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# Fabrication of highly cross-linked reversed-phase monolithic columns via living radical polymerization

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ABSTRACT

New monolithic reversed-phase liquid chromatography (RPLC) stationary phases based on single multi-acrylate/methacrylate-containing monomers [i.e., 1,12-dodecanediol dimethacrylate (1,12-DoDDMA), trimethylolpropane trimethacrylate (TRIM) and pentaerythritol tetraacrylate (PETA)] were synthesized using organotellurium-mediated living radical polymerization (TERP), which was expected to produce more efficient monolithic columns than conventional free-radical polymerization. The rationale behind selection of porogens, relative concentrations of reagents and polymerization conditions are described. The new monolithic columns were applied to the separation of small molecules (i.e., alkylbenzenes) under isocratic conditions. Chromatographic efficiencies as high as 60,200 plates/m (71,300 plates/m when corrected for extra-column variance) were obtained, showing a general improvement over previous RPLC monoliths.



## 1. Introduction

Organic monolithic stationary phases have made inroads as stationary phases for liquid chromatography (LC) since their introduction in the late 1980s and early 1990s [1–6]. Organic monoliths are typically prepared via conventional free radical polymerization. Compared to more conventional columns (i.e., columns packed with 5 μm or sub-5 μm particles) and silica monolithic columns, organic polymer monoliths do not perform as well for the separation of small molecules. This is primarily due to their high porosity, low mesopore volume and inherent structural heterogeneity [7,8], which result from free radical polymerization [9–13]. It is very difficult to control the free radical polymerization process and resultant monolith morphology because propagation of individual polymer chains from initiation to termination takes only seconds [14]. This characteristic of free radical polymerization usually results in the formation of microgels containing polymer chains with a heterogeneous distribution of cross-linking points [15,16] and, finally, heterogeneous polymer network structures that provide mediocre separation performance. Obviously, more homogeneous structures with well-defined skeletal and pore sizes are desirable for obtaining better separation performance.

During the past decade, controlled/living radical polymerization (CRP) was introduced and investigated for the synthesis of organic monoliths containing polar functional groups, which cannot be prepared under ionic and metal-catalyzed polymerization conditions [17–22]. Controlled/living radical polymerization is a reversible activation/deactivation process. Because of this reversible character, the growth rate of an individual chain is controlled by the balance between the growing radical and the dormant species. Therefore, the chain propagation period in CRP is much longer than in free radical polymerization, which gives the chains sufficient time to relax so that the reaction species distribute uniformly [23,24]. The most important aspect of CRP is the formation of a reversibly generated active radical. When a radical is formed, it can react with a monomer, which propagates a polymer chain and then becomes dormant [25,26]. Due to reaction reversibility, the resultant polymers exhibit narrower molecular weight distributions and more homogeneous cross-linked structures compared to polymers obtained from conventional free radical polymerization. There have been several reports of using CRP for controlling porous structures of polymer monoliths [17–22,27–32]. Yu et al. reported the use of atom transfer radical polymerization (ATRP), a CRP method, to prepare poly(ethylene glycol dimethacrylate) (PEGDMA) [33] and poly(ethylene glycol dimethacrylate-ethylene glycol methyl ether

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methacrylate) (PEGDMA-PEGMEMA) [14] monoliths. Poly(styrene-*co*-divinylbenzene) (PS-DVB) monoliths were successfully prepared from nitroxide-mediated living radical polymerization (NMP) [10,15,16] and reversible addition–fragmentation chain transfer (RAFT) polymerization [13,18,32].

Organotellurium-mediated living radical polymerization (TERP) is a new branch of CRP. The Yamago group investigated a series of organotellurium compounds which produce carbon-centered radicals by thermolysis to initiate polymerization reactions in the presence of an azo initiator (i.e., AIBN) [17,25,26,34,35]. This polymerization method takes place under gentle polymerization conditions, is versatile, is compatible with polar functional groups, and provides good molecular weight control [17,25,34,35]. Moreover, the reaction components involved in TERP are fewer compared to ATRP, thereby simplifying the optimization of reaction conditions. Recently, PS-DVB [11], PDVB [36], GDMA [37], and poly(*N*,*N*-methylenebisacrylamide) [12] monoliths were successfully prepared using TERP.

A typical polymerization system for monolith preparation includes initiator, monomers (functional and cross-linking monomers), and porogen(s). High cross-linker concentration has been reported to provide high mechanical stability and high surface area [38,39]. Cross-linkers which contain specific functional groups provide both monolith rigidity and chromatographic selectivity [40,41]. Recent work has demonstrated that use of a single-monomer/cross-linker in the preparation of monolithic columns provides simpler optimization of the reaction system, improved column-to-column reproducibility, better mechanical stability and higher surface area due to the highly cross-linked network [42–46].

In this study, organic monolithic capillary columns were synthesized from three different single monomers [1,12-dodecanediol dimethacrylate (1,12-DoDDMA), trimethylolpropane trimethacrylate (TRIM) and pentaerythritol tetraacrylate (PETA)] by TERP. All columns gave good separations of alkylbenzenes under isocratic conditions. This is the first report of the separation of small molecules using methacrylate/acrylate monoliths synthesized via TERP.

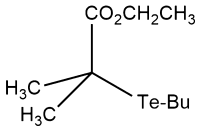
## 2. Experimental

### 2.1. Chemicals and reagents

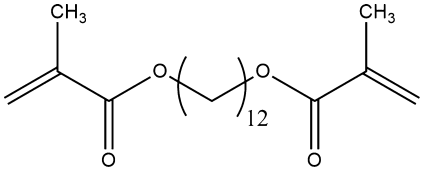
Reagents 2,2′-azobis(2-methylpropionitrile) (AIBN, 98%) and 3-(trimethoxysilyl)propyl methacrylate (TPM, 98%) were purchased from Sigma–Aldrich (St. Louis, MO, USA); 1,12-dodecanediol dimethacrylate (1,12-DoDDMA), trimethylolpropane trimethacrylate (TRIM) and pentaerythritol tetraacrylate (PETA) were gifts from Sartomer (Exton, PA, USA). Ethyl-2-methyl-2-butyltellanyl propionate (BTEE; see Fig. 1 for structure) was kindly supplied by Dr. Takashi Kameshima, Otsuka Chemical Co. (Osaka, Japan). Since BTEE is oxygen sensitive, it was stored in vials that had been carefully cleaned and dried, and all transfers were conducted inside a nitrogen glove box. Water, 1,4-butanediol, propylbenzene, butylbenzene, amylbenzene and uracil were obtained from Sigma–Aldrich; acetonitrile, *N*,*N*-dimethylformamide and ethylbenzene were purchased from Fisher Scientific (Pittsburgh, PA, USA); and toluene, cyclohexanol and ethylene glycol were purchased from Mallinckrodt (Phillipsburg, NJ, USA). All solvents and chemicals for preparation of monoliths and mobile phase buffers were HPLC grade or analytical reagent grade, and they were used as received.

### 2.2. Fused silica capillary pretreatment

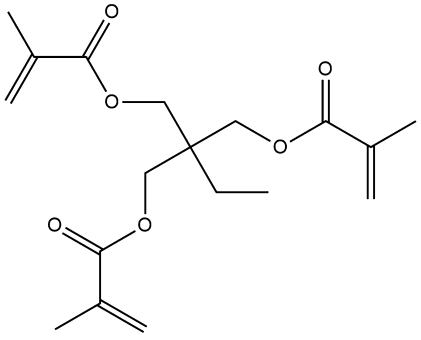
First, UV-transparent fused silica capillary tubing (75-μm, 100-μm, and 150-μm i.d., 375-μm o.d., Polymicro Technologies, Phoenix, AZ, USA) was treated with TPM in order to anchor the polymer to the capillary wall. The treatment procedures were reported by Vidič et al. [47] and Courtois et al. [48]. The capillary was connected to a syringe pump and washed with ethanol and then water for 30 min each. The inner surface of the capillary tubing was treated with 1 M NaOH solution at room temperature for 1 h. Both ends were then sealed with GC septa and the capillary was heated in a GC oven at 120 °C for 3 h. Then, the tubing was washed with



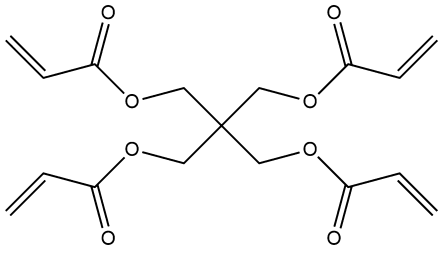

Ethyl-2-methyl-2-butyltellanyl propionate (BTEE)




1,12-Dodecanediol dimethacrylate (1,12-DoDDMA)



Trimethylolpropane trimethacrylate (TRIM)



Pentaerythritol tetraacrylate (PETA)

**Fig. 1.** Chemical structures of BTEE and multi-methacrylate/acrylate monomers.