Soluble Supports Tailored for Organic Synthesis: Parallel Polymer Synthesis *via* Sequential Normal/Living Free Radical Processes

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Abstract: To expand the availability and solubility range of polymer supports for liquid-phase organic synthesis (LPOS) we have applied a sequence of normal and "living" free radical polymerization to generate a library of block copolymers possessing either block or graft architecture with initiators **1**−**4** and a diverse set of vinyl monomers **5**−**9**. The structure, molecular weight, and polydispersity (PD) of the individual library members have been determined by size exclusion chromatography (SEC), ^{1}H and ^{13}C NMR, and as a function of the solubility of each polymer in a range of solvents. One copolymer, poly**BS-DS** (M_n = 17 000, PD = 1.54) derived from 4-*tert*-butylstyrene (**6**, **BS**), 3,4-dimethoxystyrene (**7**, **DS**), and initiator **1** has a solubility profile [soluble in toluene, tetrahydrofuran (THF), ether, acetone and methylene chloride (DCM), insoluble in methanol and water] that is different from the present polymer of choice for LPOS, poly(ethylene) glycol (PEG), and has been studied in some detail as a new support in LPOS. The α-nitrile groups of poly**BS-DS** are reduced smoothly with $LiAlH_4$ in THF to give the amino functionalized copolymer **22** (0.14 mmol g^{-1} of amino groups based on a quantitative ninhydrin analysis). Kinetic studies have revealed that derivatization of the amino groups of **22** with 4-dimethylaminocinnamaldehyde **23** occurs at a comparable rate to a solution counterpart (k_{poly22} = 0.49 L mol^{-1} h^{-1} vs $k_{aminohexane}$ = 0.69 L mol^{-1} h^{-1}). Following reaction of poly**22** with *N*-glutaroyl-(2*S*,4*S*)-4-diphenylphosphino-2-[(diphenylphosphino)methyl]pyrrolidine (**26**) and exchange of Rh(I), the resulting phosphine containing copolymer Rh(I)-**27**, catalyzes the enantioselective hydrogenation of 2-*N*-acetamidoacrylic acid (**28**) to *N*-acetylalanine (**29**) in THF. An 87% enantiomeric excess (ee) of (*S*)-**29** is obtained, comparable to that observed with a homogeneous phosphine ligand. This work highlights the power of a parallel polymer synthesis strategy, from conception to application, for the generation of polymers possessing unique solubility profiles and functionality which can serve as novel supports in LPOS.

Introduction

Currently, there is a tremendous effort in the pharmaceutical industry being directed toward the discovery of lead compounds possessing activity against an increasing number of biological targets highlighted *via* a combination of focused medical research, bioinformatics, and combinatorics.[1] This perforce has led to an exponential increase in the demand for novel compounds and the speed at which they are generated. This reality is driving the emergent fields of high-throughput and combinatorial chemistry, which are founded on the necessity of converting standard solution-phase organic chemistry onto polymer supports for optimal speed of compound production, purification, and structure elucidation.[1−3] Often, the rate-limiting step in these areas is the incompatibility of the solution chemistry when transferred to a solid-phase environment. To address this problem, liquid-phase chemistry with *soluble* polymer supports such as poly(ethylene) glycol (PEG) is being developed in parallel and is receiving increasing use in high-throughput and combinatorial chemistry.[4,5] However, a problem common to both solid- and liquid-phase polymer supports is that the chemistry associated with them is limited to a fairly narrow range of organic solvents. This is a major drawback because successful chemical transformations often require a specific solvent, and the demand for solvent-dependent reactions can only be expected to rise in the foreseeable future. Therefore, there is an increasing need for alternative polymer supports that can be adapted to various reaction conditions and thus allow the incorporation of a broader spectrum of organic synthetic methodology into polymer supported high-throughput organic synthesis.

In an attempt to overcome the dearth of soluble polymer supports available for organic synthesis and to rapidly generate new soluble supports that not only conform to the solvent conditions dictated across the whole spectrum of solution

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chemistry (organic and aqueous) but also include positions amenable for suitable chemical derivatization and functionalization, we have utilized a spatially addressable parallel approach to polymer library synthesis.

It is known that a greater number of monomers are amenable to radical polymerization than either anionic or cationic methods,[6] therefore a higher diversity of polymers may be obtained through free radical polymerization. Additional structural variation can be achieved through the synthesis of polymers based on either one monomer (homopolymers) or multiple monomers (copolymers). Although a single polymerization of a mixture of monomers yields copolymers, block and graft copolymerization offer the tantalizing possibility of a controlled alteration of physical properties, including solubility, by varying polymer block and graft length and composition.[7−10] Traditionally, block copolymers have been synthesized by anionic methods to control chain length and polydispersity (PD); however, anionic polymerizations are incompatible with many commercially available monomers.[8−19] To draw from a larger pool of monomers and increase the diversity of block copolymers, several laboratories have developed methods to transform the propagating center of one living polymerization into a reactive center suitable for polymerization of a second monomer (for example, by changing from anionic to cationic polymerization).[20−22] Recently, methods of living radical polymerization, mediated by 2,2,6,6-tetramethylpiperidinyl-1-oxy (TEMPO) or atom transfer radical polymerization (ATRP) initiated by CuCl/2,2′-bipyridine complexes have produced block copolymers with well-defined molecular weights and narrow PDs.[8−19]

However, block and graft copolymerization that occurs exclusively by a radical mechanism, while being less easy to control in terms of the molecular weight outcome and PD of the polymer products, allows the greatest number of monomers to be chosen at all stages of the polymerization. In this paper, we describe the utilization of a sequence of normal and living free radical processes with the initiators **1**−**4** and monomers **5**−**9** to generate a parallel array of either block (derived from bifunctional initiators **1**−**3**) or graft (derived from initiator **4**) copolymers which exhibit unique solubility profiles (Figure 1).

These new block (class **10**−**12**) or graft (class **13**) copolymers, by virtue of the structural remnants of the initiators that generated them, contain loci that are amenable for derivatization and as discussed *vide infra* makes them of ultimate value in LPOS (Scheme 1).

Results and Discussion

Bifunctional Initiator Design and Synthesis. Having settled upon a radical polymerization strategy, the next stage was the design and synthesis of suitable initiators. Diazene and TEMPO moieties are known to initiate/mediate free radical polymerization at 70 and 130 °C, respectively. Therefore we have synthesized bifunctional free radical initiators **1**−**3**[23,24] (Scheme 1), which contain an α-nitrile diazene core (−N═N−) linked via a spacer to two TEMPO molecules. This inherent bifunctionality of **1**−**3** is designed to provide for two independent rounds of polymerization, thus block copolymers can be obtained in a temperature controlled manner through sequential normal and "living" polymerizations to give block copolymers of the type **10**−**12** (Scheme 1).[23,24] The synthesis of initiators **1** and **2** has been described elsewhere.[23,24] Initiator **3** was synthesized in four steps from commercially available 4-amino TEMPO **14** by an initial Boc protection to give the TEMPO derivative **15** in 76% yield (Scheme 2). The critical reaction of styrene **5**, dibenzoyl peroxide, and **15** then gave the key benzoyl protected derivative **16** in acceptable yield (38%) following silica gel chromatography. Saponification of **16** proceeded smoothly in a 10 N NaOH/MeOH/THF (3:1:1) mixture to give the TEMPO alcohol derivative **17** in 98% yield. The bis esterification of 4,4′-azobis(4-cyanovaleric acid) (**18**) with **17** occurred via EDC/HOBt coupling conditions in tetrahydrofuran (THF) to give initiator **3** in 76% yield.

As discussed *vide supra* sequential normal/"living" polymerizations can produce graft (or comb) copolymers in addition to block copolymers (Scheme 1).[11−13] To expand the structural diversity of our copolymer library and to explore the solubility properties of comb polymers *vs* block polymers, TEMPO-functionalized methacrylate **4** was synthesized as the final initiator/mediator in our strategy *via* esterification of 1-hydroxy-2-phenyl-2-(2′,2′,6′,6′-tetramethyl-1-piperidinyloxy)ethane (**19**) with methacryloyl chloride (**20**) in good yield (65%) (Scheme 2). In contrast to initiators **1**−**3**, **4** participates as a monomer in the first polymerization with monomer A, resulting in statistical copolymers of type **21** (Scheme 1). The TEMPO

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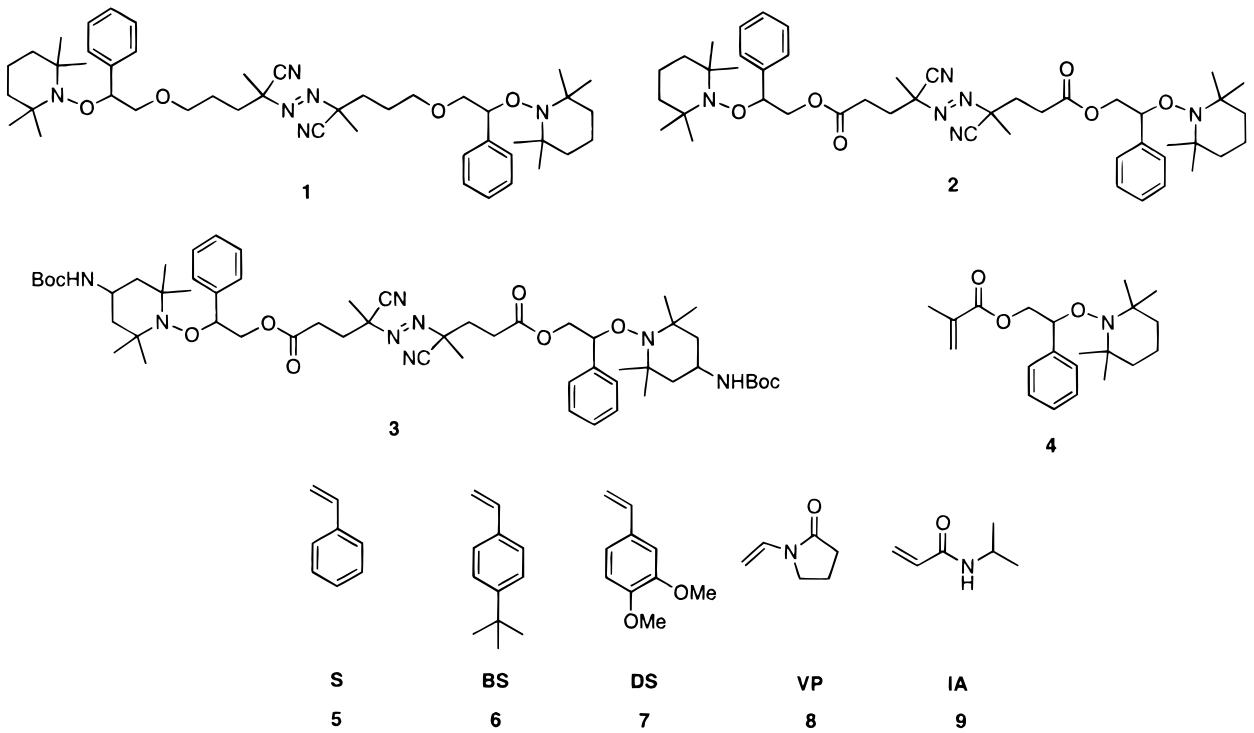
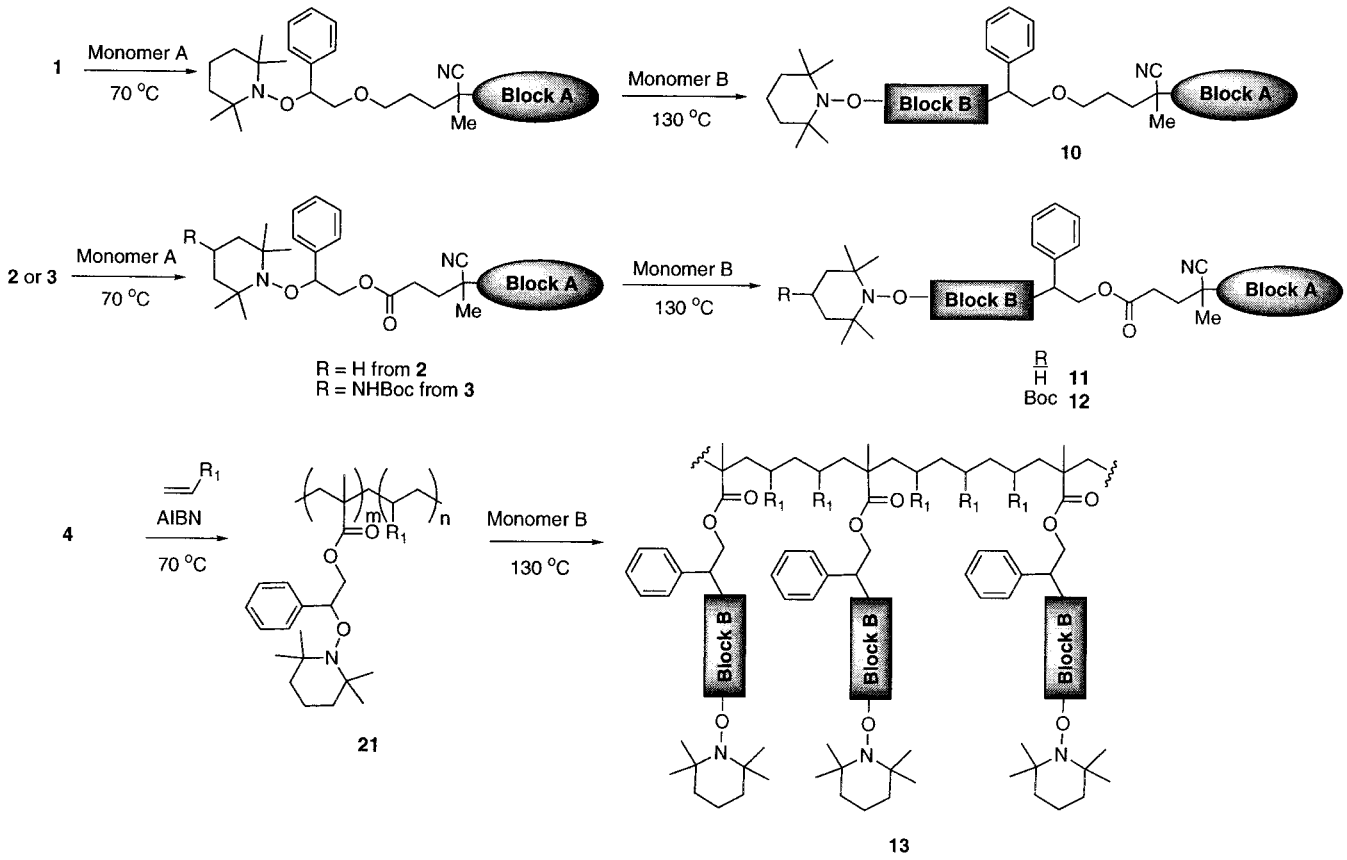


Figure 1. Free radical initiators **1**−**4** and vinylic monomers **5**−**9** utilized for copolymer library construction.

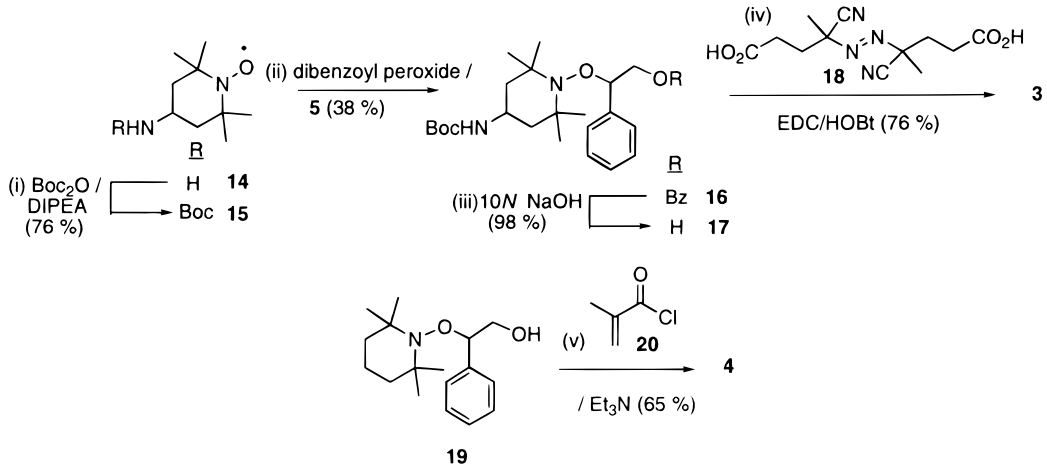
Scheme 1. Sequence of Normal/"Living" Polymerization with Initiators **1**−**4** and Monomers A and B Showing the Potential Architecture of the Block and Graft Copolymer Products and the End Groups for Derivatization



functionalized residues then mediate the "living" polymerization at 130 °C with monomer B giving rise to comb copolymers of type **13**.

Intrinsic in the structures of **1**−**4** is that the copolymers formed by the normal and "living" free radical sequence of polymerization, either di- or tri-block, will contain residues amenable for derivatization and hence be of use in LPOS (Scheme 1). The block copolymers **10**−**12** derived from initiators **1**−**3** possess α-nitrile residues, which can be converted into amino groups by reduction. A structural feature common

Scheme 2. Synthetic Route to Initiators **3** and **4**



to all the classes of copolymers **10**−**13** formed by this strategy, a result of the known termination mechanism of "living" free radical polymerization,[9−16] is that the end of the copolymer chains may possess TEMPO groups. It is known that the TEMPO functionality can be removed under reductive conditions (Zn/acetic acid or Zn/NH_4Cl)[25,26] to give terminal hydroxyl groups. Additionally, implicit in the design of initiator **3** is that the Boc group of the 4-amino TEMPO residues (class **12** copolymers) may be facilely removed with TFA, hence generating a terminal amino group serving to increase the loading of these polymer supports.

The final component of the initiators' **1**−**4** design requiring discussion is the moiety that links the α-diazene core and the TEMPO end groups. For initiator **1** this is a dialkyl ether whereas in **2**−**4** this is a substituted homobenzylic ester. Again it should be noted from Scheme 1 that these linkages become incorporated into the block or graft copolymers during the polymerization sequence, which is an advancement of tandem "living" free radical polymerization methodology. Existing methods utilizing either ATRP or TEMPO produce block copolymers that do not provide linkages between polymeric blocks. While "link-functionalized" polymers (LFPs) have been synthesized with bis-initiators that link together two active polymerization centers to form both blocks simultaneously,[27] our methodology provides for polymerization of each block independently with different monomers.

The incorporation of a chemically robust dialkyl ether linkage between the polymer blocks by initiator **1** was seen as fundamental for library construction of copolymers being considered for ultimate application in LPOS. Initiators **2**−**4** were utilized when the lability of the ester linkage was to be exploited either during SEC analysis of polymer digests (to help confirm di- or tri-block structures) or during a process we have dubbed "oscillating liquid-phase" (OLP) where the solubility of the polymer support can be modified during a synthetic strategy by saponification of the homobenzylic ester moiety thus fragmenting the copolymer into its constituent blocks.

Parallel Block Copolymer Synthesis Utilizing Initiator 1. Library synthesis occurred in a two-dimensional spatially addressable array format with five vinylic monomers **S** (**5**), **BS** (**6**), **DS** (**7**), **VP** (**8**), and **IA** (**9**). Polymerization reactions were conducted in a thick-walled reaction tube in a heated reactor/stirrer block affixed to an orbital shaker. Where possible the polymerizations were conducted neat; however, in certain cases a minimum of solvent [dimethylformamide (DMF) or 1,2-dichlorobenzene (DCB)] was added to ensure homogeneous reaction conditions. Only the minimum amount of solvent was added because polydispersity (PD) has been reported to be directly proportional to the amount of solvent used in TEMPO-mediated polymerizations.[9−16]

Following polymerization of initiator **1** with the first monomer (rigorously degassed by freeze−thawing with liquid nitrogen) at 70 °C for 8−10 h, homopolymeric material was isolated from the reaction mixtures by precipitation with a suitable solvent. The resultant homopolymer was then dissolved in the second monomer, deoxygenated as described *vide supra*, and then heated to 130 °C for 8−10 h. This library of 20 crude block copolymers (polymers of the 5 × 5 array containing all blocks of the same monomer were not synthesized) was isolated by precipitation following addition of suitable solvent mixtures. At this stage, selective solvents were used to remove unwanted homopolymer "impurities" from the isolated residues. In some cases, however, such solvent systems could not be found and occasionally addition of selective solvents to crude polymeric products produced intractable suspensions that could not be easily filtered. However, it should be stressed that residual amounts of homopolymers produced as a result of chain transfer and/or termination events common to free radical polymerization approach, while elevating the value of the PDs observed, do not affect at all the ultimate use of these materials as soluble polymer supports in liquid-phase synthesis. Solubility characteristics and other physical properties of the polymer library are reported in Tables 1 and 2.

Solubility properties of the twenty polymer supports were assayed in a panel of 10 commonly used solvents (Table 1). Because solubility properties changed by linking together different polymer blocks, new supports were obtained that exhibited solubility profiles not matched by any other block copolymer or homopolymer studied. All polymer supports were soluble in tetrahydrofuran (THF) and dichloromethane (DCM). However, only copolymers containing blocks of both **S** and **BS** were soluble in diethyl ether (Et_2O), while polymer supports based on blocks of two of the three polar monomers **DS**, **VP**, and **IA** were soluble in dimethyl sulfoxide (DMSO). Polymerization of **BS** followed by **VP** yielded the block copolymer poly**BS-VP**, which is insoluble in all solvents except THF, acetone, and DCM, but the copolymer formed from a first polymerization of **DS** followed by **VP** is soluble in all solvents

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Table 1. Solubility of the Block Copolymer Library Members from Initiator **1**

polymerization[a] order	solubility[b,c]									
	A	B	C	D	E	F	G	H	I	J
S	S	S	S	S	sw	S	S	I	I	I
BS	S	S	S	sw	I	S	I	I	I	I
DS	S	I	S	S	S	S	S	S	I	I
VP	I	I	S	sw	S	S	S	S	S	S
IA	sw	I	S	S	S	S	S	S	S	S
S-BS	S	S	S	S	sw	S	sw	I	I	I
S-DS	S	sw	S	S	S	S	S	I	I	I
S-VP	S	sw	S	S	sw	S	S	I	I	I
S-IA	I	I	S	S	S	S	S	sw	S	I
BS-S	S	S	S	sw	I	S	I	I	I	I
BS-DS	S	S	S	S	I	S	I	I	I	I
BS-VP	I	I	S	I	S	I	I	I	I	I
BS-IA	sw	I	S	sw	I	S	sw	I	I	I
DS-S	S	I	S	S	S	S	S	sw	I	I
DS-BS	S	sw	S	S	sw	S	S	sw	I	I
DS-VP	S	I	S	S	S	S	S	S	S	I
DS-IA	sw	I	S	S	S	S	S	S	sw	sw
VP-S	sw	I	S	S	S	S	S	sw	sw	I
VP-BS	I	I	S	sw	I	S	I	I	I	I
VP-DS	I	I	S	S	S	S	S	S	sw	I
VP-IA	I	I	S	S	S	S	S	S	S	S
IA-S	I	I	S	S	I	S	S	I	I	I
IA-BS	sw	I	S	sw	I	S	I	I	I	I
IA-DS	sw	I	S	S	S	S	S	S	sw	I
IA-VP	I	I	S	S	S	S	S	S	S	S

[a] Monomers: styrene **5** (**S**), 4-*tert*-butylstyrene **6** (**BS**), 3,4-dimethoxystyrene **7** (**DS**), *N*-vinylpyrrolidinone **8** (**VP**), *N*-isopropylacrylamide **9** (**IA**). [b] Solvents: toluene (A), diethyl ether (B), tetrahydrofuran (C), acetone (D), acetonitrile (E), dichloromethane (F), dimethylformamide (G), dimethyl sulfoxide (H), methanol (I), water (J). [c] S = soluble; sw = swell; I = insoluble.

studied except Et_2O and water. In some cases, the solubility profiles of the block copolymers differed slightly between two polymer supports derived from the same monomers but polymerized in opposite order; however, these differences might also be attributable to differences in block lengths.

The only water soluble block copolymers contained blocks of both **VP** and **IA**. Homopolymers of **VP** and **IA** are both soluble in water, but upon heating above the cloud point of 31−32 °C poly**IA** precipitates.[28] This inverse solubility behaviour, characterized by a lower critical solution temperature (LCST), has been exploited previously to produce polymer supports that act as a temperature controlled switch for catalytic hydrogenation.[29] Interestingly, aqueous solutions of poly**VP-IA** and poly**IA-VP** also clouded upon heating, with LCSTs measured at 38 and 35 °C, respectively.

Characterization of all the copolymer library members by ^{1}H and ^{13}C NMR spectroscopy gave results consistent with block copolymer structures. However, molecular weights measured by SEC [utilizing three Styrogel (Waters) columns in series] often did not increase significantly, from the homopolymer isolated from the first polymerization after the second polymerization as may be expected for block copolymerization. It should be stressed that SEC elution times can be influenced by polymer chemical composition,[30] and discrepancies may result from molecular weight calculations of block copolymers based on their SEC elution times relative to polystyrene standards.[31] Even changing functional groups at polymer termini can lead to longer elution times and consequently an apparently lower molecular weight value.[32] In fact, we observed that between polystyrene samples produced by an anionic method (M_n = 1700, PD = 1.06, reported by Polymer Laboratories) and "living" radical polymerization (M_n = 1000, PD = 1.12, by SEC with THF),[15] the order of elution from the SEC columns *reversed* upon changing the solvent from THF to chloroform ($CHCl_3$). Consequently with $CHCl_3$ as the mobile phase, the molecular weight of TEMPO-functionalized polystyrene was recalculated to be M_n = 3200, PD = 1.16 relative to the SEC elution times of the polystyrene standards. Thus, molecular weights calculated from data obtained from our SEC system serve only as an estimate of the true polymer chain lengths.

Table 2. Physical Properties of the Block Copolymer Library Derived from Initiator **1**

polymerization order	$M_{n(SEC)}$[a]/$\times 10^3$	PD[a]	solvent[b]	F_2[c]	yield,[d] %
S	8.0	2.11	A	na[e]	80
BS	24.0	2.36	A	na	85
DS	19.0	1.67	A	na	75
VP	5.1	1.44	B	na	74
IA	18.1	1.40	B	na	54
S-BS	7.8	2.42	A	2.5	44
S-DS	8.5	2.00	A	1.9	33
S-VP	8.4	1.75	A	3.2	5
S-IA	16.2	1.61	A	0.42	16
BS-S	19.3	3.07	A	3.5	35
BS-DS	19.5	2.44	A	2.5	59
BS-VP	20.5	2.52	A	2.4	6
BS-IA	27.1	2.04	A	3.1	19
DS-S	17.8	1.73	A	3	20
DS-BS	18.9	1.72	A	2.7	30
DS-VP	9.8	2.34	A	1.3	17
DS-IA	17.0	1.77	A	3.5	12
VP-S	10.6	4.10	A	1.3	26
VP-BS	5.7	3.21	A	0.36	25
VP-DS	47.1	2.63	A	0.59	54
VP-IA	7.1	1.57	B	0.42	35
IA-S	49.1	1.53	B	1.1	15
IA-BS	20.4	5.92	A	0.45	41
IA-DS	109.0	1.56	A	0.59	45
IA-VP	2.3	1.78	B	0.63	5

[a] M_n and PD measured on three Styrogel (Waters) columns in series (7.8 × 300 mm: 10^4, 10^3, 500 Å) calibrated with 10 monodisperse (M_w/M_n < 1.13) polystyrene standards (M_n: 3.15×10^6, 1.29×10^6, 6.30×10^5, 1.71×10^5, 6.60×10^4, 2.85×10^4, 1.29×10^4, 5.46×10^3, 1.70×10^3, 580). [b] SEC mobile phase solvent: A = THF, B = $CHCl_3$. [c] Molar ratio of the second monomer in the copolymer as measured by ^{1}H NMR. [d] Yield calculated from the theoretical yield (see experimental section). [e] Not applicable: homopolymer.

To help confirm the nature of the block copolymers synthesized by our strategy, a separate series of normal and "living" polymerizations were undertaken with the **S** monomer and initiator **2**. Heating **S** and **2** at 70 °C overnight and precipitating the product, by addition of methanol (MeOH), yielded poly**S** with an M_n = 8200 and a PD = 1.69 (Figure 2a). A sample of the poly**S** homopolymer then was heated at 130 °C with additional **S** to produce poly**S-S** of higher molecular weight (M_n = 264 000, PD = 1.30) (Figure 2b). The ester bond between the polymer blocks (*vide supra*) was hydrolyzed with NaOH in a THF:MeOH:H_2O (3:1:1) mixture, and SEC analysis revealed complete loss of the peak of M_n = 264 000 and concomitant formation of two peaks of M_n = 118 000 (PD = 1.22) and 8700 (PD = 1.44) (Figure 2c).[33] Therefore, the measured molecular weight of 264 000 reported seems consistent with a *triblock* copolymer wherein two TEMPO-mediated blocks

(28) Heskins, M.; Guillet, J. E. *J. Macromol. Sci. Chem.* **1968**, 1441.
(29) Bergbreiter, D. E.; Caraway, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 6092.
(30) *Handbook of Size Exclusion Chromatography*; Wu, C.-S., Ed.; Marcel Dekker: New York, 1995; p 149.
(31) Hawker, C. J.; Elce, E.; Dao, J.; Volksen, W.; Russell, T. P.; Barclay, G. G. *Macromolecules* **1996**, *29*, 2686.
(32) (a) Spychaj, T. *J. Appl. Polym. Sci. Appl. Polym. Symp.* **1991**, *48*, 199. (b) Zhong, X. F.; Varshney, S. K.; Edsenberg, A. *Macromolecules* **1992**, *25*, 7160.

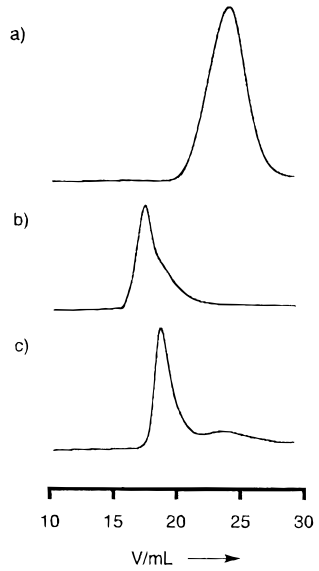

Figure 2. SEC traces of block copolymer polystyrene (poly**S-S**) synthesized by using bifunctional initiator **2** after (a) first polymerization at 70 °C, (b) second polymerization at 130 °C, and (c) hydrolysis of ester linkages between poly**S-S** blocks.

of $M_n = 118\,000$ are attached to one central diazene-initiated polystyrene block of $M_n = 8700$.

The formation of the triblock structure is most likely a consequence of head-to-head combination of two polymer chains during the first polymerization at 70 °C.[34] This is the predominant mode of termination during normal free radical polymerization of **S**; however, other modes of termination are known to occur. In fact, the observed peak for poly**S-S** in Figure 2b is asymmetric and suggests the presence of polymeric structures other than triblock. Chain transfer events and/or disproportionation that occur during diazene-initiated polymerization increase polydispersity and may lead to diblock, branched, or homopolymers following the second polymerization mediated by TEMPO. Ideally, such termination events should be absent in "living" radical polymerization; however, homopolymer production *via* thermal initiation is a known side reaction during TEMPO-mediated polymerization.[9−16] Another piece of evidence suggesting that side reactions have occurred is given by the measured PD of 1.22 for the cleaved TEMPO-mediated block, as "living" radical polymerizations normally yield PDs < 1.1.[9−16] Finally, it should be pointed out that pathways of termination may differ for the monomers other than **S** and lead to polymeric structures with varying proportions of triblock, diblock, and homopolymeric components.

For most applications in materials science, side reactions must be minimized to produce polymers with narrow molecular weight distributions. However, narrow PD is less important for polymer supports with ultimate use in organic synthesis. For example, a copolymer with PD = 3.54 has been used successfully to prepare water-soluble, polymer-bound hydrogenation catalysts that were recovered by precipitation by alteration of pH.[35] Of course there is a genuine concern that polymer supports with broad PD may suffer material losses of very short polymer chains which will remain in solution during the precipitation step, however, such low molecular weight polymers can be removed by performing several precipitations prior to using the polymer support for organic synthesis. In fact, this fractionation technique is a well-known method for lowering PD.[36]

To highlight the effectiveness of selective precipitation of contaminating homopolymer from copolymers, poly**IA-S** was chosen for study because of the contrasting solubility profiles of its constituent homopolymers. Polystyrene swells or dissolves (depending on its molecular weight) in diethyl ether (Et_2O) and is insoluble in MeOH. Poly(*N*-isopropylacrylamide) is insoluble in Et_2O but completely miscible with MeOH. After **IA** was heated at 70 °C with either azobisisobutyronitrile (AIBN) as a control or **1**, the polymeric products were precipitated from ether, dried, and heated at 130 °C in **S** with minimal DMF as a cosolvent. The final reaction mixtures then were dissolved in dichloromethane (DCM) and precipitated into MeOH to remove homopolymers of poly**IA**. Subsequently, the collected solids were collected by filtration, dried, dissolved in DCM, and precipitated into Et_2O to remove poly**S** homopolymer. From the control reaction with AIBN as the initiator, a sticky gel was recovered in 3% yield. This material contained a 1:16 ratio of **IA**:**S** residues based on ^{1}H NMR analysis. However, a white solid was obtained in 22% yield from the polymerization with initiator **1**, and integration of the ^{1}H NMR spectrum suggested a 3:1 ratio of **IA**:**S** residues. Although NMR analysis does not discriminate definitively between either a block copolymer structure or a blend of homopolymers, a polymer blend would be expected to yield little solid, if any, using the combination of precipitations described. Thus, the significant yield of polymer derived from **2** supplies strong evidence that the product formed was a block copolymer of **IA** and **S**.

It is a well observed phenomenon that in the solid state, block copolymers exhibit interesting morphology due to immiscibility between blocks derived from different monomers.[37] Although immiscible homopolymers can separate into two phases, the polymer chains of block copolymers can only separate from unlike polymer chains to a limited extent because of the covalent coupling between blocks. This microphase separation leads to similar blocks aggregating into domains within the matrix of the other blocks; the resulting domain morphology can be observed by transmission electron microscopy (TEM)**.** Following extensive solid−liquid extractions of the copolymer poly**IA-S** described above with a Soxhlet apparatus, thin films of this polymer were prepared and examined by TEM. The solid material recovered from the Soxhlet extractor formed transparent solutions in THF and $CHCl_3$, but a translucent mixture was observed in acetone:MeOH (1:1). Acetone swells or dissolves both homopolymers of poly**S** and poly**IA**, but MeOH is a selective nonsolvent for poly**S**. Amphiphilic block copolymers with a suitable hydrophilic/hydrophobic balance

(33) The peak assigned to the polystyrene block initiated by the diazene functionality (first block of M_n 8200) was not detected by SEC upon direct injection of the hydrolysis reaction (after removing water with Na_2SO_4). Instead, only the TEMPO-mediated block ($M_n = 118\,000$; PD = 1.22) was observed, which was not unexpected as the block copolymer contained at a maximum 3.2% of the first block by weight. However, it was discovered that addition of ether to the hydrolysis reaction not only induced phase separation, but also caused the higher molecular weight polystyrene to partition out of the organic layer and collect at the interface as an emulsion. Thus, observation by SEC of the lower molecular weight polystyrene was achieved by concentrating the organic layer and adding only a small sample of emulsion found at the interface.

(34) Moad G.; Solomon, D. H. *The Chemistry of Free Radical Polymerization;* Pergamon: Oxford, 1995; p 228.

(35) Bergbreiter, D. E.; Liu, Y.-S. *Tetrahedron Lett.* **1997**, *38*, 3703.

(36) (a) *Polymer Fractionation*; Cantow, M. J. R., Ed.; Academic Press: New York, 1967. (b) Noshay A.; McGrath J. E. *Block Polymers;* Academic Press: New York, 1977; p 49.

(37) Elias, H.-G. *An Introduction to Plastics*; VCH: Weinheim, 1993; p 100.

(38) (a) Kotaka, T.; Fukuda, T.; Inagaki, H. *Polym. J. (Tokyo)* **1972**, *3*, 327. (b) Tuzar, Z.; Kratochvil, P. *Adv. Colloid Interface Sci.* **1976**, *6*, 201. (c) Kotaka, T.; Fukuda, T.; Hattori, M.; Inagaki, H. *Macromolecules* **1978**, *11*, 138.

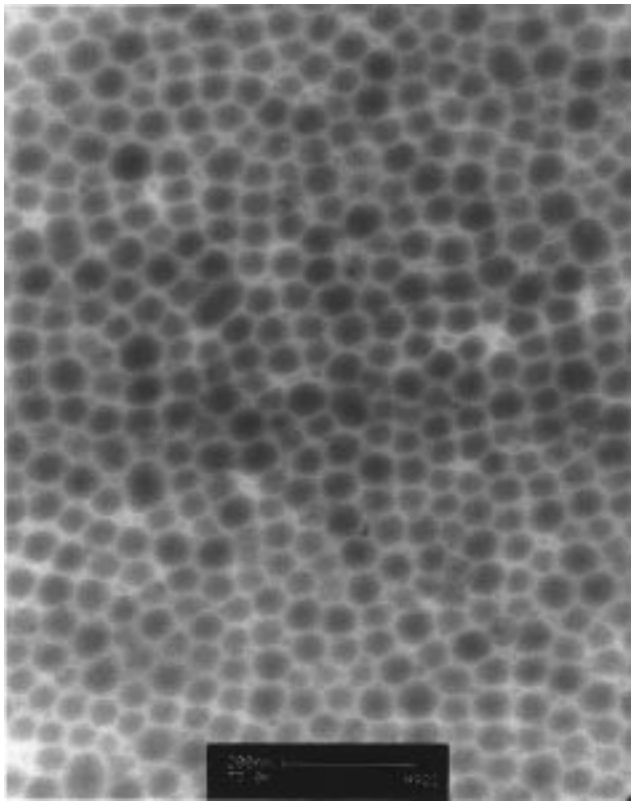

Figure 3. Transmission electron micrograph of the block copolymer obtained by sequential polymerization of *N*-isopropylacrylamide (**IA**) and styrene (**S**) using initiator **2**.

form micelle structures in the presence of selective solvents,[38] and the use of MeOH in our polymer solution may assist microphase separation upon drying to the solid state. The thin polymer films were cast by dipping copper grids[39] into a poly**IA-S** solution [1% (w/v) in 1:1 acetone:MeOH], dried, and analyzed by TEM. Blends of homopolymers macrophase separate into large amorphous domains as observed by TEM;[23] however, the pattern observed for poly**IA-S** appeared as an ordered array of microspheres (Figure 3). Their spherical shape was confirmed by rotating the copper disk and observing the resulting TEM image. This observed morphology for poly**IA-S** is consistent with microphase separation of poly**S** blocks from poly**IA** blocks in a copolymer.

Finally it should be noted that there is a wide range of molecular weights obtained after the "living" polymerization step (2 300 poly**IA-VP** to 109 000 poly**IA-DS**) with no obvious correlation between monomer and molecular weight. The yields from the polymerizations are, as expected, highest for homopolymer synthesis (54−85%). Following the second "living" polymerization step the amount of block copolymer isolated is far more variable. Repeatedly where the "living" polymerization utilizes the **VP** monomer with any homopolymer, the observed yield of copolymer is very low (5−17%), suggesting that "living" polymerization with the **VP** monomer is particularly inefficient.

Parallel Graft Copolymer Synthesis Utilizing Initiator 4. Synthesis of the graft copolymers began by simply heating AIBN with **4** and a subset of three vinyl monomers **S**, **DS**, and **VP** at 70 °C to generate linear statistical copolymers of class **13** [poly**S(4)**, poly**DS(4)** and poly**VP(4)**] containing pendant TEMPO groups. These copolymers were then polymerized at 130 °C with **S**, **DS**, and **VP**.

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Table 3. Solubility of the Graft Copolymer Library from Initiator **4**

polymerization[a] order	solubility[b,c]									
	A	B	C	D	E	F	G	H	I	J
S(4)	S	S	S	S	sw	S	S	I	I	I
DS(4)	S	sw	S	S	S	S	S	I	I	I
VP(4)	sw	I	S	sw	sw	S	S	sw	S	I
S(4)-DS	S	I	S	S	S	S	S	S	I	I
S(4)-VP	S	I	S	S	S	S	S	S	S	I
DS(4)-S	S	sw	S	sw	I	S	S	I	I	I
DS(4)-VP	S	sw	S	S	S	S	S	I	I	I

[a] Monomers: styrene **5** (**S**), 3,4-dimethoxystyrene **7** (**DS**), *N*-vinylpyrrolidinone **8** (**VP**). [b] Solvents: toluene (A), diethyl ether (B), tetrahydrofuran (C), acetone (D), acetonitrile (E), dichloromethane (F), dimethylformamide (G), dimethyl sulfoxide (H), methanol (I), water (J). [c] S = soluble; sw = swell; I = insoluble.

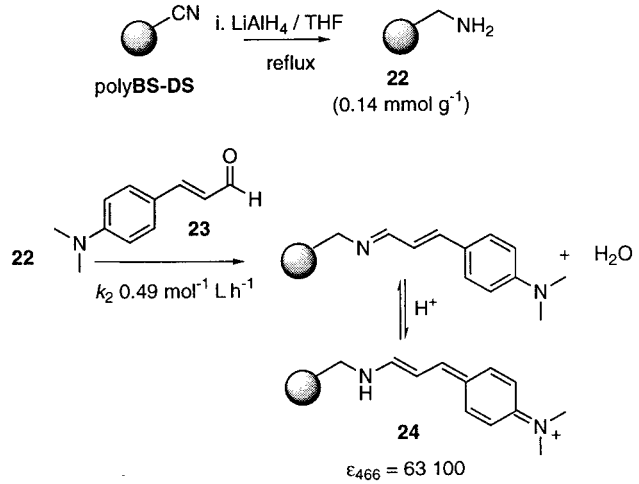
Heating of the copolymer poly**VP(4)** at 130 °C with either **S** or **DS** produced gelatinous reaction mixtures that were insoluble in any solvents listed (Table 3). Gels formed after heating for only 3 min, in contrast to the synthesis of the other comb polymers which were viscous solutions after heating overnight. Hyperbranched polymers have been synthesized previously with use of a monomer similar in structure to **4** and no observation of any insoluble or cross-linked material was made, although **VP** monomer was not used.[11−13] No gelation was observed when poly**VP** was mixed with poly**S(4)** and heated with either **S** or **DS**. These results suggest that gel formation is dependent upon the statistical copolymer poly**VP(4)**. In fact, poly**VP(4)** differed from poly**S(4)** and poly**DS(4)** in that its SEC analysis exhibited a bimodal distribution. The exact basis for gelation in this system is speculative, but we postulate that side reactions during polymerization at 130 °C may be leading to cross-linking.

Combinations of **S**, **DS**, and **VP** produced soluble comb polymers with interesting profiles (Table 3). Both solubility properties and molecular weights changed considerably after the second polymerization. In contrast to that observed for the block copolymers, the solubility profiles of the comb polymers were generally determined by the second monomer, although not exclusively. For example, both poly**S(4)-VP** and poly**DS(4)-VP** are soluble in MeOH although poly**S(4)** and poly**DS(4)** are not. However, the presence of poly**S(4)** and poly**DS(4)** confers water insolubility on these comb polymers since the homopolymer poly**VP** is highly soluble in water.

Solubility profiles of block and graft copolymers derived from the same pair of monomers exhibited minor differences (Tables 1 and 3). For example, the block copolymer poly**DS-S** was found to be soluble in both acetone and acetonitrile, whereas poly**DS(4)-S** only swelled or remained undissolved. Such variances might originate from the acrylate structure derived from **4** in addition to differences in polymer composition and molecular weight. Whatever their source of diversity, these comb polymers provide additional versatility as supports for soluble polymer organic synthesis while exploiting the same monomer set as before.

Selection and Utility of a Block Copolymer for LPOS. After screening the solubility profiles of the individual members of the copolymer library (Table 1) poly**BS-DS** was selected for further study. Of critical importance is its solubility in Et_2O and THF and its insolubility in H_2O. This is in complete contrast to the present soluble polymer of choice in LPOS, poly(ethylene) glycol (PEG). The poor solubility of PEG in Et_2O and THF has meant that the breadth of chemistry that can be achieved with this support is ultimately limited. An additional

Scheme 3. Reduction of the α-Nitrile Groups in PolyBS-DS To Give Poly**22** and Subsequent Kinetic Evaluation of Imine Formation with **23**



problem with PEG-supported chemistry is the polymer's high solubility in H_2O, meaning that aqueous extractions to remove salts cannot easily be performed. Therefore poly**BS-DS** seemed an ideal starting point for the characterization of a new soluble support for LPOS.

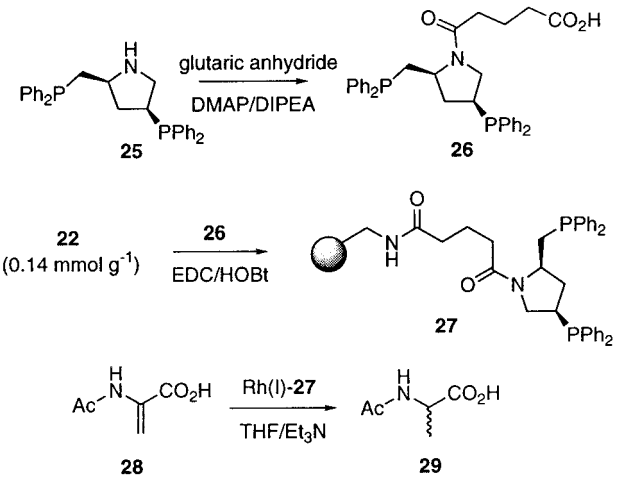
As described *vide supra* block copolymers derived from bifunctional initiators **1**−**3** contain an α-nitrile group at the linkage between the blocks. Reduction of these α-nitrile groups yields amines that can serve as loci for polymer-supported organic chemistry. Reaction of the copolymer poly**BS-DS** with $LiAlH_4$ in refluxing THF for 2 h gave the amino functionalized poly**BS-DS-NH$_2$** (**22**) (Scheme 3).[40]

Quantitative ninhydrin analysis[41] revealed a loading of 0.14 mmol g^{-1} of amine which, based on the SEC determined value of $M_n = 17\,000$, approximates to 2 amino groups per polymer chain as expected. This value compares favorably with the maximal loading capacity of 0.20 mmol g^{-1} calculated for PEG monomethyl ether ($M_n = 5000$).

Kinetic Analysis of Imine Formation with polyBS-DS-NH$_2$ (22). While the functional basis of LPOS is that molecules which are bound to soluble polymer supports often exhibit similar reactivity as their unbound counterparts,[42] it was important to determine that this was the case for our new support poly**22**. Given that the location of the amino groups of poly**22** is in the middle of the block copolymer it was a concern that either one of the polymer blocks may impede their availability for reaction. A comparative kinetic analysis was performed between poly**22** and 1-aminohexane for their reaction with 4-dimethylaminocinnamaldehyde (**23**) (Scheme 3). The rate of iminium ion **24** formation was determined by the method of initial rates in a UV assay by repetitive scanning of a $CHCl_3$ solution at 466 nm.[43]

The second-order rate constants for imine formation were measured as $k_{poly22} = 0.49$ L mol^{-1} h^{-1} and $k_{aminohexane} = 0.69$ L mol^{-1} h^{-1}, suggesting that the amino groups of poly**22** are indeed sufficiently solvent exposed to make them amenable for derivatization and hence that poly**BS-DS** is a suitable support for LPOS.

Scheme 4. Synthetic Route to Polymer Supported Phosphine Ligand **27** and Subsequent Catalytic Reduction of **28** to **29**



For an application of poly**BS-DS** in a different setting, we studied its utility as a ligand support in a well-characterized rhodium(I)-catalyzed asymmetric hydrogenation (Scheme 4).[44]

The commercially available diphosphine ligand **25** was treated with glutaric anhydride to generate the glutaroyl derivative **26**. An excess of **26** (5 equiv) was then reacted with poly**BS-DS**−**NH$_2$** (**22**) ($M_n = 17\,000$, 0.14 mmol g^{-1}) under EDC/HOBt coupling conditions in DCM. The reaction was followed by quantitative ninhydrin analysis, which showed the reaction to be complete after 4 h. The workup involved simple dropwise addition of the reaction mixture to cold, anhydrous MeOH. The diphosphine derivatized polymer **27** then was collected by filtration, washed repeatedly with MeOH, and dried *in vacuo*. The reaction of **27** with rhodium(I) in the form of [Rh(1,5-cyclooctadiene)Cl]$_2$ in THF gave a light yellow polymer of a Rh(I)-**27** complex after isolation by filtration following precipitation into cold, anhydrous MeOH. The reduction of 2-*N*-acetamidoacrylic acid (**28**) to 2-*N*-acetylalanine (**29**) was performed at 20 psi H_2 and 20 °C in THF, with a rhodium/phosphine ratio of 0.5 and a substrate/rhodium ratio of 50. As described previously the excess of phosphine ensures that any phosphine sites that had been oxidized during complex formation would not coordinate to rhodium.[44] Rh(I)-**27** catalyzed the reduction of **28** with a rate comparable to that of the unbound ligand (2*S*,4*S*)-1-*tert*-butoxycarbonyl-4-diphenylphosphino-2-(diphenylphosphinomethyl)pyrrolidine, 50% *vs* 40% after 2.5 d, respectively. The enantiomeric excess (ee) was determined by NMR and an HPLC assay following reaction of the products with an excess of (*R*)-(+)-1-(1-naphthyl)ethylamine. The Rh-(I)-**27** support gave a comparable ee (*S*-**29**, 87% ee) to that of the solution-based phosphine ligand (*S*-**29**, 81% ee). The use of the Rh(I)-**27** polymer support had the advantages that precipitation of the polymer-bound ligand with methanol simplified the reaction workup and allowed near quantitative recovery of the expensive ligand essentially unchanged such that recycling was possible.

Polymer Supports with Functionality Derived from TEMPO. As discussed *vide supra* "living" free radical

(40) For reduction of polymeric nitriles in the presence of ester linkages derived from initiator **1**, catalytic hydrogenation with PtO_2 in dioxane/$CHCl_3$ has been shown to be successful.

(41) Sarin, V. K.; Kent, S. B. H.; Tam, J. P.; Merrifield, R. B. *Anal. Biochem.* **1981**, *117*, 147.

(42) (a) Bayer E.; Mutter, M.; Uhmann, R.; Polster, J.; Mauser, H. *J. Am. Chem. Soc.* **1974**, *96*, 5614. (b) Bayer E.; Mutter, M.; Polster, J.; Uhmann, R. In *Peptides 1974*; John Wiley & Sons: New York, 1975; p 129. (c) Mutter, M. *Int. J. Peptide Protein Res.* **1979**, *13*, 274. (d) Mutter, M.; Bayer E. In *The Peptides*; Academic: New York, 1979; Vol. 2, p 285.

(43) Gargiulo, D.; Ikemoto, N.; Odingo, J.; Bozhkova, N.; Iwashita, T.; Berova, N.; Nakanishi, K. *J. Am. Chem. Soc.* **1994**, *116*, 3760.

(44) For leading papers on polymer-supported transition metal-catalyzed reactions, see: (a) Masuda T.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 268. (b) Baker, G. L.; Fritschel, S. J.; Stille, J. K. *J. Org. Chem.* **1981**, *46*, 2954.

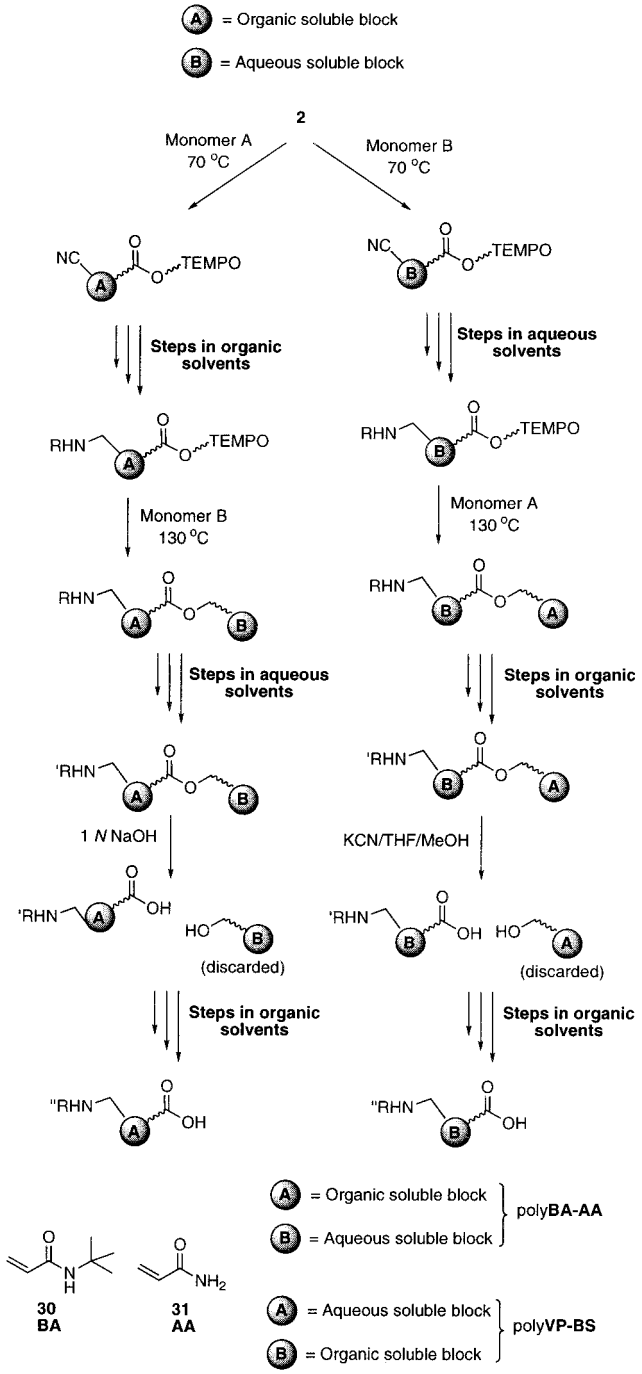
polymerization with initiators **1**−**4** may produce polymer chains terminated by TEMPO[9−16] that, in principle, may be removed by hydrolysis to reveal hydroxyl moieties suitable as orthogonal tether points for functionalization. It was envisioned primarily that the orthogonal nature of loci unmasked from the α-nitrile and TEMPO groups may serve in combinatorial library construction for example, where tagging and/or encoding strategies are required alongside the library development.

Treatment with Zn/AcOH or Zn/NH_4Cl is a well-characterized process for cleavage of the N−O bond of TEMPO in small molecules.[25,26] However, in our hands this method gave inconsistent results for the library of block copolymers described. Of preliminary concern was the insolubility of a number of the library members in the Zn/AcOH reaction mixture. Attempts to solubilize these copolymers by addition of cosolvents lowered the yield of TEMPO deprotection in control reactions. Other reductive methods employing Ra−Ni/H_2, Pd−C/H_2, and SmI_2 reportedly failed to cleave the N−O bond of TEMPO,[26] and in fact we have found that using freshly activated zinc, $NiCl_2$−$LiAlH_4$,[45] or $Mo(CO)_6$[46] also did not give satisfactory results.

To be able to reproducibly derivatize end groups based on the known termination mechanism of TEMPO in the "living" free radical mechanism of polymerization we have developed initiator **3** (see Figure 1). The TEMPO groups are themselves now functionalized with Boc protected amino groups. Sequential polymerization of monomers **BS** followed by **DS** with initiator **3** produced the soluble support poly**BS-DS-(NBoc)** (M_n = 20 400), a homologue of poly**BS-DS** described *vide supra*. A second support, poly**VP-S-(NBoc)** (M_n = 52 200), was formed from tandem polymerization of **VP** and **S**. The ease of Boc deprotection was studied for both of these polymer supports in a TFA/DCM (1:10) mixture. Quantitative ninhydrin analysis revealed that the deprotection was complete after stirring overnight. Loadings were measured as 0.06 (1.3 amino groups per polymer chain) and 0.01 mmol g^{-1} (0.5 amino groups per polymer chain),[47] respectively. No cleavage of the ester linkages was detected by SEC during this deprotection strategy. Thus, soluble supports derived from initiator **3** may contain up to four uniformly distributed amino groups after reaction with both H_2/PtO_2[40] and TFA.

Oscillating Liquid-Phase (OLP) Supports. Bifunctional initiators provide for two independent rounds of polymerization to produce block copolymers in a temperature-controlled manner. After the first polymerization, the solubility properties of the newly formed polymer support can be altered considerably by the second round of polymerization, which provides the block copolymer support with solubility properties intermediary between the two homopolymers. It is this two-dimensional polymerization approach that allows access to a concept we have dubbed "oscillating liquid-phase" (OLP) synthesis (Scheme 5).

Scheme 5. Outline of the "Oscillating Liquid Phase Strategy" Showing the Potential for Changing Polymer Support Solubility from Organic to Aqueous to Organic with an Organic Polymer Block (A) and an Aqueous Polymer Block (B) and *Vice Versa*[a]



[a] Block copolymers polyBA-AA and polyBS-VP have been investigated for their utility in this approach.

In this OLP strategy, it is envisioned that molecules can be attached to the homopolymer created by heating bifunctional initiator **2** at 70 °C with a selected monomer (either organic soluble or aqueous soluble). After performing reactions with the homopolymer-bound substrate, the solubility properties of the polymer support then can be changed by the second polymerization (at 130 °C) with a monomer of opposite solubility properties. Finally, if required the ester linkage between the copolymer blocks may be cleaved during a synthesis to reduce the support to its original solubility as a homopolymer.

(45) Tufariello, J. J.; Meckler, H.; Senaratne, K. P. A. *Tetrahedron* **1985**, *41*, 3447.

(46) Cicchi, S.; Goti, A.; Brandi, A.; Guarna, A.; De Sarlo, F. *Tetrahedron Lett.* **1990**, *31*, 3351.

(47) Low loading capacity indicated either incomplete deprotection of BOC or the presence of polymers lacking TEMPO end groups that might arise by either homopolymer production or termination events during polymerizations.

(48) (a) Elmore, D. T.; Guthrie, D. J. S.; Wallace, A. D.; Bates, S. R. E. *J. Chem. Soc., Chem. Commun.* **1992**, 1033. (b) Schuster, M.; Wang, P.; Paulson, J. C.; Wong, C.-H. *J. Am. Chem. Soc.* **1994**, *116*, 1135. (c) Halcomb, R. L.; Huang, H.; Wong, C.-H. *J. Am. Chem. Soc.* **1994**, *116*, 11315. (d) Kopper, S. *Carbohydr. Res.* **1994**, *265*, 161. (e) Waldmann, H.; Reidel: A. *Angew. Chem.* **1997**, *109*, 642. (f) Yamada, K.; Nishimura, I. *Tetrahedron Lett.* **1995**, *36*, 9493. (g) Sauerbrei, B.; Jungmann, V.; Waldmann, H. *Angew. Chem.* **1998**, *110*, 1187.

Thus solubilities can change from organic to aqueous and then back to organic, or *vice versa*, and therefore may be of considerable use in chemistries that require a combination of organic and bioorganic syntheses.[48]

To demonstrate the feasibility of OLP, poly(*N-tert*-butylacrylamide) (poly**BA**) was synthesized from initiator **2** (containing an ester linkage) and *N-tert*-butylacrylamide (**30**). Poly**BA** is completely insoluble in water; however, a second polymerization with **AA** yielded a polymer support, poly**BA-AA**, that forms a translucent aqueous solution. Following treatment with aqueous NaOH, the homopolymer poly**BA** was recovered by extraction with ethyl acetate. Cleavage of ester linkages under nonaqueous conditions can also be performed with a methanolic solution of KCN in THF. Similarly, the homopolymer poly**VP** derived from initiator **2** is a water-soluble support that swells in THF. A second polymerization with **BS** greatly increases the THF solubility of the block copolymer poly**VP-BS**. The transformed copolymer support was also water insoluble, therefore reactions on this new support can involve workups that involve aqueous extractions to remove water-soluble impurities.

These results suggest that it is possible to conduct reactions first in organic solvents (after the first polymerization), then aqueous mixtures (after a second polymerization with a water-soluble monomer), and finally back into organic solutions (after cleavage of the ester linkages between blocks).

Conclusions

Libraries of block and graft copolymers have been generated by a sequence of normal and "living" free radical polymerization with a variety of vinyl monomers **5**−**9** and initiators **1**−**4**. One block copolymer selected from these libraries, poly**BS-DS**, has a solubility profile that is complementary to the current soluble polymer of choice in LPOS, PEG, and hence may be even more useful when applied in soluble polymer organic synthesis. Hydrolysis of the terminal TEMPO residues of the copolymers to generate hydroxyl residues has proven to be difficult by standard methodologies. However, the α-nitrile groups of poly**BS-DS** are facilely reduced with $LiAlH_4$ or PtO_2/H_2. Kinetic studies have revealed that the accessibility of these amino functionalities for reaction is essentially equivalent to a small molecule in solution. As an example of poly**BS-DS** in LPOS, a rhodium(I) phosphine poly**BS-DS** complex Rh(I)-**27** catalyzes the asymmetric reduction of 2*N*-acetylacrylic acid (**28**) at the same rate and with a similar optical yield to a rhodium(I)−phosphine ligand in solution.

Other features of this work are that copolymers poly**BS-DS-(NBoc)** and poly**VP-S-(NBoc)** derived from inititator **3** possess TEMPO end groups functionalized with Boc protected amino residues which can be easily hydrolyzed with a TFA/DCM (1:10) mixture to incorporate additional sites for derivatization. In addition an "oscillating liquid-phase" strategy can be performed (with polymers derived from initiators **2**−**4**) where the solubility of the copolymer support can be modified during a synthetic strategy by either a second polymerization during a synthetic scheme or hydrolysis of the ester linkage between the blocks to free the component homopolymer fragments.

Finally, the adaptability of these new soluble polymer supports makes them ideal for additional applications in high-throughput organic synthesis such as potential fluorous phase compatibility[3] and offers soluble polymer analogues to resin-capture,[49] polymer-quench,[50] and complementary molecular recognition (CMR) strategies.[51]

Experimental Section

General Procedures. Unless otherwise stated, all reactions were performed under an inert atmosphere with dry reagents and solvents and flame-dried glassware. Analytical thin-layer chromatography (TLC) was performed with 0.25 mm coated silica gel Kieselgel 60 F_{254} plates. Visualization was by UV absorbance, methanolic sulfuric acid, iodine, and bromocresol green. ^{1}H NMR spectra were recorded on a Bruker AMX-500, AMX-400, or AC-250 spectrometer at 500, 400, or 250 MHz, respectively. Chemical shifts are reported in parts per million (ppm) on the δ scale from an internal standard. ^{13}C NMR spectra were recorded on either a Bruker AMX 500 spectrometer at 125 MHz or a Bruker AMX 400 spectrometer at 100 MHz. High-resolution mass spectra were recorded on a VG ZAB-VSE mass spectrometer. UV−vis spectroscopy was performed on a Hewlett-Packard 8452A diode array spectrophotometer. Lower critical solution temperatures (LCST) were measured by observing a droplet of polymer solution set directly on a Koffler hot stage melting point apparatus. Size exclusion chromatography (SEC) was performed on a Hitachi L-6200 Intelligent liquid chromatograph pump equipped with a Hitachi D-2000 integrator and either a Hitachi L-4000 UV−vis detector (254 nm) or a Hewlett-Packard HP 1047A refractive index detector. THF or $CHCl_3$ (due to low solubilities of some polymers in THF) was used as the mobile phase with a flow rate of 1 mL/min. Three Styrogel (Waters) columns were run in series (7.8 × 300 mm; 10^4, 10^3, 500 Å) and calibrated with 10 monodisperse (M_w/M_n < 1.13) polystyrene standards obtained from Polymer Laboratories (M_n = 3.15 × 10^6, 1.29 × 10^6, 6.295 × 10^5, 1.706 × 10^5, 6.60 × 10^4, 2.85 × 10^4, 1.29 × 10^4, 5.46 × 10^3, 1.70 × 10^3, 580).

Transmission Electron Microscopy (TEM) was performed with a Philips CM100 electron microscope at 80 kV and data documented on Kodak SO163 film. Polymer films were prepared for imaging by dipping copper mesh grids (3 mm diameter, 200 mesh) into a 1% (w/v) polymer solution (1:1 acetone:methanol) and dried at ambient pressure (overnight) and under vacuum (4 h). 1-Hydroxy-2-phenyl-2-(2′,2′,6′,6′-tetramethyl-1-piperidinyloxy)ethane and the bifunctional initiators **1** and **2** were prepared as previously reported.[24] Reversed phase HPLC was performed on a Hitachi LC6000 series machine with an Adsorbosphere HS RP-C18 analytical column.

Synthesis of Initiators 3 and 4. 4-(*tert*-Butoxycarbonylamino)-2,2,6,6-tetramethyl-1-piperidinyloxyethane (15). A solution of 4-amino-(2,2,6,6-tetramethyl-1-piperidinyloxy)ethane (2 g, 11.6 mmol), di-*tert*-butyl dicarbonate (3.2 mL, 14 mmol) and diisopropylethylamine (DIPEA, 4.2 mL, 24 mmol) in DCM (100 mL) was stirred for 4 h at room temperature. The reaction mixture then was diluted with DCM (100 mL) and washed with 1 N HCl (3 × 250 mL) and brine (2 × 250 mL). The combined organic fractions were combined, dried (Na_2SO_4), and evaporated *in vacuo*, to give a crude orange oil that was purified by silica gel chromatography (DCM/MeOH 95:5). This gave **15** as a pale orange solid (2.4 g, 76%). ^{1}H NMR ($CDCl_3$) δ 4.4 (bs, 1H), 3.9 (bs, 1H), 2.0 (bd, 1H), 1.56 (s, 9H, *tert*-butyl), 1.51 (s, 3H, CH_3), 1.49 (bs, 2H), 1.48 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.15 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 155.45, 80.09, 60.48, 45.99, 31.78, 28.90, 28.14, 27.37; LRESMS$^+$ $(M + Na)^+$ 295.

1-Benzoyloxy-(4-*tert*-butoxycarbonylamino)-2-phenyl-2-(2,2,6,6-tetramethyl-1-piperidinyloxy)ethane (16). A solution of **15** (1.7 g, 6.3 mmol) and benzoylperoxide (1.52 g, 6.3 mmol) in styrene **5** (50 mL) was stirred at 50 °C overnight. Following evaporation of the volatiles *in vacuo* the residue was purified by silica gel chromatography (DCM/MeOH 98:2). This gave **16** as a fluffy white solid (1.2 g, 38%). ^{1}H NMR ($CDCl_3$) δ 7.8 (d, 2H, Ar−H), 7.4 (t, 1H, Ar−H), 7.30−7.05 (complex m, 7H, Ar−H), 4.95 (t, 1H, CH), 4.80 (dd, 1H, CH), 4.3 (dd, 1H, CH), 4.2 (bs, 1H), 3.80 (bs, 1H), 1.94−1.72 (complex m, 2H), 1.60 (s, 9H, *tert*-butyl), 1.51 (s, 3H, CH_3), 1.48, (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.15 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$) δ 166.31, 155.21, 140.29, 133.41, 132.89, 130.08, 129.66, 128.39, 128.33, 128.23, 84.07, 79.31, 66.61, 60.45, 46.55, 42.03, 33.91, 28.40, 20.93; HR-FABMS calcd for $C_{29}H_{41}N_2O_5$ 497.3015; obsd 497.3002.

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1-Hydroxy-2-phenyl-2-(4-*tert*-butoxycarbonylamino-2,2,6,6-tetramethyl-1-piperidinyloxy)ethane (17). The ester **16** (0.9 g, 1.8 mmol) was dissolved in a 10 N NaOH/THF/MeOH (3:1:1) mixture (16 mL) and stirred for 8 h at room temperature. The reaction mixture was then diluted with diethyl ether (50 mL) and partitioned. The organic fraction was washed with brine (2 × 50 mL), dried (Na_2SO_4), and evaporated *in vacuo*. The crude residue was purified by silica gel chromatography (DCM/MeOH 95:5) to give alcohol **17** as a white solid (700 mg, 98%). ^{1}H NMR ($CDCl_3$) δ 7.25 (bm, 5H, Ar−H), 5.2 (dd, 1H, CH), 4.35 (bs, 1H), 4.2 (dd, 1H, CH), 3.87 (bs, 1H), 3.75 (dd, 1H, CH), 1.95−1.85 (complex m, 2H), 1.65 (s, 3H, CH3), 1.60 (s, 9H, *tert*-butyl), 1.35−1.00 (complex m, 11H, 3 × CH_3 and CH_2); ^{13}C NMR ($CDCl_3$) δ 155.19, 139.92, 128.21, 127.93, 127.67, 83.89, 79.28, 66.62, 60.48, 46.52, 32.97, 28.40, 20.90; HRFABMS calcd for $C_{22}H_{36}N_2O_4$ 393.3675; obsd 393.3672.

Diazene 3. A solution of alcohol **17** (700 mg, 1.78 mmol), the diacid **18** (180 mg, 0.71 mmol), EDC (544 mg, 2.84 mmol), hydroxybenzotriazole (HOBt, 383 mg, 2.84 mmol), and DIPEA (0.74 mL, 4.26 mmol) in THF (10 mL) was stirred for 8 h at room temperature. The reaction mixture was then diluted with diethyl ether (50 mL) and washed sequentially with 1 N HCl (3 × 50 mL), saturated $NaHCO_3$ (3 × 50 mL), and brine (2 × 50 mL). The combined organic fractions were then combined, dried (Na_2SO_4), and evaporated *in vacuo* to give a crude colorless oil that was purified by silica gel chromatography (Et_2O/hexane 1:1). This gave initiator **3** as a white crystalline solid (557 mg, 76%). ^{1}H NMR ($CDCl_3$) δ 7.34−7.2 (complex m, 10H, Ar−H), 4.89 (dd, 2H, CH), 4.60 (m, 2H, CH), 4.31−4.24 (complex m, 3H), 3.75 (bs, 1H), 2.39−2.17 (complex m, 8H, 4 × CH_2), 1.79 (d, 2H), 1.67 (d, 2H), 1.60 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 1.42 (s, 18H, 2 × *tert*-butyl), 1.42 (s, 6H, 2 × CH_3), 1.32 (s, 6H, 2 × CH_3), 1.30−1.28 (m, 2H), 1.16 (s, 6H, 2 × CH_3), 0.65 (s, 6H, 2 × CH_3); ^{13}C NMR ($CDCl_3$) δ 170.84, 155.19, 139.92, 129.02, 127.93, 127.67, 117.41, 83.89, 79.28, 71.76, 66.40, 60.48, 46.52, 41.99, 33.84, 32.97, 30.29, 28.96, 23.81, 23.47, 20.90; HRFABMS calcd for $C_{56}H_{84}N_8O_{10}Cs$ 1161.5365; obsd 1161.5437.

1-Methacryloyloxy-2-phenyl-2-(2′,2′,6,6′-tetramethyl-1-piperidinyloxy)ethane (4). 1-Hydroxy-2-phenyl-2-(2′,2′,6′,6′-tetramethyl-1-piperidinyloxy)ethane (**19**, 15 g, 54 mmol, 1 equiv) was dissolved in dry DCM (150 mL). Triethylamine (12.2 mL, 87.5 mmol, 1.6 equiv) was added followed by methacryloyl chloride (**20**, 7.9 mL, 82 mmol, 1.5 equiv), and an ice bath was applied briefly. After being stirred under a nitrogen atmosphere for 2.5 h, the reaction mixture was washed with 1 N HCl (3 × 100 mL) and brine (100 mL), dried (Na_2SO_4), and evaporated to dryness. The crude product was purified by column chromatography (19:1 hexane:ethyl acetate). This gave **4** as a white solid (12.1 g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.22 (m, 5H, Ar−H), 5.98 (s, 1H, CH_2), 5.47 (s, 1H, CH_2), 4.95 (t, 1H, CH), 4.62 (dd, 1H, CH), 4.33 (dd, 1H, OH), 1.84 (s, 3H, CH_3), 1.62, 1.48, 1.37, 1.31, 1.17, 1.03, 0.70 (each br s, 18H, 3 × CH_2 and 4 × CH_3); ^{13}C NMR ($CDCl_3$) δ 167.14, 140.64, 136.15, 127.93, 127.52, 125.53, 83.83, 66.47, 60.03, 40.37, 33.96, 20.28, 18.26, 17.10; HRFABMS calcd for $C_{21}H_{31}NO_3$ $(M + Na)^+$ 368.2202; obsd 368.2214.

General Procedure for Block and Graft Copolymer Synthesis. Monomers were distilled prior to use except for acrylamide and its derivatives which were used as received. Polymerization yields were determined gravimetrically and calculated from a theoretical yield based on 100% monomer conversion. Although often too small and/or broad to accurately determine, some initiator-derived resonances were observed by ^{1}H and ^{13}C NMR analysis and are reported in those instances. The general method for copolymer synthesis is illustrated once each for formation of the block copolymer poly**S-BS** and graft copolymer poly**S(4)-DS**. For homopolymer synthesis only the first polymerization at 70 °C occurs. Note that the precipitation solvents change for each copolymer.

Blockpolymer Synthesis. 1. Homopolymers. Polystyrene (S). A solution of 300 mg of **1** (300 mg, 0.39 mmol) and styrene (**5**, 0.89 mL, 7.75 mmol) in DCB (3 mL) was freeze-thawed 3 times with liquid nitrogen and then heated at 70 °C for 8 h. The solution was precipitated by dilution in DCM followed by dropwise addition into MeOH to give a white solid, yield 80%. M_n(THF) = 8000 and PD = 2.11; ^{1}H NMR ($CDCl_3$) δ 7.25−6.8 (br m, Ar−H), 6.8−6.2 (br m, Ar−H), 2.1−1.65 (br s, polymer backbone), 1.65−1.2 (br s, polymer backbone); ^{13}C NMR ($CDCl_3$) δ 145.27, 127.83, 125.66, 85.38, 73.35, 70.44, 40.47, 34.05, 20.38, 17.16.

Poly(4-*tert*-butylstyrene) (BS). Reaction: 300 mg of **1** (0.39 mmol, 1 equiv) and 4-*tert*-butylstyrene (**6**, 1.42 mL, 7.75 mmol, 20 equiv) in DCB (3 mL). Precipitation: DCM/methanol to give a white solid, yield 85%. M_n(THF) = 24 000 and PD = 2.36; ^{1}H NMR ($CDCl_3$) δ 7.35−6.8 (br m, Ar−H), 6.8−6.05 (br m, Ar−H), 2.15−1.5 (br m, polymer backbone), 1.5−1.1 (br s, *tert*-butyl group and polymer backbone); ^{13}C NMR ($CDCl_3$) δ 147.95, 142.72, 127.21, 124.61, 85.33, 40.47, 39.79, 34.23, 31.53, 20.32, 17.16.

Poly(3,4-dimethoxystyrene) (DS). Reaction: 300 mg of **1** (0.39 mmol, 1 equiv) and 3,4-dimethoxystyrene (**7**, 1.15 mL, 7.75 mmol, 20 equiv) in DCB (3 mL). Precipitation: DCM/methanol to give a white solid, yield 75%. M_n(THF) = 19 000 and PD = 1.67; ^{1}H NMR ($CDCl_3$) δ 6.75−6.25 (br m, Ar−H), 6.25−5.75 (br m, Ar−H), 3.95−3.4 (br d, $-OCH_3$), 2.2−1.6 (br s, polymer backbone), 1.6−1.2 (br s, polymer backbone); ^{13}C NMR ($CDCl_3$) δ 148.34, 147.02, 137.94, 127.71, 127.13, 119.42, 110.49, 85.26, 73.26, 70.33, 55.59, 44.72, 40.13, 33.99, 20.25, 17.07.

Poly(*N*-vinylpyrrolidinone) (VP). Reaction: 140 mg of **1** (0.18 mmol, 1 equiv) and *N*-vinylpyrrolidinone (**8**, 0.39 mL, 3.6 mmol, 20 equiv) in DCB (1.5 mL). Precipitation: methanol/diethyl ether, then DCM/hexane to give a white powder, yield 74%. M_n($CHCl_3$) = 5100 and PD = 1.44; ^{1}H NMR ($CDCl_3$) δ 4.05−3.5 (br m, 1H, CH), 3.5−3.05 (br s, 2H, CH_2), 2.55−1.3 (br m); ^{13}C NMR ($CDCl_3$) δ 175.45, 127.78, 73.27, 44.81, 43.52, 42.34, 31.39, 19.93, 18.26, 18.00.

Poly(*N*-isopropylacrylamide) (IA). Reaction: 131 mg of **1** (0.17 mmol, 1 equiv) and *N*-isopropylacrylamide (**9**, 388 mg, 3.4 mmol, 20 equiv) in DMF (1.5 mL). Precipitation: THF/diethyl ether to give a white solid, yield 54%. M_n($CHCl_3$) = 18 100 and PD = 1.40; ^{1}H NMR ($CDCl_3$) δ 6.8−5.7 (br s, 1H, NH), 4.1−3.9 (br s, 1H, CH), 2.4−1.2 (br m), 1.2−0.95 (br s, 6H, CH_3); ^{13}C NMR ($CDCl_3$) δ 174.54, 127.69, 73.09, 70.76, 42.19, 41.24, 35.10, 22.46, 20.83, 17.45.

2. Copolymers. Polystyrene−Poly(4-*tert*-butylstyrene) (S-BS). A solution of the homopolymer poly**S** 102 mg (0.98 mmol of styrene residues estimated, 1 equiv) in 4-*tert*-butyl styrene (**6**, 0.197 mL, 1.08 mmol, 1.1 equiv) was freeze−thawed 3 times at −70 °C and then heated at 130 °C for 12 h. The reaction mixture was then diluted with DCM and added dropwise to MeOH. The resultant precipitate was collected by filtration to give poly**S-BS** as a white powder, yield 44%. M_n(THF) = 7800 and PD = 2.42; ^{1}H NMR ($CDCl_3$) δ 7.35−6.05 (br m, Ar−H), 2.15−1.1 (br m, includes *tert*-butyl group); ^{1}H signal integration, 2.5:1 ratio of styrene:4-*tert*-butylstyrene residues; ^{13}C NMR ($CDCl_3$) δ 148.18, 145.10, 142.54, 127.31, 125.65, 124.67, 40.38, 34.26, 31.49.

Polystyrene−Poly(3,4-dimethoxystyrene) (S-DS). Reaction: 53 mg of poly**S** (0.51 mmol of styrene residues estimated, 1 equiv) and 3,4-dimethoxystyrene (**7**, 0.114 mL, 0.77 mmol, 1.5 equiv). Precipitation: DCM/methanol to give a white powder, yield 33%. M_n(THF) = 8500 and PD = 2.00; ^{1}H NMR ($CDCl_3$) δ 7.25−5.75 (br m, Ar−H), 3.95−3.4 (br d, $-OCH_3$), 2.2−1.2 (br m); ^{1}H signal integration, 1.9:1 ratio of styrene:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 148.41, 146.95, 145.27, 136.48, 127.96, 125.65, 119.46, 110.62, 55.67, 40.37.

Polystyrene−Poly(*N*-vinylpyrrolidinone) (S-VP). Reaction: 42 mg of poly**S** (0.40 mmol of styrene residues estimated, 1 equiv) dissolved first in 0.07 mL of DMF, *N*-vinylpyrrolidinone (**8**, 0.344 mL, 3.2 mmol, 8 equiv), heated for 40 h. Precipitation: THF/methanol to give a white powder, yield 5%. M_n(THF) = 8400 and PD = 1.75; ^{1}H NMR ($CDCl_3$) δ 7.25−6.8 (br m, Ar−H), 6.8−6.2 (br m, Ar−H), 4.05−3.5 (br m, CH), 3.5−3.05 (br s, CH_2), 2.55−1.2 (br m); ^{1}H signal integration, 3.2:1 ratio of styrene:*N*-vinylpyrrolidinone residues; ^{13}C NMR ($CDCl_3$) δ 176.23, 145.16, 127.66, 125.62, 44.10, 43.48, 42.30, 40.36, 18.11.

Polystyrene−Poly(*N*-isopropylacrylamide) (S-IA). Reaction: 43 mg of poly**S** (0.41 mmol of styrene residues estimated, 1 equiv) dissolved first in 0.07 mL of DMF, *N*-isopropylacrylamide (**9**, 0.284 g, 2.5 mmol, 6 equiv), heated for 40 h. Precipitation: THF/diethyl ether to give poly**S-IA** as a white powder, yield 16%. M_n(THF) = 16 200 and PD = 1.61; ^{1}H NMR ($CDCl_3$) δ 7.25−6.2 (br m), 4.1−3.9 (br s, NCH), 2.4−0.95 (br m, includes $-CH_3$); ^{1}H signal integration,

1:2.4 ratio of styrene:*N*-isopropylacrylamide residues; ^{13}C NMR ($CDCl_3$) δ 174.38, 145.09, 127.84, 125.61, 42.34, 41.35, 40.37, 22.57.

Poly(4-*tert*-butylstyrene)−Polystyrene (BS-S). Reaction: 51 mg of poly**BS** (0.32 mmol of 4-*tert*-butylstyrene residues estimated, 1 equiv) and styrene (**5**, 0.109 mL, 0.95 mmol, 3 equiv). Precipitation: DCM/methanol to give poly**BS-S** as a white solid, yield 35%; M_n(THF) = 19 300 and PD = 3.07; ^{1}H NMR ($CDCl_3$) δ 7.35−6.05 (br m, Ar−H), 2.15−1.1 (br m, includes *tert*-butyl group); ^{1}H signal integration, 3.5:1 ratio of 4-*tert*-butylstyrene:styrene residues; ^{13}C NMR ($CDCl_3$) δ 145.23, 148.01, 142.72, 127.51, 125.25, 124.64, 40.32, 39.81, 34.31, 31.55.

Poly(4-*tert*-butylstyrene)−Poly(3,4-dimethoxystyrene) (BS-DS). Reaction: 100 mg of poly**BS** (0.62 mmol of 4-*tert*-butylstyrene residues estimated, 1 equiv) and 3,4-dimethoxystyrene (**7**, 0.102 mL, 0.69 mmol, 1.1 equiv). Precipitation: DCM/methanol to give poly**BS-DS** as a white solid, yield 59%. M_n(THF) = 19 500 and PD = 2.44; ^{1}H NMR ($CDCl_3$) δ 7.35−5.75 (br m, Ar−H), 3.95−3.4 (br d, −OCH_3), 2.2−1.1 (br m, includes *tert*-butyl group); ^{1}H signal integration: 2.5:1 ratio of 4-*tert*-butylstyrene:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 148.34, 148.00, 146.79, 142.78, 137.64, 127.21, 124.61, 119.43, 110.59, 55.66, 40.08, 39.83, 34.24, 31.54.

Poly(4-*tert*-butylstyrene)−Poly(*N*-vinylpyrrolidinone) (BS-VP). Reaction: 52 mg of poly**BS** (0.32 mmol of 4-*tert*-butylstyrene residues estimated, 1 equiv) dissolved first in 0.085 mL of DCB, *N*-vinylpyrrolidinone (**8**, 0.174 mL, 1.6 mmol, 5 equiv). Precipitation: DCM/methanol to give poly**BS-VP** as a white solid, yield 6%. M_n(THF) = 20 500 and PD = 2.52; ^{1}H NMR ($CDCl_3$) δ 7.35−6.8 (br m, Ar−H), 6.8−6.05 (br m, Ar−H), 4.05−3.5 (br m, −NCH−), 3.5−3.05 (br s, NCH_2), 2.55−1.1 (br m, includes *tert*-butyl group); ^{1}H signal integration, 2.4:1 ratio of 4-*tert*-butylstyrene:*N*-vinylpyrrolidinone residues; ^{13}C NMR ($CDCl_3$) δ 175.43, 147.79, 142.60, 127.34, 124.59, 45.09, 43.94, 42.78, 40.04, 34.23, 31.50, 17.93.

Poly(4-*tert*-butylstyrene)−Poly(*N*-isopropylacrylamide) (BS-IA). Reaction: 52 mg of poly**BS** (0.32 mmol of 4-*tert*-butylstyrene residues estimated, 1 equiv) and *N*-isopropylacrylamide (**9**, 148 mg, 1.3 mmol, 4 equiv). Precipitation: THF/methanol to give poly**BS-IA** as a white solid, yield 19%. M_n(THF) = 27 100 and PD = 2.04; ^{1}H NMR ($CDCl_3$) δ 7.35−6.8 (br m, Ar−H), 6.8−6.05 (br m, Ar−H), 4.1−3.9 (br s, −NCH−), 2.4−0.95 (br m); ^{1}H signal integration: 3.1:1 ratio of 4-*tert*-butylstyrene:*N*-isopropylacrylamide residues; ^{13}C NMR ($CDCl_3$) δ 175.24, 147.96, 142.78, 127.31, 124.62, 42.29, 41.35, 39.78, 34.25, 31.50, 22.43.

Poly(3,4-dimethoxystyrene)−Polystyrene (DS-S). Reaction: 58 mg of poly**DS** (0.35 mmol of 3,4-dimethoxystyrene residues estimated, 1 equiv) and styrene (**5**, 0.101 mL, 0.88 mmol, 2.5 equiv). Precipitation: DCM/methanol to give poly**DS-S** as a white solid, yield 20%. M_n(THF) = 17 800 and PD = 1.73; ^{1}H NMR ($CDCl_3$) δ 7.25−5.75 (br m, Ar−H), 3.95−3.4 (br d, −OCH_3), 2.2−1.2 (br m); ^{1}H signal integration, 3:1 ratio of 3,4-dimethoxystyrene:styrene residues; ^{13}C NMR ($CDCl_3$) δ 148.24, 146.70, 145.23, 137.24, 127.94, 125.63, 119.45, 110.48, 55.64, 40.23.

Poly(3,4-dimethoxystyrene)−Poly(4-*tert*-butylstyrene) (DS-BS). Reaction: 54 mg of poly**DS** (0.34 mmol of 3,4-dimethoxystyrene residues estimated, 1 equiv) dissolved first in 0.09 mL of DCB, 4-*tert*-butylstyrene (**6**, 0.182 mL, 0.99 mmol, 3 equiv). Precipitation: THF/methanol to give poly**DS-BS** as a white solid, yield 30%. M_n(THF) = 18 900 and PD = 1.72; ^{1}H NMR ($CDCl_3$) δ 7.35−5.75 (br m, Ar−H), 3.95−3.4 (br d, −OCH_3), 2.2−1.1 (br m, includes *tert*-butyl group); ^{1}H signal integration, 2.7:1 ratio of 3,4-dimethoxystyrene:4-*tert*-butylstyrene residues; ^{13}C NMR ($CDCl_3$) δ 142.93, 148.29, 147.95, 146.81, 137.65, 127.16, 124.76, 119.10, 110.49, 55.62, 40.17, 39.85, 34.29, 31.47.

Poly(3,4-dimethoxystyrene)−Poly(*N*-vinylpyrrolidinone) (DS-VP). Reaction: 48 mg of poly**DS** (0.29 mmol of 3,4-dimethoxystyrene residues estimated, 1 equiv) dissolved first in 0.063 mL of DMF, *N*-vinylpyrrolidinone (**8**, 0.125 mL, 1.2 mmol, 4 equiv). Precipitation: THF/methanol, filtered solid [poly**DS**, identified by ^{1}H NMR], concentrated filtrate, then precipitated with hexane to give poly**DS-VP**, yield 17%. M_n(THF) = 9800 and PD = 2.34; ^{1}H NMR ($CDCl_3$) δ 6.75−6.25 (br m, Ar−H), 6.25−5.75 (br m, Ar−H), 4.05−3.05 (br m), 2.55−1.2 (br m); ^{1}H signal integration, 1.3:1 ratio of 3,4-dimethoxystyrene:*N*-vinylpyrrolidinone residues; ^{13}C NMR ($CDCl_3$) δ 175.41, 148.28, 146.73, 137.08, 119.30, 110.56, 55.62, 44.73, 43.44, 42.50, 40.20, 31.38, 18.30.

Poly(3,4-dimethoxystyrene)−Poly(*N*-isopropylacrylamide) (DS-IA). Reaction: 54 mg of poly**DS** (0.33 mmol of 3,4-dimethoxystyrene residues estimated, 1 equiv) and *N*-isopropylacrylamide (**9**, 381 mg, 3.4 mmol, 10 equiv). Precipitation: DCM/diethyl ether to give poly**DS-IA** as a white solid, yield 12%. M_n(THF) = 17 000 and PD = 1.77; ^{1}H NMR ($CDCl_3$) δ 6.75−6.25 (br m, Ar−H), 6.25−5.75 (br m, Ar−H), 4.1−3.4 (br m), 2.4−0.95 (br m); ^{1}H signal integration, 3.5:1 ratio of 3,4-dimethoxystyrene:*N*-isopropylacrylamide residues; ^{13}C NMR ($CDCl_3$) δ 174.16, 148.29, 146.73, 137.56, 119.55, 110.52, 55.62, 42.47, 41.25, 40.13, 22.62.

Poly(*N*-vinylpyrrolidinone)−Polystyrene (VP-S). Reaction: 41 mg of poly**VP** (0.37 mmol of *N*-vinylpyrrolidinone residues estimated, 1 equiv) dissolved first in 0.105 mL of DMF, styrene (**5**, 0.211 mL, 1.8 mmol, 5 equiv). Precipitation: DCM/hexane to give poly**VP-S** as a white solid, yield 26%. M_n(THF) = 10 600 and PD = 4.10; ^{1}H NMR ($CDCl_3$) δ 7.25−6.8 (br m, Ar−H), 6.8−6.2 (br m, Ar−H), 4.05−3.5 (br m, NCH), 3.5−3.05 (br s, NCH_2), 2.55−1.2 (br m); ^{1}H signal integration, 1.3:1 ratio of *N*-vinylpyrrolidinone:styrene residues; ^{13}C NMR ($CDCl_3$) δ 175.45, 145.24, 127.92, 125.62, 44.82, 43.63, 42.12, 40.30, 31.58, 18.31.

Poly(*N*-vinylpyrrolidinone)−Poly(4-*tert*-butylstyrene) (VP-BS). Reaction: 32 mg of poly**VP** (0.29 mmol of *N*-vinylpyrrolidinone residues estimated, 1 equiv) dissolved first in 0.10 mL of DMF, 4-*tert*-butylstyrene (**6**, 0.263 mL, 1.4 mmol, 5 equiv), heated for 58 h. Precipitation: THF/methanol to give poly**VP-BS** as a white solid, yield 25%. M_n(THF) = 5700 and PD = 3.21; ^{1}H NMR ($CDCl_3$) δ 7.35−6.8 (br m, Ar−H), 6.8−6.05 (br m, Ar−H), 4.05−3.5 (br m, NCH), 3.5−3.05 (br s, NCH_2), 2.55−1.1 (br m, includes *tert*-butyl group); ^{1}H signal integration, 1:2.8 ratio of *N*-vinylpyrrolidinone:4-*tert*-butylstyrene residues; ^{13}C NMR ($CDCl_3$) δ 175.54, 148.01, 142.76, 127.34, 124.60, 44.87, 43.58, 42.73, 39.74, 34.29, 31.51, 31.28, 18.32.

Poly(*N*-vinylpyrrolidinone)−Poly(3,4-dimethoxystyrene) (VP-DS). Reaction: 33 mg of **VP** (0.30 mmol of *N*-vinylpyrrolidinone residues estimated, 1 equiv) dissolved first in 0.044 mL of DMF, 3,4-dimethoxystyrene (**7**, 0.088 mL, 0.059 mmol, 2 equiv). Precipitation: THF/diethyl ether, washed with methanol to give poly**VP-DS** as a white solid, yield 54%. M_n(THF) = 47 100 and PD = 2.63; ^{1}H NMR ($CDCl_3$) δ 6.75−6.25 (br m, Ar−H), 6.25−5.75 (br m, Ar−H), 4.05−3.05 (br m), 2.55−1.2 (br m); ^{1}H signal integration, 1:1.7 ratio of *N*-vinylpyrrolidinone:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 175.56, 148.34, 146.81, 137.95, 119.40, 110.48, 55.59, 44.75, 43.46, 42.39, 40.17, 31.42, 18.27.

Poly(*N*-vinylpyrrolidinone)−Poly(*N*-isopropylacrylamide) (VP-IA). Reaction: 35 mg of poly**VP** (0.31 mmol of *N*-vinylpyrrolidinone residues estimated, 1 equiv) dissolved first in 0.1 mL of DMF, *N*-isopropylacrylamide (**8**, 0.182 g, 1.6 mmol, 5 equiv). Precipitation: THF/diethyl ether to give poly**VP-IA** as a white solid, yield 35%. M_n-($CHCl_3$) = 7100 and PD = 1.57; ^{1}H NMR ($CDCl_3$) δ 6.8−5.7 (br s, NH), 4.1−3.5 (br m), 3.5−3.05 (br s, NCH_2), 2.55−0.95 (br m, includes −CH_3); ^{1}H signal integration, 1:2.4 ratio of *N*-vinylpyrrolidinone:*N*-isopropylacrylamide residues; ^{13}C NMR ($CDCl_3$) δ 175.48, 174.61, 44.79, 43.66, 42.41, 41.38, 31.46, 22.52, 18.29; LCST(H_2O) = 38 °C.

Poly(*N*-isopropylacrylamide)−Polystyrene (IA-S). Reaction: 27 mg of poly**IA** (0.24 mmol of *N*-isopropylacrylamide residues estimated, 1 equiv) dissolved first in 0.035 mL of DMF, styrene (**5**, 0.19 mL, 1.66 mmol, 7 equiv), heated for 8 h. Precipitation: THF/diethyl ether to give poly**IA-S** as a white solid, yield 15%. M_n(THF) = 49 100 and PD = 1.53; ^{1}H NMR ($CDCl_3$) δ 7.25−6.2 (br m), 4.1−3.9 (br s, −NCH−), 2.4−0.95 (br m, includes −CH_3); ^{1}H signal integration, 1.1:1 ratio of *N*-isopropylacrylamide:styrene residues; ^{13}C NMR ($CDCl_3$) δ 174.55, 145.38, 127.64, 125.65, 42.36, 41.28, 40.33, 22.58.

Poly(*N*-isopropylacrylamide)−Poly(4-*tert*-butylstyrene) (IA-BS). Reaction: 24 mg of poly**IA** (0.21 mmol of *N*-isopropylacrylamide residues estimated, 1 equiv) dissolved first in 0.10 mL of DMF, 4-*tert*-butylstyrene (**6**, 0.269 mL, 1.47 mmol, 7 equiv); heated for 58 h. Precipitation: THF/methanol to give poly**IA-BS** as a white solid, yield 41%. M_n(THF) = 20 400 and PD = 5.92; ^{1}H NMR ($CDCl_3$) δ 7.35−6.8 (br m, Ar−H), 6.8−6.05 (br m, Ar−H), 4.1−3.9 (br s, −NCH−),

2.4−0.95 (br m); ^{1}H signal integration, 1.2:2 ratio of *N*-isopropylacrylamide:4-*tert*-butylstyrene residues; ^{13}C NMR ($CDCl_3$) δ 174.62, 148.00, 142.76, 127.35, 124.63, 42.18, 41.32, 39.88, 34.26, 31.53, 22.30.

Poly(*N*-isopropylacrylamide)−Poly(3,4-dimethoxystyrene) (IA-DS). Reaction: 31 mg of poly**IA** (0.27 mmol of *N*-isopropylacrylamide residues estimated, 1 equiv) dissolved first in 0.1 mL of DMF, 3,4-dimethoxystyrene (**7**, 0.2 mL, 1.35 mmol, 5 equiv). Precipitation: THF/methanol yielded a milky solution that was filtered through cotton to remove solid homopolymer [poly**DS**, identified by ^{1}H NMR]. The filtrate was concentrated *in vacuo* and added dropwise to hexane. The precipitate was collected by filtration to give poly**IA-DS** as a white solid, yield 45%. M_n(THF) 109 000 and PD = 1.56; ^{1}H NMR ($CDCl_3$) δ 6.75−6.25 (br m, Ar−H), 6.25−5.75 (br m, Ar−H), 4.1−3.4 (br m), 2.4−0.95 (br m); ^{1}H signal integration, 1:1.7 ratio of *N*-isopropylacrylamide:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 174.55, 148.37, 146.85, 136.45, 119.42, 110.54, 55.62, 42.54, 41.35, 40.14, 22.55.

Poly(*N*-isopropylacrylamide)−Poly(*N*-vinylpyrrolidinone) (IA-VP). Reaction: 24 mg of poly**IA** (0.21 mmol of *N*-isopropylacrylamide residues estimated, 1 equiv) and *N*-vinylpyrrolidinone (**8**, 0.455 mL, 4.26 mmol, 20 equiv), heated for 4.5 h (formed a glassy solid/gel). Precipitation: reaction mixture extracted with THF [discarding gelatinous homopolymer poly**VP**], precipitated with diethyl ether to give poly**IA-VP**, yield 5%. M_n($CHCl_3$) = 2300 and PD = 1.78; ^{1}H NMR ($CDCl_3$) δ 6.8−5.7 (br s, NH), 4.1−3.5 (br m), 3.5−3.05 (br s, NCH_2), 2.55−0.95 (br m, includes CH_3); ^{1}H signal integration, 1:1.6 ratio of *N*-isopropylacrylamide:*N*-vinylpyrrolidinone residues; ^{13}C NMR ($CDCl_3$) δ 174.49, 44.75, 43.53, 42.81, 41.25, 22.53, 18.49; LCST(H_2O) = 35 °C.

Parallel Graft Copolymer Synthesis. 1. Statistical Copolymers. Poly(styrene-*stat*-4) [S(4)]. A solution of **4** (311 mg, 0.90 mmol, 1 equiv), AIBN (90 mg, 0.55 mmol, 0.6 equiv), and styrene (**5**, 1.05 mL, 9.2 mmol, 10 equiv) in DCB (3 mL) was freeze−thawed three times and then heated to 70 °C for 8 h. Precipitation: DCB/methanol gave poly**S(4)** as a white solid, yield 92%. M_n(THF) = 12 600 and PD = 2.84; ^{1}H NMR ($CDCl_3$) δ 7.5−6.7 (br m, Ar−H), 6.7−6.1 (br m, Ar−H), 4.6−4.2 (br s, 2H), 4.0−3.1 (br m), 2.6−0.65 (br m), 0.65−0.0 (br m, TEMPO); ^{1}H signal integration, 11.2:1 ratio of styrene:**4** residues; ^{13}C NMR ($CDCl_3$) δ 176.20, 145.33, 127.96, 127.65, 125.65, 88.55, 65.55, 59.87, 40.39, 33.96, 20.35, 17.15.

Poly(3,4-dimethoxystyrene-*stat*-4) [DS(4)]. Reaction: 282 mg of **4** (0.82 mmol, 1 equiv), AIBN (92 mg, 0.56 mmol, 0.7 equiv), and 3,4-dimethoxystyrene (**7**, 1.2 mL, 8.1 mmol, 10 equiv) in DCB (3 mL). Precipitation: THF/methanol, to give poly**DS(4)** as a white solid, yield 70%. M_n(THF) = 18 500 and PD = 2.30; ^{1}H NMR ($CDCl_3$) δ 7.3−6.9 (br s, Ar−H), 6.75−6.3 (br m, Ar−H), 6.3−5.75 (br m, Ar−H), 4.69 (br s), 4.42 (br s), 4.0−3.3 (br d, $-OCH_3$), 2.3−0.8 (br m), 0.8−0.2 (br m); ^{1}H signal integration, 11.0:1 ratio of 3,4-dimethoxystyrene:phenyl (derived from **4**) residues; ^{13}C NMR ($CDCl_3$) δ 176.02, 148.41, 147.03, 137.89, 128.07, 124.94, 119.49, 110.58, 83.67, 65.83, 60.19, 55.63, 40.14, 33.92, 20.28, 17.17.

Poly(*N*-vinylpyrrolidinone-*stat*-4) [VP(4)]. Reaction: 291 mg of **4** (0.84 mmol, 1 equiv), AIBN (93 mg, 0.57 mmol, 0.7 equiv), and *N*-vinylpyrrolidinone (**8**, 0.90 mL, 8.4 mmol, 10 equiv) in DCB (3 mL). Precipitation: THF/diethyl ether to give poly**VP(4)** as a white solid, yield 90%. M_n($CHCl_3$) = 65 700 and PD = 1.49; ^{1}H NMR ($CDCl_3$) δ 7.3−6.95 (br m, Ar−H), 4.71 (br s), 4.28 (br s), 4.1−3.35 (br m, 1H, NCH), 3.35−2.8 (br s, 2H, NCH_2), 2.8−0.4 (br m); by integration: 4.1:1 ratio of *N*-vinylpyrrolidinone:phenyl (derived from **4**) residues; ^{13}C NMR ($CDCl_3$) δ 175.29, 127.68, 83.46, 66.30, 59.94, 44.72, 43.46, 42.00, 33.94, 31.37, 20.32, 17.06.

2. Graft Copolymers. Poly(styrene-*stat*-8)-*graft*-poly(3,4-dimethoxystyrene) [S(4)-DS]. Reaction: 109 mg of poly**S(4)** and 3,4-dimethoxystyrene (**7**, 1.0 mL). Precipitation: DCM/methanol to give poly**S(4)-DS** as a white solid, yield 72%. M_n(THF) = 94 300 and PD = 1.39; ^{1}H NMR ($CDCl_3$) δ 7.2−5.75 (br m), 4.0−3.3 (br d, $-OCH_3$), 2.3−0.8 (br m); ^{1}H signal integration, 11.0:1 ratio of 3,4-dimethoxystyrene:styrene residues; ^{13}C NMR ($CDCl_3$) δ 148.00, 146.87, 137.67, 127.98, 125.43, 119.38, 110.58, 55.63, 40.18.

Poly(styrene-*stat*-8)-*graft*-poly(*N*-vinylpyrrolidinone) [S(4)-VP]. Reaction: 104 mg of poly**S(4)** and *N*-vinylpyrrolidinone (**8**, 1.0 mL). Precipitation: DCM/diethyl ether to give poly**S(4)-VP** as a white solid, yield 13%. M_n($CHCl_3$) = 9200 and PD = 1.84; ^{1}H NMR ($CDCl_3$) δ 7.3−6.2 (br m, Ar−H), 4.1−3.5 (br m, 1H, NCH), 3.5−2.9 (br s, 2H, NCH_2), 2.5−0.85 (br m); ^{1}H signal integration, 1.6:1 ratio of styrene:*N*-vinylpyrrolidinone residues; ^{13}C NMR ($CDCl_3$) δ 175.40, 145.84, 127.96, 125.67, 60.55, 44.20, 43.42, 42.84, 40.30, 31.45, 18.36.

Poly(3,4-dimethoxystyrene-*stat*-8)-*graft*-polystyrene [DS(4)-S]. Reaction: 105 mg of poly**DS(4)** and styrene **5** (1.0 mL). Precipitation: DCM/methanol to give poly**DS(4)-S**, yield 49%. M_n(THF) = 136 000 and PD = 1.42; ^{1}H NMR ($CDCl_3$) δ 7.55−5.8 (br m), 4.0−3.4 (br d, $-OCH_3$), 2.4−0.9 (br m); ^{1}H signal integration, 9.9:1 ratio of styrene:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 148.65, 147.35, 145.27, 137.41, 127.64, 125.68, 119.19, 111.05, 55.79, 40.43.

Poly(3,4-dimethoxystyrene-*stat*-8)-*graft*-poly(*N*-vinylpyrrolidinone) [DS(4)-VP]. Reaction: 102 mg of poly**DS(4)** and *N*-vinylpyrrolidinone **8** (1.0 mL). Precipitation: DCM/diethyl ether to give poly**DS(4)-VP** as a white solid, yield 18%. M_n($CHCl_3$) = 12 100 and PD = 1.40; ^{1}H NMR ($CDCl_3$) δ 7.3−6.7 (br s, Ar_4−H), 6.7−6.3 (br m, Ar_{DS}−H), 6.3−5.7 (br m, Ar_{DS}−H), 4.1−2.8 (br m), 2.6−0.8 (br m), 0.8−0.1 (br s); by integration, 2.3:1 ratio of *N*-vinylpyrrolidinone:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 175.23, 148.52, 146.86, 137.89, 119.34, 110.53, 65.78, 55.62, 43.56, 42.47, 40.13, 31.39, 20.29, 18.25, 16.99.

Verification of Block Copolymer Structures Derived from Initiator 2 *via* Saponification (Figure 2). The general procedure for the synthesis and verification of the block copolymer structure is a three-step process. Following two rounds of polymerizations the ester linker between the polymer blocks is cleaved by saponification. SEC analysis occurs after each of the three stages. The generation of a block copolymer of polystyrene (poly**S-S**) as detailed below is illustrative.

First polymerization: A solution of initiator **2** (224 mg, 0.28 mmol, 1 equiv) and styrene (**5**, 0.65 mL, 5.7 mmol, 20 equiv) in DCB (3 mL) was degassed by 3 cycles of freezing/thawing under vacuum then heated at 70 °C under nitrogen with mixing for 18 h. The reaction mixture was precipitated into hexane, dissolved in DCM, precipitated into methanol, and dried to give poly**S** as a white solid (392 mg, 66%). M_n(THF) = 8200 and PD = 1.69.

Second polymerization: The homopolymer poly**S** obtained from the first polymerization (20 mg, 0.19 mmol of styrene residues estimated, 1 equiv) was dissolved in styrene (**5**, 1.09 mL, 9.5 mmol, 50 equiv), degassed as described *vide supra*, and then heated at 130 °C for 18 h. The reaction mixture then was diluted and precipitated twice (DCM/methanol) to give the block copolymer poly**S-S** as a white solid (619 mg, 61%). M_n(THF) = 264 000 and PD = 1.30.

Ester Hydrolysis. Poly**S-S** (15 mg) was dissolved in THF (4 mL) and mixed with methanol (1 mL) and 2 N NaOH (1 mL) forming an emulsion that was rapidly stirred at room temperature. After 3 h, stirring was stopped and phase separation was assisted by addition of water (2 mL) and diethyl ether (2 mL). A portion of the organic phase was mixed with a small sample of the thin layer of emulsion at the interface of phases, evaporated to dryness, dissolved in THF, and analyzed by SEC (M_n(THF) = 118 000 and PD = 1.22; M_n(THF) = 8700 and PD = 1.44).

Synthesis of Block Copolymer polyIA-S for TEM Analysis. First polymerization: 92 mg of **1** (0.12 mmol, 1 equiv) and *N*-isopropylacrylamide (**9**, 3.38 g, 30 mmol, 250 equiv) were dissolved in DMF (10 mL), and polymerization was performed as described *vide supra*. Precipitation occurred from THF/diethyl ether to give poly**IA** as a white solid, yield 88%. M_n($CHCl_3$) = 9300 and PD = 1.40; ^{1}H NMR ($CDCl_3$) δ 7.0−6.2 (br s, 1H, NH), 3.95 (br s, 1H, NCH), 2.4−1.25 (br m), 1.25−0.9 (br s, 6H, CH_3); ^{13}C NMR ($CDCl_3$) δ 174.62, 42.34, 41.28, 22.53.

Second polymerization: 1.12 g of poly**IA** from the first polymerization (9.9 mmol of *N*-isopropylacrylamide residues estimated, 1 equiv) was dissolved first in 1.4 mL of DMF with gentle warming, and styrene (**5**, 2.26 mL, 19.7 mmol, 2 equiv) was added. The second polymerization then was performed as described *vide supra*. Precipitation occurred with DCM/methanol followed by DCM/diethyl ether to give poly**IA-S** as a white solid, yield 22%; ^{1}H NMR ($CDCl_3$) δ 7.4−6.25

(br m, Ar−H), 4.00 (br s, −NCH−), 2.4−0.95 (br m, includes $-CH_3$); ^{1}H signal integration, 3.2:1 ratio of styrene:*N*-isopropylacrylamide residues.

Solid−liquid extraction: poly**IA-S** (594 mg) was placed into a Soxhlet extractor, extracted with diethyl ether (17 h), dried, and then extracted with methanol (23 h) and dried. Yield 515 mg of a white solid (87%). M_n(THF) = 145 000 and PD = 1.28; ^{1}H signal integration, 4.1:1 ratio of styrene:*N*-isopropylacrylamide residues; ^{13}C NMR ($CDCl_3$) δ 174.53, 145.08, 127.41, 125.62, 42.37, 41.28, 40.33, 22.60.

Control Polymerization with AIBN Initiator. First polymerization: 21 mg of AIBN (0.13 mmol, 1 equiv) and *N*-isopropylacrylamide (**9**, 3.46 g, 30.6 mmol, 240 equiv) in DMF (10 mL). Precipitation: THF/diethyl ether to give poly**IA** as a white solid, yield 96%; ^{1}H NMR ($CDCl_3$) δ 6.9−6.1 (br s, 1H, −NH), 3.92 (br s, 1H, −NCH−), 2.35−1.2 (br m), 1.2−0.9 (br s, 6H, $-CH_3$).

Second polymerization: 1.113 g of poly(*N*-isopropylacrylamide) (9.8 mmol of *N*-isopropylacrylamide residues estimated, 1 equiv) dissolved first in 1.4 mL of DMF with gentle warming, styrene (**5**, 2.26 mL, 19.7 mmol, 2 equiv). Precipitation: DCM/methanol, then DCM/diethyl ether, yield 3%; M_n(THF) = 386 000 and PD = 1.68; ^{1}H NMR ($CDCl_3$) δ 7.45−6.85 (br m, Ar−H), 6.85−6.25 (br m, Ar−H), 4.1−3.9 (br s, 1H, −NCH−), 2.4−1.25 (br m, aliphatic polymer backbone), 1.25−1.05 (br s, 6H, $-CH_3$); ^{1}H signal integration, 16:1 ratio of styrene:*N*-isopropylacrylamide residues; ^{13}C NMR ($CDCl_3$) δ 175.30, 145.32, 127.94, 125.66, 42.90, 41.61, 40.37, 22.66.

Methods Incorporating polyBS-DS into LPOS. Reduction of α-Nitriles. (a) Metal Hydride Reduction To Form polyBS-DS-NH_2 (22). $LiAlH_4$ (0.51 g, 13.4 mmol, 76 equiv) was added portionwise to copolymer poly**BS-DS** (1.5 g, M_n(THF) = 17 000 and PD = 2.45; 0.088 mmol, 2 equiv) dissolved in THF (100 mL) and heated to reflux for 2 h. After being cooled and quenched carefully with water (1 mL) and 1 N NaOH (1 mL), the reaction mixture was filtered twice through Celite, concentrated (ca. 2 mL), precipitated into methanol (50 mL), and dried to give **22** as a white solid, yield 83%. M_n($CHCl_3$) = 16 400 and PD = 1.58; ^{1}H NMR ($CDCl_3$) unchanged from poly**BS-DS** reported *vide supra*. CH_2NH_2 resonances overlap with those of polymer backbone; quantitative ninhydrin: 0.14 mmol of amine per gram of polymer (ninhydrin assay was negative for poly**BS-DS** prior to $LiAlH_4$ treatment).

(b) Hydrogenation. A homopolymer of poly**S** (derived from **2**, 2.0 g, M_n($CHCl_3$) = 8400 and PD = 1.98; 0.24 mmol estimated from SEC, 2 equiv) was dissolved in dioxane (50 mL) in a Parr bottle. After adding PtO_2 (0.25 g, 1.1 mmol) and $CHCl_3$ (1 mL), the solution was degassed by bubbling with N_2 and then shaken overnight under a H_2 atmosphere (40 psi). The catalyst was removed by filtration through Celite, and the filtrate concentrated (ca. 8 mL). The polymer product was precipitated into methanol (200 mL), and dried to a white solid, yield 89%. M_n($CHCl_3$) = 8500 and PD = 1.79; ^{1}H NMR ($CDCl_3$) unchanged (CH_2NH_2 resonances overlap with those of polymer backbone); quantitative ninhydrin: 0.21 mmol of amine per gram of polymer (ninhydrin assay was negative for poly**S** prior to $LiAlH_4$ treatment).

Kinetics of Imine Formation. Copolymer amine **22** from above and 1-aminohexane were prepared as a series of solutions of varying concentrations (30, 20, 10 mM) in $CHCl_3$ and equimolar 4-dimethylaminocinnamaldehyde (**23**) was added. The mixture was stirred over a small amount of Na_2SO_4 at room temperature. Periodically, aliquots (10 μL) were removed and diluted to 20 μM with 150 μM trifluoroacetic acid in $CHCl_3$, and the absorbance was measured at 466 nm (ϵ_{466},polymeric Schiff base = 63 100; ϵ_{466},Schiff base of 1-aminohexane = 79 000). A plot of $x/[a(a - x)]$ versus time where x = concentration of Schiff base and a = initial concentration of amine gave a straight line indicative of second-order kinetics with the rate constant equal to the slope (Maher, J. J.; Furey, M. E.; Greenberg, L. J. *Tetrahedron Lett.* **1971**, 27).

Preparation of polyBS-DS Supported Chiral Diphosphine Ligand 27. (2*S*,4*S*)-*N*-Glutaroyl-4-diphenylphosphino-2-(diphenylphosphinomethyl)-pyrrolidine (26). A solution of (2*S*,4*S*)-4-diphenylphosphino-2-(diphenylphosphino)methylpyrrolidine (**25**, 58 mg, 0.13 mmol), glutaric anhydride (19 mg, 0.16 mmol), diisopropylethylamine (DIPEA, 58 mg, 0.33 mmol), and (dimethylamino)pyridine (DMAP, 1.6 mg, 0.013 mmol) in degassed DCM (1.0 mL) was stirred under an argon atmosphere at room temp (8 h). The reaction mixture then was concentrated *in vacuo* and applied to a Kieselghur 1 mm preparative TLC plate. The product **26** was isolated as a colorless oil (57 mg, 78%): R_F = 0.4 (95:5 DCM/MeOH with 2% AcOH); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.2−1.5 (m, 1H), 2.0−2,4 (m, 10 H), 2.6−3.1 (m, 6H), 7.0−7.7 (m, 20H); HRFABMS calcd for $C_{34}H_{36}NO_3P_2$ 568.2092, obsd 568.2094.

Polymer Supported Phosphine Ligand 27. A solution of carboxyamide **26** (35 mg, 62 μmol), EDC (30 mg, 152 μmol), DMAP (13 mg, 106 μmol), and poly**BS-DS-NH_2** (**22**, 0.14 mmol g^{-1} amino groups, 135 mg) in degassed DCM was stirred at room temperature for 8 h or until quantitative ninhydrin analysis was negative. The reaction mixture was then added dropwise into cold MeOH (50 mL) and the precipitate collected by filtration, redissolved in DCM, and reprecipitated by addition into MeOH. The precipitate was collected by filtration to give **27** as a free flowing white powder, yield 99%. ^{1}H NMR (CDCl3) δ 7.35−5.75 (br m, Ar−H (masks phenyl protons of ligand), 3.95−3.4 (br d, $-OCH_3$), 3.0−2.9 (m, ligand protons), 2.2−1.1 (br m, includes *tert*-butyl group).

Catalytic Hydrogenation with 27. To an argon-purged flask was added the polymer-supported ligand **27** (126 mg, 0.14 mmol of diphosphine per gram of polymer), μ-dichloro-bis(1,5-cyclooctadiene)-dirhodium(I) (4 mg, 0.008 mmol), and degassed THF (5 mL). The homogeneous mixture was stirred for 4 h and then evaporated under argon and resuspended in degassed DCM (1.5 mL). The rhodium-supported polymer, Rh(I)-**27**, was then precipitated by dropwise addition into cold, degassed, anhydrous methanol (50 mL). The polymer (pale yellow) was recovered by filtration and dried *in vacuo*. The Rh(I)-**27** complex was then dissolved in degassed THF (10 mL) and 2-*N*-acetamidoacrylic acid (**28**, 52 mg, 0.4 mmol) was added. The reaction was stirred under H_2 (20 psi). After 2 d, the reaction mixture was evaporated to dryness, dissolved in DCM (2 mL), and precipitated as described above. The polymer was recovered by filtration (126 mg, 100%), the methanolic mother liquor was evaporated to dryness, and the products were analyzed by ^{1}H NMR. The ratio of ^{1}H NMR integrations between *N*-acetylalanine (**29**, CD_3OD, δ 1.99) and starting material **28** (CD_3OD, δ 2.06) *N*-acetyl peaks was used to determine a conversion of 50% after 2.5 d. No attempt to optimize this reaction was made.

Catalytic Hydrogenation with Soluble Ligand: (2,*S*,4,*S*)-1-*tert*-Butoxycarbonyl-4-diphenylphosphino-2-(diphenylphosphinomethyl)pyrrolidine. The method and relative equivalents of all the reagents is as described above for **27**. Conversion (as determined by ^{1}H NMR) = 40% after 2.5 d. No attempt to optimize this reaction was made.

Enantiomeric Excess Determination. The reaction products from the catalytic hydrogenations with either polymer-supported ligand **27** or the soluble ligand *vide supra* were dissolved in DCM (5 mL), and (*R*)-(+)-1-(naphthyl)ethylamine (12 mg, 66 μmol), EDC (13 mg, 70 μmol), and DMAP (8.5 mg, 70 μmol) were added. The reaction mixtures were stirred at room temperature (2 h). The crude reaction mixtures were then analyzed by HPLC [mobile phase 30:70 acetonitrile water (0.1% TFA); *R*T (*S*)-**29** = 43.01 min, *R*T (*R*)-**29** = 43.73 min], and ^{1}H NMR [(400 MHz, $CDCl_3$) δ 1.98 (s, CH_3, (*R*)-**29**), 1.85 (s, CH_3, (*S*)-**29**), 1.36 (d, CH_3, (*S*)-**29**), 1.20 (d, CH_3, (*R*)-**29**); poly**27** = 87.0 ± 0.2% ee; **26** = 81.2 ± 2.4% ee].

Synthesis of NBoc Block Copolymer Supports with Initiator 3. 1. polyBS-DS-(NBoc). First polymerization: 101 mg of **3** (0.098 mmol, 1 equiv) and 4-*tert*-butylstyrene (**6**, 0.36 mL, 1.97 mmol, 20 equiv) in DCB (1 mL). Precipitation: DCM/methanol to give poly**BS** as a white solid, yield 81%. M_n(THF) = 5000 and PD = 2.43; ^{1}H NMR ($CDCl_3$) δ 7.5−6.8 (br m, Ar−H), 6.8−6.0 (br m, Ar−H), 4.87 (br d, CH**3**), 4.57 (br d, CH**3**), 4.25 (br m, CH**3**), 3.76 (br s, CH**3**), 2.5−1.6 (br m), 1.42 (br s, *tert*-butyl$_{\mathbf{BOC}}$), 1.27 (br s,*tert*-butyl$_{\mathbf{BS}}$), 0.88 (br s), 0.66 (br d); ^{1}H signal integration, 15:1 ratio of 4-*tert*-butylstyrene: phenyl (derived from 4 residues); ^{13}C NMR ($CDCl_3$) δ 171.67, 148.13, 142.91, 128.47, 127.65, 124.88, 83.96, 66.07, 60.12, 46.34, 39.57, 34.02, 33.58, 31.58, 28.13, 20.51, 19.11.

Second polymerization: 209 mg of poly**BS** derived from **3** (1.3 mmol of 4-*tert*-butylstyrene residues estimated, 1 equiv) dissolved in 3,4-dimethoxystyrene (**7**, 0.21 mL, 1.4 mmol, 1.1 equiv). Precipita-

tion: DCM/methanol to give poly**BS-DS-(NBoc)** as a white solid, yield 74%. $M_n(CHCl_3) = 24\,300$ and PD = 1.87; ^{1}H NMR ($CDCl_3$) δ 7.3−6.8 (br m, Ar−H), 6.8−5.75 (br m, Ar−H), 3.95−3.4 (br d, $-OCH_3$), 2.5−0.2 (br m), 1.43 (br s, *tert*-butyl$_{\mathbf{BOC}}$), 1.27 (br s,*tert*-butyl$_{\mathbf{BS}}$); ^{1}H signal integration, 1.2:1 ratio of 4-*tert*-butylstyrene:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 148.79, 148.04, 147.13, 142.85, 137.34, 127.54, 124.84, 119.82, 110.77, 55.47, 39.90, 38.53, 33.95, 31.19.

2. polyVP-S-(NBoc). First polymerization: 100 mg of **3** (0.097 mmol, 1 equiv) and *N*-vinylpyrrolidinone (**8**, 0.21 mL, 1.97 mmol, 20 equiv) in DCB (1 mL). Precipitation: DCB/diethyl ether to give poly**VP** as a white solid, yield 78%. $M_n(CHCl_3) = 33\,200$ and PD = 1.66; ^{1}H NMR ($CDCl_3$) δ 7.23 (br s, Ar−H), 4.82 (br s, CH**3**), 4.51 (br s, CH**3**), 4.23 (br s, CH**3**), 4.1−3.45 (br m, NCH), 3.45−2.85 (br s, NCH_2), 2.6−1.4 (br m), 1.35 (br s, *tert*-butyl$_{\mathbf{BOC}}$), 1.27, 1.20, 1.04, 0.60 (each br s, CH_2 and/or CH_3 of TEMPO); ^{1}H signal integration, 27:1 ratio of *N*-vinylpyrrolidinone:phenyl (derived from **3**) residues; ^{13}C NMR ($CDCl_3$) δ 175.27, 171.53, 128.06, 127.58, 83.84, 65.76, 60.39, 46.45, 44.75, 43.47, 41.99, 33.76, 31.40, 28.34, 18.24.

Second polymerization: 54 mg of poly**VP** derived from **3** (0.49 mmol of *N*-vinylpyrrolidinone residues estimated, 1 equiv) dissolved first in 0.4 mL of DMF with gentle warming, styrene (**5**, 1.0 mL, 8.7 mmol, 18 equiv). Precipitation: DCM/methanol to give poly**VP-S-(NBoc)** as a white solid, yield 53%. M_n(THF) = 48 800 and PD = 1.41; ^{1}H NMR ($CDCl_3$) δ 7.4−6.9 (br m, Ar−H), 6.9−6.3 (br m, Ar−H), 4.15−3.55 (br m, NCH), 3.55−3.05 (br s, NCH_2), 2.8−0.9 (br m); ^{1}H signal integration, 10.9:1 ratio of styrene:*N*-vinylpyrrolidinone residues; ^{13}C NMR ($CDCl_3$) δ 175.48, 145.36, 127.47, 125.54, 44.84, 43.91, 42.73, 40.39, 31.47, 18.40.

Boc Deprotection of polyBS-DS-(NBoc). poly**BS-DS-(NBoc)** (92 mg) was dissolved in DCM (0.25 mL) and trifluoroacetic acid (TFA) (25 mL) was added. After the mixture was stirred for 15 h, the volatiles were evaporated under a stream of N_2, and the residue was dissolved in DCM (1 mL) and washed with 1 N $NaHCO_3$ (3 × 1 mL) and brine (1 mL). After being dried over Na_2SO_4, the polymer solution was concentrated and precipitation induced by dropwise addition to methanol. The filtrate was collected to give deprotected poly**BS-DS-(NBoc)** as a white solid, yield 81%. $M_n(CHCl_3) = 20\,400$ and PD = 2.00; ^{1}H NMR ($CDCl_3$) δ 7.35−5.75 (br m, Ar−H), 3.95−3.45 (br d, $-OCH_3$), 2.25−0.65 (br m), 1.28 (br s, *tert*-butyl$_{\mathbf{BS}}$); by integration, 1:1 ratio of 4-*tert*-butylstyrene:3,4-dimethoxystyrene residues; ^{13}C NMR ($CDCl_3$) δ 148.27, 147.97, 147.08, 142.71, 137.97, 127.13, 124.60, 119.45, 110.52, 55.66, 40.19, 39.79, 34.26, 31.52.

Deprotection of polyVP-S-(NBoc). Poly**VP-S-(NBoc)** (92 mg) was dissolved in dry DCM (0.25 mL) and TFA (25 mL) added. After the mixture was stirred for 15 h, the reaction was worked up as above to give Boc deprotected poly**VP-S** as a white solid, yield 64%. M_n(THF) = 52 200 and PD = 1.43; ^{1}H NMR ($CDCl_3$) δ 7.35−6.85 (br m, Ar−H), 6.85−6.3 (br m, Ar−H), 4.1−3.5 (br m, NCH), 3.5−3.05 (br s, NCH_2), 2.5−0.9 (br m); ^{1}H signal integration, 10.6:1 ratio of styrene:*N*-vinylpyrrolidinone residues; ^{13}C NMR ($CDCl_3$) δ 175.43, 145.30, 127.97, 125.66, 44.82, 43.46, 42.26, 40.34, 31.39, 18.32.

Synthesis of Copolymers for "Oscillating Liquid-Phase" (OLP) Synthesis (Scheme 5). (a) Organic−Aqueous−Organic. First polymerization: 900 mg of **2** (1.1 mmol, 1 equiv) and *N-tert*-butylacrylamide (**31**, 1.43 g, 11 mmol, 10 equiv) in DMF (5 mL). Precipitation: THF/water, then purified through a short bed of silica (95:5 DCM:methanol), yield 42%; $M_n(CHCl_3) = 32\,100$ and PD = 2.44; ^{1}H NMR ($CDCl_3$) δ 7.2 (br m, Ar−H), 4.85 (br s), 4.70 (br s), 4.53 (br s), 4.23 (br s), 2.3−1.4 (br m), 1.4−1.1 (br s, *tert*-butyl group), 0.94 (br s), 0.63 (br s); ^{13}C NMR ($CDCl_3$) δ 174.99, 127.98, 127.60, 83.71, 42.78, 40.32, 36.47, 33.95, 20.34, 17.02.

Second polymerization: 58 mg of poly**BA** (0.46 mmol of *N-tert*-butylacrylamide residues estimated, 1 equiv) dissolved first in 0.45 mL of DMF, acrylamide (**32**, 327 mg, 4.6 mmol, 10 equiv). Precipitation: water/methanol, yield 21% (incompatibility of SEC column with aqueous solvents precluded analysis). ^{1}H NMR (D_2O) δ 2.4−1.4 (br m), 1.3 (br s, *tert*-butyl group); ^{1}H signal integration, 1:140 ratio of *N-tert*-butylacrylamide:acrylamide residues; ^{13}C NMR (D_2O) δ 181.79, 44.08, 37.63, 36.77, 28.83.

Ester hydrolysis: 42.5 mg of copolymer poly**BA-AA** stirred with 1 N NaOH (5 mL) for 7 d. Extraction with ethyl acetate gave poly**BA** as a white solid, yield 89% [based on the weight of poly**BA** contained in block copolymer poly**BA-AA** (estimated from ^{1}H NMR integration)]. $M_n(CHCl_3) = 46\,500$ and PD = 2.29; ^{1}H NMR ($CDCl_3$) δ 2.3−1.45 (br m), 1.45−1.15 (br s, *tert*-butyl group).

(b) Aqueous−Organic−Aqueous. First polymerization: 146 mg of **2** (0.18 mmol, 1 equiv) and *N*-vinylpyrrolidinone (**8**, 0.39 mL, 3.6 mmol, 20 equiv) in DCB (1.5 mL). Precipitation: THF/diethyl ether to give a white solid, yield 77%; $M_n(CHCl_3) = 1100$ and PD = 1.46; ^{1}H NMR ($CDCl_3$) δ 7.3−6.9 (br m, Ar−H), 4.80 (br s), 4.62 (br s), 4.49 (br s), 4.3−3.35 (br m, 1H, NCH), 3.35−2.8 (br s, 2H, NCH_2), 2.55−1.15 (br m), 1.06 (br s), 0.91 (br s), 0.57 (br s); ^{1}H signal integration, 15:1 ratio of *N*-vinylpyrrolidinone:phenyl (derived from **2**) residues; ^{13}C NMR ($CDCl_3$) δ 175.34, 127.92, 127.56, 83.61, 44.79, 43.54, 42.32, 40.27, 33.84, 31.33, 20.15, 18.18, 16.98.

Second polymerization: 54 mg of poly**VP** (0.49 mmol of *N*-vinylpyrrolidinone residues estimated, 1 equiv) dissolved first in 0.36 mL of DMF, then 4-*tert*-butylstyrene (**6**, 0.89 mL, 4.9 mmol, 10 equiv). Precipitation: DCM/methanol to give a white solid, yield 59%. M_n(THF) = 129 000 and PD = 1.66; ^{1}H NMR ($CDCl_3$) δ 7.35−6.8 (br m, Ar−H), 6.8−6.05 (br m, Ar−H), 4.05−3.5 (br m, NCH), 3.5−3.05 (br s, NCH_2), 2.55−1.1 (br m, includes *tert*-butyl group); ^{1}H signal integration, 1:8 ratio of *N*-vinylpyrrolidinone:4-*tert*-butylstyrene residues; ^{13}C NMR ($CDCl_3$) δ 174.30, 147.98, 142.71, 127.19, 124.59, 45.05, 43.53, 42.56, 39.75, 34.25, 31.51, 18.28.

Ester hydrolysis: 105 mg of copolymer poly**VP-BS** dissolved in THF (6 mL) mixed with a solution of KCN (16 mg) in methanol (3 mL), overnight. Evaporated solvents, dissolved/slurried solids in $CHCl_3$ (0.5 mL), precipitated poly**BS** by addition of methanol (5 mL), and isolated by filtration. poly**VP** was recovered from the filtrate, yield 32% (based on weight of poly-*N*-vinylpyrrolidinone contained in block copolymer estimated from ^{1}H NMR integration). $M_n(CHCl_3) = 1000$ and PD = 1.90; ^{1}H NMR ($CDCl_3$) δ 4.05−3.5 (br m, 1H, −NCH−), 3.5−3.05 (br s, 2H, $-NCH_2-$), 2.55−1.3 (br m).

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