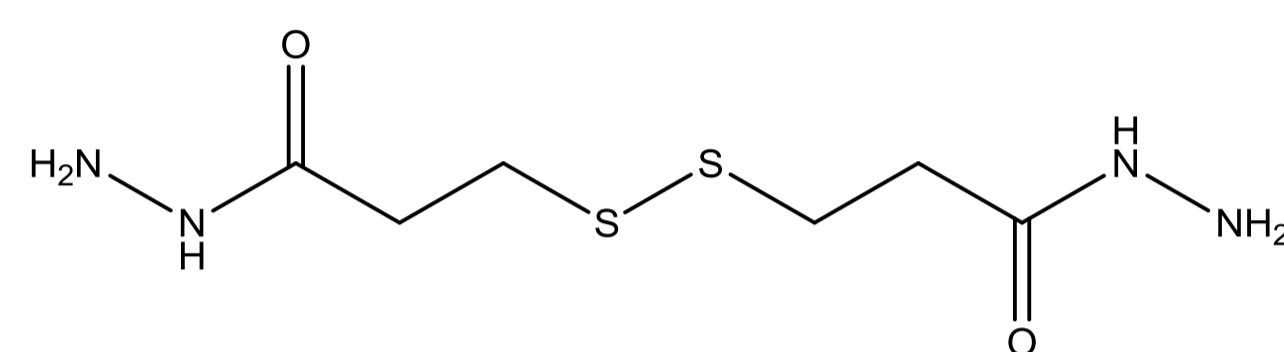


Quantifying Compositional Changes in Polymer-Scaffolded Dynamic Combinatorial Libraries

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Objectives

- Determine the hydrodynamic radii of polymer-scaffolded dynamic combinatorial libraries (PS-DCL) of varying chain lengths by use of dynamic light scattering (DLS) and investigate the relationship between the hydrodynamic radius and length of the polymer chain.
- Synthesise a dihydrazide cross-linker **1** and use this to produce single chain polymer nanoparticles.
- Synthesise functionalised polymers and co-polymers.



Dihydrazide cross-linker **1**, 3,3'-disulfanediyldi(propanehydrazide)

Experimental/Methods

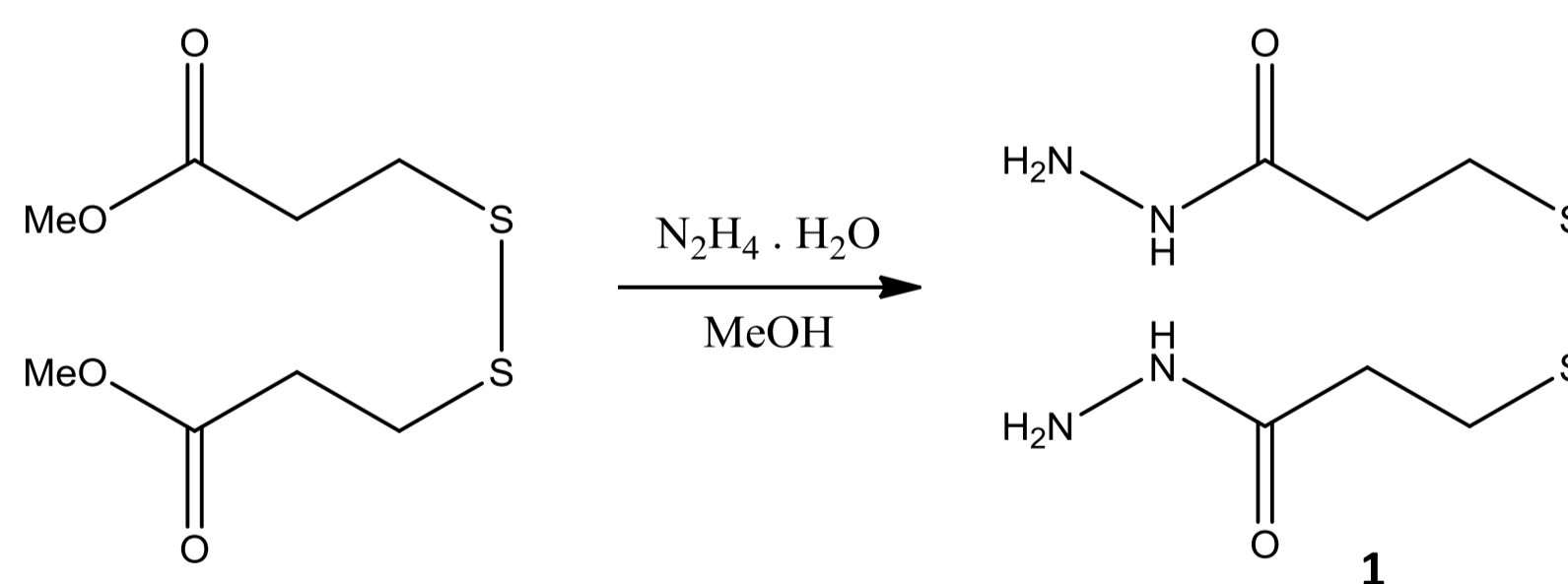
Dynamic light scattering (DLS) is essentially a technique used to find the size of particles using data obtained from how those particles scatter light. Light is shone on the particle(s) and consequently the light will be scattered, this is detected and after some maths a trace of intensity against size is produced.

The 'particles' measured by DLS are polymer-scaffolded dynamic combinatorial libraries (PS-DCL) which are, in simple terms, a polymer chain (the scaffold) with residues attached. These residues can change their concentration on the polymer scaffold depending on the environment the PS-DCL is in.

The purpose of the cross-linker **1** was to produce nanoparticles upon reaction of it with a PS-DCL; these experiments were unsuccessful but the cross-linker **1** synthesis is shown below in scheme 1.

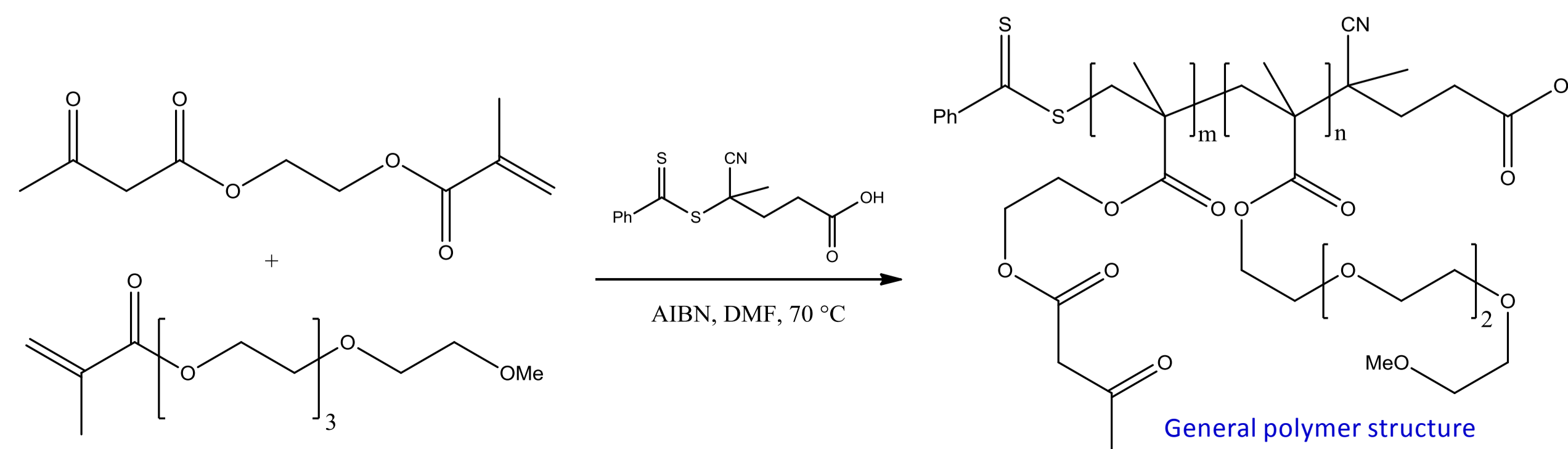
3,3'-dithiopropionic acid dimethyl ester (0.599 g, 2.51 mmol) and hydrazine hydrate (0.74 cm³, 15.1 mmol) were combined in methanol (15 cm³) and left to stir overnight at room temperature.

The experiment was very simple. Several samples of polymer were prepared in aqueous solution. Several concentrations were used, from 1 mg cm⁻³ to 0.125 mg cm⁻³ decreasing each time by a factor of 2, then the DLS was ran.



Scheme 1: Synthesis of dihydrazide cross-linker **1**

Several polymers were synthesised and the general structure is shown in scheme 2. All of the reagents were combined in N,N-dimethyl formamide and the solution was degassed using the freeze-pump-thaw technique. The reactions were then heated to 70 °C and left overnight. They were worked-up by precipitation in petroleum ether 40 - 60.



Scheme 2: General polymer synthesis

General polymer structure
 $m + n = 100$ residues

Results/Discussion

All of the DLS traces gave multimodal distributions; multimodal meaning that there were multiple peaks in the trace. The expectation was a monomodal distribution (only one peak) corresponding to the PS-DCL. The expected hydrodynamic diameter (size) of the PS-DCL was about 2 nm.

One of the data sets is shown below in table 1, picked from multiple sets

Polymer	$M_n / \text{g mol}^{-1}$	Hydrodynamic Radius / nm		
		Peak 1	Peak 2	Peak 3
P6	7400	0.621	5.61	7.53
P7	9800	6.50	7.53	7.53
P2	19300	6.50	7.53	7.53
P3	23000	10.1	13.5	15.7

Table 1: Variation of size of PS-DCL as the molecular weight (M_n) is increased. Concentration = 0.125 mg cm⁻³

At first glance it seems that as we increase the molecular weight (M_n) the size of the PS-DCL increases. The values in the **Peak 2** column begin at 5.61 nm which is too large for a particle of that molecular weight and similarly in **Peak 3**, so whatever is causing those values has remained in solution despite filtering through cotton wool and syringe filtering the solutions.

The values of interest are in **Peak 1**, but 0.621 nm is too small to be a PS-DCL and there is a massive jump to get to 6.50 nm, which seems quite large.

The experiments started at a concentration of 1 mg cm⁻³ and the values obtained were similar to those in table 1 (which were ran at a concentration 8 times more dilute). The larger values could be a result of dust particles entering the cuvette or aggregation of the PS-DCL molecules. This is the reason for the set of dilutions, to try and avoid aggregation but it was unsuccessful and the DLS experiments were side-lined.

The dihydrazide cross-linker **1** synthesis was fairly simple and the first time yielded 45 %. This was improved to a 70 % yield when the reaction was performed for a second time. The cross-linker **1** was obtained as a white powder.

The polymer syntheses were successful. The first set of co-polymers made were not consistent, the chain length of the polymer scaffold was not kept constant and so they couldn't be used for any experimentation. But this was rectified and the polymers were used in another set of experiments which aren't included here.

Conclusions

- The DLS experiments didn't give any meaningful results considering the approximate, expected particle size.
- Both the dihydrazide cross-linker **1** and the polymers were synthesised successfully