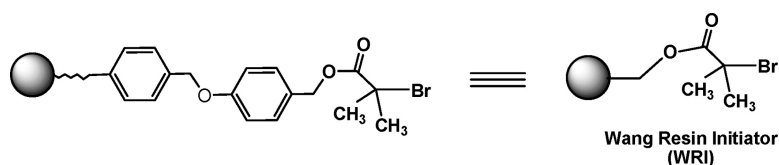Article

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Well-Defined Azlactone-Functionalized (Co)polymers on a Solid Support: Synthesis via Supported Living Radical Polymerization and Application as Nucleophile Scavengers

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Wang resin has been converted to a supported initiator for transition metal-mediated living radical polymerization often called atom-transfer radical polymerization (ATRP) of 2-vinyl-4,4-dimethyl-5-oxazolone (VDM) and styrene (S). Several "Rasta" resins with well-defined macromolecular architectures, including homopolymers PVDM, PS, statistical P(S-*stat*-VDM), block P(S-*b*-VDM), and P[S-*b*-(S-*stat*-VDM)] copolymers, have been elaborated. For the homopolymerization of VDM and S, a sacrificial initiator, benzyl 2-bromoisobutyrate (BBI), has been introduced to monitor the evolution of molar masses and polydispersity indexes (PDIs) of PS and PVDM onto the Wang resin support without cleavage. After 6 h, 86.7% conversion of VDM is reached, with the isolated PVDM chains having a molar mass of 18 000 g mol^{-1} and a PDI value of 1.22. Block copolymers have been synthesized in two steps, involving the synthesis of the PS block isolated at low conversions (<15%) to maintain the bromine end-chain functionality and the subsequent synthesis of the second PVDM or P(S-*stat*-VDM) block. Polydispersity indexes of the cleaved (co)polymers were low (PDI = 1.11−1.44), and high azlactone loadings have been reached (loading = 6.0 mmol g^{-1}). Such azlactone-functionalized Wang resins have shown high efficiency during the scavenging process of benzylamine as monitored by HPLC. Moreover, grafted statistical copolymers have shown the best behavior for removing benzylamine because of an improvement of the accessibility of azlactone rings by the dilution with styrene units.

Introduction

Much of work carried out in combinatorial chemistry has typically been associated with the solid-phase synthesis methodology pioneered by Merrifield more than 40 years ago.[1] In solid-phase synthesis, a starting reagent, covalently attached to a solid support is modified by one or more reactions. The final product is cleaved from the support and is recovered in a pure form. Solid-phase synthesis has gained in popularity as a result of the ease of separation of the final product from the reaction mixture and the ability to use a large excess of reagents to drive reactions to high yields.

However, solution-phase synthesis is often preferred as it provides a wide range of organic reactions.[2] The difficulties associated with this process include the purification processes required after each step of the synthesis to remove excess reagents and byproducts from the mixture. This has led to the development of solid-supported scavengers[3,4] which can selectively remove one or more components from the reaction mixture leaving a purified product in the solution. Different designs of such solid-supported scavengers have been reported. Recent studies have shown that porous polymer monoliths[5,6] and polyHIPE[7,8] materials can be used under flow-through conditions. However, most of the solid-supported scavengers are based on cross-linked functionalized polystyrene beads. Such materials are prepared by suspension copolymerization of monomers, such as styrene and divinylbenzene (DVB), with a functional monomer bearing a scavenging group, such as an isocyanate,[9] aldehyde,[10] or azlactone.[11] Another strategy is the introduction of a scavenging group onto the commercial polystyrene-based supports by chemical reactions. Since the pioneering work of Kaldor et al.[3] with the anchored isocyanate group, many electrophilic functional groups, such as aldehyde,[12,13] acid chloride,[3,14] or anhydride,[15] have been studied. A different approach to increase the density of the scavenging groups is grafting polymer chains from each surface active site of the solid support. Fréchet et al.[16,17] performed free radical polymerization of an azlactone-based monomer from porous polymer monolithic disks containing a conventional polymerization initiator. A polymer-supported ruthenium alkylidene metathesis catalyst has been reported[18] to initiate a ring-opening metathesis polymerization of norbornene derivatives to prepare novel high-loading resins for use in combinatorial chemistry. On the other hand, Hodges et al.[19] used nitroxide-

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mediated polymerization (NMP) to copolymerize 3-isopro-penyl-α,α-dimethylbenzylisocyanate with styrene onto Merrifield resin. Moreover, the use of NMP allows the length of all polymer arms to be controlled. These supports have been termed "Rasta" resins.[19]

In the present paper, supported copper-mediated living radical polymerization (ATRP) will be used to (co)polymerize 2-vinyl-4,4-dimethyl-5-oxazolone (VDM) onto a Wang resin to obtain "Rasta" resins with well-defined electrophilic functional polymers from the core bead.

Since the discovery of ATRP,[20−22] (co)polymers have been widely grafted onto many solid supports,[23,24] including silica, cross-linked polymers, gold, and carbon. Haddleton et al. polymerized N,N-dimethylacrylamide[25] and methyl methacrylate[26] from Wang resin via living radical polymerization using both CuBr/N-(n-octyl)-2-pyridylmethanimine and CuBr/N-(n-propyl)-2-pyridylmethanimine catalysts. Well-defined PMMA has been obtained with a low polydispersity index (PDI = 1.18) after 62% conversion. More recently, grafted copolymers, such as poly(*tert*-butyl acrylate-*b*-styrene), have been synthesized[27] onto a tritrpticin-functionalized Wang resin (tritrpticin is an antimicrobial peptide). Thereafter, hydrolysis of the *tert*-butyl acrylate units and the ester linkage between the beads and tritrpticin allowed tritrpticin-*b*-poly-(acrylic acid-*b*-styrene) with a molar mass of approximately 6100 g mol^{-1} to be obtained in solution. In an appropriate solvent, polymer micelles have been observed with the tritrpticin inside. Moreover, the polymers have shown biological activity.

We have previously demonstrated that well-defined (co)-polymers based on VDM can be obtained via ATRP[28] in solution. This present work consists of the homopolymerization and copolymerization by ATRP of VDM with styrene onto Wang resin to obtain a high azlactone loading (i.e., 6.0 mmol g^{-1}). The main advantage of using azlactone-functionalized solid supports as scavenging supports is that the ring-opening reaction by amines, alcohols, or thiols occurs without byproduct elimination.[29] Such materials, with well-defined macromolecular architecture arms, have been evaluated in the scavenging of benzylamine as a model compound.

Experimental Section

Materials. Benzylamine (99.5%), anisole (99%), styrene (Sty, 99%, Acros), and 2-vinyl-4,4-dimethyl-5-oxazolone (VDM, 99.4%, ISOCHEM) were vacuum distilled and stored at −15 °C following purification. N,N,N',N',N''-Pentamethylethylenetriamine (PMDETA, 99+%), toluene (99%), methanol (99%), diethyl ether, 2-bromoisobutyryl bromide (98%), trifluoroacetic acid (TFA, 99%), and Wang resin (0.9−1.1 mmol g^{-1}, 75−150 μm) were purchased from Acros and used as received. Triethylamine (Et$_3$N, 99%, Aldrich) was distilled prior to use. Tetrahydrofuran (THF, SDS), CDCl$_3$ (Euriso-Top, 99.9%), and basic alumina (Prolabo) were used as received. The ligand Me$_6$Tren[30] and the initiator benzyl 2-bromoisobutyrate[31] were prepared according to reported procedures. Copper(I) bromide (Aldrich, 99.99%) was purified according to the published procedure.[32]

Measurements. Monomer conversion was determined by ^{1}H NMR. ^{1}H NMR spectra were measured in CDCl$_3$ on a Bruker AC 200 MHz spectrometer. ^{13}C NMR spectra of the grafted PVDM onto Wang resin was carried out in CDCl$_3$ by gel-phase NMR on a Bruker 300 MHz NMR. Molar masses and molar mass distributions were measured using size exclusion chromatography (SEC) at 35 °C on a system equipped with a SpectraSYSTEM AS1000 autosampler a guard column (Polymer Laboratories, PL gel 5 μm Guard, 50 × 7.5 mm), 2 analytical columns (Polymer Laboratories, 2 PL gel 5 μm MIXED-D columns, 2 × 300 × 7.5 mm), and a SpectraSYSTEM RI-150 detector. The eluent used was THF at a flow rate of 1.0 mL min^{-1}. Polystyrene standards (580−483 × 10^3 g mol^{-1}) were used to calibrate the SEC. FTIR spectra of the Wang resin were recorded using a Nicolet Avatar 370 DTGS spectrometer in ATR mode. HPLC analyses were achieved on a Waters system with UV detector (254 nm) and a Prévail amide column 3 μm (4.6 mm ID, 150 mm length) at 40 °C. The mobile phase (1.0 mL min^{-1}) is based on an acetonitrile/buffer pH 4 in a volume ratio of 75/25. Elemental analyses were performed by the Service Central d'Analyses du Centre National de Recherche Scientifique, Gif-sur-Yvette (France).

Synthesis of Wang Resin Initiator (WRI). In a round-bottom flask, 10 g of commercial Wang resin (0.020 mol), THF (200 mL), triethylamine (6 mL, 0.042 mmol), and 2-bromoisobutyryl bromide (5.0 mL 0.04 mmol) were introduced. The reaction was carried out with mechanical stirring (100 rpm) at ambient temperature for 12 h. The beads were subsequently washed with THF, methanol, and water. The resins were then introduced into a Soxhlet apparatus and kept at reflux in THF for 12 h to remove residual salts. The product was filtered and dried overnight. FTIR (ATR): $\nu_{C=O}$ 1732 cm^{-1}. Elemental analysis: C, 79.1; H, 6.9; O, 5.7; Br , 8.3. A loading of approximately 1.0 mmol g^{-1} was calculated.

Typical ATRP onto Wang Resin. Wang resin initiator was introduced with CuBr in a reactor that was deoxygenated with three vacuum/argon fill cycles. A Schlenk tube was charged with monomers, toluene, anisole (internal standard), and if necessary, the soluble initiator; all liquids were degassed using the freeze/pump/thaw method. The solution was added to the reactor containing resin and CuBr via a cannula. The mixture was stirred with an orbital stirrer (Advanced ChemTech, PLS-6) at the desired temperature under argon, and then, the previously degassed ligand was added ($t = 0$). Samples were removed periodically via a degassed syringe for conversion monitoring and SEC analysis (after the cleavage procedure). After the reaction, the grafted resins were washed with THF and diethyl ether followed by a Soxhlet extraction in THF under argon for 12 h. Resins were then dried under vacuum to a constant mass.

Cleavage Procedure. The grafted beads (0.1 g) were introduced into a vial with 15 mL of dichloromethane, and trifluoroacetic acid (2 mL) was added dropwise. The mixture was kept under magnetic stirring at ambient temperature for 30 min. Filtration was ensured to isolate cleaved polymer. The polymer mixture was precipitated in methanol, recovered by evaporation, and dried under vacuum overnight prior to analysis.

Scheme 1. Synthesis of Wang Resin Initiator for Atom Transfer Radical Polymerization
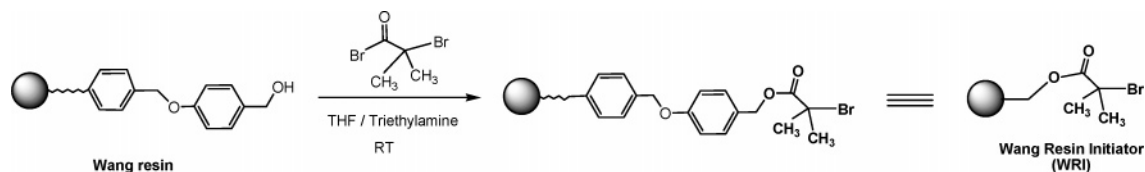
Scheme 2. Synthesis of Different Supported Architectures Based on VDM from Wang Resin Initiator
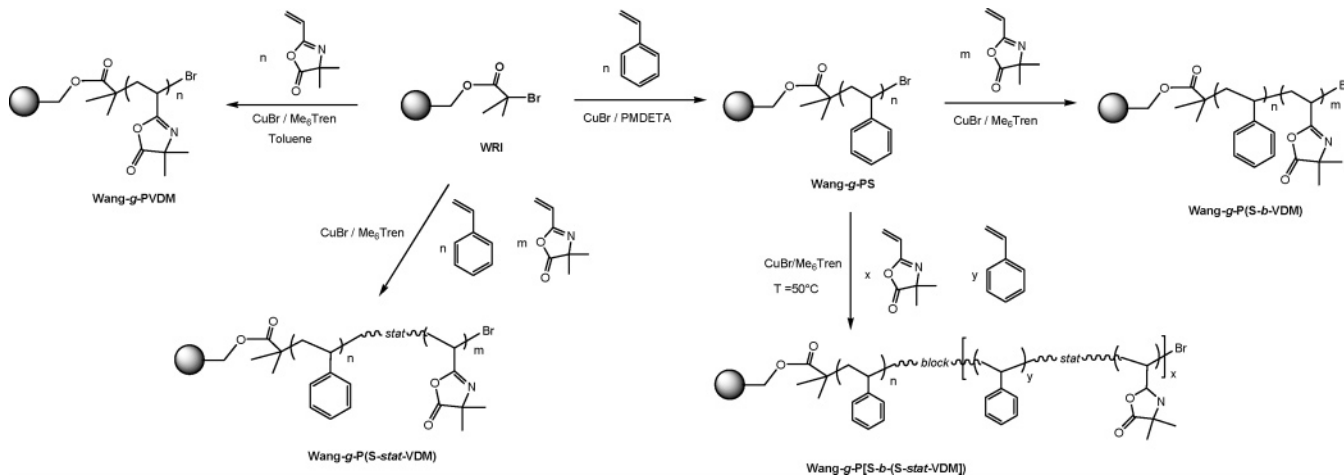
General Procedure for Scavenging Benzylamine with Azlactone Beads. Resin (100 mg, 1 equiv) and a small magnetic bar were introduced into a glass tube. Benzylamine (molar concentration = 0.08−0.1 mol L^{-1}, 1 equiv), toluene (internal standard, same volume as benzylamine), and THF (3−5 mL) were introduced ($t = 0$), and reactions were carried out at room temperature. After fixed time intervals, samples were withdrawn (volume = 50 μL) from the reaction mixture using a syringe and immediately injected into the HPLC apparatus to follow the disappearance of benzylamine versus toluene.

Results and Discussion

Synthesis of Well-Defined Supported Architectures. The synthesis of initiator-functionalized solid supports from Wang resins has already been reported[26] (Scheme 1). The reaction of Wang resin with a hydroxyl loading of 1 mmol g^{-1} with 2-bromoisobutyrate bromide was performed in the presence of triethylamine in THF at room temperature to get a Wang resin initiator (WRI).

WRI was characterized by FTIR spectroscopy, and the acylation of the benzylic hydroxyl groups of the resin is shown by the appearance of a C=O (ester) band at 1732 cm^{-1}; the bromine loading, determined by elemental analysis, is equal to 1.0 mmol g^{-1}. The copper-mediated living radical polymerization of VDM from the surface of the Wang resin was performed to provide solid supports with high azlactone loading. In this way, WRI was used as initiator, and CuBr/Me$_6$Tren was the catalytic system (Scheme 2) in 72/1/1/1 molar ratio (VDM/WRI/CuBr/Me$_6$Tren). Such a catalytic system was previously used to synthesize well-defined (co)-polymers based on VDM in solution.[28]

After 7 h, 65.5% conversion of VDM is reached, and the azlactone loading, determined by elemental analysis, is equal to 5.8 mmol g^{-1}. The PVDM-functionalized support was

characterized by FTIR spectroscopy and gel-phase ^{13}C NMR spectroscopy. The FTIR spectrum (Figure 1) showed strong stretching bands from azlactone rings at 1818 ($\nu_{C=O}$), 1203 (ν_{C-O-C}), and 1670 cm^{-1} ($\nu_{C=N}$).

The gel-phase ^{13}C NMR spectrum (Figure 2) shows signals from the azlactone group at 180.1 (C=O), 163.2 (C=N), 65.1 (C(CH$_3$)$_2$), and 24.3 ppm (C(CH_3)$_2$). The other peaks in the NMR spectrum originate from carbons in the poly-(styrene-co-divinylbenzene) core between 120 and 130 ppm. The cleavage of the polymer from the resin support via the benzylic ester linkage was performed using an excess of trifluoroacetic acid (TFA)[26] to monitor the molar masses and polydispersity index of the grafted PVDM. Unfortunately, the resulting polymer was not soluble in THF because of the opening of the azlactone group by traces of water which prove to be difficult to remove from TFA. The FTIR spectrum showed the appearance of a band at 1730 cm^{-1}, corresponding to an acid group, and the disappearance of the band at 1816 cm^{-1} relative to the carbonyl group of the azlactone ring. To circumvent this problem, a soluble initiator ("sacrificial" initiator), benzyl 2-bromoisobutyrate (BBI), was
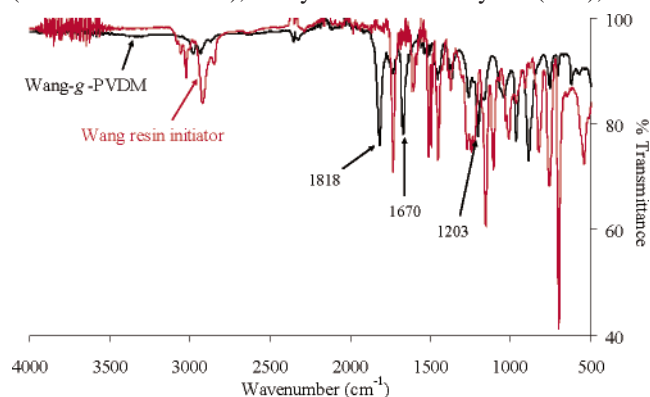

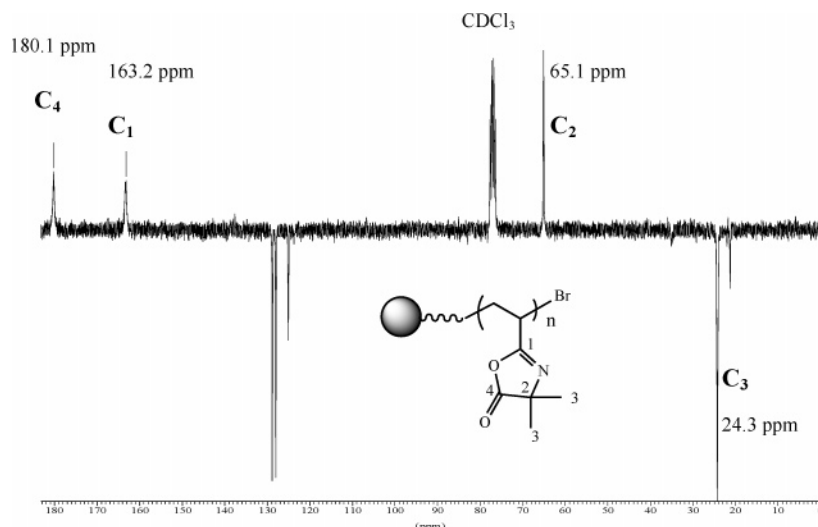**Figure 1.** FTIR spectra of Wang resin initiator and Wang-g-PVDM.

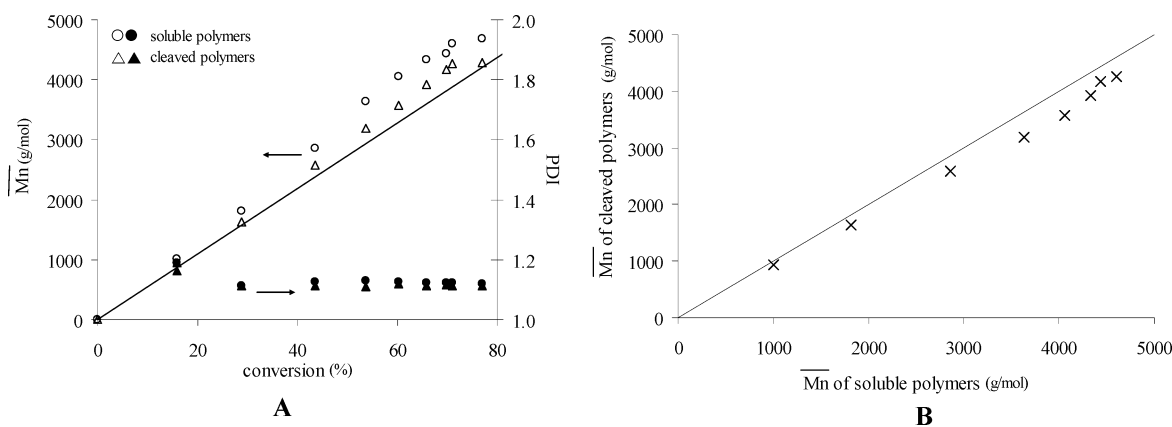**Figure 2.** 300 MHz gel-phase ^{13}C NMR spectrum of Wang-*g*-PVDM.

Figure 3. Dependence of molar mass and PDI on monomer conversion for solution and supported polymerization of styrene (A) and the relationship of molar mass between cleaved PS and soluble PS (B) (solid lines are the theoretical values): [styrene]$_0$/[WRI]$_0$/[BBI]$_0$/[CuBr]$_0$/[PMDETA]$_0$ = 100/1/1/2/2 in toluene (50% v/v) and anisole (5% v/v) at 90 °C.

added. Such a strategy was first applied by Fukuda et al.[33–36] who found that PMMA formed in solution and on a solid support have similar macromolecular characteristics (molar masses and PDIs). In this work, this approach was first used with styrene as monomer. ATRP of styrene with the supported initiator (WRI) and the soluble initiator (BBI) was carried out in toluene at 90 °C using styrene/WRI/BBI/CuBr/PMDETA in a 100/1/1/2/2 molar ratio. After the polymerization, soluble PS and cleaved PS were analyzed by SEC to compare the evolution of experimental molar masses and polydispersity indexes.

Figure 3A shows that the molar masses of both soluble PS and cleaved PS increased linearly when monomer conversion increased up to nearly 80% and the PDI decreased to 1.11. On the other hand, Figure 3B shows that the $\overline{M_{n,\text{SEC}}}$ values of cleaved PS are similar to the $\overline{M_{n,\text{SEC}}}$ values of soluble PS, indicating that the growth of polymer chains from the BBI initiator in solution and from WRI is similar. This very useful strategy was applied to VDM as the monomer. Subsequently, a copper-mediated radical polymerization of VDM with the supported initiator (WRI) and the soluble initiator (BBI) was carried out using VDM/WRI/BBI/CuBr/Me$_6$Tren in a 144/1/1/2/2 molar ratio. The polymerization

was performed in toluene at 50 °C, and 86.7% conversion of VDM was reached after 6 h.

The kinetic plot (Figure 4) shows that, although the reaction was initially fast, the propagation rate decreases after 1 h. This reveals a decrease of the active species concentration probably resulting from irreversible terminations which seems to be confirmed by higher experimental molar masses than theoretical ones (Figure 4). However, prominent irreversible terminations would have led to much higher PDI values than those obtained in our case (1.11 < PDI < 1.25). Another explanation of the decrease in the number of active species could be a progressive reduction of the concentration of the available catalyst by PVDM complexation.[28]

The addition of a sacrificial initiator resulted in the conversion of VDM reaching a very high value in a shorter time (conversion = 64.8% after 1 h) than in ATRP without BBI where the conversion reached 65.5% in 7 h. Moreover, the azlactone loadings of such materials, determined by elemental analysis, are high (between 5.8 and 6.0 mmol g^{-1}).

To investigate the potential to prepare block copolymers based on VDM and styrene on a Wang resin, the synthesis was attempted in two steps. First, a PS block was synthesized on the Wang resin. After it was isolated and purified, the Wang-*g*-PS was used in the second step as the supported
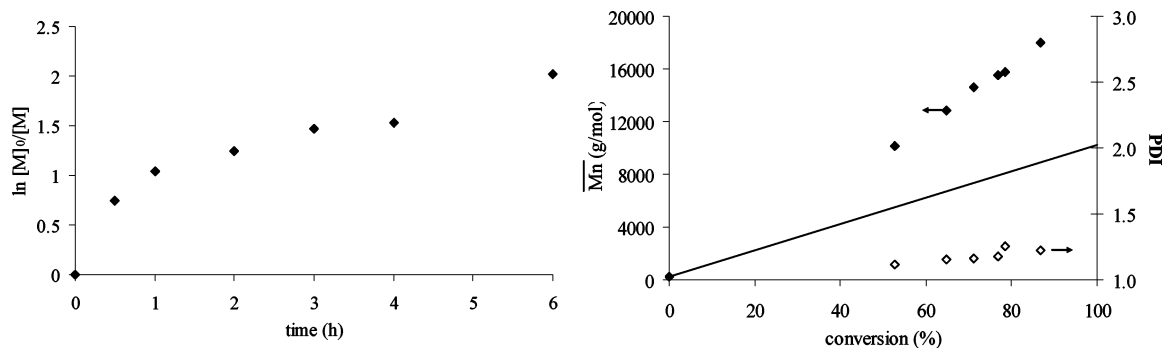
Figure 4. (A) Kinetic plot of the ATRP of VDM on WRI with sacrificial initiator added at 50 °C and (B) the dependence of the experimental molar masses and PDI on monomer conversion: $[VDM]_0/[WRI]_0/[BBI]_0/[CuBr]_0/[Me_6Tren]_0 = 144/1/1/2/2$ in toluene (66% v/v) and anisole (5% v/v) at 50 °C.

Table 1. Supported Block Copolymerization of VDM and Styrene[a]

	1st block PS					2nd block PVDM			Wang-g-P(S-b-VDM)				
	[Sty]/ [WRI]	$M_{n,SEC}$[c] (g mol^{-1})	$M_{n,theo}$[c] (g mol^{-1})	PDI	τ[d] (%)	[VDM]/ [Wang-g-PS]	τ[d] (%)	time (h)	$M_{n,SEC}$[b] (g mol^{-1})	$M_{n,theo}$[c] (g mol^{-1})	PDI	loading[e] (mmol g^{-1})	F_{VDM}[f]
WB$_{0.10}$	100/1	7000	4 780	1.08	44.3	100/1	8.8	24	7500	8200	1.11	nd	0.10
WB$_{0.81}$	100/1	1 500	1 620	1.17	14.0	100/1	55.1	5	$-$[g]	9200	$-$[g]	5.8	0.81
WB$_{0.64}$	250/1	3 950	4 100	1.10	15.1	200/1	23.9	2	7000	10 600	1.26	4.1	0.64
WB$_{0.68}$	250/1	3 950	4 100	1.10	15.1	200/1	36.3	1.2	10 750	14 000	1.44	4.2	0.68

[a] WB$_X$: W for Wang, B for block copolymer, and X for the VDM molar ratio in the copolymer. 1st block: $[WRI]_0/[CuBr]_0/[PMDETA]_0 = 1/1/1$, $T = 90$ °C, toluene (50% v/v), anisole (5% v/v). 2nd block: $[Wang-g-PS]_0/[CuBr]_0/[Me_6Tren]_0 = 1/1/1$, $T = 50$ °C, toluene (66% v/v), anisole (5% v/v). [b] SEC calibrated with PS standards. [c] $M_{n,theo} = ([monomer]_0/[initiator]_0) \times \tau_{monomer} \times M_{monomer} + M_{initiator}$. [d] Conversion calculated by ^{1}H NMR. [e] Determined by elemental analysis; azlactone loading = (%N/14)/100. [f] Molar ratio in the block copolymer. [g] The cleaved copolymer was insoluble.

macroinitiator for the ATRP of VDM (Scheme 2) to obtain Wang-g-P(S-b-VDM), also called WB$_X$ (W for Wang, B for block copolymer, and X for the VDM molar ratio in the copolymer).

A PS block was synthesized at 90 °C using a system based on WRI/CuBr/PMDETA in a 1/1/1 molar ratio. Several styrene/WRI molar ratios were used to get different experimental molar masses. Thus, several supported PS macroinitiators with experimental molar mass values between 1500 and 7000 g mol^{-1} and low polydispersity indexes (PDI < 1.17, Table 1) were obtained. These were subsequently used as macroinitiators to synthesize a second PVDM block. The first polymerization attempt was carried out with the macroinitiator having $\overline{M_{n,SEC}}$ of 7000 g mol^{-1} and led only to a small increase of the block copolymer molar mass ($\overline{M_{n,SEC}}$ = 7500 g mol^{-1}, WB$_{0.10}$, Table 1). This is the result of a loss of the bromine end-functional groups on the PS macroinitiator. To overcome this problem, conversions below 15% were targeted for the other PS macroinitiators (Table 1). In this case, well-defined block copolymers were obtained with low PDI (1.11 < PDI < 1.44). As an example, SEC traces of the cleaved PS macroinitiator and of the cleaved P(S-b-VDM) resulting the THF-soluble block copolymer (Figure 5) originating from the WB$_{0.68}$ sample (Table 1) show monomodal curves with no detectable quantities of unreacted macroinitiator. It indicates that the polymerization of the second block was initiated in high yield. The polydispersity index of the final block copolymer increased, indicating a slightly broad distribution of the PVDM block (PDI = 1.44). The azlactone loadings of such modified supports varied from 4.1 to 5.8 mmol g^{-1}.
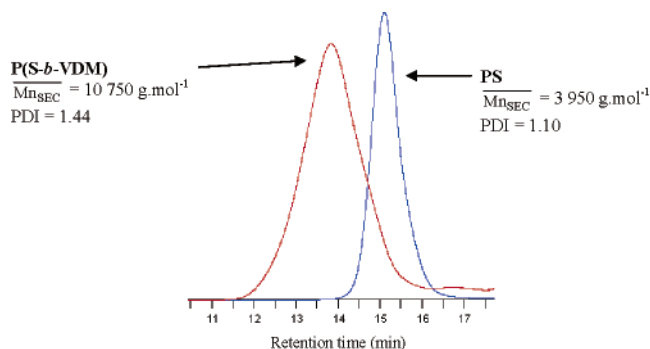

Figure 5. SEC traces of cleaved block copolymer PS-b-PVDM and macroinitiator PS-Br (WB$_{0.68}$, Table 1).

Statistical copolymers have been also prepared from Wang resin by ATRP to incorporate styrene units between VDM units. Copolymerizations of VDM ($r_{VDM} = 0.59$[37]) and styrene ($r_S = 0.50$[37]) were carried out in toluene at 60 °C using the system based on styrene/VDM/WRI/CuBr/Me$_6$Tren (Scheme 2) with an equimolar ratio of WRI/CuBr/Me$_6$Tren.

Characteristics of grafted statistical copolymers Wang-g-P(S-stat-VDM), also called WS$_X$ (W for Wang, S for statistical copolymer, and X for the VDM molar ratio in the copolymer) are summarized in Table 2.

When a high molar mass is targeted (WS$_{0.30}$, Table 2), the $\overline{M_{n,SEC}}$ is higher (14 700 g mol^{-1}) than the theoretical one (9300 g mol^{-1}), but the PDI value remains quite low (PDI = 1.30). In this case, the azlactone loading is equal to 2.6 mmol g^{-1}. Conversely, when lower molar masses are targeted (WS$_{0.33}$ and WS$_{0.50}$, Table 2), the $\overline{M_{n,SEC}}$ values are close to the theoretical values, and the PDI values are low

Table 2. Results from the Synthesis of Supported Statistical Copolymers[a]

	$[Sty]_0/[VDM]_0$	$\overline{M_{n,SEC}}$[b] (g mol^{-1})	$\overline{M_{n,theo}}$[c] (g mol^{-1})	PDI	τ_S[d] (%)	τ_{VDM}[d] (%)	F_{VDM}[e]	loading[f] (mmol g^{-1})
WS$_{0.30}$	160/40	14700	9300	1.30	34.7	60.4	0.30	2.6
WS$_{0.33}$	80/20	5650	6550	1.33	46.3	90.7	0.33	2.0
WS$_{0.50}$	50/50	3900	3400	1.30	26.7	26.5	0.50	3.1

[a] WS$_X$: W for Wang, S for statistical copolymer, and *X* for the VDM molar ratio in the copolymer. $[WRI]_0/[CuBr]_0/[Ligand]_0 = 1/1/1$, $T = 60\,°C$ (ligand Me$_6$Tren, WS$_{0.30}$, and WS$_{0.33}$), $T = 90\,°C$ (ligand PMDETA, WS$_{0.50}$), toluene (50% v/v), and anisole (5% v/v). [b] SEC calibrated with PS standards. [c] $\overline{M_{n,theo}} = ([VDM]_0/[WRI]_0 \times \tau_{VDM} \times M_{VDM}) + ([Sty]_0/[WRI]_0 \times \tau_S \times M_S) + M_{initiator}$. [d] Monomer conversion calculated by ^{1}H NMR. [e] Molar ratio in the statistical copolymer. [f] Determined by elemental analysis; azlactone loading = (%N/14)/100.

Table 3. Synthesis of Supported Copolymers P[S-*b*-(S-*stat*-VDM)] Obtained by ATRP[a]

|	1st PS block					2nd P(S-*stat*-VDM) block				P[S-*b*-(S-*stat*-VDM)]			support
	$[Sty]/[WRI]$	$\overline{M_{n,SEC}}$[b] (g mol^{-1})	$\overline{M_{n,theo}}$[c] (g mol^{-1})	PDI[a]	τ_S[d] (%)	time (h)	τ_{VDM}[d] (%)	τ_S[d] (%)	F_{VDM}[e]	$\overline{M_{n,SEC}}$[b] (g mol^{-1})	$\overline{M_{n,theo}}$[f] (g mol^{-1})	PDI[b]	loading[g] (mmol g^{-1})
WBS$_{0.30}$	100/1	1 900	1 600	1.13	13.8	8	41.7	24.9	0.30	12 000	8 400	1.40	2.2
WBS$_{0.24}$	250/1	3 950	4 100	1.10	15.1	3.75	19.0	21.3	0.24	7 750	8 560	1.20	1.2

[a] WBS$_X$: W for Wang, B for block copolymer, S for statistical copolymer, and *X* for the VDM molar ratio in the copolymer. 1st block: $[WRI]_0/[CuBr]_0/[PMDETA]_0 = 1/1/1$, $T = 90\,°C$, toluene (50% v/v), anisole (5% v/v). 2nd block: $[Sty]_0/[VDM]_0/[Wang-g-PS]_0/[CuBr]_0/[Me_6Tren]_0 = 160/40/1/1/1$ (WBS$_{0.30}$), 147/53/1/1/1 (WBS$_{0.24}$), $T = 60\,°C$, toluene (66% v/v), anisole (5% v/v). [b] SEC calibrated with PS standards. [c] $\overline{M_{n,theo}} = ([Sty]_0/[WRI]_0) \times \tau_S \times M_S + M_{initiator}$. [d] Monomer conversion calculated by ^{1}H NMR. [e] Molar ratio in the second statistical block. [f] $\overline{M_{n,theo}} = M_{PS} + ([VDM]_0/[Wang-PS]_0) \times \tau_{VDM} \times M_{VDM}) + ([Sty]_0/[Wang-PS]_0 \times \tau_S \times M_S)$. [g] Determined by elemental analysis; azlactone loading = (%N/14)/100.

(PDI = 1.33 and 1.30). Furthermore, the azlactone loadings are equal to 2.1 (WS$_{0.33}$, Table 2) and 3.0 mmol g^{-1} (WS$_{0.50}$, Table 2).

Finally, a copolymer based on a first PS block followed by a statistical copolymer P(S-*stat*-VDM) was synthesized by ATRP, namely, WBS$_X$ (W for Wang, B for block copolymer, S for statistical copolymer, and *X* for the VDM molar ratio in the copolymer). Such an architecture based on methacrylates has been previously reported in only one step by Haddleton et al.:[26] Wang-*g*-P[MMA-*b*-(BMA-*stat*-MMA)]. The strategy chosen in our case consisted of the synthesis of Wang-*g*-P[S-*b*-(S-*stat*-VDM)] in two steps (Scheme 2).

The first step is the synthesis of a well-defined supported PS block by ATRP, and the second step is the synthesis of a statistical copolymer. In this way, the advantages of block and statistical copolymers previously described were combined. PS macroinitiators were synthesized by the ATRP of styrene at 90 °C with a system based on styrene/WRI/CuBr/PMDETA. Two different styrene/WRI molar ratios (100/1 and 250/1) were used to get two different lengths of macroinitiators. Conversions below 15% were targeted for the bromine end-group to survive the reaction.

For the lower styrene/WRI molar ratio, a macroinitiator with a $\overline{M_{n,SEC}}$ value of 1900 g mol^{-1} and a PDI value of 1.13 was obtained after a 13.8% conversion of styrene. This was then used to reinitiate the styrene and VDM mixture in a 160/40 molar ratio using CuBr/Me$_6$Tren in a 1/1 molar ratio. Copolymerization was been carried out in toluene at 60 °C (WBS$_{0.30}$, Table 3). The experimental molar mass ($\overline{M_{n,SEC}} = 12\,000$ g mol^{-1}) of the resulting P[S-*b*-(S-*stat*-VDM)] copolymer was slightly higher than the theoretical one ($\overline{M_{n,theo}} = 8400$ g mol^{-1}), and the polydispersity index was 1.40, indicating a slightly broad distribution of the second statistical block.
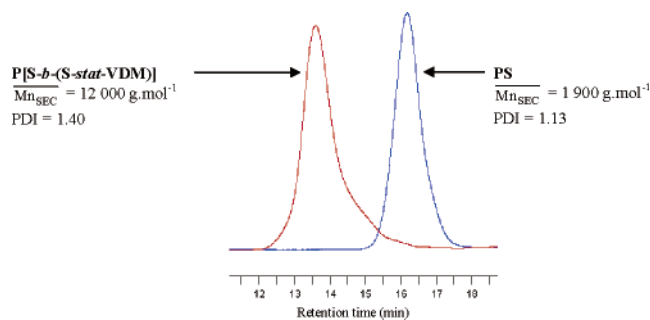
Figure 6. SEC traces of cleaved block copolymer P[S-*b*-(S-*stat*-VDM)] and macroinitiator PS-Br (WBS$_{0.30}$, Table 3).

With a styrene/WRI molar ratio of 250/1, a macroinitiator with a slightly higher molar mass was obtained ($\overline{M_{n,SEC}} = 3950$ g mol^{-1}) at 15.1% conversion (PDI = 1.10). The statistical copolymerization using this second macroinitiator led to a P[S-*b*-(S-*stat*-VDM)] copolymer ($\overline{M_{n,SEC}} = 7750$ g mol^{-1}) of low polydispersity (PDI = 1.20).

Figure 6 shows the SEC traces of the P[S-*b*-(S-*stat*-VDM)] and the PS macroinitiator for the WBS$_{0.30}$. A monomodal curve with no detectable amount of unreacted macroinitiator was observed indicating efficient polymerization of the second block. Azlactone loadings remained high (1.2 and 2.2 mmol g^{-1}), even when styrene units were incorporated into the copolymer.

Use of the Azlactone-Functionalized Wang Resins in the Scavenging Process. The previous azlactone-functionalized (co)polymers grafted onto Wang resin, including homopolymers (WH, H for homopolymer, corresponding to Wang-*g*-PVDM), block (WB), and statistical (WS) copolymers, have been tested as amine scavengers. The main advantage of such an azlactone ring-opening addition is that this reaction occurs without byproduct elimination.[29] In this study, a primary amine, benzylamine, was selected as a model compound. The scavenging experiments were per-
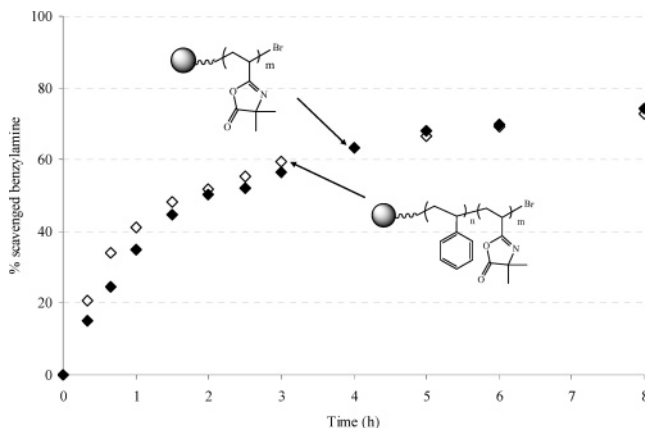
Figure 7. Effect of a PS spacer on the rate of benzylamine scavenging with support WH (◆) and support $WB_{0.68}$ (◇) at ambient temperature with an azlactone/benzylamine molar ratio of 1/1.

Figure 8. Scavenging studies using block copolymers Wang-*g*-P(S-*b*-VDM) with support $WB_{0.64}$ (○) and support $WB_{0.68}$ (△) at ambient temperature with an azlactone/benzylamine molar ratio of 1/1.

Figure 9. Scavenging studies using statistical copolymers Wang-*g*-P(S-*stat*-VDM) with support $WS_{0.30}$ (○), support $WS_{0.33}$ (△), and support $WS_{0.50}$ (◇) at ambient temperature with an azlactone/benzylamine molar ratio of 1/1.

formed in THF at 25 °C. The kinetics of benzylamine consumption was monitored by HPLC using toluene as an internal standard. The influence of a PS spacer on the amount of scavenged benzylamine was studied by comparison of WH with WB structures and WS with WBS structures. The kinetics of the benzylamine scavenging using WH and $WB_{0.68}$ are shown in Figure 7.

Figure 7 shows that the reactivity of the azlactone-functionalized supports is similar; after 24 h of reaction, 86.1% of the benzylamine has reacted with WH and 84.1% with $WB_{0.68}$. It appears that a PS spacer ($\overline{M}_{n,SEC}$ = 3950 g mol^{-1}) does not lead to a significant improvement of the scavenging. Similar results are observed regarding the comparison between the azlactone materials $WS_{0.30}$ and $WBS_{0.30}$. The results of the scavenging process have shown that 79% of the benzylamine has reacted after 24 h with $WS_{0.30}$ and 65.7% of the benzylamine with $WBS_{0.30}$ after 24 h. It indicates also that anchoring a PS spacer ($\overline{M}_{n,SEC}$ = 1900 g mol^{-1}) did not improve the efficiency of such azlactone supports.

In the block copolymers, $WB_{0.64}$ and $WB_{0.68}$, the first PS block is similar ($\overline{M}_{n,SEC}$ = 3950 g mol^{-1}) in both cases, but the molar mass of the second PVDM block is lower for $WB_{0.64}$ ($\overline{M}_{n,SEC}$ = 3050 g mol^{-1}) than for $WB_{0.68}$ ($\overline{M}_{n,SEC}$ = 6 800 g mol^{-1}). The kinetic behavior of the benzylamine scavenged, reported in Figure 8, shows that the rates of immobilization reaction are very close for $WB_{0.64}$ and $WB_{0.68}$.

After 24 h of reaction, it was found that 1 equiv of $WB_{0.64}$ and of $WB_{0.68}$ was able to remove 81.4 and 84.1%, respectively, of the benzylamine. Thus, in this case, the size of the second block appears to have no effect on the efficiency of the scavenger. Moreover, whatever the grafted polymers (homopolymers or block copolymers) used as scavengers, incomplete reactions were achieved, and therefore, a portion of the azlactone groups do not participate in the reaction with the amine. In the VDM blocks, after the opening of the azlactone rings, amide links are created at each monomer unit. As THF is a nonsolvent for polyacrylamides and its derivatives,[38,39] a plausible explanation for the incomplete reaction could be the presence of coils surrounding the bead because of the presence of a nonsolvent.
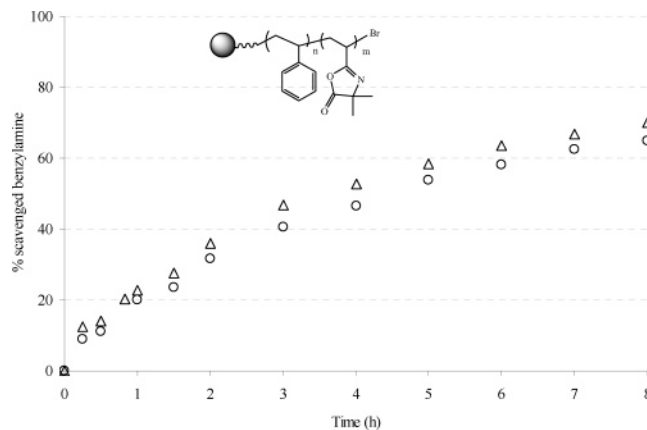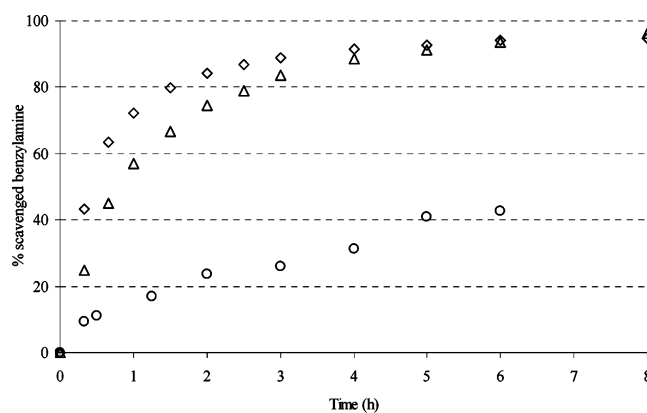
To overcome this problem, a study on benzylamine scavenging process was performed using different grafted statistical copolymers, $WS_{0.50}$, $WS_{0.33}$, and $WS_{0.30}$, in which the distance between azlactone rings is effective because of the incorporation of styrene units. The grafted statistical copolymers have different experimental molar masses ($WS_{0.50}$, $\overline{M}_{n,SEC}$ = 3900 g mol^{-1}; $WS_{0.33}$, $\overline{M}_{n,SEC}$ = 5 650 g mol^{-1}; $WS_{0.30}$, $\overline{M}_{n,SEC}$ = 14 700 g mol^{-1}). The VDM molar ratios in the copolymer (F_{VDM}) are 0.50, 0.33, and 0.30, respectively.

Two different behaviors were observed during the scavenging process: $WS_{0.50}$ and $WS_{0.33}$ supports reacted very rapidly to a nearly complete reaction (98.5% of the benzylamine was removed from the solution for $WS_{0.50}$ and 96.8% for $WS_{0.33}$ after 24 h), while the immobilization of benzylamine is much slower with $WS_{0.30}$ (79.0% of scavenged benzylamine after 24 h). Thus, to explain the difference of reaction rate, $WS_{0.33}$ and $WS_{0.30}$ supports must be considered as they contain the same VDM proportion in the copolymer, while the molar mass of the grafted copolymer from $WS_{0.30}$ is higher ($\overline{M}_{n,SEC}$ = 14 700 g mol^{-1}, Table 2) than that from $WS_{0.33}$ ($\overline{M}_{n,SEC}$ = 5650 g mol^{-1}, Table 2). Better results were then obtained with arms of a lower molar mass. When the arms are longer, the copolymer could be confined around
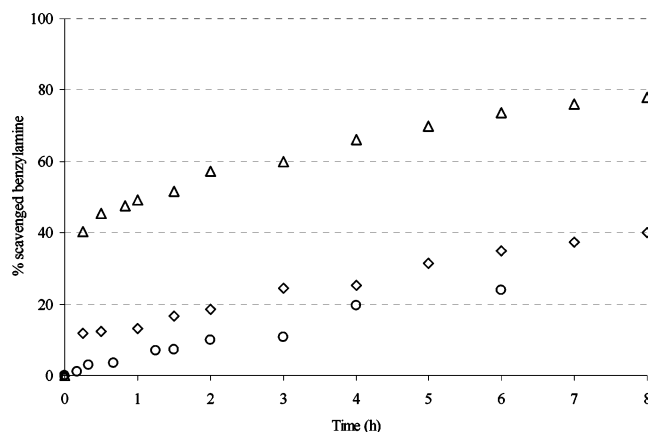
Figure 10. Scavenging studies using grafted copolymers Wang-*g*-P[S-*b*-(S-*stat*-VDM)] with support WBS$_{0.24}$ (○), support WBS$_{0.30}$ (△), and support WBS$_{0.48}$ (◇) at ambient temperature with an azlactone/benzylamine molar ratio of 1/1.

itself, limiting the accessibility of the azlactone rings. Thus, the structure of statistical copolymers P(S-*stat*-VDM) involves a distance between the azlactone rings and improves the efficiency in the scavenging process with regard to the Wang-*g*-PVDM resins when experimental molar masses, in our case, are not too high.

The last studied architecture was Wang-*g*-P[S-*b*-(S-*stat*-VDM)] which combines both advantages previously described: a PS spacer to move the azlactone rings away from the core of the beads and a second statistical block to create a distance between each VDM unit. Figure 10 shows the kinetic behavior of benzylamine scavenged for the three different supports (Table 3).

It appears that WBS$_{0.48}$ scavenges benzylamine at a higher rate than the other supports tested. Moreover, at the end of the reaction (24 h), 90.3% of the benzylamine was anchored onto WBS$_{0.48}$, while 65.7 and 68.3% were anchored onto WBS$_{0.30}$ and WBS$_{0.24}$, respectively. In the case of the WBS$_{0.30}$ and WBS$_{0.48}$ supports, the first PS block is similar, but the length of the second statistical block is higher in the case of WBS$_{0.30}$ ($\overline{M_{n,SEC}}$ = 12 000 g mol^{-1}) compared to that of WBS$_{0.48}$ ($\overline{M_{n,SEC}}$ = 2600 g mol^{-1}). Thus, a longer statistical copolymer block seems to be a drawback because it confined itself, as observed with the simple statistical copolymers. When the molar mass is not too high, a good efficiency can be reached to remove benzylamine from the medium.

Conclusions

The modification of Wang resin into a supported ATRP initiator was successfully used for the ATRP of VDM and styrene to obtain "Rasta"-functionalized resins. Well-defined homopolymers, based on PVDM and PS, were synthesized using the sacrificial initiator strategy. Block copolymers P(S-*b*-VDM) were also elaborated via ATRP, and well-defined architectures were obtained (PDI = 1.11−1.44). In addition, different statistical copolymers P(S-*stat*-VDM) were synthesized by changing the VDM molar ratio (F_{VDM}) in the copolymer from 0.30 to 0.50. Experimental molar masses between 3900 and 14 700 g mol^{-1} with low polydispersity indexes (PDI = 1.30−1.33) were obtained. Wang-P[S-*b*-(S-*stat*-VDM)] was successfully elaborated in two steps with

low polydispersity indexes (PDI = 1.20 and 1.40). The azlactone loadings reach high values (i.e., 6.0 mmol g^{-1}).

Thus, supported ATRP has allowed the preparation of "Rasta" resins with different well-defined architectures containing electrophilic groups. The supports have been studied in a scavenging process with benzylamine. The results illustrate the influence of the architecture of the grafted (co)polymer: grafted homopolymers and block copolymers show good efficiency in the removal of benzylamine, although the proximity of the azlactone rings prevents the reaction from being quantitative. The best results in terms of reactivity and efficiency toward benzylamine were observed with grafted statistical copolymers. Such result could be explained by an improvement of the accessibility of the azlactone rings by the presence of styrene units between azlactone units.

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