Functional Monoliths for Flow Processes by RAFT Polymerisation[1]

Kristine J. Barlow, Victor Bernabeu, Xiaojuan Hao, Timothy C. Hughes, Oliver E. Hutt, Anastasios Polyzos, Kathleen A. Turner, Graeme Moad

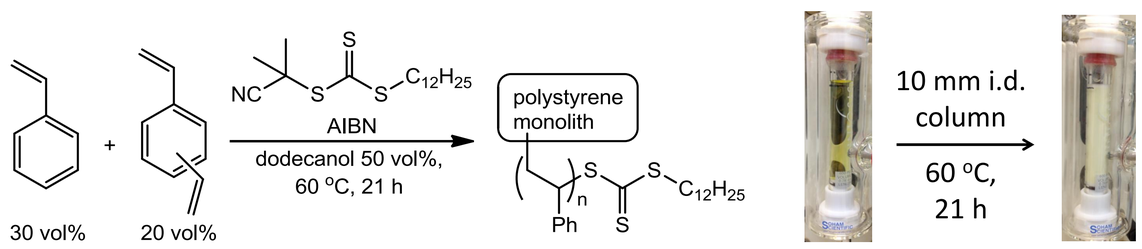
CSIRO MATERIALS SCIENCE & ENGINEERING
www.csiro.au

Introduction

Polymeric monoliths have recently emerged as a new class of solid supports for stoichiometric and catalytic reactions in continuous flow synthesis.[2] We sought to use Reversible Addition-Fragmentation Chain Transfer (RAFT) polymerisation to synthesise these monoliths: RAFT provides control over polymer-chain growth in linear radical polymerisation, and should provide control over pore size distribution and functionality distribution in crosslinking polymerisation. This work aims to develop such solid supports, in order to target important reactions for the pharmaceutical industry (eg. amide coupling).[3]

Monolith synthesis and characterisation

The process of monolith synthesis uses a high proportion of crosslinkers and a poor solvent deliberately chosen to behave as a porogen: these conditions are quite different to those "typical" polymerisations in which RAFT has been utilized. Using 2-cyano-2-propyl dodecyl trithiocarbonate as a RAFT agent, we recently found that suitable polystyrene monoliths were obtained when 0.4 to 2 equivalents of RAFT / AIBN were used.[1]



Scheme 1: Poly(styrene-*co*-divinyl benzene) monolith synthesis in the presence of 2-cyano-2-propyl dodecyl trithiocarbonate. Molar ratio of monomer to AIBN was fixed at 144.

A linear relationship between backpressure and flow rates was obtained when MeOH or CH_2Cl_2 was pumped through the monoliths, indicating laminar flow of liquid through the material.

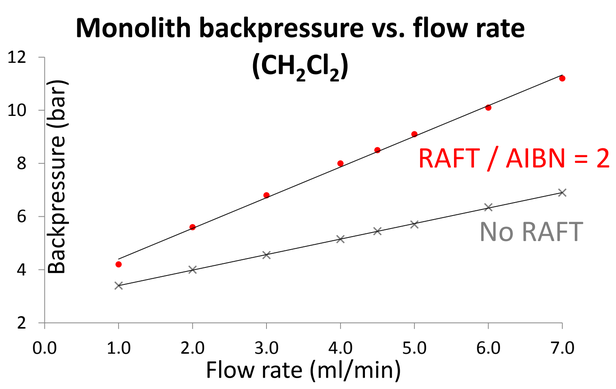
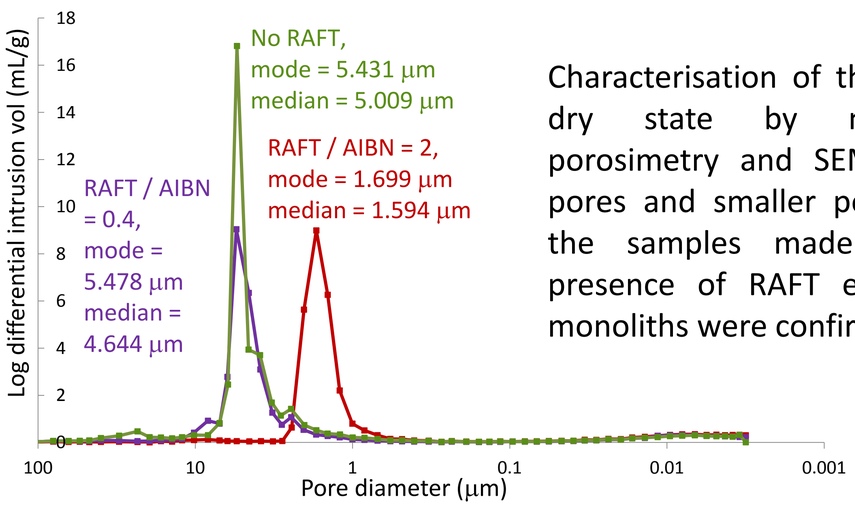


Figure 1: CH_2Cl_2 was flowed through a 2.8 bar backpressure regulator and the corresponding monolith.

A. Differential pore size distribution



Characterisation of the monoliths in the dry state by mercury intrusion porosimetry and SEM revealed smaller pores and smaller polymer globules for the samples made with RAFT. The presence of RAFT end groups on the monoliths were confirmed by EDX.

B. SEM images

C. EDX mapping of sulfur

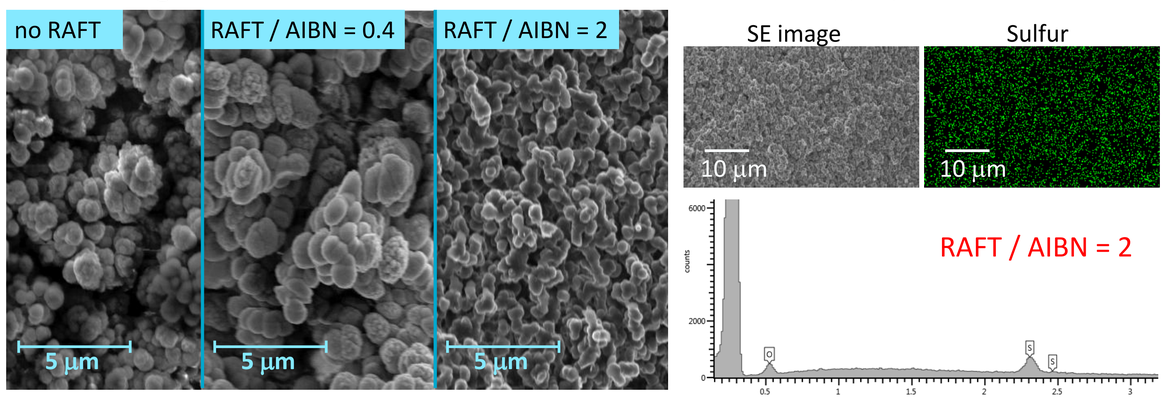


Figure 2: A. Differential pore diameter distribution obtained by mercury intrusion porosimetry. B. SEM images of monoliths. C. EDX detection of sulfur.

Monolith-bound RAFT end-groups

Reaction with hydrazine

The solid-bound thiocarbonylthio groups are available for heterogeneous reaction in a flow setting, as shown by reaction with hydrazine.[4]

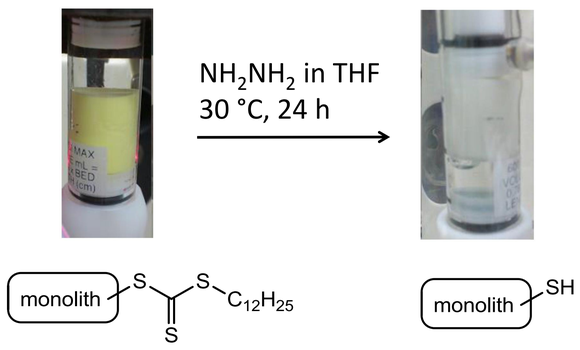
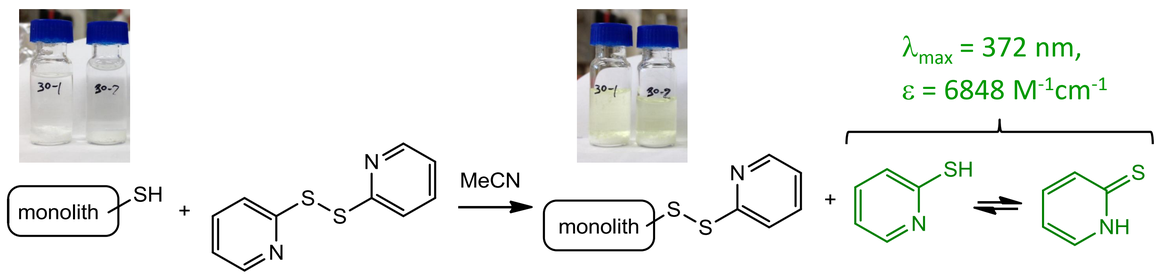


Figure 3: Reaction of a RAFT-monolith with NH_2NH_2.

The monolith decolourised and an aliphatic C12 residue due to the reacted RAFT group was detected in the reaction solution. Using a monolith made with RAFT/AIBN = 4, the amount of available RAFT groups was quantified by elemental analysis. Since a third of sulfur remained in the monolith after treatment with hydrazine, the end groups are quantitatively available for reaction in a swelling solvent such as THF.

Post-reaction, a qualitative assay with 2,2′-dipyridyl disulfide[5] demonstrated the presence of thiol functionality on the monolith.



Scheme 2: Determination of thiol functionality by reaction with 2,2′-dipyridyl disulfide.

Surface grafting

To develop a potential solid-supported catalyst, poly(vinylphenylboronic acid) was successfully grafted onto a monolith using the RAFT end groups.

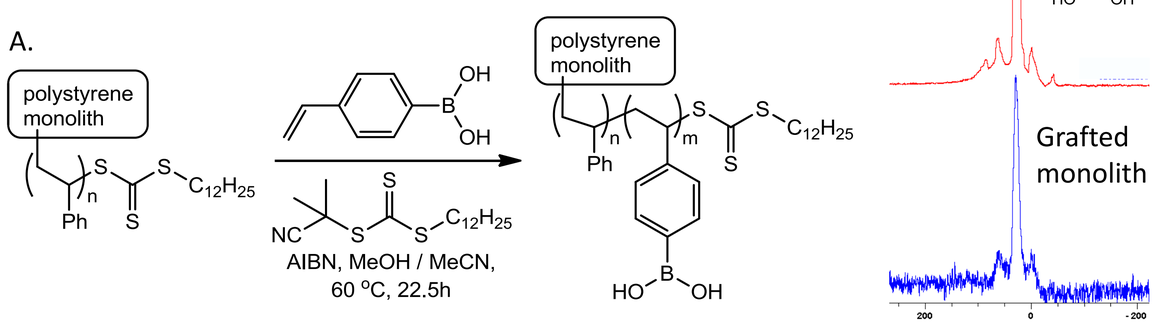


Figure 4: A. Surface-grafting conditions with 4-vinylphenylboronic acid. B. ^{11}B solid state NMR spectra of monomer and grafted monolith. Spectra are background subtracted and externally referenced to boric acid at 19.3 ppm.

Conclusions

Monolith synthesis with a RAFT agent enables control of pore size and polymer globules, while maintaining good flow properties. Our synthetic protocol provides a convenient route to monoliths containing RAFT end-groups, which are accessible for surface modification or grafting reactions. These reactive groups provide a platform for introducing a wide range of functionality. The utility of these grafted monoliths as catalysts in flow synthesis are currently being explored.

REFERENCES

[1] *Polym. Chem.* **2014**, Advance Article (**DOI**: 10.1039/C3PY01015E).
[2] Recent examples: *Org. Biomol. Chem.* **2008**, *6*, 1587; *Synlett* **2011**, 869; *Beilstein J. Org. Chem.* **2011**, *7*, 1648; *Org. Lett.* **2012**, *14*, 3920.
[3] *Green Chem.* **2007**, *9*, 411; *Org. Process Res. Dev.* **2008**, *12*, 807; *Org. Process Res. Dev.* **2010**, *14*, 770.
[4] *Macromol. Rapid Commun.* **2010**, *31,* 1444.
[5] *Anal. Chim. Acta*, **2005**, *533*, 179.

ACKNOWLEDGEMENTS

Drs Roger Mulder, Jo Cosgriff, Almar Postma, Christian Hornung, Thomas Gengenbach and Mr Mark Greaves; CPSE Characterisation Facility; Particle & Surface Sciences Australia

FOR FURTHER INFORMATION

Dr Kristine J. Barlow (née Tan)
e kristine.barlow@csiro.au
t +61 3 9545 2535
w www.csiro.au/cmse