

Silica Monolith Particles of Improved Separation Efficiency and Their Modification with Polystyrene by RAFT Polymerization

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Abstract. Silica monolith particles of ca 2 μm size having proper particle size distribution were prepared and modified to give polystyrene attached silica monolith particles as a new chromatographic stationary phase of high separation efficiency. Attachment of 4-chloromethylphenylisocyanate to silica particles was catalyzed by dibutyltin dichloride and the ligand was reacted with diethyldithiocarbamate to yield initiator attached silica particles. Reversible addition-fragmentation chain transfer (RAFT) polymerization was used to attach polystyrene layers to initiator attached silica monolith particles. This new stationary phase was packed in a microcolumn of 0.5 mm ID and its separation performance was examined. The optimum flow rate was found 7 uL /min in 60/40 (v/v) acetonitrile /water (0.1 % TFA). The numbers of theoretical plates of the column (0.5 ×300 mm) were over 30,000.

Keywords: Ground silica monolith particles, Initiator attachment, RAFT Polymerization, Polystyrene attached phase, High separation efficiency.

1. Introduction

The capability of porous and nonporous inorganic surface for the attachment of initiators to form controlled polymer layers ultimately leading to organic-inorganic hybrid polymeric stationary phases have been documented in several review articles [1-6]. Such hybrid phases can be used for chromatographic purposes [2]. Atom transfer radical polymerization (ATRP) and reversible addition-fragmentation chain transfer (RAFT) polymerization have been listed to be involved in preparation of such chromatographic phases.

The detailed mechanism and application of ATRP have been introduced in some review articles [7-9]. Briefly, ATRP is activated by a surface initiator having terminal halogen on silica surface with an aid of a catalytic mixture composed of cuprous/cupric halides and an amine base. Although some of the resultant stationary phases prepared by ATRP showed some better separation selectivities in comparison to conventional C18 phases, their separation efficiencies were quite lower than those of conventional C18 phases in most cases. Although formation of polymer layers upon organic monolith with ion exchange capabilities by ATRP has also been reported in a specific study [10], inorganic silica monoliths or spheres are the most versatile materials involved in surface modification for preparation of chromatographic media.

The detailed mechanism and application of RAFT polymerization have been introduced in several review articles [5-6, 11-12]. Since its introduction by the group of Rizzardo et al in 1998 [13], RAFT polymerization have been used extensively by various research groups. RAFT polymerization includes a surface-attached initiator prepared by the reaction of sodium diethyldithiocarbamate with a halogen containing ligand chemically attached to inorganic surface.

According to the RAFT polymerization mechanism, the polymer chain is grown in the C-S bond located between the spacer moiety and the diethyldithiocarbamate moiety [5-6, 11-12]. The resultant stationary

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phases prepared by making use of different halogen containing ligands have shown lower separation efficiencies in general than conventional C18 phases.

Several studies on preparation of polystyrene attached- silica particles by RAFT polymerization have been carried out in our laboratory [14-17]. Making initiator-attached silica particles by reaction with 3-chloropropyltrimethoxysilane and sodium diethyldithiocarbamate in sequence followed by RAFT polymerization resulted in stationary phases of improved separation efficiency [15-17]. The polystyrene-attached silica spheres made by using 4-chloro-methylphenylisocyanate as the ligand moiety showed somewhat inferior separation performance [14].

Preparation of ground silica monolith particles of better chromatographic separation performance than conventional silica spheres has been another research topic of our laboratory [17-19]. We have coupled the two research areas in a recent study to make polystyrene-attached ground silica monolith particles [17]. The particle size of the previous studies was 3-5 μm . We have been improving the process of production of silica monolith particles.

In this study, silica monolith particles of ca 2 μm size have been prepared by a much simplified process, and modified to give polystyrene-attached stationary phase by RAFT polymerization where the surface initiator was made by reacting silica particles with 4-chloromethylphenylisocyanate and sodium diethyldithiocarbamate in sequence. The resultant stationary phase has shown improved selectivities and separation efficiencies (number of theoretical plates above 30,000).

2. Experimental

2.1. Chemicals and Materials

Glacial acetic acid, urea, polyethylene glycol (PEG) 10000, trimethylorthosilicate (TMOS), 4-chloromethylphenylisocyanate, sodium diethyldithiocarbamate, anhydrous toluene, tetrahydrofuran (THF), styrene were purchased from Sigma-Aldrich (St. Louis, MO, USA). HPLC grade methanol, acetonitrile, acetone, and water were obtained from Mallinckrodt Baker (Phillipsburg, NJ, USA). All the reagents were used as received. Screen frits (1.6mm diameter, 0.08mm thickness, and 0.5 μm pore size) were obtained from Valco (Houston, TX, USA). Glass lined stainless steel tubing (30cm, 0.5 mm ID, 1.6 mm OD) and silica capillary (50 μm ID, 365 μm OD) were purchased from Alltech (Deerfield, IL, USA).

2.2. Synthesis of Ground Silica Monolith

The manufacturing procedure for ground silica monolith was modified in this study to get ca 2 μm particle size. 1600 mg PEG and 2200 mg Urea were dissolved in 15 mL 0.01N acetic acid in a Teflon vial, and magnetically stirred for 10 minutes in ice/water. Then, 5mL TMOS was added, and the mixture was kept under stirring for 40 min. The solution was incubated at 40°C for 48 h then at 120°C (in an autoclave) for 48 h. The residual water due to shrinkage (sol-gel process) was decanted off and the solid cake of monolith was dried at 70°C overnight, ground for 10min, and calcined at 550°C for 48h.

2.3. Synthesis of Initiator Attached Silica Monolith Particles

4-Chloromethylphenylisocyanate 130 mg was dissolved in 12mL anhydrous toluene and purged with N₂ for 10min. Dibutyltin dichloride 50 mg was added to catalyze the reaction. Ground silica monolith 500 mg (calcined at 550°C) dried at 120°C (12 h) was suspended in it and was stirred for 10 min. Thermal treatment of the reaction mixture was carried out at 80°C for 50h. The product was washed with anhydrous toluene followed by acetone, filtered and dried in a vacuum desiccator at room temperature. A solution of 350 mg sodium diethyldithiocarbamate in 12mL anhydrous THF was sonicated for 10min followed by N₂ purging for 10min. The ligand attached silica monolith particles were suspended in the solution and treated at 55°C for 12 h. The product was thoroughly washed with THF, methanol/water (60/40, v/v %) and acetone in sequence, filtered, dried, and kept in a vacuum desiccator overnight.

2.4. Styrene Polymerization

A solution of 4 mL styrene in 12 mL anhydrous toluene was subjected to sonication for 10 min followed by N₂ purging for 10 min and 200 mg of initiator attached silica particles were dispersed. Radical

polymerization was carried out under reflux at 110°C for 30 h under N₂ environment. The residual polystyrene-attached stationary phase was washed with toluene and acetone, and dried at 60°C overnight. The whole procedure of polystyrene-attached silica monolith particles including initiator attachment and RAFT polymerization was illustrated in Fig. 1.

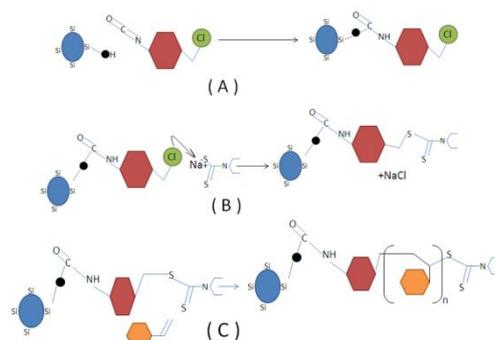


Fig. 1. Reaction schemes: (A) attachment of ligand 4-chloromethylphenylisocyanate, (B) attachment of initiator sodium dithylditiocarbamate, (c) styrene polymerization

2.5. Micro Liquid Chromatography (μ LC)

A 10AD pump (Schimadzu, Tokyo Japan), a Valco (Houston, TX, USA) C14W.05 injector with 50nL injection loop, membrane degasser (Schimadzu DGU-14A), a UV-VIS capillary window detector (Jasco UV-2075), a homemade 0.5mm I.D glass lined micro column were assembled to construct the μ LC system. The software Multichro 2000 from Youlingisul (Seoul, Korea) was used for acquisition and processing chromatographic data. Packing of micro columns was carried out according to the procedure published [14-19] with some modification. The slurry was prepared by suspending the 110 mg stationary phase in methanol by sonication for 10 min and the supernatant was removed. This procedure was repeated thrice. The final 1.2 mL slurry (methanol + stationary phase) was fed into reservoir. A pressure of 17,000 psi for 5 min, 11,000 psi for 10 min and 8,000 psi for 30 min was applied in sequence. The stock test mix sample solution was prepared by dissolving phenol (0.88 μ L), acetophenone (0.14 μ L), 4-methyl-2-nitroaniline (0.32 mg), benzene (2.93 μ L), and toluene (1.46 μ L) in 1mL mobile phase and was stored at 4°C. The sample was further diluted for injection.

3. Result and Discussion

3.1. Architecture of Stationary Phases

Microscopic and SEM views of silica monolith particles of previous and this study are compared in Fig. 2. The average particle size of silica monolith particles of current study was ca 2 μ m as compared to previous study (3.7 μ m). The modifications of this study such as reduction of particle size coupled with catalyzed initiator attachment have resulted in a new polystyrene-attached ground silica monolith phase that has shown better separation performance than those of previous studies as shown in Table 1. The chromatogram of the test mix obtained with the stationary phase of this study is given in Fig. 3. As reported in the previous studies, the superiority of this stationary phase is owing to pseudo-core/shell like architecture of polystyrene phase and the specific shape of silica monolith particles (bent, irregular, and oval) enabling faster mass transfer kinetics in comparison to spherical particles as well as the reduced particle size.

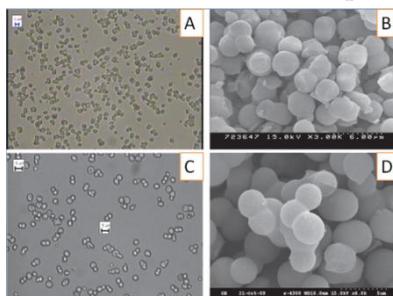


Fig 2. (A) Microscopic and (B) SEM views of current study (C) Microscopic and (D) SEM views of previous study [17].

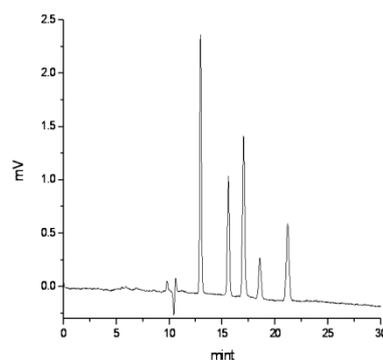


Fig 3. The chromatogram of the test mix obtained in 60/40(v/v %) acetonitril/water (0.1% TFA) at 7 $\mu\text{L}/\text{min}$ and 214 nm. The solutes eluted in the following order except for the first system peak: phenol, acetophenone, 4-methyl-2-nitroaniline, benzene, toluene.

Table1: Comparative analysis of number of theoretical plates of current and previous batches of stationary phases.

Solute	Polystyrene bound silica monolith (this study)	Polystyrene bound silica monolith (previous study) [17]	C18 bound silica monolith (previous study) [17]	Polystyrene bound conventional silica [17]	C18 bound conventional silica [17]
Phenol	31000 \pm 200	29800 \pm 300	27000 \pm 500	26000 \pm 500	21200 \pm 600
Acetophenone	30100 \pm 400	28100 \pm 400	26900 \pm 600	24100 \pm 400	20300 \pm 400
4-Methyl-2-nitroaniline	29600 \pm 250	26400 \pm 800	29700 \pm 900	22000 \pm 900	22100 \pm 800
Benzene	30500 \pm 300	31900 \pm 400	29700 \pm 900	21800 \pm 400	20800 \pm 500
Toluene	33600 \pm 200	31100 \pm 500	24600 \pm 600	19500 \pm 800	21100 \pm 600
Average	31000 \pm 250	29500 \pm 220	26400 \pm 2300	22700 \pm 2500	21100 \pm 700

4. Conclusion

The modifications of this study such as reduction of particle size (ca 2 μm) of silica monolith particles coupled with catalyzed initiator attachment have resulted in a new polystyrene-attached ground silica monolith phase that has shown better separation performance than those of previous studies.

5. Acknowledgements

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6. References

- [1] A. Olivier, F. Meyer, J. Raquez, P. Damman, P. Dubois. Surface-initiated controlled polymerization as a convenient method for designing functional polymer brushes: From self-assembled monolayers to patterned surfaces. *Prog. Polym. Sci.* 2012, **37**: 157-181.
- [2] H. Wang, X. Dong, M. Yang. Development of separation materials using controlled/livingradical polymerization. *Trends Anal. Chem.* 2012, **31**: 96-108.
- [3] G. J. A. A. Soler-Illia, O. Azzaroni. Multifunctional hybrids by combining ordered mesoporous materials and macromolecular building blocks. *Chem. Soc. Rev.* 2011, **40**, 1107-1150.
- [4] S. Edmondson, S. P. Armes. Synthesis of surface-initiated polymer brushes using macro-initiators. *Polym. Int.* 2009, **58**: 307-316.
- [5] M. Beija, J. Marty, M. Destarac. RAFT/MADIX polymers for the preparation of polymer/inorganic nanohybrids.

Prog. Polym. Sci. 2011, **36** (3): 845-886.

- [6] G. Moad, M. Chen, M. Häussler, A. Postma, E. Rizzardo, S.H Thang. Functional polymers for optoelectronic applications by RAFT Polymerization. *Polym. Chem.* 2011, **2**(3): 492-519.
- [7] K. Matyjaszewski, N. V. Tsarevsky. Nanostructured functional materials prepared by atom transfer radical polymerization. *Nat. Chem.* 2009, **1**: 276-288.
- [8] K.Y. Qiu, P. Li. New initiation systems for atom transfer radical polymerization. Chinese. *J. Polym. Sci.* 2004, **22** (2): 99-110.
- [9] V. Coessens, T. Pintauer, K. Matyjaszewski. Functional polymers by atom transfer radical polymerization. *Prog. Polym. Sci.* 2001, **26**: 337-377.
- [10] E. Unsal, B. Elmas, B. Caglayan, M. Tuncel, S. Patir, A. Tuncel, Preparation of an ion-Exchange chromatographic support by a "grafting from" strategy based on atom transfer radical polymerization. *Anal. Chem.* 2006, **78**: 5868-5875.
- [11] A. Favier, M. Charreyre. Experimental Requirements for an Efficient control of Free-Radical Polymerization via the Reversible Addition-Fragmentation Chain Transfer (RAFT) process. *Macromol. Rapid Comm.* 2006, **27** (9): 653-692.
- [12] S. Perrier, P. Takolpuckdee, Macromolecular design via reversible addition-fragmentation chain transfer (RAFT)/Xanthates (MADIX) polymerization. *J. Polym. Sci. Pt. A: Polym. Chem.* 2005, **43** (22): 5347-5393.
- [13] T. P. T. Le, G. Moad, E. Rizzardo, S. H. Thang. E.I. Dupont de Nemours and Company, *WO 98/01478*. 1998.
- [14] S.S. Kim, W.J. Cheong. A new stationary phase prepared by polymerization of styrene on initiator bonded porous silica. *Bull. Korean Chem. Soc.* 2009, **30** (3): 722- 725.
- [15] D.G. Hwang, S.A. Zaidi, W.J. Cheong. A new stationary phase with improved ligand morphology prepared by polymerization of styrene upon initiator-attached Lichorsorb silica particles. *Bull. Korean Chem. Soc.* 2009, **30** (12): 3127-3130.
- [16] D.G. Hwang, S.A. Zaidi, W.J. Cheong. Use of chain transfer agent attached to silica particles in preparation of polystyrene-based stationary phases. *J. Sep. Sci.* 2010, **33**: 587-593.
- [17] S.M. Lee, S.A. Zaidi, W.J. Cheong. A new stationary phase prepared from ground silica monolith particles by reversible addition-fragmentation chain transfer polymerization. *Bull. Korean Chem. Soc.* 2010, **31** (10): 2943-2948.
- [18] J.H. Ko, Y.S. Baik, S.T. Park, W.J. Cheong. Ground, sieved, and C18 modified monolithic silica particles for packing material of microcolumn high-performance liquid chromatography. *J. Chromatogr. A* 2007, **1144**, 269-274.
- [19] K.M. Han, W.J. Cheong. C18 Modified Monolith silica particles of 3-5 μ m. *Bull. Korean Chem. Soc.* 2008, **29** (11): 2281-2283.