Automated Synthesis of Methacrylate (MA) Polymers using RAFT

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CHEMSPEED TECHNOLOGIES

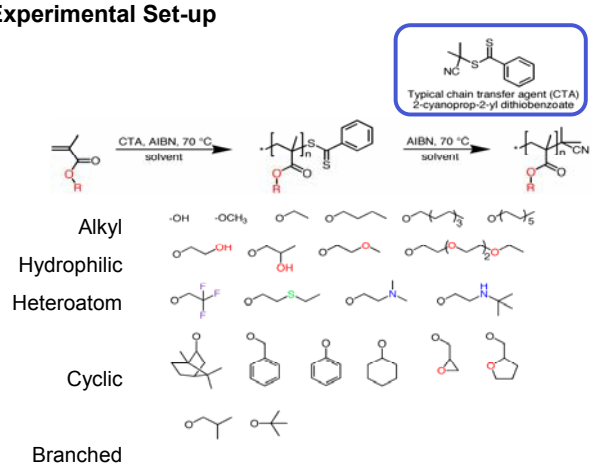
Pharmaceuticals & Agrochemicals

Objective

To create a polymethacrylate library for the rapid screening of cell-material interactions and the development of *in silico* modeling technique. Polymethacrylates are widely studied and used for intraocular lens, orthopedic applications, bone cement, and cartilage substitutes.

A library of these polymers has not yet been explored for studies of biological interactions. This was the first study with a polymer library of this size (> 40,000 polymers). Approx. 100 polymers were synthesized for use as a training set for a computational model, to subsequently demonstrate the value of computational modeling. The study will also validate the effectiveness of Chemspeed's Automated Synthesizer.

Experimental Set-up



- Synthesis of polymethacrylates using reversible addition-fragmentation transfer (RAFT) polymerization
- Homopolymers, copolymers and terpolymers
- Removal of RAFT end group in a second step to ensure biological response not affected by RAFT end group
- Instrumentation: Chemspeed Automated Synthesizer

Figure 1. Chemspeed glass reactor arrays for parallel automated synthesis.

Results

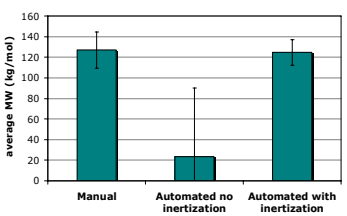


Figure 2. Validation of automated synthesis under inert conditions: Comparison of weight-average of molecular weights from polymers obtained using free radical solution polymerization of isobutyl methacrylate with manual and automated synthesis.

Table 1. Determination of optimum ratio of $[CTA]_0$:$[AIBN]_0$. Optimum ratio of $[CTA]_0$:$[AIBN]_0$ is typically 4 versus 10 (faster rate of polymerization and low polydispersity); solvent effect is more important than $[CTA]_0$:$[AIBN]_0$ for methacrylic acid.

polymer	Mn (kg/mol)	PDI	Solvent	$[CTA]_0/[AIBN]_0$
benzyl-MMA (50-50)	43	2.1	toluene	10
benzyl-MMA (50-50)	144	1.5	MEK	4
tetrahydrofurfuryl	44	1.8	DMF	10
tetrahydrofurfuryl	137	1.6	DMF	4
methacrylic acid	48	1.5	DMF	10
methacrylic acid	98	1.6	DMF	4
methacrylic acid	221	1.5	dioxane	10

Table 2. The effect of solvent on the RAFT polymerization. The use of methylethylketone as the reaction solvent resulted in a dramatic increase in MW.

Polymer	Mn (kg/mol)	PDI	Solvent	$[CTA]_0/[AIBN]_0$
benzyl-MMA (25-75)	22	1.9	toluene	10
benzyl-MMA (25-75)	97	1.4	MEK	10
hydroxypropyl-MMA (75-25)	54	1.8	DMF	10
hydroxypropyl-MMA (75-25)	154	1.4	MEK	10
Phenyl	16	1.5	EtOAc	10
Phenyl	135	1.6	MEK	10
t-butyl	32	1.5	EtOAc	10
t-butyl	31	2	toluene	4
t-butyl	49	1.6	MEK	10
Undecyl	19	1.8	toluene	4
Undecyl	85	1.6	MEK	4
Undecyl	185	1.8	none	4

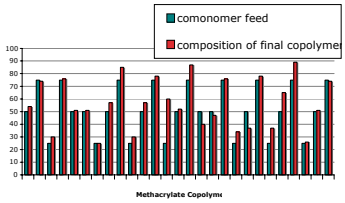


Figure 3. Copolymer composition: Comparison of mol% A in comonomer feed and in final copolymer as determined from ^1H NMR spectroscopy.

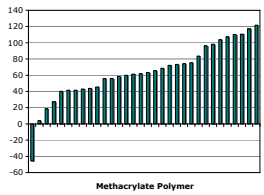


Figure 4. Thermal properties of methacrylate polymers: Glass transition temperatures of methacrylate homo- and co-polymers as measured using DSC.

Summary

- Approx. 100 polymers were synthesized
- Materials subset exhibits range of thermal properties
- Validation of RAFT polymerization on a Chemspeed automated synthesizer
- Automated synthesis was successful in providing a library of polymers

References

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