# Investigating Thermoresponsive Polymers

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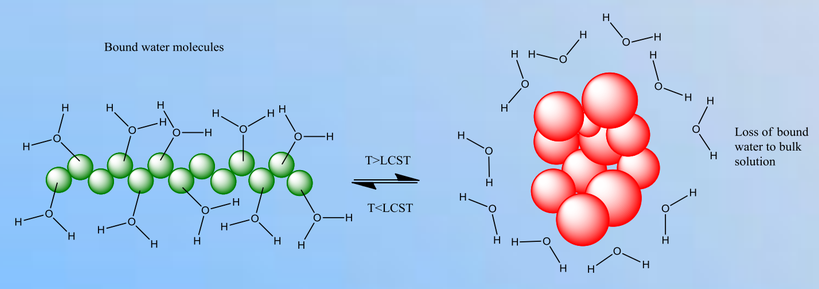
## Aims and Introductions

Thermoresponsive polymers are large molecules that are soluble or insoluble in water depending on the temperature of the solution. This gives them a large range of potential applications, such as in the biomedical and nanotechnological areas. This project's aim was to further investigate some of the more unusual aspects of these polymers. The first task was to synthesise a series of these polymers in order to investigate their properties. However, this proved to be a more difficult task than initially thought, so the focus of the project turned to developing a sound synthesis route for them.

## Background Chemistry

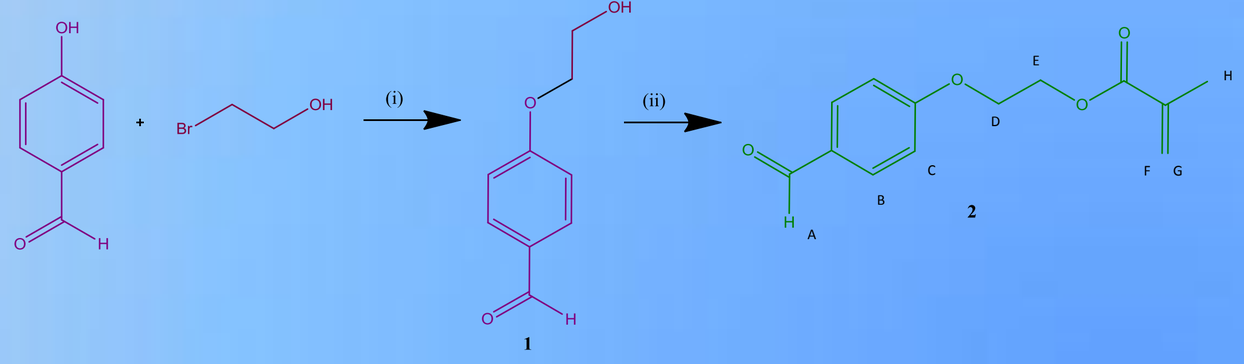
Thermoresponsive polymers are a class of materials that possess a unique ability to reversibly undergo a phase transition from hydrophilic to hydrophobic when they pass through their lower critical solution temperature (LCST). It was previously thought that the temperature at which polymers undergo this phase transformation was directly proportional to how hydrophobic or hydrophilic the polymer is. However, recent work by Dr Fulton's group found a thermoresponsive polymer that broke this assumption.

A polyoligo(ethylene glycol) methacrylate polymer was chosen as a scaffold. This relatively new class of thermoresponsive polymer has a tunable LCST and is very biocompatible (there are no known toxic side effects of it). We aimed to create a series of copolymers with $OEGMA_{300}$ and MAEBA. The $OEGMA_{300}$ provides the scaffold, and has a well known LCST value of ~60°C, whereas the MAEBA provides a reactive aldehyde group to functionalize the polymer. An aldehyde is a popular group for the functionalization of polymers, since it can form hydrolytically stable oxime or hydrazone bonds with readily available nitrogen donors thus adjusting the hydrophilicity of the polymer.



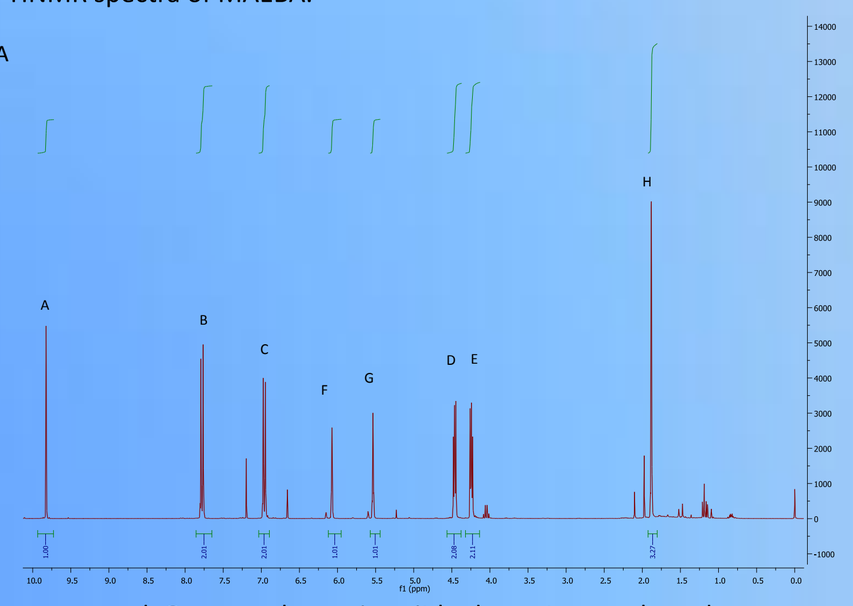

## Reactions and method

The initial step was to synthesise a precursor p-(hydroxyethoxy)benzaldehyde (**1**), and subsequently react it with methacrolyl chloride to create the monomer unit p-(2-methacryloxyethoxy)benzaldehyde (MAEBA)(**2**) . Diagram 1 is an assigned $^1$HNMR spectra of MAEBA.




(i)$K_2CO_3$, DMF, reflux 90 minutes. (ii) Methacrolyl chloride, $Et_3N$, $CH_2Cl_2$

**Diagram 1**:$^1$HNMR spectra of MAEBA




N.b. a small amount of an inhibitor, hydroquinone was added to the purified MAEBA due to the high reactivity of the compound. On several occasions it had spontaneously undergone an irreversible self-polymerisation process. Before the MAEBA could be used in a polymerisation reaction, the inhibitor had to be removed first. This was done by passing a solution(in dioxane(~0.5ml)) of the monomer through a very small column of basic alumina. This monomer was to undergo Reversible Addition-Fragmentation chain Transfer (RAFT) polymerisation reactions with another monomer oligo(ethylene glycol) methyl ether methacrylate ($OEGMA_{300}$). The general synthesis is outlined below.

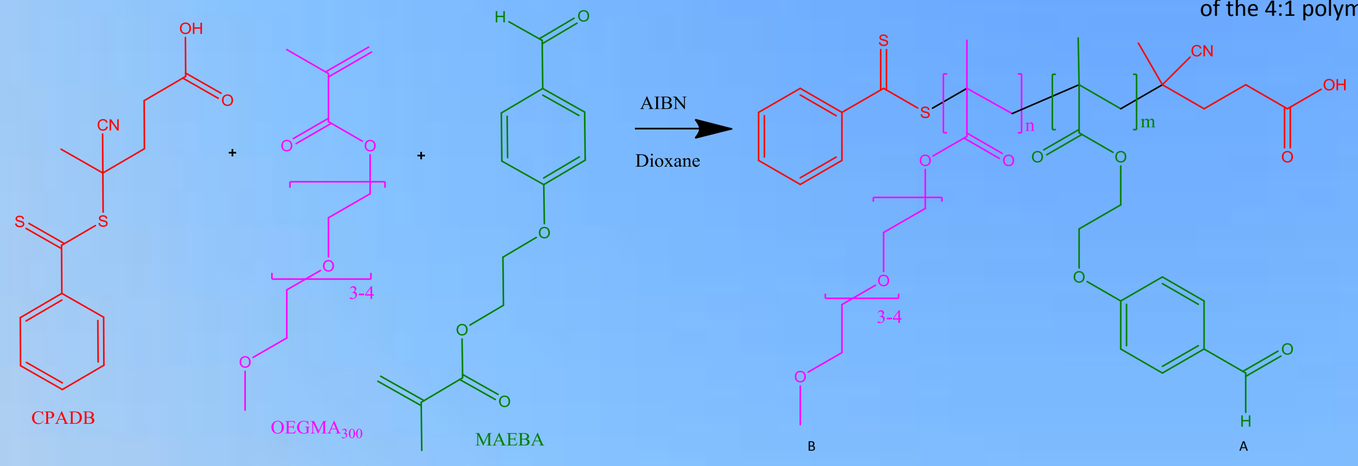
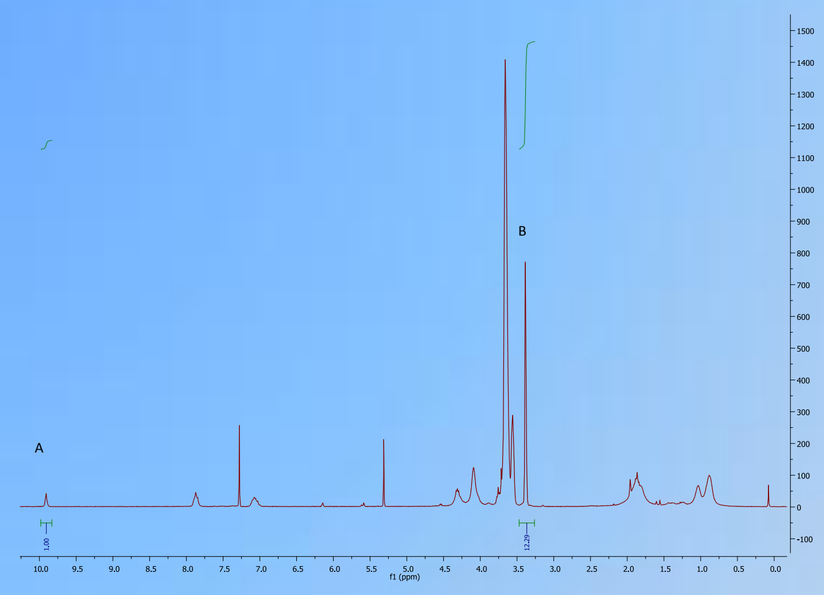



**Diagram 2**: Sample $^1$HNMR spectra of the 4:1 polymer




General RAFT co-polymerisation of $OEGMA_{300}$ and MAEBA(4:1): The chain transfer agent, CPADB (1eq) and radical initiator AIBN (0.2 eq) were added to a small schlenk tube. To this, $OEGMA_{300}$(80 eq) and MAEBA(20 eq) were added, followed by dioxane (5ml). The system was then degassed 5 or 6 times via the freeze–pump-thaw method, backfilled with $N_2$, purged with $N_2$ then allowed to reach room temperature. The reaction mixture was then placed in an oil bath at 70°C for 23 hours. Polymerisation was quenched after this time by placing in liquid nitrogen. The polymer was then purified, and $^1$HNMR and GPC (gel permeation chromatography) was processed to assess the purity. **Diagram 2** shows the $^1$HNMR spectra of the 4:1 polymer obtained, the ratio's of A and B are 1:12. This is expected since B is a methyl group corresponding to 3 protons each.

The aim was to create a series of 6 copolymers with the following ratios of $OEGMA_{300}$ : MAEBA : 2:1, 3:1, 4:1, 8:1, 16:1 and a homo-polymer containing just $OEGMA_{300}$. In order to synthesise these polymers, the following equivalents of $OEGMA_{300}$ and MAEBA were to be used. See **table 1**.

**Table 1**

| Polymer ratio | Eq. $OEGMA_{300}$ | Eq. MAEBA |
|---|---|---|
| 2:1 | 66 | 33 |
| 3:1 | 75 | 25 |
| 4:1 | 80 | 20 |
| 8:1 | 89 | 11 |
| 16:1 | 94 | 6 |
| Homo-polymer | 100 | 0 |

## Results, discussion and further work

Results from successful polymerisation reactions shown in **table 2**:

Mn and Mw are number average and weight average molecular weights, and the PDI is a measure of the distribution of molecular mass in a given polymer sample, measured by GPC analysis. The PDI is calculated as the weight average molecular weight divided by the number average molecular weight. The assumed ratios were confirmed by the NMR analysis. Unfortunately, adequate samples of the 2:1 and 3:1 polymers could not be obtained, and this is believed to be due to unsuccessful removal of the inhibitor in MAEBA. In these polymers, a larger proportion of MAEBA was used, meaning a larger amount of inhibitor being present. If the removal of inhibitor wasn't thorough enough, (i.e. some inhibitor got into the reaction vessel) the polymerisation success rates would decrease.

| **Table 2** | Mn | Mw | PDI |
|---|---|---|---|
| Homopolymer | 28,100 | 32,950 | 1.17 |
| 16:1 polymer | 23,100 | 29,500 | 1.28 |
| 8:1 polymer | 13,850 | 16,500 | 1.19 |
| 4:1 polymer | 21,650 | 27,750 | 1.28 |

The next steps in this project would be to synthesise the two remaining polymers in the series, then measure all their LCST values. Once the LCST values are known, some hydrophobic groups should be conjugated to the polymer series and LCSTs re-measured. These values can then be compared to the LCST values of the parent copolymer to observe any changes between the two values.