products
			33%	17%	23%	8%	14%	3%	2%

6	 (**10**)	**2a**[i,j]	 23%		**2a** 62%	**2b** 11%				
7	 (**10**)	**1a**[j,k]		 1%		**1b** 28%	**1c** 40%	**1d** 23%		Disulphide products 8%
8	 (**12**)	**1a**[l,m]	No cross products		**1a** 24%	**1b** 40%	**1c** 24%	**1d** 3%		Disulphide products 9%
9	 (**13**)	**1a**[n,o]	No cross products		**1a** <1%	**1b** 26%	**1c** 40%	**1d** 28%		Disulphide products 5%
10	 (**14**)	**1a**[p]	 17%	 11%	 22%	 11%	**14** 36%	**1a** 1%	**1b** 1%	**1c** 1%

11	 **(9)**	**2b**[q,r]			**2a**	**2b**	**2c**	Disulphide products
			84%	6%	1%	3%	1%	5%
12	 **(9)**	**2c**[q,s]			**2a**	**2b**	**2c**	Disulphide products
			73%	5%	2%	10%	7%	3%
13	 **(9)**	**3a**[q,t]						Disulphide products
			81%	3%				14%
14	 **(9)**	**2a**[q,u]			**2a**	**2b**		
			41%		37%	22%		

[a] All reactions performed in a microwave reactor with 1.2M K_2CO_3, in H_2O, 120°C, 60 min (unless otherwise stated). [b] Area % by GC-MS. [c] 0.2M **2a**, 0.2M **8**. [d] 0.2M **1a**, 0.2M **8**, 1.2M $NaHCO_3$, 45 min. [e] 0.4M **2a**, 0.15M **12a**, 1.6M K_2CO_3. [f] 0.14M **2b**, 0.27M **11**. [g] Unreacted methyl thiol is not detected by GC-MS method used. [h] 0.17M **2a**, 0.17M **5s**. [i] 0.4M **2a**, 1M **10**, no added base. [j] Residual **10** (in excess) not included in percentage [k] 0.1M **1a**, 1.1M **10**. [l] 0.2M **1a**, 0.2M **13**. [m] Unreacted **12** not included in percentage. [n] 0.2M **1a**, 0.2M **13**. [o] Unreacted **13** not included in percentage. [p] 0.2M **1a**, 0.2M **14**, 1.2M $NaHCO_3$, 45 min. [q] Residual **9** (in excess) not shown in percentage. [r] 0.1M **2b**, 0.6M **9**. [s] 0.06M **2c**, 0.4M **9**, 20 min. [t] 0.1M hydrochloride salt of **3a**, 0.4M **9**, 0.5M K_2CO_3, 20 min. [u] 0.2M **2a**, 1M **9**, 1.8M K_2CO_3, 15 min.

8. References

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2. D. Berkovich-Berger, N. G. Lemcoff, S. Abramson, M. Grabarnik, S. Weinman, B. Fuchs, *Chem. Eur. J.,* 2010, **16**, 6365.

3. (a) DTT and the erythritol isomer have been shown to form intramolecular products under vigorous conditions, *i.e.* concentrated HCl at reflux: R. A. Sanchez, *Synthesis,* 1982, 148; (b) See also: S. H. Lee, H. Kohn, *Heterocycles*, 2003, **60**, 47.