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Direct Synthesis of Well-Defined Alcohol-Functionalized Polymers via Acyclic Diene Metathesis (ADMET) Polymerization

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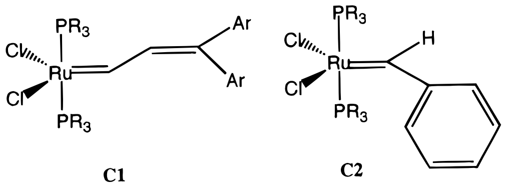
ABSTRACT: Because of its robust nature, Grubbs' ruthenium benzylidene catalyst $RuCl_2(=CHPh)(PCy_3)_2$ promotes the successful acyclic diene metathesis (ADMET) bulk polymerization of alcohol-functionalized dienes, thus providing a method for the direct synthesis of linear polymers containing hydroxy groups. Primary, secondary, and tertiary alcohol functional groups can be placed at precise intervals along an unsaturated hydrocarbon backbone. Exhaustive hydrogenation of the secondary alcohol homologue produces a well-defined ethylene−vinyl alcohol copolymer. Only the unsaturated and saturated secondary alcohol polymers crystallize, a phenomenon likely attributed to the enhanced packing propensity of these macromolecules in comparison with those of their primary and tertiary analogues.

Introduction

Poly(vinyl alcohol) and its copolymers are widely used commercially, with the vinyl alcohol polymer being the largest volume water-soluble synthetic resin in the world.[1] These polymers are made by indirect means using chain propagation techniques, since the direct polymerization or copolymerization of vinyl alcohol is not possible. The unfavorable keto−enol tautomerization (K = [enol]/[keto] $\approx 3 \times 10^{-7}$)[2] of the "monomer" vinyl alcohol precludes its use in direct polymerization, and consequently poly(vinyl alcohol) and its copolymers are prepared commercially by the free radical polymerization of vinyl acetate, followed by hydrolysis or alcoholysis. These polymers and copolymers are analogous to substituted low-density polyethylene in that they experience the same inter- and intramolecular chain-transfer events that lead to branching.[3,4] This procedure produces a polymer (either homo- or copolymer) with little control over both repeat unit identity and the degree of branching. Recently, Novak and coworkers[5] have addressed the challenge of direct polymerization of an alcohol monomer by generating vinyl alcohol in situ, followed by attempts to polymerize the monomer "kinetically." While homopolymerization has not yet proven possible using radical or cationic initiation, a spontaneous donor/acceptor type copolymerization has been observed.

Alternate synthetic approaches toward aliphatic polymers containing alcohol groups have consisted of combining metathesis chemistry with chain propagation techniques. This method has stemmed from the development of new metathesis catalysts that are more tolerant to various functional groups.[6−8] However, the inherent Lewis acidity of these catalysts has precluded their use with various olefins containing Lewis basic functional groups (specifically alcohol groups).

To avoid this problem, functionalized metathesis polymers have been made by protecting the functional group prior to polymerization. An example of this approach was described by Chung et al., who produced alcohol-functionalized polymers through the ring-opening metathesis polymerization (ROMP) of boron-functionalized monomers, followed by the oxidation of the boron-containing polymer.[9] While this method produces an unsaturated polymer with the hydroxyl functionality in well-defined sequences, absolute regiospecific placement is not possible. Instead, regioisomers form as a result of random head-to-tail (HT), head-to-head (HH), and so forth connections between monomers.



C1 **C2**

Figure 1. Ruthenium-based metathesis catalysts: R = cyclohexyl or phenyl.

Hydroxyl functionalities also can be placed on hydrocarbon metathesis polymers by taking advantage of the unsaturated group that is inherently maintained in the repeat unit. For example, Ramakrishnan[10] reported the synthesis of ethylene−vinyl alcohol copolymers by the hydroboration of the metathesis polymer's olefin groups, followed by the oxidation of the boron moiety to an alcohol group. This method provides considerable control over the polymer's sequence distribution, but the nonselective nature of the hydroboration reaction (1,2 or 2,1 addition) causes the hydroxyl-functionalized polymer to be irregular in structure.

Alcohol-containing dienes were cyclized by Fu et al.[11] using the well-defined ruthenium alkylidene **C1** (Figure 1), demonstrating that the alcohol functional group could be tolerated in ring closing metathesis, and consequently Hillmyer,[12] used the same initiator to polymerize 5-hydroxy-1-cyclooctene via ROMP techniques. As is true in all chain polymerization chemistry of unsymmetrical monomers, the resulting polymer's microstructure still displays a randomness in the location of the alcohol functionality. Nonetheless, all of this methodology represents an important advance in the direct synthesis of alcohol-containing polymers via chain techniques.

We are interested in applying metathesis chemistry for the direct synthesis of precisely defined polyalcohols.

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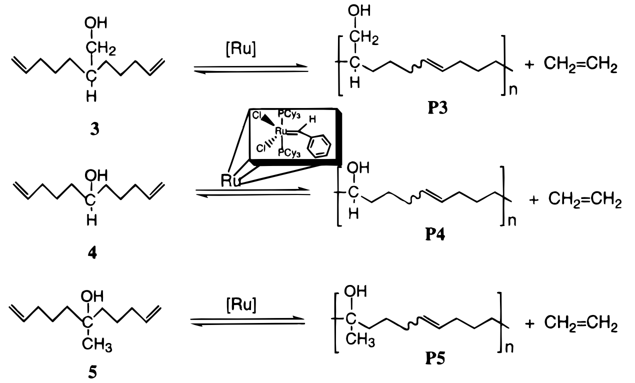

Figure 2. The acyclic diene metathesis (ADMET) polymerization of primary (**3**), secondary (**4**), and tertiary (**5**) alcohol-functionalized dienes.

This interest is driven by the desire to create well-defined materials that can lead to a better understanding of their structure–property relationships, a goal which is significant in light of the commercial value of ethylene–vinyl alcohol copolymers.[14] Further, we believe that the increased control of functional group placement by this route might lead to materials that have potential as substrates in drug delivery systems.

Consequently, we have approached the direct synthesis of alcohol-containing polymers via the acyclic diene metathesis (ADMET) step polymerization of symmetrical diene monomers rather than employing chain polymerization techniques. Catalyst **C2** (Figure 1) has been chosen for this work. It displays a high tolerance to Lewis bases and is more active than catalyst **C1**.[12] Further, it has been used in ADMET chemistry before.[15]

Alcohol-functionalized terminal dienes were exposed to Grubbs' ruthenium benzylidene **C2** (Figure 1), resulting in their condensation to form the corresponding unsaturated polymers (Figure 2). These unsaturated alcohol-functionalized polymers were fully characterized, and the secondary alcohol polymer was hydrogenated to yield a polymer structure similar to that of a poly(ethylene)/poly(vinyl alcohol) copolymer. Since these polymers are constructed by the step condensation polymerization of symmetrical monomers, the sequence distribution is controlled exactly, and no branching is observed. In fact, the range of functional group identity and placement is limited only by the synthesis of the corresponding symmetrical acyclic terminal diene. Consequently, this methodology can be used to model the substituent effect (branch and or functional group identity and frequency) on the physical properties of the polymer. This synthetic strategy provides the first example of the direct synthesis of well-defined aliphatic polyalcohols via condensation reactions.

Experimental Section

Instrumentation and Analysis. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a General Electric QE-Series NMR superconducting spectrometer system or a Varian Associates Gemini 300 spectrometer. All NMR spectra were recorded in $CDCl_3$ and/or CD_3OD with 0.03% v/v TMS as an internal reference. Chemical shifts reported were internally referenced to residual chloroform. Infrared data were recorded on a BioRad FTS/40A infrared spectrometer. Analyses were performed between NaCl plates neat or with chloroform as a solvent. The purity of compounds and reaction conversions were determined on either a Hewlett-Packard HP5880A gas chromatograph using a capillary column with a flame ionization detector or on silica-coated TLC plates with mixtures of pentane and ethyl acetate as the mobile phase. Pertinent GC peaks were confirmed by mass spectrometry or NMR on the isolated compound. Low and high-resolution mass spectrometry (LRMS and HRMS) was recorded on a Finnigan 4500 gas chromatograph/mass spectrometer using either electron ionization or chemical ionization conditions. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA.

Gel permeation chromatography (GPC) was performed using a Waters Associates liquid chromatograph U6K equipped with a tandem ABI Spectroflow 757 UV absorbance detector and a Perkin-Elmer LC-25 RI detector. All molecular weights are relative to polystyrene standards. Polymer samples were prepared in HPLC grade $CHCl_3$ and MeOH (80:20 respectively) (~1% w/v) and filtered before injection (a volume of 20–40 μL). The gel permeation chromatograph was equipped with a Ultrastyragel linear mixed-bed column. HPLC grade chloroform and methanol (80:20) were used as the eluents at a constant flow rate of 1.0 mL/min. Retention times were calibrated against narrow molecular weight polystyrene standards (Scientific Polymer Products, Inc.). All standards were selected to have M_p or M_w values well beyond the expected polymers' range. A minimum of five data points were acquired for a calibration curve.

Differential scanning calorimetry (DSC) analyses were performed using a Perkin-Elmer DSC 7 at a heating rate varying between 2 and 20 °C/min. All samples were first cooled to −120 °C (using liquid nitrogen as the coolant with a helium flow at a rate of 30 mL/min) and underwent isothermal cooling for 2–5 min before scanning up to 200 °C followed by isothermal heating for 2–5 min. Multiple cycles were performed with data collection on the second heating cycle or later. When transitions were identified, the samples were then slowly scanned over the pertinent temperature range. Reported values are T_m(peak) (first-order transition peak position), T_m(onset), and T_g (glass transition). Thermal calibrations were done using indium and cyclohexane as standards for both peak temperature transitions as well as for heats of fusion. All samples were run using an empty pan as a reference and empty cells as a subtracted baseline. Thermogravimetric analysis was performed on a Perkin-Elmer TGA 7. All samples were heated from room temperature to 700 °C in nitrogen at a scan rate of 10 °C/min. The onset of weight loss was taken as the reported value.

Materials. Grubbs' ruthenium catalyst, $RuCl_2(=CHR)(PCy_3)_2$, where Cy = cyclohexyl, (**C2**) was synthesized using a literature procedure.[16] *p*-Toluenesulfonohydrazide (TSH) was purchased from Aldrich and was recrystallized from methanol prior to use. Tripropylamine (TPA), 5-bromo-1-pentene, and *o*-xylene were purchased from Aldrich and distilled from calcium hydride prior to use. Tetrahydrofuran (THF) and dimethoxyethane (DME) were first distilled from NaK alloy using benzaldehyde as an indicator. Two molar potassium *tert*-butoxide was prepared in a dry Schlenk tube by combining the salt (Aldrich) with dry THF or DME. "Super dry" ethanol was prepared as described in the literature.[17] All other reagents mentioned were used as received.

Synthesis and Characterization. 6-(4-Pentenyl)-1-heptene-7-ol (3) was synthesized in a three-step reaction sequence as shown below.

Step 1 (One-Pot, Two-Step Synthesis). Synthesis of Ethyl 2-Acetyl-2-(4-pentenyl)-6-heptenoate (1). A 11-g (84-mmol) sample of ethyl acetoacetate (Aldrich) and 200 mL of dry DME (Aldrich) were placed in an argon-purged 500-mL three-neck flask equipped with a magnetic stir bar and a condenser. Forty-two milliliters of potassium *tert*-butoxide (2.0 M in THF) was added to this stirring solution. During the addition the solution turned lime-green in color. This solution was allowed to stir for 0.5 h at room temperature followed by slowly adding 13 g (84 mmol) of 5-bromo-1-pentene by syringe and raising the temperature to reflux. White salts were formed upon reflux. The first addition was complete in 18 h, as shown by GC. The reaction was then cooled to room temperature, and the second addition of 42 mL of the 2 M solution of potassium *tert*-butoxide in THF was performed followed by the addition of alkenyl bromide as above. The reaction was again followed by GC with the majority of product formation complete in 24 h. The reaction was then quenched with 3 M HCl, and the reaction mixture was extracted with ether. The ether was dried over $MgSO_4$ and then evaporated, yielding ~80% of **1**. The following spectral properties were observed: ^1H NMR 1.11 (m, br, 4H), 1.19 (t, 3H), 1.79 (m, br, 4H), 1.98 (q, 4H), 2.04 (s, 3H), 4.12 (q, 2H), 4.91 (m, 4H), 5.70 ppm (m, 2H); ^{13}C NMR 14.06, 23.21, 26.62, 30.79, 33.84, 61.09, 63.36, 115.1, 137.94, 172.5, 205.1 ppm. The low-resolution mass spectrum (LRMS, EI) also confirms the structure with a parent ion at 266 (calcd for $C_{16}H_{26}O_3$: 266).

Step 2. Retro-Claisen Condensation: Synthesis of Ethyl 2-(4-Pentenyl)-6-heptenoate (2). To an argon-purged dry 250-mL three-neck round-bottom flask, equipped with a condenser and a magnetic stir bar, were added 22 g (84 mmol) of **1** and 100 mL of dry ethanol. To this solution was added 35 mL of a 21% solution of sodium ethoxide in ethanol (Aldrich) was added. (This solution was also prepared by the addition of 21 wt % of sodium metal into “dry” ethanol. **Caution**: This addition should be done under an inert atmosphere using “super dry” ethanol. Any contact of sodium with water in the presence of oxygen can cause a fire. Super dry ethanol was prepared as described in the literature.[17]) The solution was allowed to reflux for 3.5 h and turned dark yellow. After the solution was cooled to room temperature, the reaction was quenched with water and 3 M HCl, followed by extraction of the reaction mixture with pentane or ether. The organic layer was then dried over $MgSO_4$ and evaporated under reduced pressure, yielding ~90% of ester **2**. The product was vacuum-distilled through a short path vacuum distillation apparatus. The product was collected between 130 and 150 °C at 4 mmHg. The following spectral properties were observed: ^1H NMR ($CDCl_3$) 1.25 (t, 3H), 1.40 (m, br, 6H), 1.62 (m, br, 2H), 2.05 (q, 4H), 2.31 (m, 1H), 4.14 (q, 2H), 4.95 (m, 4H), 5.79 ppm (m, 2H); ^{13}C NMR 14.5, 26.9, 32.0, 33.8, 45.5, 60.0, 114.9, 138.6, 176.0 ppm. The low-resolution mass spectrum (LRMS, EI) also confirms the structure with a parent ion at 224 (calcd for $C_{14}H_{24}O_2$: 224).

Step 3. Reduction of Ester: Synthesis of 2-(4-Pentenyl)-6-hepten-1-ol (3). To a flame-dried 250-mL three-neck round-bottom flask equipped with a stir bar and condenser were added 9.3 g (42 mmol) of **2** and 125 mL of dry THF. This solution was kept under an inert atmosphere and cooled to 0 °C. To this stirring solution was added 25 mL (2 equiv) of a 1 M solution of $LiAlH_4$ (Aldrich) in THF over a period of 5 min. Some bubbling was observed during this addition. The reaction mixture was allowed to warm to room temperature and stir for 2 h. The reaction was then slowly quenched with water followed by 3 M HCl. The solution was extracted with ether dried over $MgSO_4$, and the solvent was evaporated. A clear oil was recovered and vacuum-distilled at 69−72 °C at 1 mmHg. The reduction resulted in 91% yield. The following spectral properties were observed: ^1H NMR ($CDCl_3$) 1.18 (m, br, 9H), 1.79 (s, 1H), 1.98 (q, 4H), 3.49 (d, 2H), 4.88 (m, 4H), 5.78 ppm (m 2H); ^{13}C NMR 26.08, 30.29, 33.98, 34.01, 40.22, 65.36, 114.28, 138.74 ppm; IR ($CDCl_3$, cm^{-1}) 3383.8 (br), 3078.1, 3013.4, 2931.0, 2860.9, 1640.4, 1460.3, 1217.1, 1030.5, 996.1, 913.1, 759.5. Elemental anal. Calcd for $C_{12}H_{23}O$: C, 79.06; H, 12.16. Obsd: C, 78.99; H, 12.16.

Synthesis of Secondary (4) and Tertiary (5) Diene Monomers. 1,10-Undecadien-6-ol (4) and 6-Methyl-1,10-undecadien-6-ol (5) were synthesized by the Grignard reaction with the appropriate ester. 5-Bromo-1-pentene was dried over freshly ground CaH_2 for 3 h and then vacuum-transferred to a Schlenk flask with 4-Å molecular sieves. To a flame-dried 100-mL three-necked round-bottom flask were added 1.6 g (67 mmol) of freshly ground magnesium turnings and 50 mL of dry ether. A crystal of iodine and a small amount of the alkenyl halide were added in order to initiate the reaction. The remainder of the starting material was then added at such a rate as to maintain reflux. After the addition was completed, the mixture was stirred and refluxed for 0.5 h. After the mixture was cooled to room temperature, either 33.5 mmol of dry ethyl formate was slowly added to produce **4** or, alternatively, 33.5 mmol of dry ethyl acetate was added to produce **5**. Refluxing occurred upon addition of the electrophilic reagents and was maintained by heating for 2 h. The reaction mixture was then cooled, and the reaction was quenched with 3 M HCl. The reaction mixture was extracted with ether and dried over anhydrous magnesium sulfate, followed by filtration and evaporation, yielding 5.18 g (84%) of clear liquid **4.** Similar yields were obtained for **5**. Both monomers were distilled under reduced pressure (70−80 °C at 1 mmHg) using a short path distillation apparatus. The secondary alcohol diene (**4**) was further purified by column chromatography using silica gel with a solvent gradient elution using 1−5% ethyl acetate and pentane. The column was monitored by TLC using a 5/95 ethyl acetate/pentane mobile phase on silica plates. The following spectral properties were observed: ^1H NMR (**4**) 1.35 (m, 9H), 1.99 (m, 4H), 3.54 (s, 1H), 4.89 (m, 4H), 5.73 ppm (m, 2H); ^{13}C NMR 24.79, 33.56, 36.79, 71.53, 114.41, 138.54 ppm. Elemental anal. Calcd: C, 78.51; H, 11.98; O, 9.51. Obsd: C, 77.61; H, 11.80. ^1H NMR (**5**) 1.14 (s, 3H), 1.43 (m, 9H), 2.05 (m, 4H), 4.98 (m, 4H), 5.80 ppm (m, 2H); ^{13}C NMR 23.12, 26.80, 34.07, 41.21, 72.52, 114.48, 138.61 ppm. Elemental anal. Calcd: C, 79.06; H, 12.16; O, 8.78. Obsd: C, 79.16; H, 12.15.

ADMET Polymerizations of Alcohol Monomers 3−5. General Metathesis Conditions. All glassware was thoroughly cleaned and flame-dried under vacuum before use. The monomers were vacuum fractionally distilled (from CaH_2 if needed) prior to polymerization. The monomers were placed over 4-Å molecular sieves in order to preserve dryness. The purity of the monomers was >98%, as determined by GC. Monomers were degassed by subjecting them to several freeze−pump−thaw cycles under high vacuum ($<10^{-4}$ Torr). The dry, degassed monomers were then vacuum-transferred into a clean dry reaction flask fitted with a Teflon vacuum valve and containing a magnetic stir bar.

All metathesis reactions were initiated in the bulk, under an inert atmosphere. A few drops of dry $CDCl_3$ was added on occasion in order to facilitate reaction initiation. After the addition of catalyst, very slow to moderate bubbling of ethylene was observed. The bubbling reactions were then exposed to intermittent vacuum until the viscosity increased, followed by exposure to high vacuum to remove ethylene, which is continuously generated during the course of the polymerization. All the reactions were started and maintained at room temperature until the increase in viscosity prevented stirring. At this point, the reaction temperature was slowly raised to 70 °C over a period of 2−3 days until a very high viscosity was obtained or bubbling ceased. The solutions were then cooled to room temperature, and the reactions were quenched by the addition of excess ethyl vinyl ether or by exposure to air. Reactions were run on a 0.5−1.5-g scale, with a monomer-to-catalyst ratio of 500:1, 300:1, or 200:1, as noted.

Polymerization of 2-(4-Pentenyl)-6-hepten-1-ol (P3). The monomer **3** was synthesized and dried as previously described. For a monomer-to-catalyst ratio of 200:1, 23 mg of catalyst, $RuCl_2({=}CHPh)(PCy_3)_2$ (**C2**), was added to 1.0 g of the monomer. The reaction was performed under typical metathesis conditions, until the contents could no longer be stirred or ethylene evolution had stopped. The reaction was quenched by exposure to air. The polymers were not precipitated before undergoing characterization. The following spectral properties were observed: ^1H NMR ($CDCl_3$) 1.09 (br, 8H), 1.35 (br, 1H), 1.71 (br, 4.4H), 3.19 (br, 1.9H), 4.67 (br, 0.04H end group), 5.15 (br, 2H), 5.60 ppm (br, 0.003H end group); IR (neat, cm^{-1}) 3341, 3005, 2926, 2856, 1726, 1457, 1440, 1036, 967, 511. Elemental anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 75.55; H, 11.41. For GPC analysis see Table 1.

Polymerization of 1,10-Undecadien-6-ol (P4). Monomer **4** was synthesized and dried as previously described. For a monomer-to-catalyst ratio of 200:1, 24 mg of catalyst, $RuCl_2({=}CHPh)(PCy_3)_2$ (**C2**), was added to 1 g of the monomer. The procedure was followed as in (**P3**). The following spectral properties were observed: ^1H NMR 1.45 (br, d, 9H), 2.00 (br, 4H), 3.55 (br, 0.7H), 4.98 (br, 0.29H end group), 5.40 (br, 2H), 5.80 ppm (br, m, 0.04H end group); ^{13}C NMR 24.8−33.4 (multiple signals), 36.4, 71.0, 129.5−130.5 ppm (multiple

Table 1[a]

polymer	monomer/ catalyst	M_n (g/mol) GPC	M_w (g/mol) GPC	PDI
primary (**P3**)	500:1	6 300	8 200	1.3
primary (**P3**)	200:1	24 000	38 000	1.6
secondary (**P4**)	500:1	10 100	13 400	1.3
secondary (**P4**)	200:1	18 600	30 400	1.4
tertiary (**P5**)	300:1	13 600	18 600	1.4
tertiary (**P5**)	200:1	13 000	17 700	1.4

[a] Samples run in 80% chloroform/20% methanol against polystyrene standards. Presence of monoene impurity discovered.

signals). Elemental anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.48; H, 11.33. For GPC analysis see Table 1.

Polymerization of 6-Methyl-1,10-undecadien-6-ol (P5). Monomer **5** was synthesized and dried as previously described. For a monomer-to-catalyst ratio of 500:1, 15 mg of catalyst **C2** was added to 500 mg of the monomer. The procedure followed was the same as that used for **P3**. The following spectral properties were observed: ^{1}H NMR 1.12 (s, 3H), 1.40 (br, 8H), 1.99 (br, 4H), 4.94 (br, m, 0.25H end group), 5.39 (br, 2H), 5.79 ppm (br, m, 0.09H end group); ^{13}C NMR 23.90, 26.94, 27.67, 33.01, 41.37, 72.72, 129.92, 130.42 ppm. Elemental anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 76.61; H, 11.50. For GPC analysis see Table 1.

Hydrogenation of Poly[1,10-undecadien-6-ol] (HP4). Hydrogenation was performed according to the Hahn method[30] in a flame-dried, 50-mL round-bottom three-neck flask equipped with a reflux condenser and a Teflon stir bar and supplied with a positive argon pressure. To this flask were added 266 mg of polymer **P4**, 25 mL of dry reagent grade toluene, 0.907 g of TSH, and 0.932 mL of TPA. The mixing solution was then heated to reflux. All of the TSH did not dissolve until the solution was close to reflux. Upon heating, some gas evolution could be observed (bubbling of N_2) before reflux was achieved. The solution was allowed to reflux for 6 h followed by cooling to room temperature. Some white precipitate was noted at this time (insoluble hydrogenated polymer). A second addition of 0.907 mg of TSH and 0.932 mL of TPA was administered, followed by refluxing for 3 h. Once the solution cooled to room temperature, the product was observed as a white solid. The polymer was then precipitated in cold methanol. Approximately 60% of the polymer was recovered. The following spectral properties were observed: ^{1}H NMR (toluene-d_8 at 100 °C) 1.55 and 1.62 (br, s, 18H), 3.72 (s, 1H), 5.18 (br, m, residual vinylic CH_2), 5.62 ppm (br, m, residual internal olefin). ^{13}C NMR 26.60, 30.50, 30.66, 38.67, 72.41 ppm. GPC analysis was not performed due to the insoluble nature of this polymer.

Results and Discussion

Monomer Design and Synthesis. Primary, secondary, and tertiary ADMET reactive alcohol monomers (structures **3**, **4**, and **5** respectively; Figure 2) were prepared for this study, where all monomers were designed to be symmetrical with a minimum of two methylene spacers between the functional group and the olefin. Symmetrical monomers avoid the irregular placement of the alcohol group (i.e., avoiding HT, HH, etc. placement), and the methyl spacers were included to avoid the negative neighboring group effect (NNGE). This phenomenon, which has been observed both in ROMP[18,19] and ADMET systems,[20−22] is a manifestation of intramolecular complexation between the lone pairs on the functional group (as a Lewis base) and the electrophilic metal center (Lewis acid) of the catalyst. Further, the length of the alkyl group—five methylenes—obviates the formation of cyclic condensation products.

Secondary alcohol **4** and tertiary alcohol **5** monomers were synthesized by forming the Grignard reagent of 5-bromo-1-pentene, followed by reacting with either ethyl acetate or ethyl formate, respectively. This simple monomer synthesis permits the construction of a series of tertiary and secondary alcohol monomers which leads to precise control over the frequency of the alcohol functional group. The procedure also controls the identity and frequency of the alkyl substituent (tertiary alcohol) in the corresponding polymer. For example, the alkyl substituent (branch point) for monomer **5** can easily be modified by changing the identity of the ester, and similarly, the frequency of the substituents can be controlled by changing the identity of the alkenyl bromide.

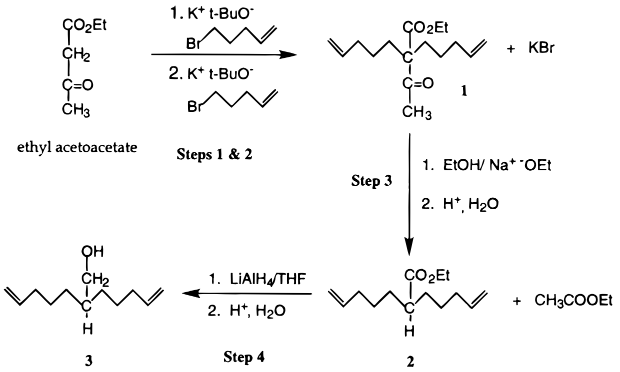

Figure 3. Four-step synthesis of primary alcohol diene (**3**).

Primary alcohol **3** was produced via a multistep synthesis (Figure 3) involving enolate chemistry on β-keto esters forming compound **1** (steps 1 and 2; Figure 3). The first step involved the deprotonation of ethyl acetoacetate by the bulky Brönsted base potassium *tert*-butoxide in dimethoxyethane (DME), followed by the addition of the alkenyl bromide. Monoalkylation, which proceeded cleanly to completion, was monitored by gas chromatography (GC). The second alkylation was performed in the same vessel by repeating the above procedure using longer reaction times, for the generation and substitution of the second enolate anion.

Compound **1** was then quantitatively deacylated via a retro-Claisen condensation[23−25] using excess sodium ethoxide (step 3; Figure 3), forming the disubstituted ester **2**. Deacylation was also observed as a side reaction during steps 1 and 2 from the addition of excess base and/or increased reaction times. The cleavage of β-keto esters at the ketone functionality has been observed during alkylation reactions and is most pronounced when the alkylated product has two α substituents,[26] as is the case for product **1**. Extended exposure of nonenolizable ketones to *tert*-butoxide in DME has also shown a similar ketone cleavage,[27,28] and proliferation of this reaction became the basis for step 3 (Figure 3) in this synthetic sequence.

In the final conversion (step 4; Figure 3), the ester was reduced to the primary alcohol **3** with near quantitative conversion at room temperature. This was accomplished by the addition of excess lithium aluminum hydride (LAH) (>2 equiv) to a solution of the ester **2** in THF.[29] The target alcohol **3** was distilled under reduced pressure ($\sim 10^{-2}$ Torr) to a purity greater than 99%.

ADMET Polymerization of Hydroxy-Functionalized Dienes. All three monomers were exposed to catalyst **C2** under ADMET conditions resulting in various degrees of metathesis condensation/polymerization (Table 1). In all cases, higher molecular weight polymers were produced using catalyst loadings somewhat higher than normal, in keeping with with results

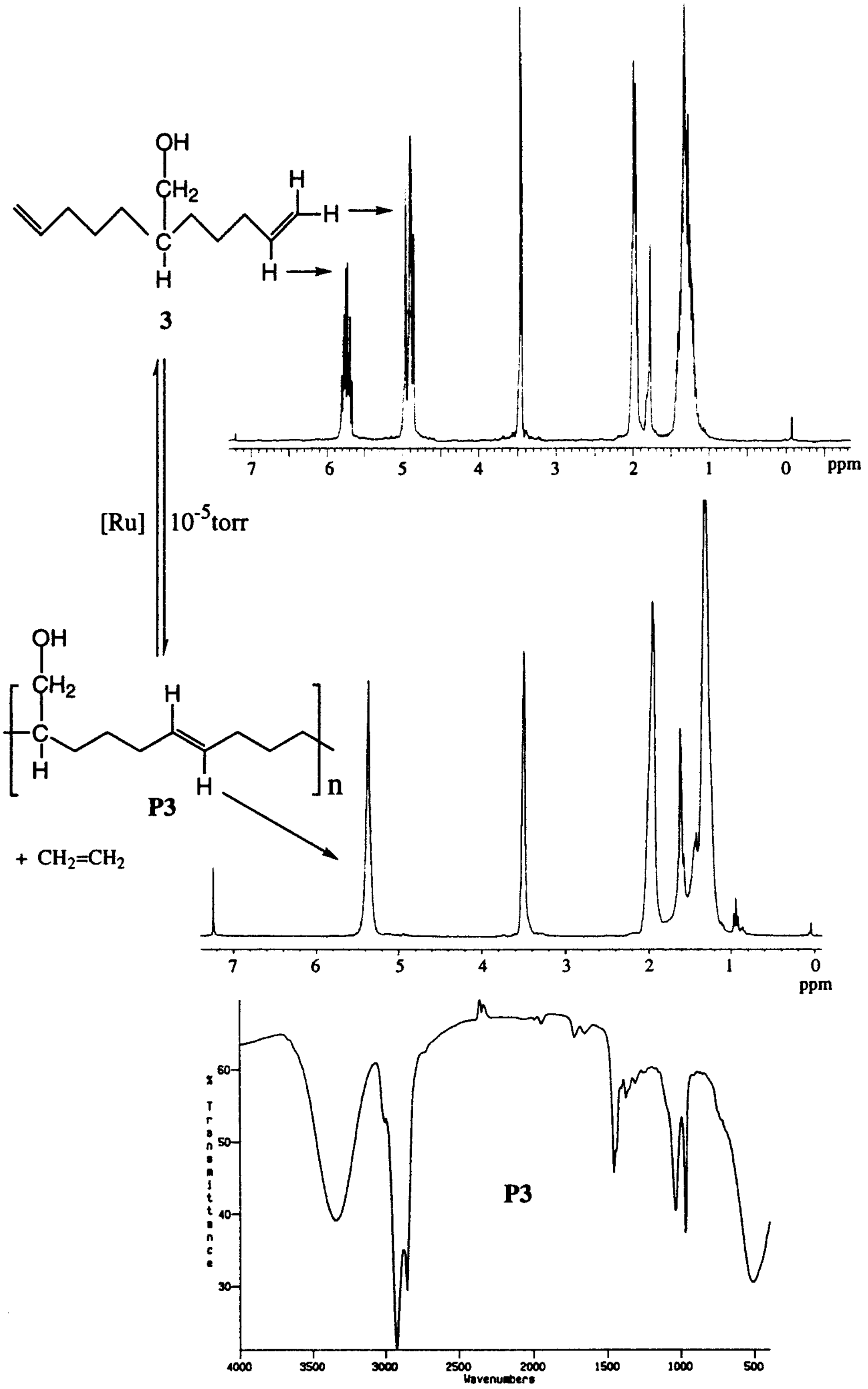

Figure 4. ^{1}H NMR end group analysis and IR transmittance spectra showing the high and clean conversion of the primary alcohol diene **3** to the linear unsaturated alcohol-functionalized polymer **P3**.

obtained from the ADMET polymerization of hydrocarbon monomers with catalyst **C2**.[15]

Polymerization of 2-(4-Pentenyl)-6-hepten-1-ol (3). This primary alcohol diene was polymerized using different catalyst ratios (500:1 and 200:1; Table 1). The lower catalyst ratio produced a highly viscous liquid, while the higher catalyst ratio generated a higher molecular weight, fibrous solid. This result is consistent with step polymerization chemistry, where higher catalyst (rather than initiator) concentrations result in faster conversions. All samples were characterized by NMR, GPC, and elemental analysis and were found to be consistent with their assigned structure. The lower molecular weight sample (Table 1) was highly soluble in common organic solvents at room temperature with little to no water solubility observed, while the higher

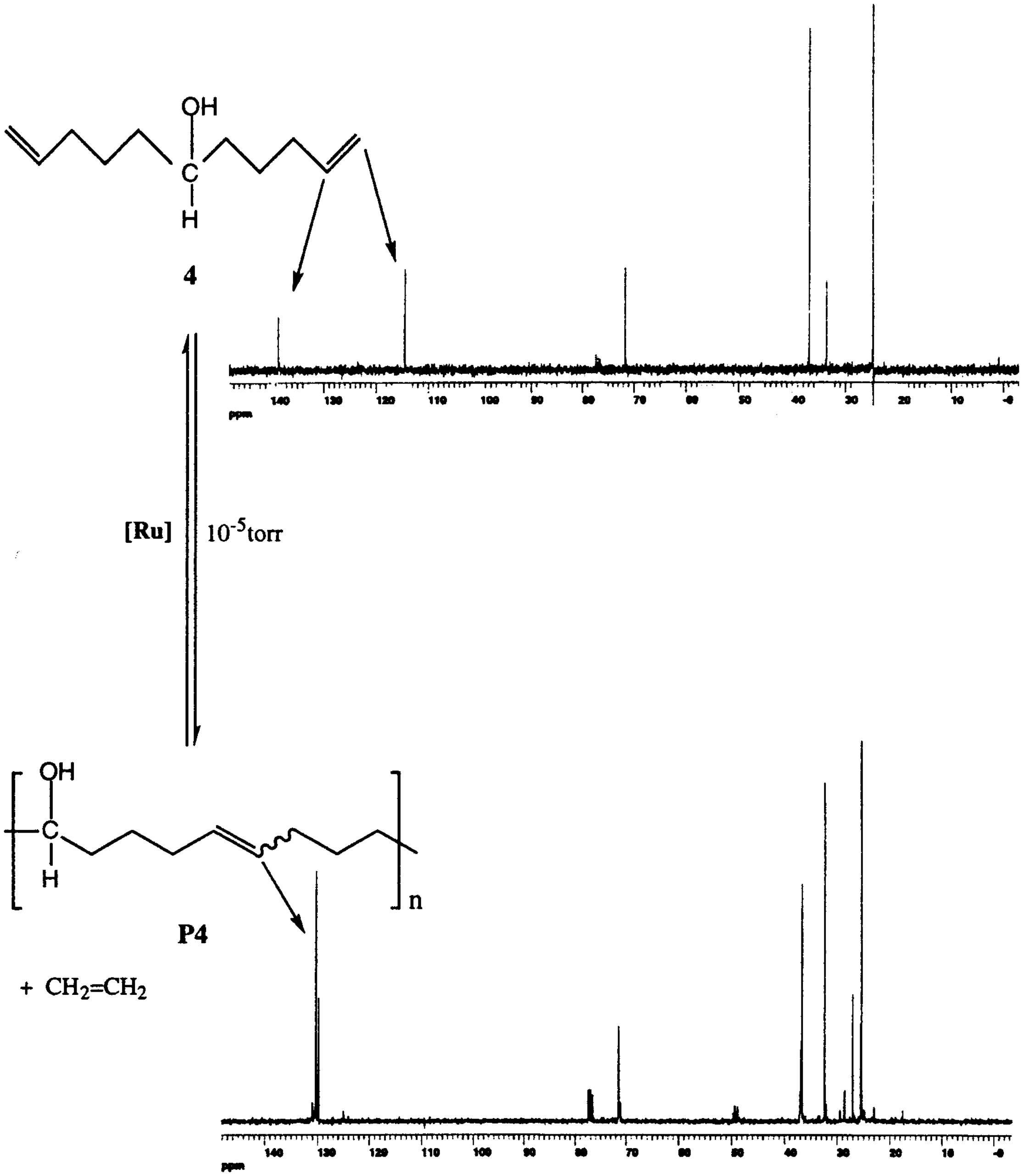

Figure 5. ^{13}C NMR spectra of the ADMET polymerization of the secondary alcohol diene **4** to its corresponding linear unsaturated polymer **P4**.

molecular weight sample (Table 1) displayed poor solubility in common organic solvents, except chlorinated ones. A solvent mixture of 80/20 chloroform/methanol was determined to be the best solvent mixture for this system.

The productive ADMET polymerization of monomer **3** is clearly demonstrated via the NMR spectra with the disappearance of the external (monomer) olefin resonances and the appearance of an internal (polymer) olefin resonance (Figure 4). Thus the multiplets at 4.9 and 5.8 ppm in the monomer are converted into a single internal olefin resonance at 5.4 ppm for the high polymer **P3**. The clean nature of this polymerization mechanism is illustrated by the absence of unidentified resonances in both the ^{1}H and ^{13}C NMR. It should be noted that the spectra are of crude polymers with *no* purification prior to analysis, again supporting the straightforward nature of this step polymerization scheme.

Infrared spectra also confirm the conversion of monomer to polymer (Figure 4), where the disappearance of the terminal olefin signal at 1640 cm^{-1} in the monomer confirms ADMET polymerization, while the alcohol functionality remains intact (broad signals in the 3300-cm^{-1} range). GPC analysis ($\bar{M}_n$ = 24 000 g/mol) and elemental analysis are consistent with the above spectral observations. These macromolecules are linear, primary polyalcohols made by direct conversion of monomer to polymer.

Polymerization of 1,10-Undecadien-6-ol (4). The polymerization of the secondary alcohol **4** represents the direct synthesis of a precisely defined, unsaturated version (prepolymer) of an ethylene–vinyl alcohol copolymer rich in ethylene content; hydrogenation then yields the saturated analogue. The secondary alcohol monomer was polymerized using two different monomer-to-catalyst ratios: 500:1 and 200:1 (Table 1), producing an opaque, waxy solid (**P4**) which was considerably less

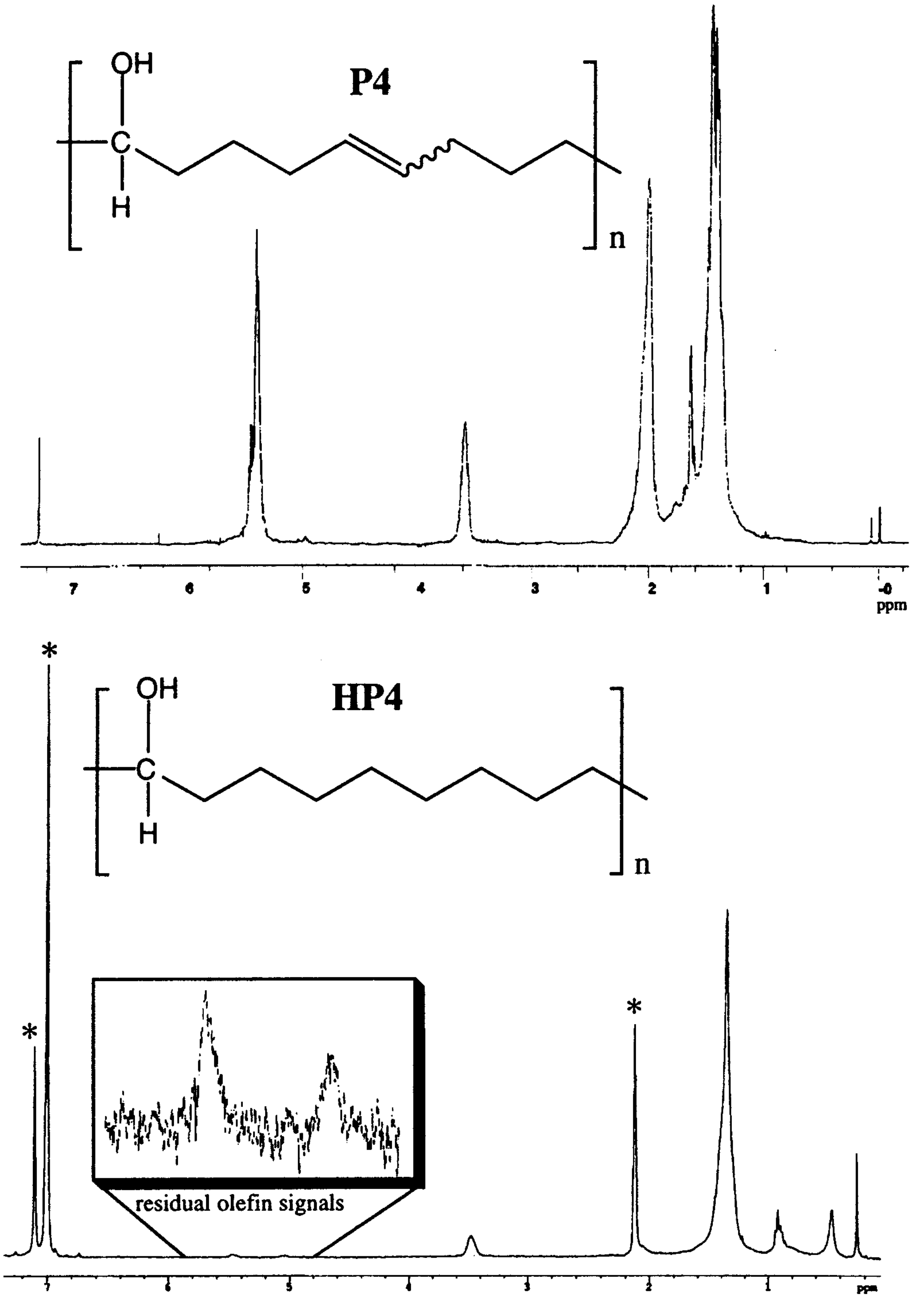

Figure 6. ^{1}H NMR of the unsaturated polymer **P4** and the diimide hydrogenated ethylene–vinyl alcohol copolymer **HP4**. The * signals are residuals from the deuterated solvent.

soluble in common organic solvents than the primary alcohol polymer. This polymer is crystalline in nature, likely due to its propensity for increased secondary chain interaction, observations which are consistent with those of Ramakrishnan and Chung in their synthesis of the ROMP polymer poly(5-hydroxyoctenylene).[9] The secondary polymer crystallizes while the primary and tertiary polymers do not, again indicative of the propensity for this polymer to more carefully pack into a crystal matrix. These comparisons are made below in the thermal analysis section of this paper.

ADMET conversion of this monomer is also observed in NMR spectra (Figure 5). Comparison of the ^{13}C and the ^{1}H spectra of this secondary alcohol polymer shows that the structure is more precise than those of similar unsymmetrical ROMP polymers.[9] The structure which results is the consequence of the symmetrical design of the monomer, which eliminates various regioisomers.

Polymerization of 6-Methyl-1,10-undecadien-6-ol (5). The tertiary alcohol monomer **5** polymerized easily using two different monomer-to-catalyst ratios (Table 1), and the polymerizations proceeded in an analogous manner to that of the primary monomer **3**. Visually, the viscosity of this tertiary monomer polymerization increased at a faster rate than that for the primary monomer, a phenomonen which may be at-

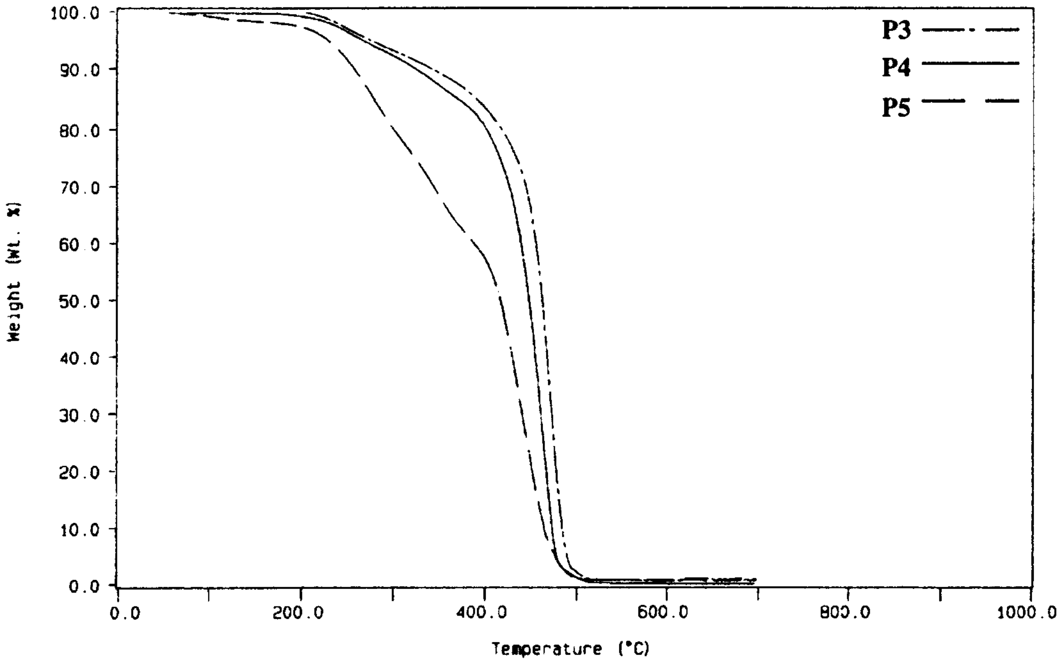

Figure 7. Thermogravimetric analysis of polymers **P3**–**P5** at a scan rate of 10 °C/min under N_2 purge.

tributed to the catalyst system being more active for this particular monomer. In this case, the more sterically hindered alcohol functionality may be less involved in complexation with the catalyst itself which in effect would increase its "apparent" activity. Regardless of the monomer/catalyst ratios, the polymer formed was a high-molecular-weight, transparent, tacky solid which was soluble in common organic solids. Molecular weight data are presented in Table 1.

Hydrogenation of Poly(6-hydroxynonenylene) P4. The further conversion of the secondary polymer to its saturated analogue is of interest, since the saturated polymer represents a precisely defined analogue of ethylene/vinyl acetate copolymers. Polymer **P4** was hydrogenated by exposure under diimide hydrogenation techniques using toluenesulfonyl hydrazide (TSH) and tripropylamine (TPA).[30] This procedure has been shown to be quantitative in its nature, and further, it can be assumed via literature results[30,31] that there was no polymer decomposition. A hard, white, granular solid was recovered and characterized by high-temperature ^{1}H and ^{13}C NMR.

The saturation of the olefin groups is confirmed by the comparison of the ^{1}H NMR spectra in Figure 6. These spectra illustrate the disappearance of the internal olefin signal at ~5.6 ppm as well as the allylic C–H signal at ~2.2 ppm; the retention of a single methine proton at ~3.7 ppm indicates the absence of regioisomers as well as the retention of the alcohol functionality. It should be noted that the absence of placement isomerism cannot be directly inferred from this spectrum due to both the simpler structure of the hydrogenated sample and the large numbers of C–C bonds between the hydroxy substituents. Precedence exists here, for Ramakrishnan[10] reported that in the presence of hydroxy groups different isomeric environments cannot be detected by NMR at a distance greater than 7 bonds. Nonetheless, the symmetry of the ADMET monomer prevents placement isomerism, resulting in a more defined microstructure. The carbon NMR confirms this simple structure, showing only five carbon environments (25.89, 29.83, 29.90, 38.00, 71.63 ppm) as well as excellent spectroscopic agreement with the assignments of Ramakrishnan's[10] ethylene–vinyl alcohol copolymers.

Thermal Analysis of the Primary, Secondary, and Tertiary Unsaturated Alcohol Polymers and the Saturated Secondary Alcohol Polymer. Generally speaking, poly(vinyl alcohol) polymers exhibit a limited degree of crystallinity (0–54%) and a wide melting temperature range (220–267 °C),[1] variations which occur due to the lack of regularity in the polymer backbone. We have used DSC and TGA techniques to compare the thermal behavior of these ADMET alcohol copolymers with that of poly(vinyl alcohol). We find that while the secondary alcohol polymers do indeed crystallize, the primary and tertiary alcohol polymers do not. The fact that the secondary polymer crystallizes is somewhat surprising, given that the polymer is atactic at the alcohol position. Nonetheless, this is consistent with observations made with other ADMET polymers, for the precise control of repeat unit regiochemistry leads to polymer crystallization.

DSC data were collected at scan rates of 20 °C/min. Each of the polymers exhibits glass transition temperatures in the range −11 to 13 °C, transitions which are observed in both the heating and cooling curves and which are reproducible on repetitive scans. TGA analysis (10 °C/min under nitrogen; Figure 7 and Table 2) shows the polymers to possess thermal stability in excess of 200 °C.

These TGA data are in keeping with prior observations on similar ROMP polymers. For example, the secondary polymer **P4** displays a rapid weight loss at 413 °C which is consistent with the case for the ROMP polymer poly(5-hydroxy-1-octenylene) reported by Chung,[9] who report an onset decomposition at 430 °C. The same ROMP polymer, directly synthesized by Hillmyer,[12] shows a decomposition temperature of 386 °C.

The two-stage TGA weight loss exhibited by polymers **P3**–**P5** may be the result of a combination of the degassing of impurities and/or the thermal elimination of water. For example, polymer **P4** loses ~15% of its

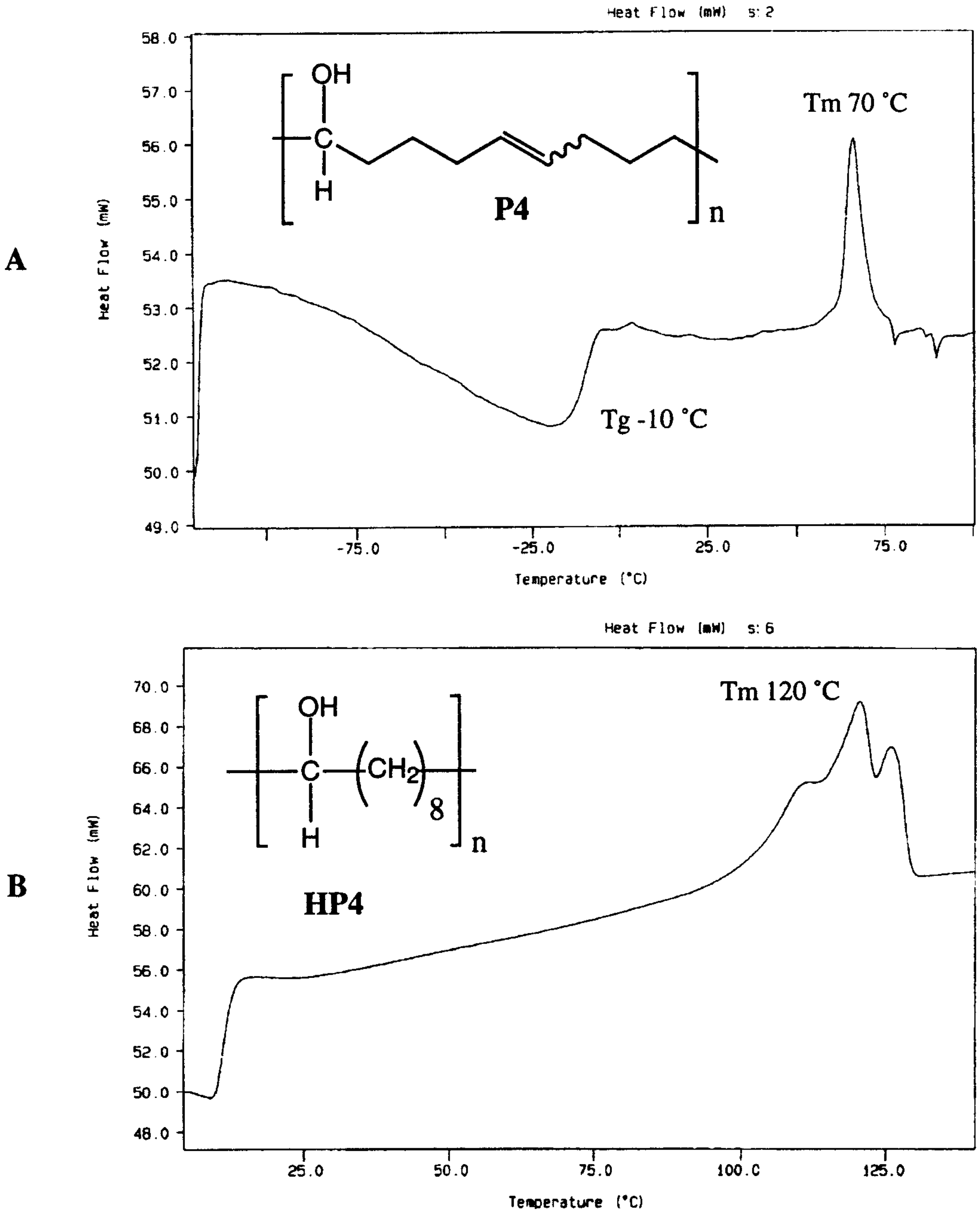

Figure 8. DSC heating scans of secondary alcohol polymers **P4** and **HP4** at a scan rate of 20 °C/min.

Table 2

sample	M_n[a] (g/mol) GPC	T_g[b] (°C)	T_m[c] (°C)	TGA[d] N_2 (°C)
P3	24 000	−11	N/A	437
P4	18 600	−10	70[e]	413
P5	13 000	13	N/A	234
HP4		N/A	120	430

[a] Relative to polystyrene standards in a 20/80 methanol/chloroform solvent mixture. [b] 20 °C/min scan rate, transition taken from second scan of thermal cycle. [c] Peak temperature from first-order endothermic transition, with a scan rate of 20 °C/min [d] Onset temperature at 10 °C/min scan rate. [e] First-order transition detected in first scan and in subsequent scans of annealed samples.

weight between 200 and 410 °C followed by the sharp decomposition to 100% weight loss. This result is consistent with the thermal elimination of H_2O (13% of the repeat unit weight) in the first stage followed by complete polymer decomposition. It is interesting to note that polymer **HP4** shows a rapid single-stage onset of decomposition at 430 °C, which is approximately 130 °C higher than that of poly(vinyl alcohol) (PVA rapidly loses weight at 300 °C).[9]

Equally as interesting is the melting behavior of these polymers (Figure 8). Both the unsaturated polymer (**P4**) and its unsaturated analogue (**HP4**) are semicrystalline materials displaying crystalline melting points at 70 and 120 °C, respectively. These melt temperatures remained unchanged following repetitive reprecipitations from water. The melt point of the saturated polymer **HPA** (120 °C and reproducible upon cycling) closely compares to that of the structurally similar sample of Ramakrishnan, which has a T_m value of 128 °C.[10]

Conclusions

Precisely defined polyalcohols can be synthesized directly via an ADMET polycondensation reaction of appropriate diene alcohol monomers using the ruthenium benzylidene $RuCl_2(=CHPh)(PCy_3)_2$ as a metathesis catalyst. The clean nature of this conversion is demonstrated by NMR and elemental analysis, where the utility of using a condensation mechanism has been demonstrated by polymerizing symmetrical primary, secondary, and tertiary alcohol diene monomers. It is evident that the precision of the structure of the resulting unsaturated polymer is limited only by the design of the monomer and is not influenced by the mechanism of polymerization. Saturated versions of the secondary polymer, in particular, offer precise models to imitate the behavior of ethylene−vinyl acetate copolymers. We intend to use these well-defined polyalcohol polymers as binding substrates in the preparation of a series of drug release macromolecules.

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