

“Exhaustive” Baeyer–Villiger Oxidation of Poly(Methyl Vinyl Ketone) and Its Copolymers

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ABSTRACT: Poly(vinyl acetate) and its copolymers represent an important class of commodity polymers. However, the preparation of copolymers of vinyl acetate (VAc) and more activated monomers (MAMs) *via* copolymerization is greatly restricted due to their disparate reactivities. Issues relating to reactivity ratios remain a fundamental challenge in copolymerization. Herein, we describe a post-polymerization modification approach using poly(methyl vinyl ketone-*co*-MAM)s as substrates to access synthetically challenging poly(VAc-*co*-MAM)s. Although the direct translations of existing small-molecule Baeyer–Villiger (BV) protocols into a post-polymerization modification method failed, a mechanism-guided multi-parameter optimization on polymer substrates disclosed a set of unique “exhaustive” BV protocols which enabled a nearly quantitative functionalization without obvious chain scission or cross-linking. Furthermore, a one-pot copolymerization/“exhaustive” BV post-modification procedure was developed to produce such copolymers in a convenient and scalable manner. This user-friendly methodology is able to access diverse poly(VAc-*co*-MAM)s including both statistical and narrow-dispersed block copolymers and could greatly facilitate the exploration of applications with such materials.

INTRODUCTION

Poly(vinyl acetate) (PVAc) homo- and copolymers such as poly(ethylene-VAc) (EVA) are essential materials in the polymer industry.^{1–3} In addition, a number of other widely used polymer materials such as poly(vinyl alcohol) (PVA), poly(vinyl acetal) (Vinylon), and ethylene-vinyl alcohol copolymer (EVOH) are prepared from either PVAc or EVA.^{4,5} Although PVAc-derived copolymers are highly valuable, many PVAc copolymers, in particular those with more activated monomers (MAMs), are rarely accessed by conventional copolymerization approaches.⁵ The ability for copolymerization of VAc with MAMs is greatly restricted by the reactivity ratios^{5,6} of the monomers. Indeed, copolymerization cannot occur effectively when two or more monomers have disparate reactivities. One notable example is that styrene (St) inhibits the polymerization of vinyl acetate (VAc) due to their marked difference in reactivity ratio.^{5,7,8} In addition to the synthesis of statistical copolymers, the synthesis of block copolymers of VAc and MAMs remains challenging as well.^{9–20} Indeed, limited access to poly(VAc-*co*-MAM) copolymers significantly deters the exploration of their material applications. It is therefore highly desirable to develop a general method for their preparation.

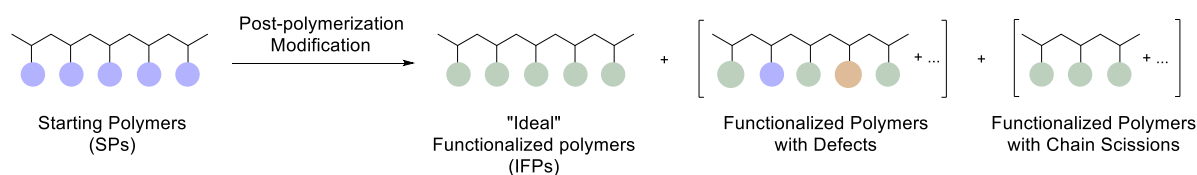
An alternative strategy for copolymer synthesis is post-polymerization modification.^{21–29} Although the majority of post-modification reactions can partially functionalize a homopolymer, post-polymerization modifications reaching

“exhaustive” (nearly quantitative) functionalization remain elusive. Notably, the development of an “ideal” or “exhaustive” post-polymerization modification reaction is even more technically challenging than that of its small-molecule prototype (Scheme 1A and Figure S1). As such, any deviation from an “ideal” post-modification will be significantly magnified with an increase in the degree of polymerization (DP) of the polymer, thereby making the post-modification of polymers with high molecular weight (MW) particularly difficult. An “exhaustive” post-polymerization modification reaction requires both a high degree of mechanistic fidelity and sufficient functionalization rates to prevent the production of defects,^{30,31} chain scission and/or cross-linking,^{26,32} since any side reaction will negatively alter the properties of the resultant polymers. Indeed, besides a number of conventional post-modification methods such as hydrolysis,^{5,22,33} isocyanate chemistry,^{22,23,25} activated ester chemistry,^{22,23,25,34} and hydrogenation,²³ only a few types of transformations have ever advanced into the category of “exhaustive” post-modification methods, most of which are “click” reactions^{35–37} and multicomponent reactions.^{25,38,39} Recently, a number of mechanistically diverse transformations have been translated into efficient post-polymerization modification methods including Hunsdiecker-type decarboxylative fluorination,⁴⁰ hydride reduction,^{41,42} organoborane oxidation,^{43,44} and Lewis acid-catalyzed silane reduction.⁴⁵

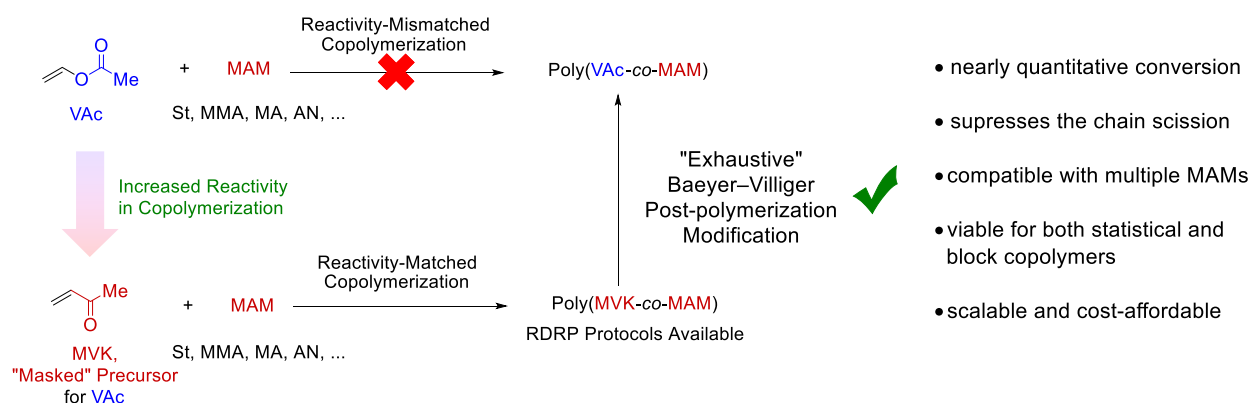
Encouraged by these accomplishments, we proposed that PVAc units within copolymers could be prepared from units of a

Scheme 1. Accessing Synthetically Challenging Poly(VAc-co-MAM)s with an “Exhaustive” Baeyer–Villiger Post-polymerization Modification

A. Fundamental Challenges in Post-polymerization Modification



B. A General Approach to Access Synthetically Challenging Poly(VAc-co-MAM)s



“masked” monomer *via* an “exhaustive” post-modification reaction. Under such circumstances, the synthesis of poly(VAc-co-MAM)s could be achieved if the “masked” monomer is more active and can thereby copolymerize with other MAMs. Preferably, the “masked” monomer would be commercially available and compatible with multiple reversible deactivation radical polymerization (RDRP) techniques. After an extensive evaluation of commercial monomers and organic transformations, we turned our attention to methyl vinyl ketone (MVK) and Baeyer–Villiger (BV) oxidation (Scheme 1B). Herein, we present an “exhaustive” BV post-modification method that is able to prepare a wide range of homopolymers, statistical, and block copolymers of VAc from commercially available poly(methyl vinyl ketone) (PMVK) and various PMVK copolymers. The efficiency of this method ensures that almost every ketone site on the PMVK segment is converted into an ester while the MW and the dispersity (D) of polymers remain essentially unchanged during oxidation.

RESULTS AND DISCUSSION

Design and Technical Considerations for an “Exhaustive” BV Post-modification of PMVK. MVK is structurally related to VAc but is much more active in radical polymerizations.⁵ It is able to copolymerize with almost all of the “more activated monomers” (MAMs) at any designated ratio.^{5,46} Furthermore, RDRP protocols of vinyl ketone monomers have been recently demonstrated by Wooley,⁴⁷ Studer,⁴⁸ Hawker,⁴⁹ Fu,⁵⁰ and others.^{51,52} Mechanistically, the conversion of PMVK to PVAc could be realized by BV oxidation. However, multiple side-reaction pathways such as aldol reaction/condensation, undesired oxidation and radical cleavage are associated with BV

oxidation.^{53–56} Although side products can be readily removed from the reaction mixtures of small-molecule reactions, this is not possible for polymer post-modification. In addition, such side reactions could negatively affect the MW and D of polymers. Additional uncertainty comes from the regioselectivity of BV oxidation since such selectivity for a polymer substrate has never been established. To provide a general approach for the synthesis of poly(VAc-co-MAM)s, we had to suppress the side-reaction pathways of BV oxidation and develop an “exhaustive” BV post-modification reaction of PMVK and its copolymers with high efficiency and regioselectivity.

Initial Attempts Using Classical BV Protocols. Pioneering efforts^{57–59} to bring BV oxidation into the field of post-polymerization modification suffered from a lack of reactivity and/or significant chain scission. Conventional BV oxidation conditions^{53,54,56} appeared to be destructive and incompatible with ketone-containing polymers. To obtain more mechanistic details, we decided to re-investigate this transformation using PMVK as a substrate.⁶⁰ We first evaluated the influence of temperature and reaction time using a commercial PMVK sample (Figure 1 and Table S2). The BV oxidations of PMVK were conducted using a typical protocol of chloroform as a solvent and *m*-chloroperoxybenzoic acid (*m*CPBA) as an oxidant. Although higher conversions were obtained with prolonged periods at elevated temperatures, the MW of the polymers decreased significantly. Noticeably, our kinetic studies revealed that the BV post-modification proceeded rapidly during the early stages, but became sluggish after 24 h. Consistent with the early investigations,^{57–59} our results also suggested that the standard BV oxidation conditions were not efficient

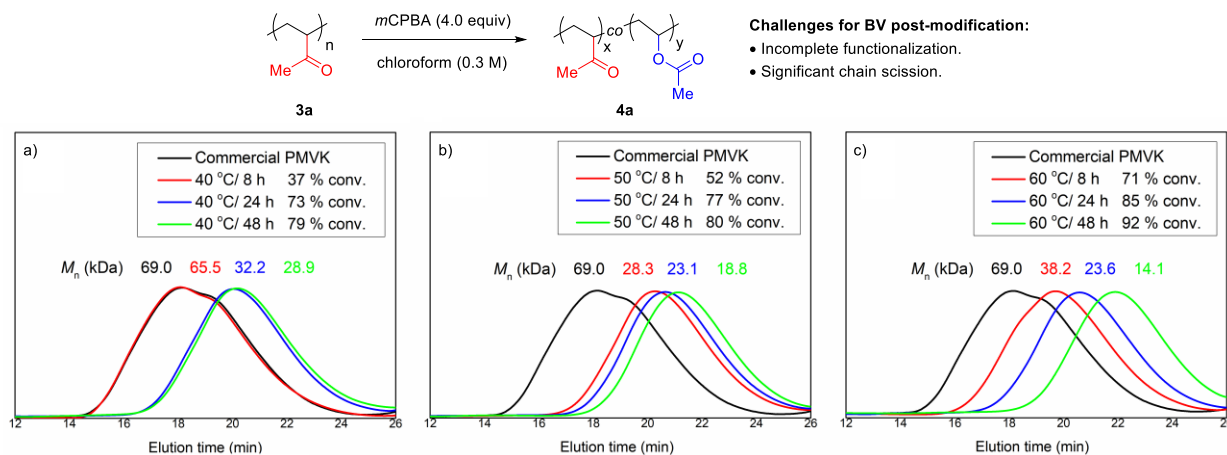


Figure 1. The influence of temperature and reaction time on the BV oxidation of PMVK in chloroform. SEC traces of commercial PMVK **3a** before and after BV oxidation at (a) 40 °C, (b) 50 °C and (c) 60 °C with different reaction time.

enough to complete the proposed post-modification of PMVK.

Attempts at the Translation of Small-molecule Protocols to PMVK. A small-molecule model using 3-hexylundecan-2-one as a substrate was established at the outset of this study. A large number of high-yielding conditions from the literature were screened and modified (Table S1). Unfortunately, the direct translation of small-molecule protocols to the post-modification of PMVK completely failed (Figure 2 and Table S3). The M_n of the polymers decreased significantly with the use of either acids or bases (Figure 2a and b). In addition, the use of alternative oxidants such as peracetic acid (PAA), trifluoroperoxyacetic acid (TFPAA), and magnesium monoperoxyphthalate hexahydrate (MMPP) gave even worse results (Figure 2c).

The failure of the translation of the small-molecule model to PMVK suggests that the reactivity of a molecule with a single functional group such as 3-hexylundecan-2-one is quite different from that of PMVK. For a polymeric substrate, the electronic and steric interactions between functional groups will significantly affect its reactivity and possibly induce additional side reactions. Therefore, a small-molecule model would not always be able to guide the development of synthetic methods for polymers and other macromolecules.

Accordingly, we turned our focus to PMVK instead of the small-molecule model compound in the following studies. Based on the estimation in Figure S1, the MW of a polymer with DP = 1000 will be cut in half even if only 0.1% chain scission were to occur during post-modification. Therefore, the suppression of side reaction pathways was considered highly important for the post-modification reaction. A literature survey revealed multiple side reaction pathways^{53–56} for BV oxidation. For example, acid-induced radical generation⁵⁵ which is reported to be able to initiate even at low temperatures could cause significant chain scission. In addition, oxidative decomposition^{61,62} instigated by excessive oxidants, or Aldol-type condensations^{63–65} promoted by acid or base could also complicate the post-polymerization modification. A combination of a literature survey and our preliminary results suggested that a comprehensive evaluation of PMVK under BV conditions was required.

Development of the BV Oxidation of Commercial PMVK Homopolymers. We first identified that the combination of carbon-13 and proton nuclear magnetic resonance spectroscopy (¹³C and ¹H NMR) was a reliable method to quantitatively

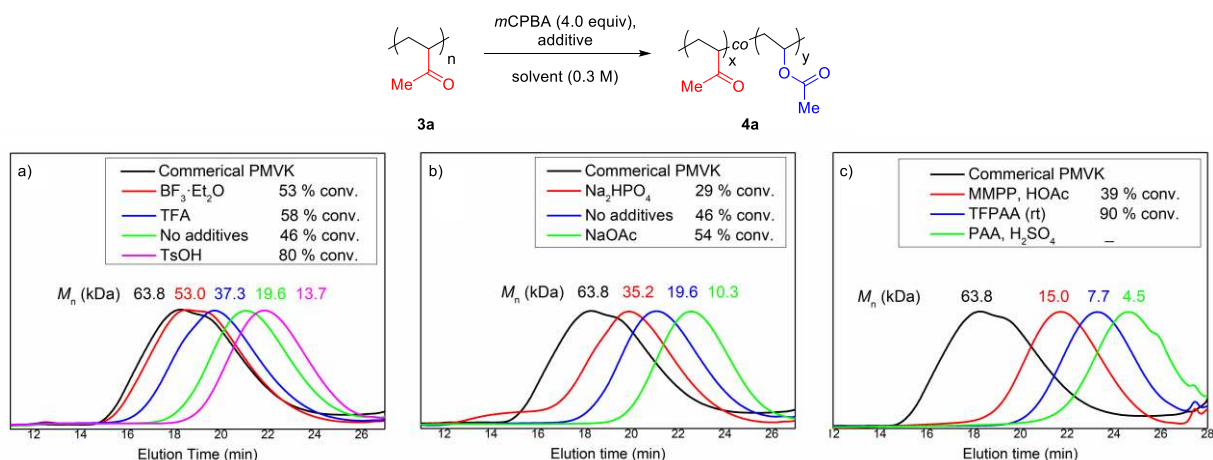


Figure 2. BV oxidation of PMVKs using high-yielding conditions optimized for the small-molecule model. SEC traces before and after BV oxidations: (a) acid catalyst, *m*CPBA as oxidant, (b) in the presence of inorganic base, *m*CPBA as oxidant, (c) MMPP and other peroxyacids as oxidant. (See the detailed conditions in Table S3.)

Table 1. The Effect of Solvent on the BV Oxidation of Commercial PMVK 3a^a

Entry	Solvent	Conversion ^b (%)	$M_{n,SEC}$ ^c (kDa)	\bar{D} ^c	Entry	Solvent	Conversion ^b (%)	$M_{n,SEC}$ ^c (kDa)	\bar{D} ^c
1	CHCl ₃	55	36.1	2.18	12	DMF	11	60.8	2.53
2	CH ₂ Cl ₂	44	41.9	2.27	13	<i>n</i> -hexane	86	64.0	2.43
3	DCE	52	61.9	2.50	14	toluene	34	63.6	2.61
4	EtOAc	23	63.9	2.45	15	(trifluoromethyl)benzene	80	63.7	2.44
5	THF	14	60.8	2.58	16	fluorobenzene	71	69.8	2.61
6	Et ₂ O	26	63.3	2.55	17	chlorobenzene	75	71.3	2.57
7	dioxane	12	62.1	2.56	18	<i>m</i> -dichlorobenzene	79	67.7	2.49
8	EtOH	22	60.8	2.53	19	<i>o</i> -dichlorobenzene	81	65.4	2.46
9	HFIP	16	55.2	2.49	20	1,2,4-trichlorobenzene	85	68.5	2.38
10	MeCN	16	54.1	2.43	21	1,2,4-trichlorobenzene ^d	>99	49.4	2.29
11	NMP	12	59.6	2.58	22	1,2,4-trichlorobenzene ^{d,e}	>99	66.4	2.42

^aStandard conditions: PMVK **3a** (41.7 mg, containing 0.60 mmol repeating units), *m*CPBA (2.40 mmol), and solvent (2.00 mL) stirred at 50 °C for 8 h. The M_n/\bar{D} of PMVK was 66.0 kDa/2.54. ^bDetermined by ¹H NMR of the crude products using 1,1,1,3-tetrachloropropane as an internal standard. ^cDetermined by SEC (THF) analysis relative to polystyrene standards. ^dReaction was run for 24 h instead of 8 h. The M_n/\bar{D} of PMVK was 61.4 kDa/2.54. ^e(TMS)₂O (1.20 mmol) and dry *m*CPBA were employed.

characterize both PMVK and its product after BV oxidation. Errors relating to C–H decoupling of ¹³C NMR were evaluated and calibrated by ¹H NMR prior to use.

The effect of solvent was first investigated under a set of standard conditions (Table 1). Less polar solvents generally gave higher conversions while polar solvents were found to be problematic. Dichloromethane and chloroform, two common solvents for BV oxidation, were not suitable for post-polymerization modification due to both significant polymer degradation and only moderate reaction rates. Surprisingly, the optimal solvents were found to be halogen-substituted aromatic solvents such as fluorobenzene, chlorobenzene and 1,2,4-

trichlorobenzene, which are rarely used in BV oxidation. Their improved performance may be partially attributed to the enhanced stability of these solvents to oxidative conditions. Among the solvents tested, 1,2,4-trichlorobenzene was found to be optimal in terms of both conversion and M_n . The post-polymerization modification proceeded smoothly in the first 24 h, but the M_n of the functionalized polymers declined with prolonged periods. We conjectured that the accumulation of *m*-chlorobenzoic acid was likely the cause of this phenomenon.

We speculated that a “precise” buffer could perhaps maintain the pH of the reaction mixture within a narrow window where

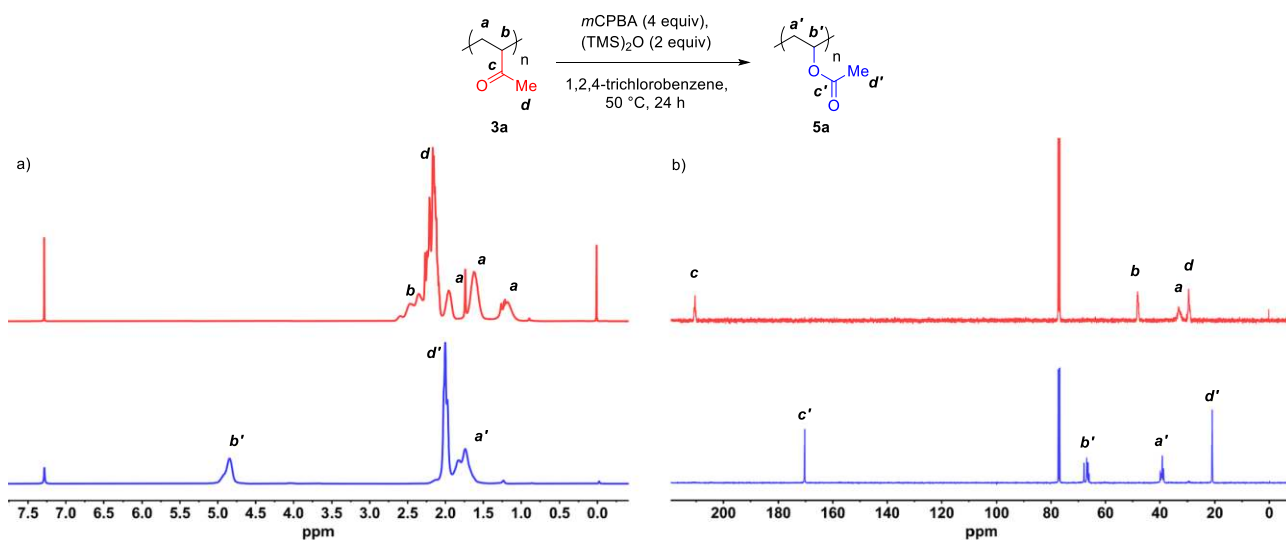


Figure 3. “Exhaustive” BV oxidation of commercial PMVK homopolymers. Comparison of (a) ¹H NMR spectra and (b) ¹³C NMR spectra before and after “exhaustive” BV oxidation of commercial PMVK **3a**. The NMR spectra were recorded using CDCl₃ as a solvent.

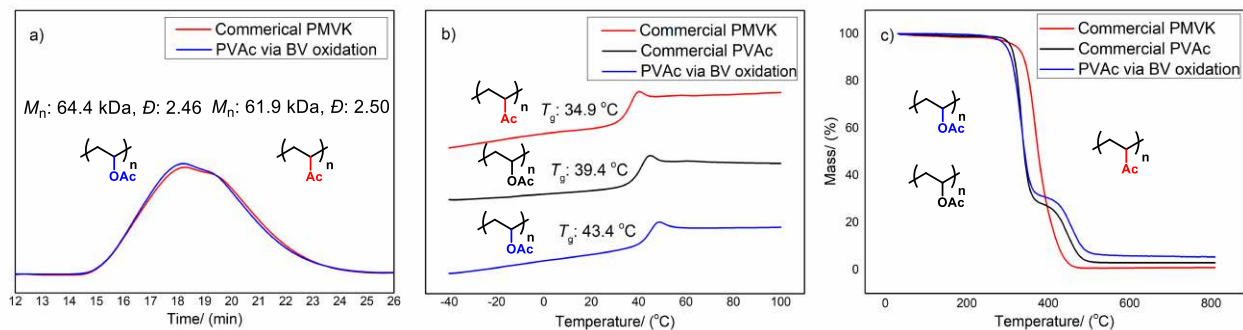


Figure 4. Characterization of PVAc **5a** prepared by “exhaustive” BV post-modification of PMVK **3a**. Comparison of (a) SEC, (b) DSC, and (c) TGA data of PMVK **3a**, commercial PVAc and PVAc **5a** obtained by BV oxidation.

polymer degradation would not occur. Indeed, even a subtle deviation from the “ideal” pH range could potentially induce chain scission. Initial efforts using various aqueous buffers were unsuccessful. Control experiments indicated that excessive water affected both the reaction rate and MW in a negative manner. Gratifyingly, an “exhaustive” screening (>700 experiments) of inorganic salts and organic additives revealed that a silicon additive (TMS)₂O (Table S5–S7) was able to buffer the system effectively. We conjectured that (TMS)₂O slowly reacted with the *m*-chlorobenzoic acid accumulating during the oxidation to form a neutral trimethylsilyl *m*-chlorobenzoate species. Further suppression of chain scission by drying the commercial *m*CPBA reagent provided an optimal BV protocol for the “exhaustive” functionalization of PMVK.

“Exhaustive” BV Oxidation of Commercial PMVK Homopolymers. With the first “exhaustive” functionalization condition in hand, we conducted a BV oxidation of commercial PMVK polymers on a preparative scale. In addition to ¹H NMR and ¹³C NMR, the resulting polymer was fully characterized by size exclusion chromatography (SEC), Fourier transform infrared spectroscopy (FT–IR), differential scanning calorimetry (DSC), and thermogravimetric analysis (TGA).

The ¹H NMR and ¹³C NMR spectra of the polymer samples before and after oxidation are displayed in Figure 3. The peak at $\delta = 4.87$ ppm was assigned to the protons attached to the carbon **b'** of the post-modified polymer (Figure 3a, bottom). Meanwhile, the peaks at $\delta = 2.3$ – 2.7 ppm corresponding to the protons attached to the carbon **b** of PMVK disappeared after the oxidation (Figure 3a, top). These results indicated that the BV oxidation completely transformed the PMVK homopolymer into a PVAc homopolymer. The ¹³C NMR spectra also provided additional evidence. In Figure 3b, the carbonyl signal of the ketone of PMVK ($\delta = 210.2$ ppm) disappeared completely after the oxidation while a carbonyl signal corresponding to an ester appeared at 170.4 ppm. In addition, the conversion of PMVK to PVAc was further confirmed by FT–IR.

The M_n and \bar{D} of the resulting PVAc polymer **5a** were obtained by SEC (Figure 4a). A slightly higher M_n and a similar \bar{D} were obtained after functionalization. The SEC traces indicated that our protocol successfully suppressed chain scission and cross-linking without affecting the MW and \bar{D} . Meanwhile, glass transition temperature (T_g) data was collected using differential scanning calorimetry (DSC) (Figure 4b). The T_g of PVAc **5a** obtained by the “exhaustive” BV oxidation was close to the T_g of the commercial PVAc sample. In contrast, the T_g of PMVK

3a was slightly lower. Furthermore, the thermogravimetric analysis (TGA) of this sample after oxidation displayed a two-staged curve, which is analogous to that of PVAc (Figure 4c). The initial degradation stage possibly relates to the elimination reaction of side groups while the second stage may relate to the degradation of the polymer backbone. As a comparison, the TGA of the original PMVK sample exhibited a one-stage curve.

“Exhaustive” BV Oxidation of Statistical Copolymers of MVK and Various Monomers. As described above, the access to poly(VAc-*co*-MAM)s by direct copolymerization is quite limited. It was much expected that our “exhaustive” BV post-modification would provide a general solution to the synthesis of poly(VAc-*co*-MAM)s.

Firstly, we prepared a number of PMVK-*co*-PSs with differing MVK/St feed ratios (20/80, 50/50, and 80/20) under AIBN-initiated free radical polymerization. The reactivity ratios of MVK and St monomers ($r_{\text{MVK}} = 0.29$, $r_{\text{St}} = 0.35$)⁵ indicate that PMVK-*co*-PS copolymers favor a statistical distribution. As expected, almost identical MVK/St ratios (28/72, 51/49 and 75/25, respectively) were obtained in the resulting copolymers. Subsequently, the prepared PMVK-*co*-PS copolymers were functionalized under the BV protocol developed for the PMVK homopolymers. Unexpectedly, it was observed that the rates of BV oxidation for PMVK-*co*-PS copolymers were higher than of the PMVK homopolymers. The enhanced rates appeared to be proportional to the percentages of styrene units within the PMVK-*co*-PSs. Following the same trend, the rates of chain scission and cross-linking also increased. Gratifyingly, with careful tuning of the reaction temperature, a set of “exhaustive” modification conditions for PMVK-*co*-PS were achieved at 45 °C (MVK/St = 75/25), 40 °C (MVK/St = 51/49), and 35 °C (MVK/St = 28/72), respectively (Table S10). Under these optimized conditions, the M_n and \bar{D} were well controlled (Figure 5). The reactivity differences between PMVK homopolymers and PMVK-*co*-PS copolymers can be tentatively attributed to the fact that phenyl groups are less electron-withdrawing than acetyl and acetoxy groups. Mechanistically, the reaction rate of BV oxidation can be affected by the electronic properties of the migrating group. Besides PVAc-*co*-PS, PVAc copolymers with other MAMs such as acrylonitrile (AN), and methyl acrylate (MA) were also successfully prepared. Under the optimized BV conditions of 50 °C and 24 hours, PMVK-*co*-PAN and PMVK-*co*-PMA copolymers were fully converted to their corresponding PVAc-*co*-PAN and PVAc-*co*-PMA copolymers, respectively. No obvious chain scission or cross-linking were

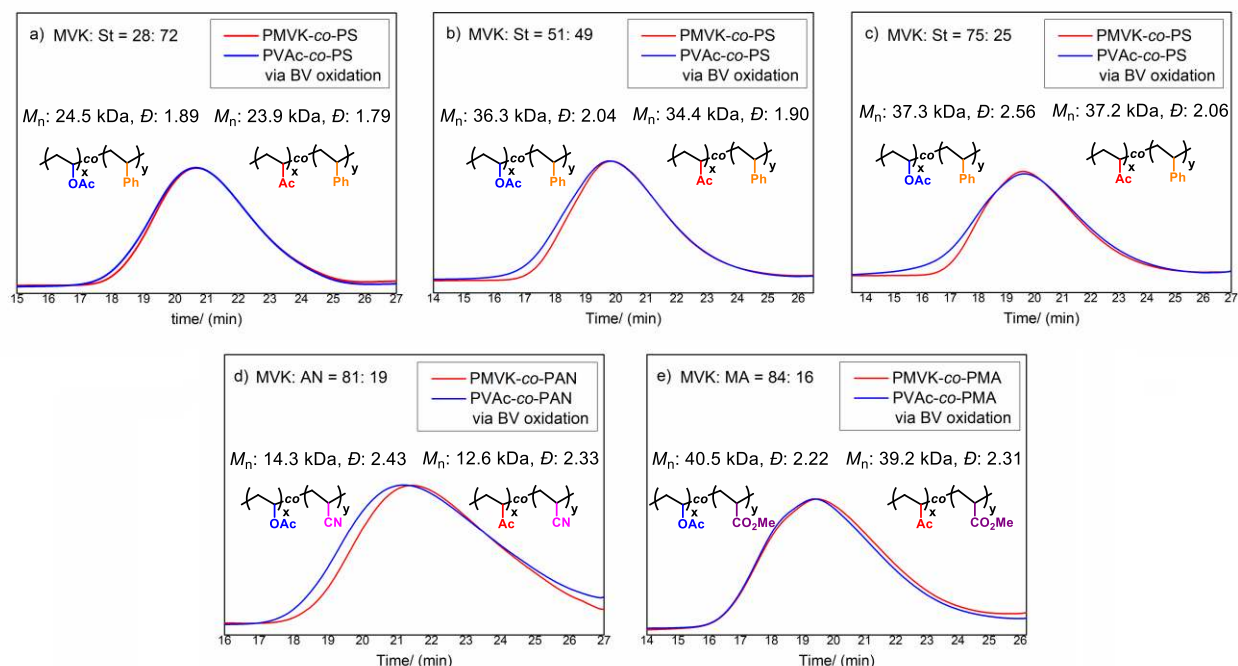


Figure 5. Synthesis of statistical copolymers of VAc and various monomers. SEC traces before and after the “exhaustive” BV oxidation of MVK statistical copolymers: (a) MVK/St (28/72) statistical copolymer **6a**, (b) MVK/St (51/49) statistical copolymer **6b**, (c) MVK/St (75/25) statistical copolymer **6c**, (d) MVK/AN (81/19) statistical copolymer **6d** and (e) MVK/MA (84/16) statistical copolymer **6e**.

observed in the SEC traces (Figure 5). All of the prepared statistical copolymers were thoroughly characterized. The “comonomer” ratios in the functionalized copolymers were consistent with the ratios of the starting copolymers (Table S10 and S12). Analysis of NMR spectral data (Figure S4–S8) confirmed that nearly all MVK units were converted to VAc units. FT–IR, DSC, and TGA data (Table S11 and S13) further supported the NMR spectra results.

“Exhaustive” BV Oxidation of Block Copolymers of MVK and Various Monomers. The synthesis of VAc block copolymers with MAMs *via* RDRP remains a significant challenge in copolymer synthesis.^{9–20} Encouraged by our success in the synthesis of statistical poly(VAc-*co*-MAM)s, we anticipated that our BV post-modification strategy could be expanded to the synthesis of PVAc block copolymers with MAMs. Firstly, we prepared a number of PMVKs and poly(MAM-*b*-MVK)s *via*

Table 2. Screening of BV Oxidation Conditions for RAFT Homopolymer **3b** in 1,2,4-Trichlorobenzene^a

Entry	Additive	Conversion ^b (%)	M_n^c (kDa)	\bar{D}^c	Entry	Additive	Conversion ^b (%)	M_n^c (kDa)	\bar{D}^c
1 ^d	(TMS) ₂ O	n.a.	2.1	1.63	9	1,3-diphenylurea	69	4.3	1.39
2 ^e	n.a.	>99	4.4	1.43	10	<i>p</i> -toluenesulfonamide	98	3.3	1.35
3	triethylamine	90	10.7	1.30	11	urea	>99	13.5	1.15
4	DIPEA	88	10.0	1.32	12	thiourea	98	11.8	1.21
5	2,6-lutidine	61	13.1	1.18	13	ammonium carbamate	87	6.9	1.37
6	NH ₄ HCO ₃	96	9.4	1.29	14	methyl carbamate	98	3.6	1.38
7	NH ₄ OAc	83	6.9	1.34	15	<i>t</i> -butyl carbamate	>99	13.0	1.16
8	benzamide	99	10.7	1.25					

^aStandard conditions: RAFT homopolymer of MVK **3b** (41.7 mg, containing 0.60 mmol repeating units), *m*CPBA (2.40 mmol), additive (0.12 mmol), and solvent (2.00 mL) stirred at 50 °C for 24 h unless noted otherwise. The M_n/\bar{D} of PMVK was 12.5 kDa/1.07. ^bDetermined by ¹H NMR of the crude products using 1,1,1,3-tetrachloropropane as an internal standard. ^cDetermined by SEC (THF) analysis relative to polystyrene standards. ^d(TMS)₂O (1.20 mmol) and dry *m*CPBA were employed. ^e*m*CPBA was used without drying.

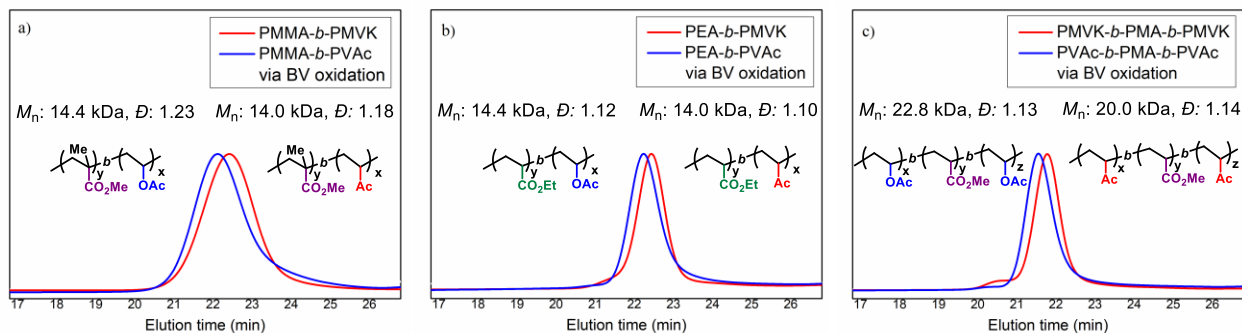


Figure 6. Synthesis of block copolymers of VAc and various monomers. SEC traces of (a) PMMA-*b*-PMVK di-block copolymer **7a**, (b) PEA-*b*-PMVK di-block copolymer **7b** and (c) PMVK-*b*-PMA-*b*-PMVK tri-block copolymer **7c** before and after “exhaustive” BV oxidation.

RDRP techniques. Although the atom transfer radical polymerization (ATRP) of vinyl ketone monomers⁵⁹ is presently inaccessible, Wooley’s RAFT protocol⁴⁷ offered us a particularly effective method to synthesize narrow-dispersed PMVKs and PMVK block copolymers. Unfortunately, none of our established BV protocols for the statistical copolymers were compatible with the narrow-dispersed PMVK homopolymers. Significant degradation of the polymer architecture occurred in all cases (Table S8). We speculated that the degradation was most likely caused by the end-group of the RAFT polymers. Indeed, this hypothesis was later verified by the fact that a RAFT-derived polymer without a sulfur-based end group^{66–68} performed well using our BV protocol (Table S8).

We speculated that sulfonic acid might be generated by the oxidation of the sulfur-based end-groups in the RAFT polymers.⁶⁹ Although TMS₂O was unable to buffer the more acidic -SO₃H group, we speculated that another additive might neutralize both *m*-chlorobenzoic acid and the additional sulfonic acid. Significant efforts at using common bases as a buffer met with little success since the pH of the reaction mixture changed dynamically. Indeed, a fluctuating pH, no matter if higher or lower, could be detrimental to the post-modification. Gratifyingly, *t*-butyl carbamate and urea were later identified as the most effective additives after a laborious screening (Table 2 and Table S9). With a modified procedure using 0.2 equiv of urea as an additive, the PMVK homopolymer prepared by RAFT was nearly quantitatively transformed into a PVAc polymer without obvious chain scission or cross-linking. The structural integrity of the resulting PVAc polymer was verified by ¹H and ¹³C NMR (Figure S3), matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF MS), and FT-IR.

The modified BV protocol using the urea additive was highly effective and thus further applied to the synthesis of PVAc block copolymers. Two di-block copolymers, poly(methyl methacrylate)-*block*-poly(methyl vinyl ketone) (PMMA-*b*-PMVK, *M_n* = 14.0 kDa, PMMA/PMVK = 7.7/6.3) and poly(ethyl acrylate)-*block*-poly(methyl vinyl ketone) (PEA-*b*-PMVK, *M_n* = 13.9 kDa, PEA/PMVK = 8.6/5.3), and one “ABA”-type tri-block copolymer, PMVK-*b*-PMA-*b*-PMVK (*M_n* = 20.0 kDa, PMVK/PMA/PMVK = 5.2/10.3/4.5), were synthesized by RAFT polymerization. Subsequently, these three PMVK block copolymers were “exhaustively” functionalized by the urea-modified BV protocol, with PMMA-*b*-PVAc, PEA-*b*-PVAc, and PVAc-*b*-PMA-*b*-PVAc being obtained without apparent degradation (Figure 6 and Figure S9–11).

Preparation of PVAc-*co*-PS via One-pot Copolymerization/“Exhaustive” BV Post-modification. To streamline the

preparation of poly(VAc-*co*-MAM)s, we developed a one-pot copolymerization/“exhaustive” BV post-modification procedure (Figure 7). This convenient and scalable process allows us to synthesize PVAc-*co*-PS on a gram scale from MVK and St monomers directly without the purification of the PMVK-*co*-PS precursor. Noticeably, the use of 1,2,4-trichlorobenzene as a solvent for copolymerization was crucial for this process. Although the comprehensive properties of PVAc-*co*-PS **10** have not been investigated, this copolymer has exhibited an improved performance over the standard PVAc adhesive in our preliminary tests, especially when applied in aqueous conditions at elevated temperatures.

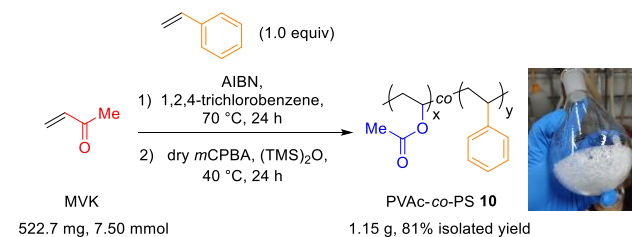


Figure 7. One-pot synthesis of PVAc-*co*-PS **10**.

CONCLUSION

Baeyer–Villiger oxidation, a historically important transformation in small-molecule organic chemistry, has now emerged to be an efficient post-polymerization modification reaction for PMVK and its copolymers. Initial unsuccessful attempts on a small-molecule model led us to develop and re-optimize the BV oxidation directly on PMVK polymers. After the elucidation of multiple factors affecting reaction kinetics and side reactions, the precise tuning of reaction parameters allowed us to identify a set of tailor-made BV oxidation conditions which were able to “exhaustively” functionalize PMVK and its copolymers without obvious chain scission or cross-linking.

With this unique BV post-modification method in hand, we successfully prepared a broad array of poly(VAc-*co*-MAM) statistical copolymers that are rarely accessed by direct copolymerization. In addition, a number of PVAc di-block and tri-block copolymers with narrow molecular weight distributions were synthesized using this post-modification method. A gram-scale one-pot process was additionally developed to demonstrate the potential of a scalable production of such copolymers. The material properties and potential applications of the prepared poly(VAc-*co*-MAM) copolymers will be reported in due course. In addition, we recognize that re-optimizing a reaction on polymer substrates could be a valuable approach for the

development of other post-polymerization modification reactions, particularly when small-molecule protocols failed in polymer post-modifications. Further work related to this topic is currently being investigated in our laboratory.

ASSOCIATED CONTENT

Supporting Information

General information, experimental procedures, supplemental data, material characterization, and spectral data.

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Author Contributions

L.L. conceived the project; L.L. and P.M. designed the research and analyzed the data; P.M. conducted the experimental work; L.L. discussed and wrote the manuscript together with P.M., C.M.P., W.L., J.P., and Y.C. All authors have given approval to the final version of the manuscript.

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CONFLICT OF INTEREST

Sun Yat-sen University has filed a patent application.

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