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Sequence-Regulated Oligomers and Polymers by Living Cationic Polymerization. 2. Principle of Sequence Regulation and Synthesis of Sequence-Regulated Oligomers of Functional Vinyl Ethers and Styrene Derivatives

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ABSTRACT: Vinyl ether oligomers with controlled repeat unit sequences were prepared by living cationic polymerization initiated with the hydrogen iodide/zinc iodide (HI/ZnI_2) system. The synthesis involved sequential and successive reactions of two, three, or four vinyl ethers (each equimolar to hydrogen iodide) in toluene at −40 to −78 °C, starting from quantitative formation of an adduct [$HCH_2CH(OR)I$] of HI and a vinyl ether, followed by activation with ZnI_2; thus, the repeat unit sequence was controlled by the order of monomer addition. The employed vinyl ethers (CH_2=CHOR) included not only alkyl (R = alkyl) but functionalized derivatives with such pendant groups as ethyl malonate [R = $CH_2CH_2CH(COOEt)_2$], benzoyloxy (R = CH_2CH_2OCOPh), methacryloyl [R = $CH_2CH_2OCOC(CH_3)$=CH_2], and chlorine (R = CH_2CH_2Cl). A sequence-regulated trimer having a *p*-methoxystyrene unit was also prepared: $CH_3CH(OC_4H_9)CH_2CH(OCH_2CH_2OCOPh)CH_2CH(C_6H_4OCH_3)OCH_3$. The yields of the sequence-regulated oligomers were greatly dependent on the order of monomer addition, and the highest yields were obtained by adding monomers in the order of their decreasing reactivity. Thermospray mass spectroscopy permitted us to determine the absolute molecular weights and the repeat unit sequence of the oligomers.

Introduction

Sequence Control in Addition Polymers. A polymer molecule consists of numerous constitutional repeat units, and there can be no doubt that the "sequence" of repeat units along a main chain is among the most important factors that determine the properties and functions of macromolecules. "Controlled" sequences of repeat units may be found in block copolymers, where a few "homosequences" (segments) of different monomer units are connected into a single macromolecule. To develop more advanced functions of polymers, it will be necessary to achieve a finer control of the repeat unit sequence that ultimately leads to, for example, an ABCDE... type completely regulated sequence (A, B, ... are monomeric repeat units).

Naturally occurring polymers and oligomers offer good instances that show the significance of regulation of repeat unit sequence. For example, the controlled amino acid and nucleotide sequences in polypeptides and genes, respectively, endow them with specific functions in vivo such as enzymatic catalysis and transmission of genetic information.

In synthetic addition polymers, it is indeed possible to obtain some regular sequences, like ...AAABBB... type block polymers and AB or ABC type alternating copolymers;[1] however, such a truly regulated sequence as ABCDE... is still beyond our reach. There has also been only limited success in attempts to control monomer sequence by template polymerization.[2]

Recently, we have shown that the hydrogen iodide/Lewis acid initiating systems (HI/I_2, HI/ZnI_2, etc.) induce living cationic polymerizations of vinyl ethers and styrene derivatives.[3] The living process enabled us to control the pendant functions, end groups, and molecular weight or molecular weight distribution of polymers. On the basis of these achievements, this study is directed toward controlling another important structural factor in polymers, i.e., the sequence of repeat units, and aims to synthesize oligomers with controlled monomer sequences via one-pot sequential reactions. Even for oligomers, the best examples thus far have still been AB type heterodimers of styrene derivatives[4] by stepwise reactions.

Strategy of the Synthesis. In the living cationic polymerization of vinyl ethers by HI/ZnI_2 (Scheme I), HI quantitatively adds to monomer to form an α-iodoether adduct, which starts living propagation via electrophilic activation of the carbon–iodine (C–I) bond of the adduct by ZnI_2.[5] We herein applied this reaction to the one-pot synthesis of sequence-regulated oligomers; Scheme II outlines our synthetic strategy. The monomers that were employed for the synthesis are listed in Table I (with

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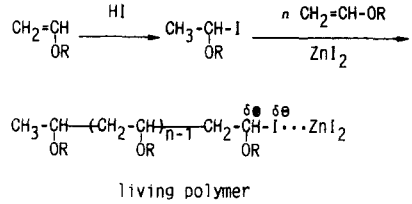
Scheme I



Scheme II

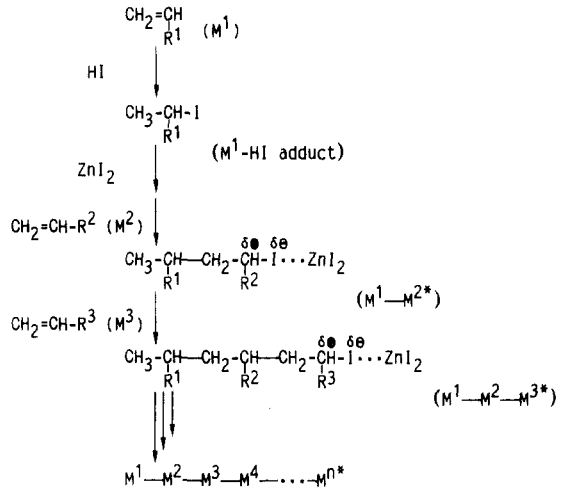


Table I
Vinyl Monomers with Various Pendant Groups

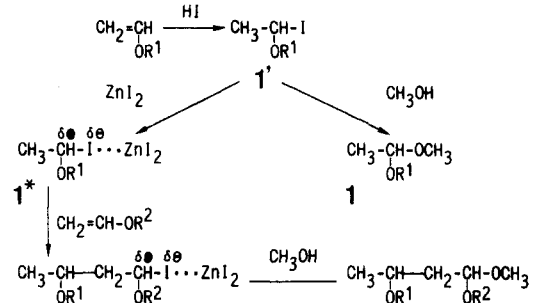
vinyl ether derivatives				styrene derivative
$CH_2=CH-OnC_4H_9$	$CH_2=CH-O-CH(COOEt)_2$	$CH_2=CH-O-CH_2CH_2OCOCH=CH_2$	$CH_2=CH-O-CH_2CH_2OCOPh$	$CH_2=CH-C_6H_4-OCH_3$
NBVE	VOEM	VEM	BzOVE	*p*MOS
$CH_2=CH-O-CH_2CH_2Cl$				
CEVE				

abbreviations). They include not only vinyl ethers but also a styrene derivative, all of which have been shown to undergo living cationic polymerization with HI/I_2 or HI/ZnI_2.[3]

Vinyl monomer M^1 is first allowed to react with an equimolar amount of HI to give the M^1–HI adduct as the initiating species. The second monomer M^2 (equimolar to HI) and ZnI_2 are then added, the latter of which activates the C–I bond of the adduct and thereby permits the insertion of M^2. The resulting dimeric living species M^1–M^{2*} again has a terminal C–I bond that can be activated by ZnI_2 for a further growth. Subsequent sequential additions of monomers M^3, M^4, ... lead to the target "sequence-regulated oligomers" (M^1–M^2–M^3–M^4–...–M^{n*}) where the repeat unit sequence is determined by the order of monomer addition.

An example of the preparation of sequence-regulated trimers and tetramers of vinyl ethers according to this strategy has been reported briefly in our preceding paper.[6] This article concerns the detailed study on the principle of the synthesis of the sequence-regulated oligomers and on the optimization of the reaction conditions.

Scheme III



code	acetal product	R^1	R^2
1a	BzOVE	CH_2CH_2OCOPh	-
1b	NBVE	C_4H_9	-
2a	BzOVE-NBVE	CH_2CH_2OCOPh	C_4H_9
2b	BzOVE-BzOVE	CH_2CH_2OCOPh	CH_2CH_2OCOPh
2c	BzOVE-CEVE	CH_2CH_2OCOPh	CH_2CH_2Cl
2d	NBVE-BzOVE	C_4H_9	CH_2CH_2OCOPh
2e	CEVE-BzOVE	CH_2CH_2Cl	CH_2CH_2OCOPh
2f	NBVE-VOEM	C_4H_9	$CH_2CH_2CH(COOEt)_2$

Results and Discussion

1. Sequence-Regulated Dimers of Vinyl Ethers. Synthesis. To obtain basic knowledge on the general strategy shown in Scheme II, selective sequential dimerization of vinyl ethers by HI/ZnI_2 was investigated (Scheme III). A particular attention was focused on the effects of the reactivity of monomers, relative to the order of their addition sequence, on the yield and selectivity for the desired AB heterodimer. Thus, BzOVE was treated with an equimolar amount of HI to give adduct **1a**',[7] followed by the addition of an equimolar amount of a second monomer (NBVE, BzOVE, or CEVE). In the presence of ZnI_2, the dimerization reaction proceeds via intermediate **1*** to form the corresponding dimeric active species **2***.[8] At each step, the reaction was quenched with methanol to afford an acetal (**1** or **2**),[9] which is more stable than the corresponding intermediate (**1*** or **2***, respectively). To suppress side reactions (such as chain transfer and termination) and homopolymerization of the added monomers, the reaction was carried out in nonpolar toluene solvent at −40 or −78 °C, at low concentrations of monomers (≅10 mM; equimolar to HI initiator) and zinc iodide (0.20 mM).

Effect of Monomer Reactivity on Product Distribution. Figure 1 shows the time–conversion curves for sequential dimerizations (the second-stage reaction in Scheme III), where three VEs (NBVE, BzOVE, and CEVE) were allowed to react with the BzOVE–HI adduct **1*** as an initiating species. Despite the extremely low monomer concentration, the reaction smoothly occurred on addition of ZnI_2 and reached ~70% conversion in 5–6 h. The overall reaction rate decreased in the order NBVE > BzOVE ≳ CEVE, which agreed with the reactivity order of the monomers in their living cationic homopolymerizations.[10-12]

Figure 2 illustrates the product distributions for the three series of sequential dimerizations. As seen in the top row (curves A, D, and G), the treatment of BzOVE with equimolar HI gave only a sharp and unimodal fraction of the acetal **1a**, $CH_3CH(OCH_2CH_2OCOPh)OCH_3$ (confirmed by ^1H NMR), which in turn demonstrated the selective and quantitative formation of the HI adduct **1a*** from BzOVE.

The product distributions in the second steps (Figure 2, middle and bottom rows) were found to depend on the

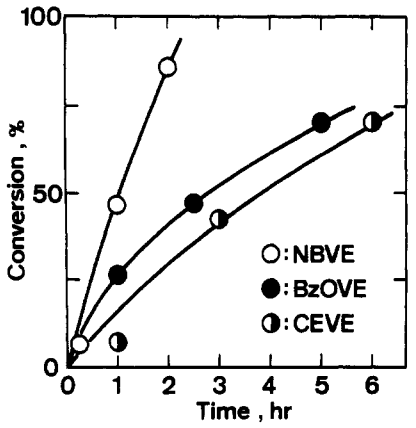


Figure 1. Time–conversion curves for the reaction of BzOVE with three VEs by HI/ZnI_2 in toluene at −78 °C: $[HI]_0 = [VE]_0 \simeq 10$ mM; $[ZnI_2]_0 = 0.20$ mM.

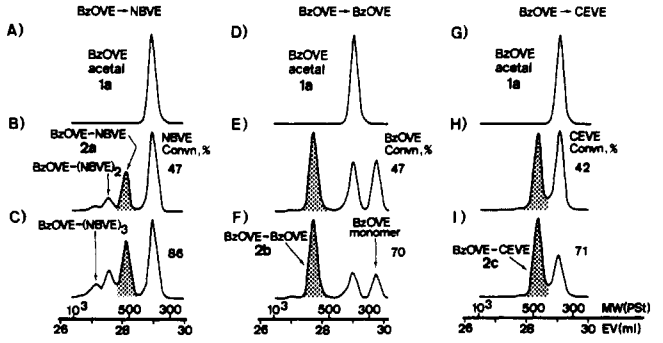


Figure 2. Product distributions in the two-stage sequential reactions of BzOVE with three VEs by HI/ZnI_2 in toluene at −78 °C: top row, the first-stage reaction; middle and bottom rows, the second-stage reaction. Added VE: (A–C) NBVE; (D–F) BzOVE; (G–I) CEVE. Monomer conversions as indicated. $[HI]_0 = [VE]_0 \simeq 10$ mM; $[ZnI_2]_0 = 0.20$ mM.

kind of the second monomers (M^2). The reaction of NBVE with the monomeric living species **1a*** yielded not only the target dimer **2a** (the shadowed fraction in curves B and C) but higher oligomers containing two or more NBVE units [BzOVE(NBVE)$_n$, $n \geq 2$]; the content of the higher oligomers increased with increasing monomer conversion. In contrast, the use of BzOVE or CEVE as the second monomer, both of which are less reactive than NBVE, led to the exclusive formation of the dimer **2b** or **2c**, respectively (curves E, F, H, and I). These results indicate that the yield of the target dimer (**2a** < **2b** ≈ **2c**) increases with decreasing reactivity of the second monomer (NBVE > BzOVE ≳ CEVE; see Figure 1).

The effects of the order of monomer addition were further studied by comparing AB and BA type heterodimerizations in relation with the relative reactivity of monomers. Figure 3 depicts the product distributions for two pairs of such heterodimers prepared by a reversed monomer sequence (curves A and B for NBVE and BzOVE and curves C and D for BzOVE and CEVE); note that the relative reactivity of these monomers is in the order: NBVE > BzOVE ≳ CEVE. In all cases, the second monomer conversion reached over 90% within 1 h at −40 °C.

The dimerization from NBVE to less reactive BzOVE led to almost quantitative formation of the target AB dimer **2d** (Figure 3, curve A), whereas the opposite order of monomer addition resulted in higher oligomers along with the BA dimer **2a** (curve B). As shown in curves C and D, even a small gap between BzOVE and CEVE in reactivity (BzOVE ≳ CEVE, cf. Figure 1) affected the product

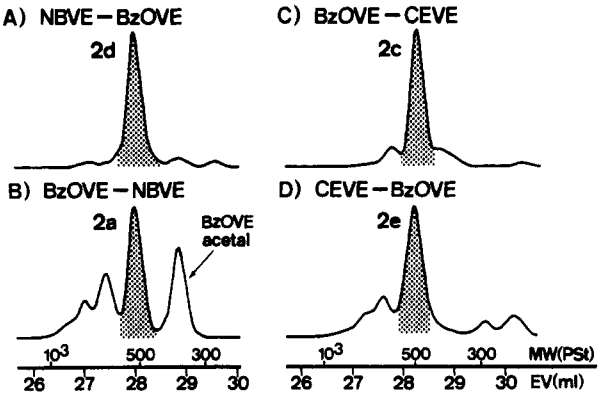


Figure 3. Product distributions in the heterodimerizations with HI/ZnI_2 in toluene at −40 °C. Monomers: (A and B) NBVE and BzOVE; (C and D) BzOVE and CEVE. The order of monomer addition (dimer sequence) is as indicated. Monomer conversions were 100% except for NBVE in curve B (ca. 90%), where the peak at ~29 mL is due to **1a** (the monomeric acetal of BzOVE) resulting from unreacted **1a*** (BzOVE–HI adduct). $[HI]_0 = [VE]_0 \simeq 10$ mM; $[ZnI_2]_0 = 0.20$ mM.

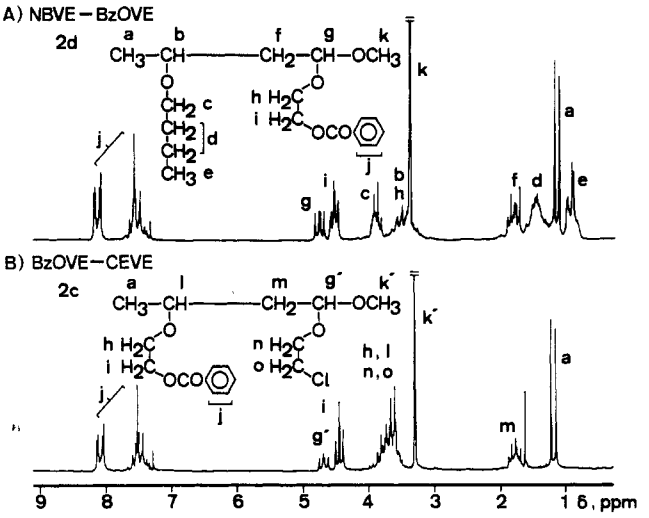


Figure 4. ^1H NMR spectra in $CDCl_3$ at 30 °C: (A) NBVE–BzOVE dimer **2d** (Figure 3A, shadowed fraction); (B) BzOVE–CEVE dimer **2c** (Figure 3C, shadowed fraction).

distribution; namely, the yield of **2c** (BzOVE–CEVE) was superior to that of **2e** (CEVE–BzOVE). Therefore, sequential addition of the VEs in the order of their decreasing reactivity was necessary in order to obtain the sequence-regulated oligomers in good yield.

Structural Analysis by ^1H NMR. The fractions of the target dimers (the shadowed areas in Figures 2 and 3) were isolated by preparative size-exclusion chromatography and analyzed by ^1H NMR spectroscopy. Figure 4 illustrates the ^1H NMR spectra of the dimers **2d** (NBVE–BzOVE, spectrum A) and **2c** (BzOVE–CEVE, spectrum B). Figure 4A exhibits two characteristic absorptions assignable to the two-component units; peak e (CH_3–, δ 0.9) for the pendant methyl of the NBVE unit and peak j (C_6H_5–, δ 7.3–8.2) for the phenyl group of the BzOVE unit. The integrated signal intensity ratio of these two peaks gave the unit ratio, NBVE/BzOVE ≃ 1/1 (see Table II), which confirmed the formation of **2d**.

Peaks g and k were assigned, respectively, to the methine and the methoxide protons [–C*H*(OCH_2CH_2OCOPh)–OCH_3] of the terminal acetal group of **2d**. The content of the acetal end group in the dimer, determined from the integrated peak area ratio, was nearly 100% relative to the NBVE unit. Thus, the dimeric living species NBVE–BzOVE* (**2d***) can survive without any loss of its activity

Table II
Characterization of Sequence-Regulated Dimers 2 Obtained with HI/ZnI_2 in Toluene at −40 °C

$HCH_2CHCH_2CHOCH_3$
OR^1 OR^2
2

code	product	R^1	R^2	mol wt obsd[a]	mol wt calcd	unit ratio[b] first monomer	unit ratio[b] second monomer
2a	BzOVE-NBVE	CH_2CH_2OCOPh	C_4H_9	324	324	1.00	1.07
2a[c]	BzOVE-NBVE	CH_2CH_2OCOPh	C_4H_9	324	324	1.00	1.02
2b[c]	BzOVE-BzOVE	CH_2CH_2OCOPh	CH_2CH_2OCOPh	416	416	1.00	(1.00)
2c[c]	BzOVE-CEVE	CH_2CH_2OCOPh	CH_2CH_2Cl	330	330	1.00	0.87
2d	NBVE-BzOVE	C_4H_9	CH_2CH_2OCOPh	324	324	1.00	1.04
2e	CEVE-BzOVE	CH_2CH_2Cl	CH_2CH_2OCOPh	330	330	1.00	1.28
2f	NBVE-VOEM	C_4H_9	$CH_2CH_2CH(COOEt)_2$	362	362	1.00	1.08

[a] Measured by thermospray mass spectroscopy; see text. [b] By ^1H NMR, relative to the first monomer unit. [c] Obtained at −78 °C.

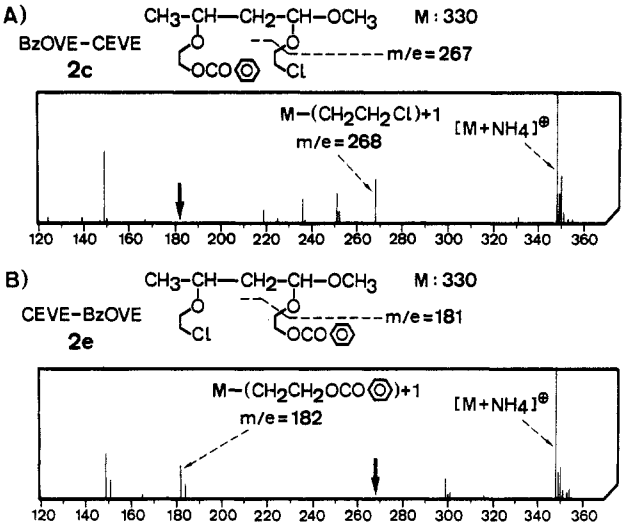


Figure 5. Thermospray mass spectra of two heterodimers obtained via opposite monomer addition sequences: (A) **2c** (BzOVE → CEVE); (B) **2e** (CEVE → BzOVE).

throughout the reaction. Similarly, spectrum B supported the expected structure of **2c** (BzOVE/CEVE ≃ 1/1; Table II).

Other AB type sequence-regulated dimers were prepared and isolated in a similar manner, as summarized in Table II with the unit ratio determined by ^1H NMR. Irrespective of the kind of the dimers (isolated by SEC), the number of each repeat unit was close to 1/oligomer chain.

Monomer Sequence Determination by Thermospray Mass Spectroscopy. In order to corroborate the structure of the obtained dimers, the isolated dimers were further analyzed by liquid chromatography/mass spectrometry (LC/MS) using a thermospray interface.[13] Thermospray ionization is generally favorable for ionic, polar, and nonvolatile samples, because the ionization process is so "soft" that undesirable complicated fragmentation can be avoided. We then determined the absolute molecular weights and the repeat unit sequences (from fragment peaks) of our sequence-regulated dimers by thermospray LC/MS. Because we employed ammonium acetate as the buffer in the LC eluent, the parent ions are expected to be $[M + NH_4]^+$ (m/e = M + 18) rather than the protonated form $[M + H]^+$.[13]

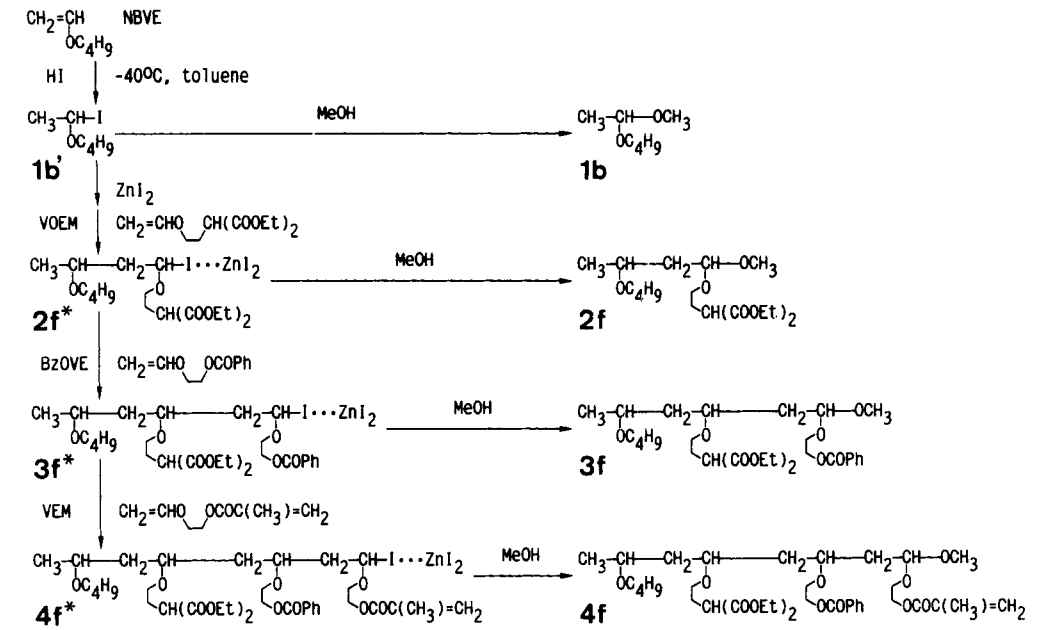
Figure 5 compares the mass spectra of **2c** (BzOVE-CEVE) and **2e** (CEVE-BzOVE), which involve reversed repeat unit sequences but possess the same molecular weight (M, 330). Actually, an $[M + NH_4]^+$ peak was found as the maximum peak in each spectrum at m/e 348 (=330 + 18), which was equal to the calculated value for the expected dimer structure. Consistent with the existence of chlorine in **2c** and **2e**, the parent peak was accompanied by a secondary isotope peak at m/e 350 due to ^{37}Cl.

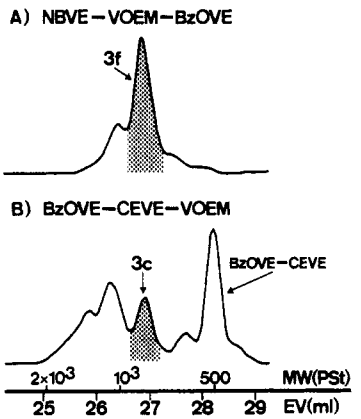
In addition to the absolute molecular weight, the repeat unit sequence in the dimers could also be identified by thermospray LC/MS from the observed fragment peaks. As shown in the structural formulas in Figure 5, cleavage occurred at the pendant C–O bond adjacent to the terminal acetal group. Thus, **2c** underwent elimination of CH_2CH_2Cl to form a fragment ion with m/e 268. This fragment could not be seen for **2d** (spectrum B), but an ion arising from elimination of the BzOVE pendant ($-CH_2CH_2OCOPh$) in turn appeared at m/e 182 (with a secondary ion at m/e 184 containing the ^{37}Cl isotope).

2. Sequence-Regulated Higher Oligomers. Trimers and Tetramers of Vinyl Ethers. On the basis of the results of the sequential dimerizations, new trimers and tetramers with controlled repeat unit sequences were prepared by our one-pot sequential reactions (unless otherwise specified, the product structure was determined by ^1H NMR spectroscopy). Scheme IV shows an example of the synthesis involving the following four VEs: NBVE with a *n*-butyl group as the first monomer, VOEM with a malonic ester function as the second, BzOVE with a benzoyloxy group as the third, and VEM with a methacrylate residue as the fourth. The resulting oligomeric living species **2f***, **3f***, and **4f*** in the respective steps were quenched with methanol and recovered in acetal forms (**2f**–**4f**).[9] Hereafter, the secondary alphabetical codes (e.g., "**f**" in **3f** and **4f**) for trimers and tetramers symbolize the precursors from which they are derived; for example, code **3f** means that this trimer is prepared from the corresponding dimeric species **2f***. The results had been reported, in part, in the previous paper,[6] and the yield for each step was fairly good except for **4f**: ca. 70% for the dimer **2f** (NBVE-VOEM); ca. 70% for the trimer **3f** (NBVE-VOEM-BzOVE); and ca. 30% for the tetramer **4f** (NBVE-VOEM-BzOVE-VEM). Figure 6A depicts the product distribution curve obtained in the third stage (the synthesis of the trimer **3f**).

In the above-discussed example, the monomer addition sequence, NBVE → VOEM → BzOVE → VEM, was in accordance with the order of monomer reactivity in the HI/ZnI_2-initiated polymerizations.[10,11,14,15] In another experiment, we attempted to synthesize trimer **3c** where the repeat unit sequence (BzOVE → CEVE → VOEM) does not follow the reactivity order (VOEM > BzOVE ≳ CEVE). In contrast to Figure 6A, the final reaction product (Figure 6B) contained a large amount of the higher molecular weight oligomers besides the target trimer **3c** (BzOVE-CEVE-VOEM; ca. 30% yield). The major reason for the lower yield of **3c** is the formation of the VOEM homosequences. These results further show that the

Scheme IV





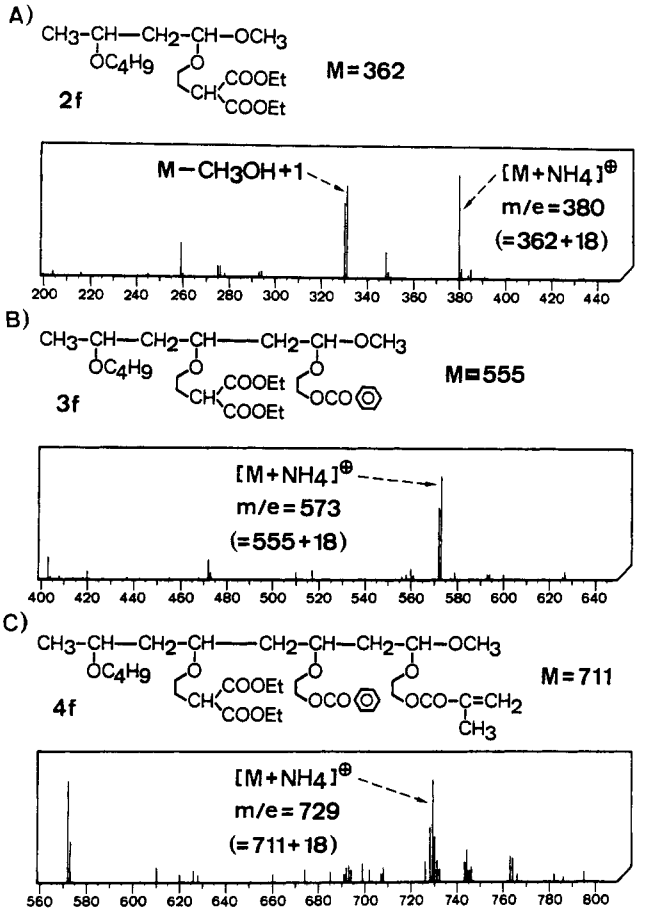


Figure 6. Product distributions in the one-pot sequential trimerizations by HI/ZnI_2 in toluene at −40 °C. Employed monomers: (A) NBVE, VOEM, and BzOVE; (B) NBVE, BzOVE, and *p*MOS. The order of the repeat unit sequence is as indicated. The peak at ~28 mL in curve B is due to **2c** (BzOVE–CEVE) resulting from unreacted **2c***. Monomer conversions: (A) BzOVE, 88%; (B) VOEM, 100%. $[HI]_0 = [VE]_0 \cong 10$ mM; $[ZnI_2]_0 = 0.20$ mM.

monomer reactivity order is of prime importance in determining the yield and selectivity for sequence-regulated oligomers.

Figure 7 shows the mass spectra of the isolated dimer **2f** (A), trimer **3f** (B), and tetramer **4f** (C). In each spectrum, the parent ion ($[M + NH_4]^+$) was observed at *m/e* 380 for **2f**, *m/e* 573 for **3f**, and *m/e* 729 for **4f**. All these observed values are identical with the calculated values (=M + 18); see Table III. Some fragment peaks were also seen. For example, spectrum A exhibits a fragment ion (*m/e* 331) assignable to the olefinic fragment, $CH_3CH(OC_4H_9)CH{=}CH[OCH_2CH_2CH(COOEt)_2]$, which forms via the elimination of methanol from the acetal group of **2f**.

Because of the ready fragmentation of vinyl ether oligomers under acidic conditions, we had not been able to obtain the parent ion by the usual chemical ionization (reagent gas, isobutane). The LC/MS with the thermospray interface, however, enabled us to accurately determine the relatively large molecular weights (500–800) of the trimer (**3f**) and the tetramer (**4f**).

Figure 7. Thermospray mass spectra of the oligomers obtained in the four-stage sequential reactions illustrated in Scheme IV: (A) dimer **2f** (NBVE–VEOM); (B) trimer **3f** (NBVE–VOEM–BzOVE); (C) tetramer **4f** (NBVE–VOEM–BzOVE–VEM).

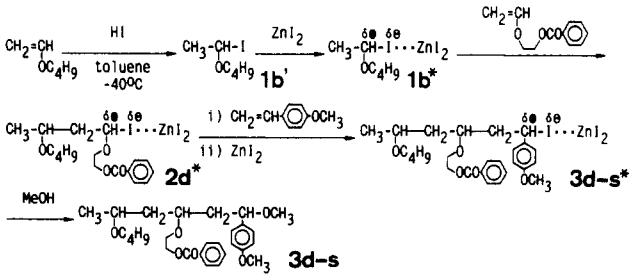
Sequence-Regulated Trimers with *p*MOS Unit. Recently, we have found that not only vinyl ethers but also *p*-methoxystyrene (*p*MOS) can be polymerized into living polymers by the HI/ZnI_2 initiating system.[16] These results prompted us to synthesize sequence-regulated oligomers that consist of vinyl ether and *p*MOS units. As illustrated in Scheme V, the synthesis of the trimer **3d-s** was carried out in a manner similar to those in Scheme IV, employing

Table III
Characterization of Sequence-Regulated Trimers 3 and Tetramers 4 Obtained with HI/ZnI_2 in Toluene at −40 °C

code	product[a]	mol wt obsd[b]	mol wt calcd	unit ratio[c] first monomer	second monomer	third monomer	fourth monomer
3c	BzOVE-CEVE-VOEM	561	561	1.00	1.00	1.08	
3f	NBVE-VOEM-BzOVE	555	555	1.00	1.13	0.97	
3f-s	NBVE-VOEM-*p*MOS	497	497	1.00	1.35	1.07	
3d-s	NBVE-BzOVE-*p*MOS	477	477	1.00	1.19	0.93	
4f	NBVE-VOEM-BzOVE-VEM	711	711	1.00	1.16	1.14	0.94

[a] See Table I for monomer codes and Schemes IV and V for the synthetic routes. [b] Measured by thermospray mass spectroscopy; see text. [c] By ^1H NMR, relative to the first monomer unit.

Scheme V



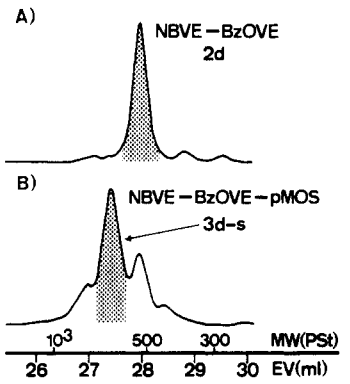


Figure 8. Product distributions in the second (A) and the third stages (B) of the sequential trimerization of NBVE, BzOVE, and *p*MOS (Scheme V) by HI/ZnI_2 in toluene at −40 °C. $[HI]_0$ = $[monomer]_0 \cong 10$ mM; $[ZnI_2]_0 = 0.20$ mM (the second stage) and 5.0 mM (the third stage). Monomer conversions: (A) BzOVE, 100%; (B) *p*MOS, 88%.

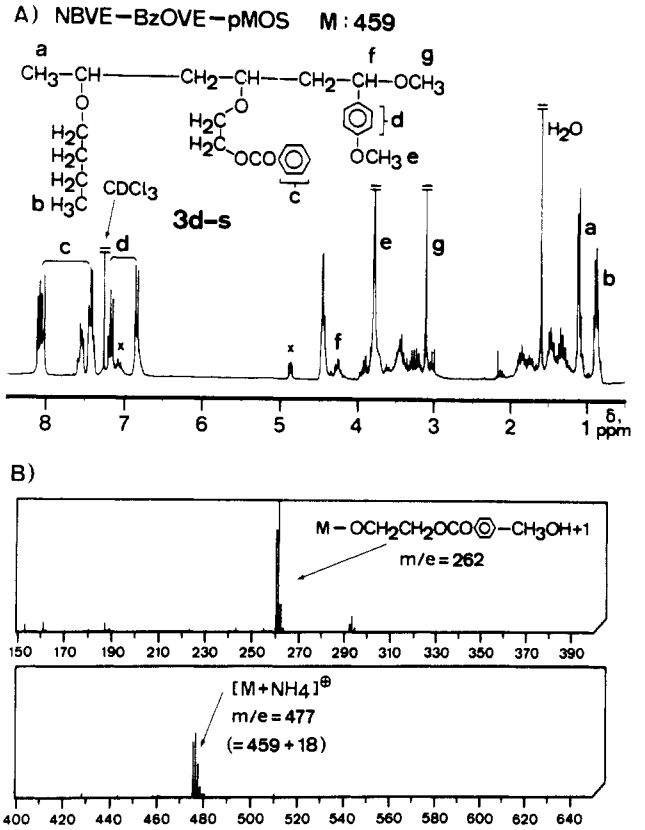


Figure 9. ^1H NMR spectrum (A) and thermospray mass spectrum (B) of trimer **3d-s** (shadowed fraction in Figure 8B).

NBVE, BzOVE, and *p*MOS in this order. Similar to the codes for the vinyl ether trimers (**3c** and **3f**), the three-component code **3d-s** indicates a trimer (**3**) that is derived from the dimeric intermediate **2d*** and contains a *p*MOS unit (**s**).

As already pointed out,[16] the living polymerization of *p*MOS needs a higher amount of ZnI_2 than that for vinyl ethers. Accordingly, the concentration of ZnI_2 was increased in the third stage from 0.20 to 5.0 mM after addition of *p*MOS. The second-stage reaction was nearly completed in ca. 15 min to give dimeric intermediate **2d***. Subsequent addition of *p*MOS and an additional amount of ZnI_2 triggered the third-stage reaction that reached 88% conversion in an additional 4 h.

The product distribution curves for the second and the third stages were presented in Figure 8. As seen in curve B, trimer **3d-s** (the shadowed area) was obtained as the major product from **2d*** (curve A).

^1H NMR structural analysis (Figure 9A) of the isolated trimer fraction established the formation of **3d-s**. For example, the four characteristic absorptions assignable to the three-component units: peak b (CH_3–, δ 0.9) for the NBVE unit; peak c (C_6H_5–, δ 7.3–8.2) for the BzOVE unit; peak d (–C_6H_4–, δ 6.8–7.2) and e (–$C_6H_4OCH_3$, δ 3.8) for the *p*MOS unit. The number of each component unit was close to 1/chain (Table III) by comparison of the peak intensity ratio, with peak b of the NBVE unit as reference. The structure of the terminal group of **3d-s** was also investigated. The two peaks f (δ 4.3) and g (δ 3.1) are assigned, respectively, to the methine and the methoxide protons $-CH(C_6H_4OCH_3)OCH_3$, which supports the structure arising from the quenching of the trimeric living species **3d-s*** with methanol.[17]

Figure 9B shows the mass spectrum of the isolated trimer fraction. The $[M + NH_4]^+$ parent ion was observed at *m/e* 477 (=459 + 18), indicating the molecular weight of the fraction to be identical with that of **3d-s** (M, 459). The intense signal at *m/e* 262 may be assignable to an olefinic fragment ion, $CH_3CH(OC_4H_9)CH_2CH^+CH{=}CH(C_6H_4OCH_3)$, which is formed by the elimination of methanol from the acetal end group and the subsequent cleavage of the BzOVE pendant group ($-OCH_2CH_2OCOPh$).

In addition to trimer **3d-s**, other trimers and tetramers were prepared by our sequential monomer addition technique. Table III lists representative examples of these sequence-regulated oligomers along with their characterization data. The slight deviations seen for some samples are most likely due to the insufficient SEC separation of high molecular weight oligomers. As seen in Table III, the

observed mass numbers ($[M + NH_4]^+$) of the isolated oligomers are all identical with the calculated values; and the repeat unit composition is also close to the expected, nearly 1 repeat unit/molecule for each monomer.

3. Conclusions. This study has demonstrated that the HI/ZnI_2 initiating system leads to the sequence-regulated oligomers by one-pot sequential reactions of functional vinyl ethers and *p*-methoxystyrene. Detailed kinetic and product analyses led to a principle for the sequence control; i.e., the sequential addition of vinyl monomers in the order of their decreasing reactivity is essential to better yields of the target oligomers. Although these sequence-regulated oligomers are small in the degree of polymerization (≤tetramer), they will be important as building blocks for the synthesis of the polymeric counterparts or highly designed periodic copolymers, as suggested in natural poly(amino acid)s and enzymes where repetition of relatively short but sequence-regulated segments plays a critical role in their functions.

Experimental Section

Materials. VOEM, BzOVE, and VEM (Table I) were prepared by the substitution reactions of 2-chloroethyl vinyl ether (CEVE) with sodiomalonic ester,[14] sodium benzoate,[11] and sodium methacrylate,[15] respectively. *p*MOS was synthesized from *p*-methoxyacetophenone by the literature method.[19] These monomers and commercial NBVE[10] and CEVE[12] were purified by distillation as reported previously. Anhydrous hydrogen iodide was obtained as an *n*-hexane solution from 57% aqueous solution by dehydration with phosphorus pentoxide.[10] The distilled monomers and the hydrogen iodide stock solution were sealed in brown ampules under dry nitrogen and stored in the freezer. ZnI_2 (Aldrich; purity >99.99%) was used as received;[5] the hygroscopic and light-sensitive salt was handled in a nitrogen-filled drybox in the dark. Toluene as polymerization solvent was purified by the usual methods and distilled twice over calcium hydride prior to use.[10]

Reaction Procedures. The synthesis of oligomers was carried out under dry nitrogen in a baked glass vessel equipped with a three-way stopcock and a stirrer bar. The mixture was magnetically stirred during the reaction, and the monomer and the initiator solution were each added with a dry syringe under dry nitrogen. In the synthesis of trimer **3d-s** (NBVE–BzOVE–*p*MOS; Scheme V), for example, a toluene solution (17 mL) of NBVE (0.20 mmol; 0.026 mL) was stirred at −40 °C, and an equimolar amount of HI (in toluene; 200 mM, 1.0 mL) was added to form adduct **1b′**. To this solution of **1b′** were added a toluene solution (1.0 mL) of BzOVE (0.20 mmol; 0.035 mL) and ZnI_2 (in diethyl ether; 4.0 mM, 1.0 mL) in this order. When the second-stage reaction reached above 90% conversion in 15 min, a toluene solution (1.0 mL) of *p*MOS (0.20 mmol; 0.027 mL) and an additional ZnI_2 solution (58 mM, 2.0 mL) were added to start the third reaction. After ca. 4 h (88% *p*MOS conversion), the reaction was terminated with prechilled ammoniacal methanol. The quenched reaction mixture was washed with 10% aqueous sodium thiosulfate solution and then with water and evaporated to dryness under reduced pressure to give the product (**3d-s**, ca. 60% by SEC) as an oil. All other oligomers (Tables II and III) were prepared in a similar way.

Measurements. The product distribution was measured in chloroform by size-exclusion chromatography (SEC) on a Jasco 880-PU precision pump equipped with three polystyrene gel columns (Shodex K-802, K-803, and K-804) that were calibrated against standard polystyrene samples in the molecular weight range 10^2–10^5. Oligomers were isolated by preparative SEC on a Jasco Trirotar chromatograph (column, Shodex H-2001; operational molecular weight range, ≤1000). ^1H NMR spectra were recorded in $CDCl_3$ on JEOL FX-90Q (90 MHz) and GSX-270 (270 MHz) instruments. Thermospray mass (LC/MS) spectrometric analyses were performed in the filament-on mode on a Shimadzu QP-1000 quadrapole mass spectrometer (maximum mass, m/e ≤900) equipped with a Vestec Model 750B thermospray unit and a Shimadzu LC-6A precision pump (eluent, methanol containing 0.1 M ammonium acetate; 1.0 mL/min). Samples were dissolved in methanol or isopropyl alcohol (usually 20–30 mg/L; 200–300 mg/L for less ionizable oligomers such as the tetramer **4f**), and 20 μL of the solution was injected into the thermospray unit through the precision pump.

References and Notes

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(8) Because the concentration of the activator ZnI_2 is much lower than that of the VE–HI adduct ($[VE–HI\ adduct]_0 \cong 10$ mM, $[ZnI_2]_0 = 0.2$ mM), the propagating species exists in the form of either $\sim\sim\sim CH_2CH(OR)–I$ (dormant) or $\sim\sim\sim CH_2CH(OR)\cdots I\cdots ZnI_2$ (activated).[5,7] However, rapid exchange of ZnI_2 between these two forms provides each potentially active C–I terminal with an equal probability of propagation. The terms "living species" and "active species" in this study refer to both of the two forms.
(9) Although acetals undergo acidolysis into aldehydes, they are stable during our workup procedures that are kept under basic or neutral conditions; see refs 7 and 14b.
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(17) In Figure 9A, some peaks (indicated with crosses) could not be assigned, but there were no signals assignable to the terminal endo olefin or the indan structure, which had been observed in the usual cationic oligomerization of styrene derivatives.[18]
(18) See, for example: Sawamoto, M.; Higashimura, T. *Macromolecules* **1981**, *14*, 467.
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Registry No. **1a**, 129708-61-8; **1b**, 75677-94-0; **2a**, 129708-62-9; **2b**, 129708-63-0; **2c**, 129708-64-1; **2d**, 129708-65-2; **2e**, 129708-66-3; **2f**, 127769-65-7; **3c**, 129708-67-4; **3d–s**, 129708-69-6; **3f**, 127769-66-8; **3f–s**, 129708-68-5; **4f**, 127769-67-9; HI, 10034-85-2; ZnI_2, 10139-47-6.