RAFT-polymerization of 2-hydroxyethylmethacrylate using different end-functionalized dithioesters as chain-transfer agents

Norma A. Cortez-Lemus[1], Angel Licea-Claverie[1*], Craig J. Hawker[2] and Curt W. Frank[3]
1.-Centro de Graduados e Investigación, Instituto Tecnológico de Tijuana, A.P. 1166, 22000 Tijuana, B.C., México.
*E-mail:*aliceac@tectijuana.mx
2.-Materials Research Laboratory, University of California, Santa Barbara, Santa Barbara, CA 93106-5121, USA
3.-Department of Chemical Engineering, Stanford University, Stanford, CA 94305-5080, USA.

1. Abstract

2-Hydroxyethyl methacrylate (HEMA) is a commercially important monomer widely used in the manufacture of soft contact lenses and intraocular lenses. Since HEMA copolymers usually exhibit excellent biocompatibility and good blood compatibility, HEMA based materials are increasingly developed for many different biomedical applications. The synthesis of controlled-structure polyHEMA and their blockcopolymers has been described via anionic and ATRP living polymerization techniques. However, the best results were obtained when the alcohol functionality was protected prior to polymerization, which involves a subsequent removal of the protecting groups. In this contribution we report the use of three different ditioester-compounds for the RAFT-polymerization of HEMA aiming to yield controlled structure HEMA polymers of different sizes containing either: carboxylic acid, primary amine or alcohol end-groups; while trying to avoid time and money consuming, protection/deprotection techniques.

2. Introduction

2-Hydroxyethyl-2-methylacrylate is a monomer with numerous applications and a large number of publications and patents have been devoted to this product and its corresponding polymer [1]. This popularity is due to several factors, such as the primary alcohol function, which allows substitution reactions in the monomer and the corresponding polymer; and their practical usage in biomedically important materials in contact lenses, in coating of surgical sutures, as hydrogel and in hemodialysis membranes [2, 3]. However, synthesis of linear high molecular weight polyHEMA is relatively difficult because chain transfer reactions to the hydroxyl group of HEMA often occur during the polymerization and thereby the resulting polymers become branched and/or cross-linked [4]. There have been several reports on the synthesis of controlled-structure HEMA-based block copolymers via anionic polymerization chemistry, but this approach requires protection of the alcohol functionality. Such syntheses involve at least three steps: synthesis of the protected monomers, its controlled polymerization subsequent removal of

the protecting groups. ATRP has been shown to be a versatile technique for the controlled polymerization of many monomers classes, including acrylates, methacrylates and styrenics. Armes *et.al.* [5] reported efficient and well-controlled PHEMA in either 50:50 methanol/water mixtures or pure methanol. Compared to the previous HEMA polymerizations via ATRP, much faster rates of polymerization, higher final conversion and lower polydispersities were achieved.

In our efforts to overcome these problems and to search for versatile synthetic tools to obtain well-defined macromolecular conjugates, we explored the potential of the reversible addition-fragmentation chain transfer radical polymerization (RAFT) process. The RAFT process offers some advantages in its ability to tolerate functional groups, allowing the controlled polymerization of a variety of functional monomers [6]. The RAFT technique is facile since the different components are not sensitive to air or moisture and can therefore be simply dissolved and deoxygenated prior to the polymerization. As the popularity of the method has grown, more novel RAFT agents have been synthesized and used for polymerization of various monomers [7].

3. Experimental Section

PolyHEMA was prepared by RAFT in *N*,*N*-dimethylformamide (DMF) or *p*-1,4-dioxane or H_2O/*p*-1,4-dioxane mixture using differents dithiobenzoate CTA´s as RAFT agents. For example, a typical RAFT polymerization to prepare a target molecular weight of 10,000 $gmol^{-1}$, a stock solution of HEMA (1.8 M, 7.69 mmol), AZO (0.0226 mmol) and CTA (0.113 mmol) in DMF was prepared. Deoxygenated solutions by four freeze-evacuate-thaw cyles were flame-sealed under vacuum. Polymerization was conducted at 70 °C in a constant temperature oil bath. PolyHEMA was dissolved in methanol followed by precipitation in hexane.

4. Results and Discussion

In this work four chain transfer agents (CTA) were used under various polymerization conditions in the hope of obtaining a final product of the required molecular weight containing an specific end-group. However, despite the methods popularity, the results of this work have clearly shown that the method has some limitations with regard to the level of control over the molecular weight distribution. Structures of the RAFT agents used are shown in Figure 1.

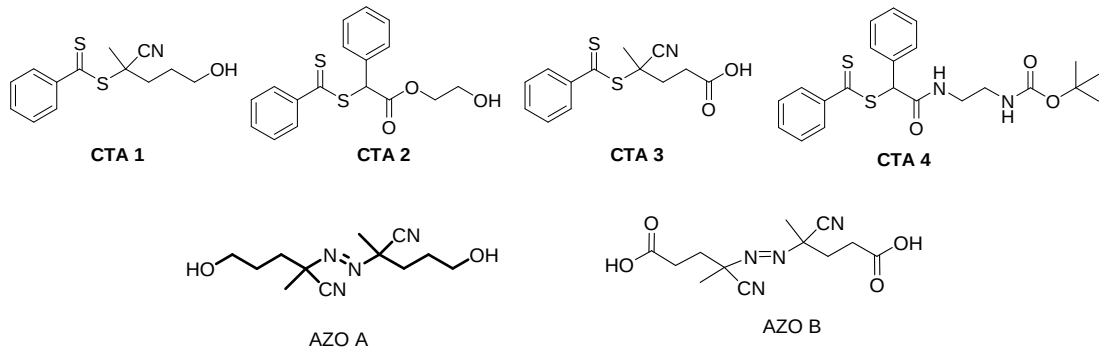

Figure 1. Structures of RAFT agents and AZO initiator used in polymerization of HEMA.

All the attemps to polymerize HEMA using the RAFT method resulted in formation of pink polymers indicating the presence of the CTA-moitety. Different solvents, concentrations and temperatures in the reaction solution were tested. The results of the polymerization and the analysis of the polymers samples are presented in Table 1.

Table 1. Molecular weight and conversion data for polymerization of HEMA in the presence of RAFT agents.

Entry	RAFT/AZO agent	T (°C)	Solvent	[HEMA]:[CTA]:[AZO]	Time, h	$M_{n,\,GPC}$ [b]	PDI	Yield %	$M_{n,target,}$ [c]
1	1/A	70	*p*-dioxane	68:1:0.2*	1.7	8276	1.22	22	8840
2	2/A	70	*p*-dioxane	68:1:0.2*	1.6	11460	1.34	25	8840
3	3/B	70	*p*-dioxane	68:1:0.2*	1.6	10240	1.35	32	8840
4	2/A	70	DMF	68:1:0.2*	7.5	14670	1.22	45	8840
5	3/B	70	*p*-dioxane:H_2O	136:1:0.2*	12	19380	1.18	54	17680
6	3/B	70	*p*-dioxane:H_2O	136:1:0.2*	18	26180	1.90	75	17680
7	4/B	70	*p*-dioxane:H_2O	136:1:0.2*	13	29100	1.40	55	17600
8	2/A	90	*p*-dioxane	136:1:0.4**	1	32410	1.44	81	17680

[a]Conversion measured by precipitating samples into ether and drying the polymer under vacuum.
[b]Molecular weigth and PDI values mesured by GPC; [c]Target molecular weights were calculated based on 100% monomer conversion . * $[HEMA]_o$ = 1.18 M; $[HEMA]_o$ = 1.9 M.

In typical free radical polymerization of HEMA, the polymers have quite broad molar mass distributions (PDI ~ 2), which is a symptom of the uncontrolled mechanism of the reaction. In this work clearly there is a living character, even if it is not ideal. Dithioesters 1,2 and 3 were effective in controlling the molecular weight, possess similar reactivities and provided narrow polydispersity (1.22-1.35). Normally, depending on the colour of the RAFT agent used, succesful

RAFT polymerization results in formation of coloured polymer, indicating incorporation of the chain transfer agent into the polymer chain. But, multimodal distributions were observed for HEMA polymerization at 90 °C (entry 8) and distributions with a shoulder were observed for polymerizations in p-Dioxane/Water mixtures (entries 5-7) although polymer was in all cases still pink colored. Therefore, in order to minimize high molecular weight peaks or shoulders it is necessary to quench reactions at moderate conversions. Unimodal molecular weight distributions were observed using *p*-dioxane and DMF at low conversion (Table 1, entries 1-4).

4.Conclusion

In this work RAFT polymerization of HEMA under various conditions was investigated; we have shown that the use of a functionalized dithiobenzoate as chain transfer agents allows us to keep a high concentration of living chains. At high conversions chain branching and/or termination trough polymer to polymer radical addition events may contribute to the broadening of the molecular weight distribution. Dithioesters 1, 2 and 3 were effective in controlling the molecular weight, possess similar reactivities and provided narrow polydispersity (1.22-1.35) at low conversion.

Acknowledgements

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5. References

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