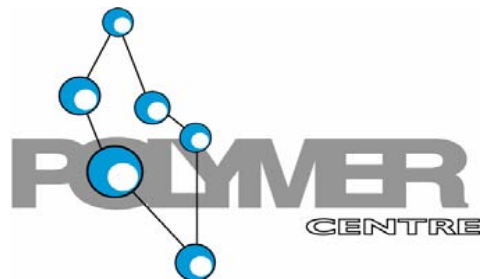




Esterification of Hydroxylated Polymers with 2-Sulfobenzoic Acid Cyclic Anhydride

Peter D. Iddon, Duan C. Vo, and Steven P. Armes

Department of Chemistry, University of Sheffield, UK

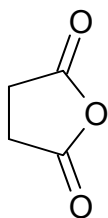


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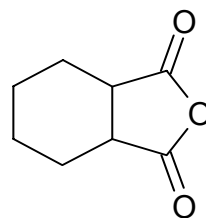


Background

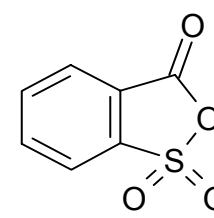
- ▶ Usually the synthesis of polyacids with narrow polydispersity (PDI) involves protecting group chemistry. Direct synthesis *via* living radical polymerisation techniques can be problematic.
- ▶ Liu and coworkers – partial esterification of P*t*BA-*b*-PHEMA diblock copolymers with succinic anhydride (SA) (13-18 mol %).¹
- ▶ Bories-Azeau *et al.* – first complete derivatisation of PHEMA, PHPMA, and PGMA using SA and 1,2-cyclohexanedicarboxylic anhydride (CDA).²
- ▶ Dr Duan Vo – esterification of diblock copolymers using SA and 2-sulfobenzoic acid cyclic anhydride (SBA).
- ▶ Benefits: synthetically undemanding (no protecting group chemistry), mild reaction conditions, and atom efficient.



Succinic anhydride
(SA)



1,2-Cyclohexanedicarboxylic anhydride
(CDA)

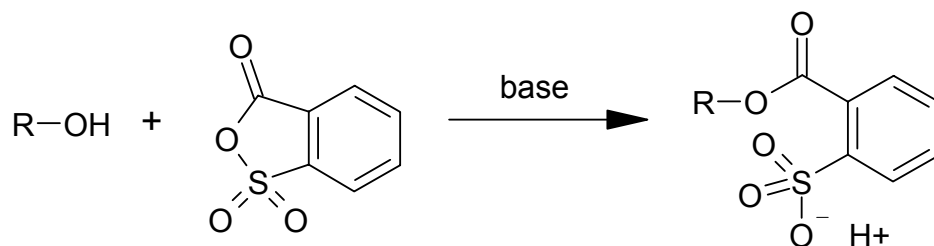


2-Sulfobenzoic acid cyclic
anhydride (SBA)

1. Li, Z.; *et al. Biomacromolecules* **2002**, 3, 984.
2. Bories-Azeau, X.; *et al. Macromolecules* **2004**, 37, 8903.

Introduction

- ▶ SA and CDA give carboxylic acid functionality – these are weak acids.
 - ▶ The pH sensitivity of these groups has been exploited to prepare block copolymers with interesting aqueous solution properties.¹
 - ▶ However there may be situations in which a pH insensitive polyacid block is required.
- ▶ SBA introduces a sulfonate group – a strong acid (pH insensitive).
- ▶ Similarity/analogous to poly(sodium 4-styrenesulfonate) (PNaStS) polymers.²
- ▶ We can derive low PDI weak polyacids from PHEMA, PHPMA or PGMA using SA – is it possible to obtain low PDI strong polyacids using SBA?
- ▶ These precursor polymers can be easily synthesised with low PDI *via* atom transfer radical polymerisation (ATRP).

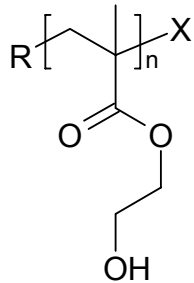


General base-catalysed reaction of SBA with a hydroxy group

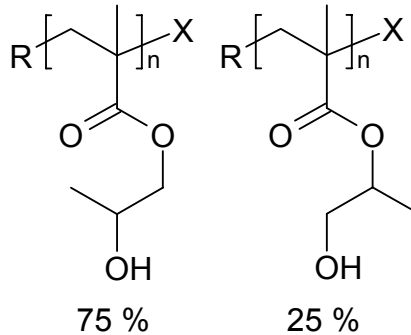
1. Bories-Azeau, X.; *et al. Macromolecules* **2004**, 37, 8903.
2. Iddon, P. D.; *et al. Polymer* **2004**, 45, 759; Choi, C. K.; Kim Y. B. *Polymer Bulletin* **2003**, 49, 433.

Hydroxylated Polymers

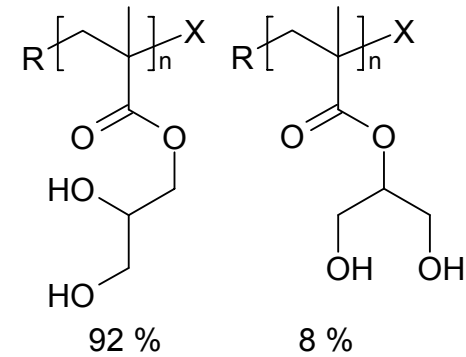
- PHEMA [poly(2-hydroxyethyl methacrylate)], PHPMA [poly(2-hydroxypropyl methacrylate)], and PGMA [poly(glycerol monomethacrylate)] homopolymers:



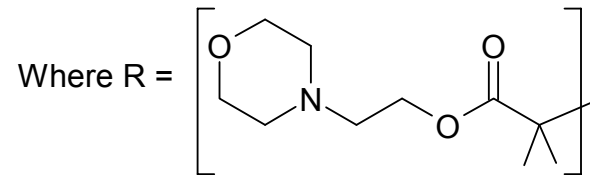
PHEMA



PHPMA isomers



PGMA isomers



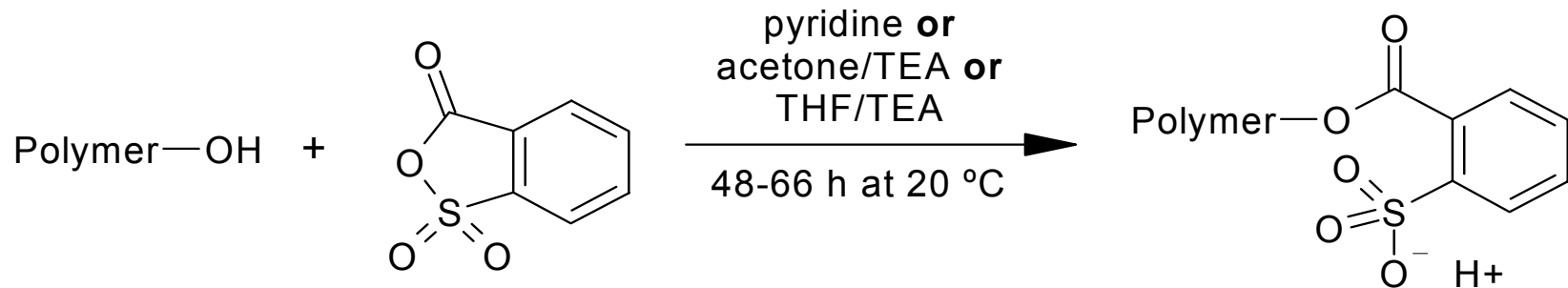
- Possible applications for sulfonated polymers include:
 - Proton conducting cell membranes for fuel cells.
 - Layer-by-layer deposition of polyelectrolyte multilayers.
 - pH-insensitive charge stabiliser for micelles.

Experimental Design

- ▶ Pyridine was the preferred solvent for the previous work using SA reported by X. Bories-Azeau *et al.*¹ However, this solvent is toxic and malodorous, so a more benign esterification solvent would be ideal.
- ▶ In addition, SBA is only slightly soluble in pyridine, and the homopolymer precursors become increasingly insoluble as the degree of esterification (D_{est}) increases.
- ▶ Preliminary experiments indicated that of the alternative solvents studied, THF gave higher D_{est} values for PHEMA and PHPMA, whereas acetone was the better reaction solvent for PGMA.
- ▶ Unfortunately, only the PHPMA homopolymer precursor is fully soluble in the alternative reaction solvent (THF). PHEMA and PGMA are only swelled in their respective alternative solvents.
- ▶ In addition, none of the esterified homopolymers are fully soluble in their reaction solvents.
- ▶ As the reaction conditions are heterogeneous, care must be taken to ensure efficient mixing during the reaction.

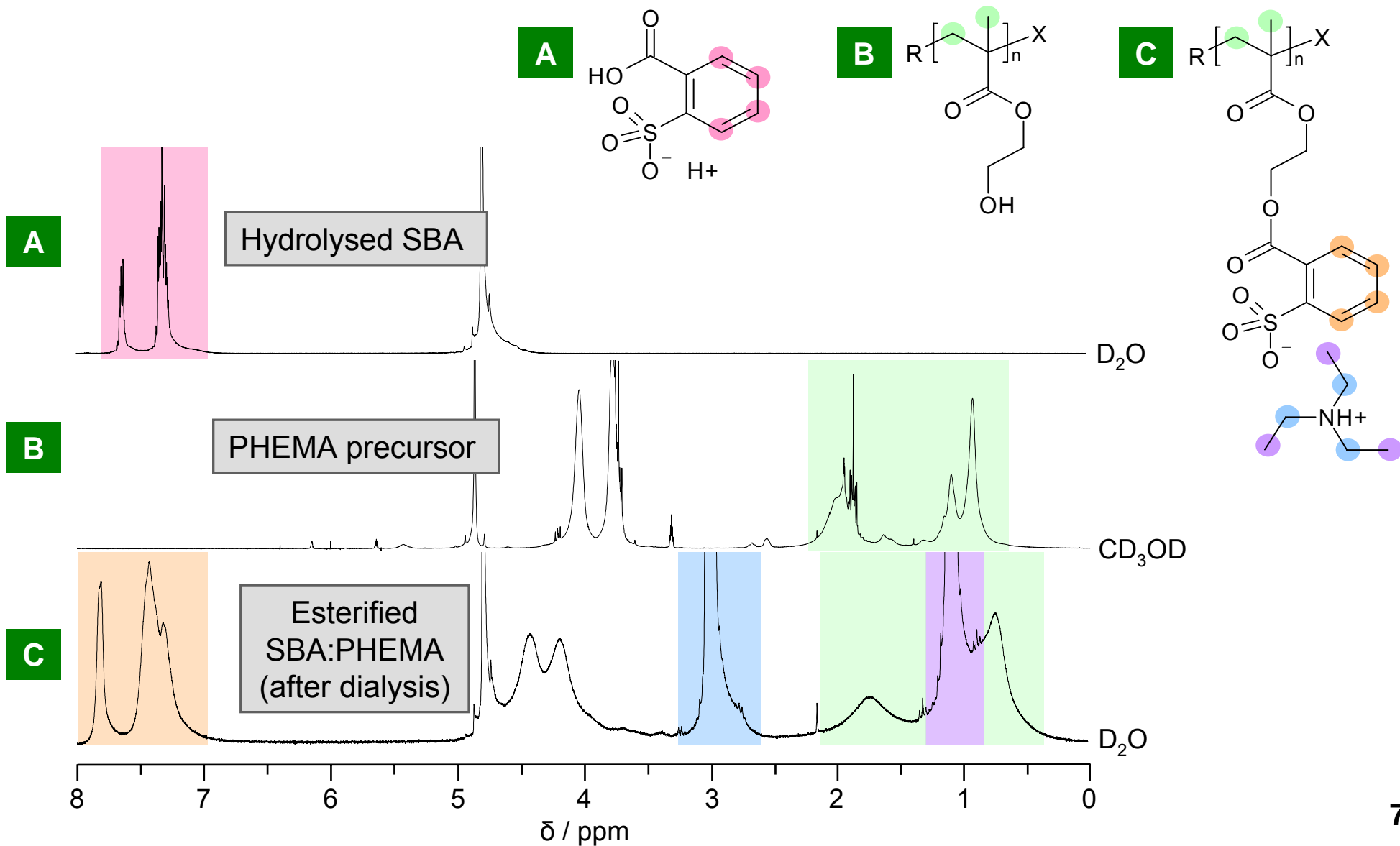
Experimental Design

- ▶ Despite the solubility issues, it is possible to obtain high D_{est} values in pyridine, THF, and acetone (depending on the homopolymer).
- ▶ Pyridine is basic, so catalyses the reaction. However, it may be necessary to add a base to catalyse reactions carried out in THF and acetone.
 - ▶ Preliminary studies showed that triethylamine (TEA) was a suitable base.
- ▶ Dialysis was used to purify the esterified polymers.
- ▶ ^1H NMR was used to determine D_{est} (after dialysis to remove excess SBA/TEA).



Esterification reaction of SBA with a polymeric hydroxy residue

Determination of D_{est} by ^1H NMR



Esterification in Pyridine

- ▶ Despite the low solubility of SBA and esterified polymers in pyridine, it is still possible to attain high D_{est} values in this solvent.

Data for the esterification of hydroxylated homopolymers with SBA, in pyridine at 20 °C.

Polymer ^a	Ratio of SBA to OH Groups	Reaction Time (h)	D_{est} of OH Groups (%) ^b
PHEMA	2.0	48	100
PHPMA	2.0	48	34
PGMA	2.0	48	87
PHEMA	2.0	168	100
PHPMA	2.0	168	87
PGMA	2.0	168	100

^a Precursor polymer concentration was 2.5 w/v %. ^b Measured by ¹H NMR

Esterification in THF or Acetone

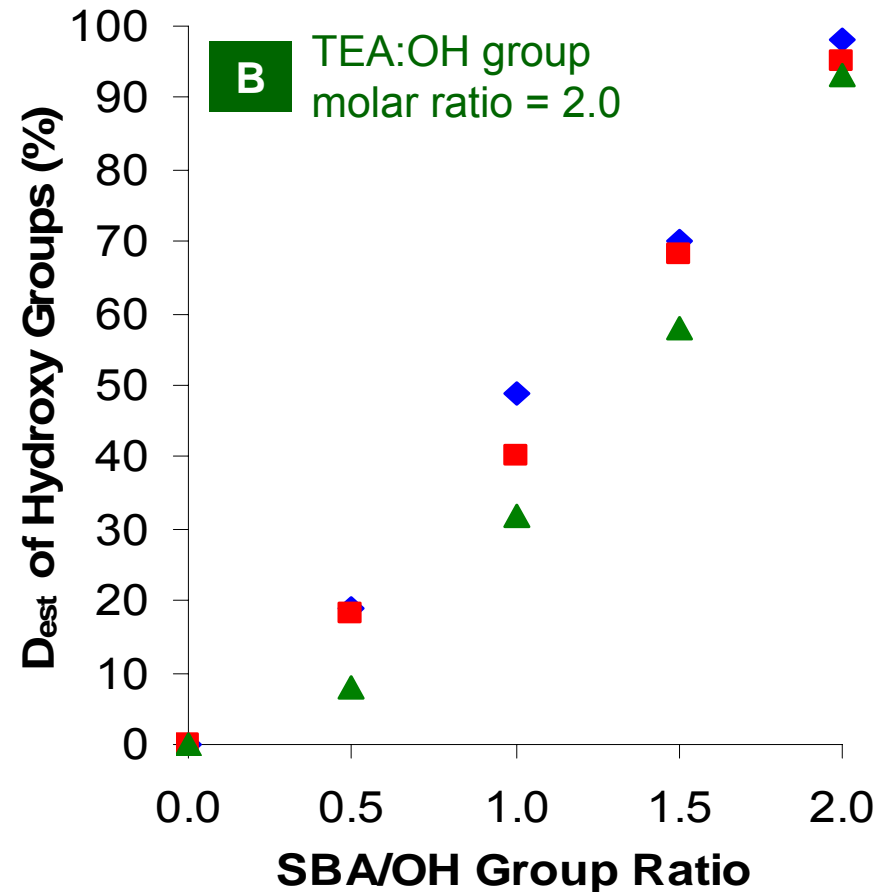
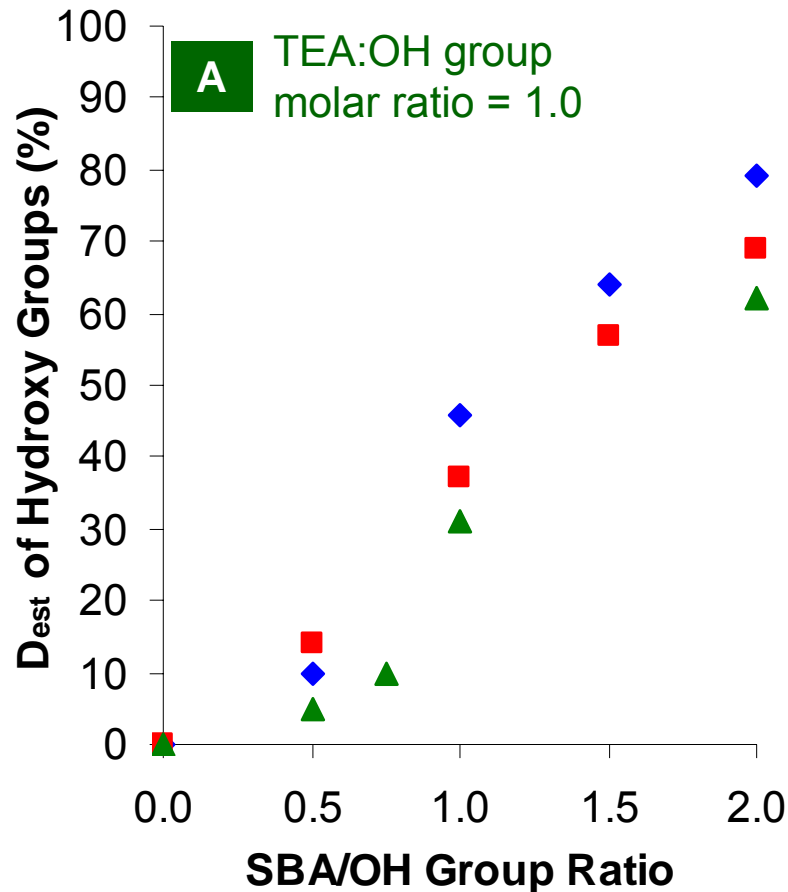
- ▶ An equimolar ratio of TEA to SBA has proved to be necessary to obtain the highest D_{est} values.
- ▶ There is evidence of side reactions in these solvents.

Data for the esterification of hydroxylated homopolymers with SBA at 20 °C for 64 h.

Polymer ^a	Solvent	Ratio of SBA to OH Groups	Ratio of TEA to OH Groups	D_{est} of OH Groups (%) ^b
PHEMA	THF	2.0	2.0	98
PHPMA	THF	2.0	2.0	95
PGMA	Acetone	2.0	2.0	93
PHEMA	THF	2.0	1.0	79
PHPMA	THF	2.0	1.0	69
PGMA	Acetone	2.0	1.0	62
PHEMA	THF	2.0	no TEA	88
PHPMA	THF	2.0	no TEA	77
PGMA	Acetone	2.0	no TEA	7

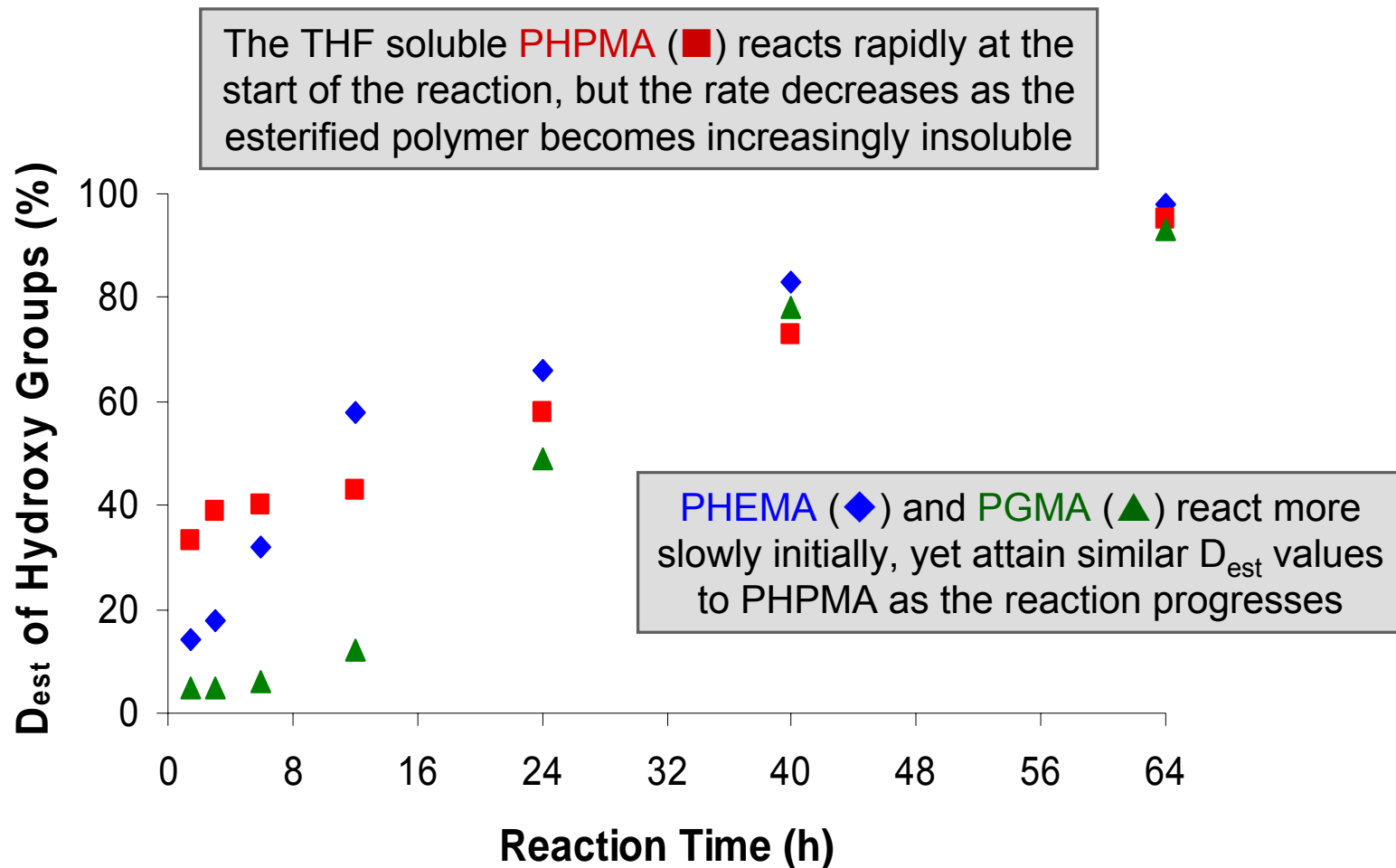
^a Precursor polymer concentration was 2.5 w/v %. ^b Measured by ¹H NMR

Effect of SBA Concentration



Degree of esterification (D_{est}) of **PHEMA** in THF (◆), **PHPMA** in THF (■), and **PGMA** in acetone (▲), with SBA at 20 °C for 66 h, with either a TEA:OH group molar ratio = 1.0 (**A**) or a TEA:OH group molar ratio = 2.0 (**B**). Precursor polymer concentration was 2.5 w/v %.

Homopolymer Esterification Kinetics



Degree of esterification (D_{est}) against reaction time for **PHEMA** in THF (◆), **PHPMA** in THF (■), and **PGMA** in acetone (▲) with SBA at 20 °C. SBA:OH group molar ratio = 2.0, TEA:OH group molar ratio = 2.0, and precursor polymer concentration was 2.5 w/v %.

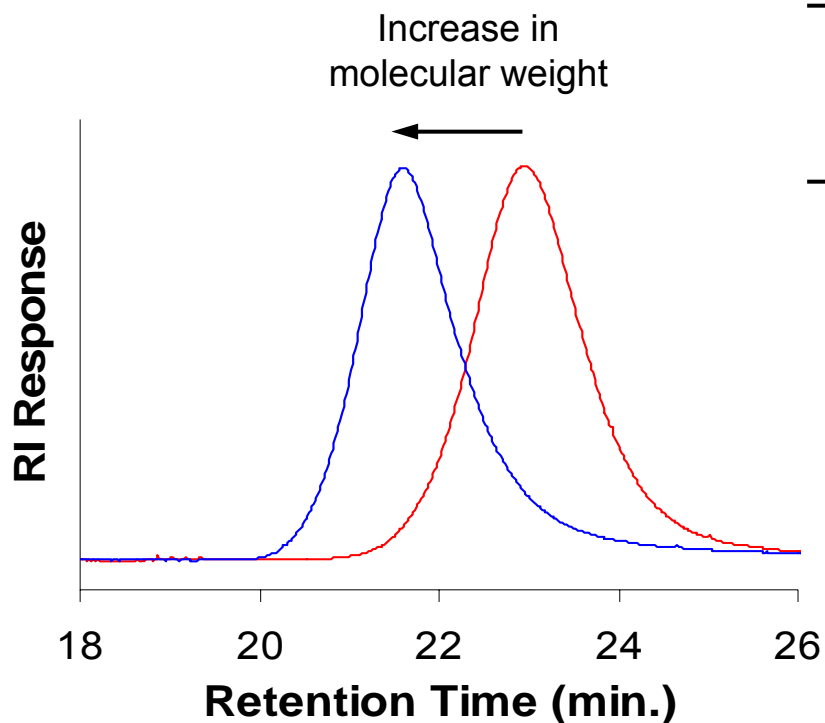
GPC Data

- ▶ GPC data obtained in a DMF eluent for the **PHPMA** precursor and corresponding **SBA:PHPMA** after esterification.
- ▶ There is a clear increase in molecular weight, and there is no apparent evidence of chain scission or cross-linking during the esterification reaction.

Polymer	M_n	M_w	PDI (M_w/M_n)
PHPMA	10,500	15,100	1.44
SBA:PHPMA	14,200	21,500	1.52

GPC analysis conditions: DMF eluent, 1.0 mL flow rate, PLgel mixed B column set, 70 °C run temperature, and calibrated with PMMA standards. Data collected by Dr Duan Vo.

Although the values for M_n and M_w GPC are not directly comparable due to the differences in chemical structure between the PMMA calibration standards, **PHPMA**, and **SBA:PHPMA**; the peaks are both unimodal and similar in shape



Esterification at Elevated Temperature

- ▶ The esterification reaction is relatively slow at room temperature.
- ▶ Previous work with a different esterification agent (SA) showed that increasing the reaction temperature decreased D_{est}^1
- ▶ A preliminary experiment esterifying PHPMA using SBA in refluxing THF (66 °C) was carried out (in collaboration with Dr Duan Vo).

Comparison of data for the esterification of PHPMA homopolymer with SBA at 66 °C for 8 h, with previous data collected at 20 °C. Ratio of SBA:OH groups = 2.0 and ratio of TEA:OH groups = 2.0.

Polymer ^a	Temperature (°C)	Reaction Time (h)	D_{est} of OH Groups (%) ^b
PHPMA	66	8	92
PHPMA	20	8	41 ^c
PHPMA	20	61	92 ^c

^a Precursor polymer concentration was 2.5 w/v %. ^b Measured by ¹H NMR. ^c Values interpolated from kinetics plot.

Conclusions

- ▶ Although THF and acetone are more benign solvents (compared to pyridine), there are some issues regarding side reactions in these solvents.
 - ▶ TEA reacts/interacts with SBA.
 - ▶ SBA reacts with acetone.
- ▶ The heterogeneous reaction conditions makes synthesis more difficult and potentially prone to reproducibility problems.
- ▶ However, high degrees of esterification for hydroxylated homopolymers are possible using SBA in THF and acetone.
- ▶ Reaction conditions are mild, and there is no evidence of chain scission or cross-linking for reactions carried out at 20 °C (by GPC).
- ▶ Initial experiments suggest that higher reaction temperatures can significantly increase the rate of reaction.
- ▶ These promising results provide a basis for investigating the esterification of block copolymers with SBA, to produce novel block copolymers with interesting properties.

Further Work

- ▶ Continue with study of high temperature esterification reactions.
 - ▶ Investigate the use of a microwave reactor to increase the reaction rate even further.
- ▶ Explore the use of DMF or DMSO as homogenous reaction solvents.
- ▶ Extend preliminary results for the esterification of diblock and triblock copolymers, using optimised reaction conditions from homopolymer study.

Acknowledgements

- ▶ Professor Steve Armes.
- ▶ EPSRC and AVECIA for funding this work.
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- ▶ The rest of the Armes Research Group.