Examples of new synthetic routes to pendant ester-ether derivatives of α-hydroxymethylacrylate polymers

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Summary

Three routes to new ester-ether derivatives of ethyl α-hydroxymethylacrylate (EHMA) and t-butyl α-hydroxymethylacrylate (TBHMA) were investigated. The first approach involved the preparation of chloroacetate derivatives of EHMA and TBHMA as intermediates followed by attempted etherification of the chloroacetate group. All attempted nucleophilic reactions of ethyl α-chloroacetoxymethacrylate (ECAM) and t-butyl α-chloroacetoxymethacrylate (TBCAM) gave Michael-type substitution products with loss of the α-chloroacetyl substituent. Polymer substitution was therefore investigated. Bulk polymerization of ECAM with AIBN gave unexpectedly high molecular weight polymer with a number average value of 1.15 million. This homopolymer was substituted with 4-phenylphenol in excellent conversion. The second approach involved the reaction of ethyl α-chloromethylacrylate (ECMA) with α-ethers of acetic acid sodium salts using phase transfer catalysis. The methoxyacetate derivative was prepared and polymerized to give a polymer with a number average molecular weight of 260,000. The third route to ester-ether derivatives involved three steps: reaction of t-butylchloroacetate with an alcohol to give the ether, conversion of the t-butyl group to the acid chloride, and reaction of the acid chloride with EHMA or TBHMA. The 2-(4-phenylphenoxy)acetate derivative of EHMA was prepared using this method, and converted to high polymer.

Introduction

It has been shown that ether derivatives of EHMA rapidly polymerize but give only low molecular weight polymers due to facile chain transfer.[1,2] For example, the highest molecular weights obtained for ethers of the ethyl ester polymers range from 23 to 90 thousand.[3] In contrast, ester derivatives of EHMA have shown surprisingly good polymerizability, giving products with number average molecular weights of 112 to 700 thousand.[4] The higher molecular weights are due to enhanced reactivity caused by the more electron withdrawing ester group. It was expected that ether derivatives linked through an ester at the β position (rather than directly attached) would polymerize well to give high molecular weight materials. We describe here examples of three synthetic approaches to such ether-ester monomers and their polymerization.

Experimental

All solvents and reagents were used as obtained. Monomers and polymers were

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characterized by ^{13}C NMR spectroscopy using a Bruker AC-200 spectrometer. Thermal analyses were done on a DuPont 9900 analyzer. Size-exclusion chromatography (SEC) was carried out with THF solvent, American Polymer Standard columns of 500, 10^3, 10^4 and 10^6 Å packing, and polystyrene calibration standards ranging from 17.5×10^3 to 3×10^6. Ethyl α-hydroxymethylacrylate (EHMA), t-butyl α-hydroxymethylacrylate (TBHMA) and ethyl α-chloromethylacrylate (ECMA) were prepared using previously reported procedures.[5,6]

Representative Procedure for the Synthesis of ECAM and TBCAM
Acid Chloride Procedure

EHMA (3.9 g, 0.03 m), chloroacetyl chloride (23.76 g, 0.21 m) and 10 ml CH_2Cl_2 were added to a 50 ml three-neck round-bottom flask in an ice bath under a dry nitrogen purge. A 20 ml CH_2Cl_2 solution of TEA (0.77 g, 7.58 mmol) was added dropwise to the flask over 15 min. The solution was stirred in an ice bath until all EHMA reacted as monitored by GC (1 h). Water was added slowly via addition funnel to the mixture in the ice bath and the aqueous phase separated. Water was added to the organic phase and the solution was neutralized with $NaHCO_3$ solution to remove excess chloroacetyl chloride. The solution was extracted with ether, the ether extract dried with $MgSO_4$ and solvents evaporated to give 85-95% yield. GC showed 3-4% residual EHMA due to hydrolysis of the product during work up. Copper(II) chloride was added as a free-radical inhibitor and the solution was distilled to give 98% pure product in 50% yd.

Synthesis of ethyl α-methoxyacetoxymethacrylate

ECMA (5.52 g, 0.037 m), methoxyacetic acid sodium salt (12.5 g, 0.11 m) and Aliquat 336 (Aldrich, 0.17 g, 0.42 mmol) in CH_2Cl_2 were added to a 100 ml round-bottom flask. The mixture was stirred at room temperature 9 days and then refluxed for 22 days until all ECMA had reacted. The solution was filtered and CH_2Cl_2 was evaporated under reduced pressure; crude yield 95%. Copper(II) chloride was added as a free-radical inhibitor and vacuum distillation gave monomer as a colorless liquid at 98.6% purity.

Synthesis of t-butyl α-(4-phenylphenoxy)acetate

t-Butyl chloroacetate (6.67 g, 44.5 mmol), 4-phenylphenol (6.81 g, 40 mmol), K_2CO_3 (6.94 g, 50 mmol) and 40 ml DMF were added to a 50 ml round-bottom flask. The reaction mixture was stirred at room temperature for 24 h. Ether was added to the mixture and the solid was separated. Ether was evaporated from the organic phase under reduced pressure and the remaining DMF solution was poured into 2 l of water. The product was isolated by filtration and vacuum dried (72% yd); mp 37 $^{\circ}$C.

α-(4-Phenylphenoxy)acetyl chloride

t-Butyl α-(4-phenylphenoxy)acetate (3.42 g, 0.012 mol) and excess thionyl chloride were added to a 50 ml round-bottom flask equipped with a condenser. A nitrogen purge was used to remove HCl gas evolved. The mixture was stirred at room temperature for 3 days and then heated to 60 $^{\circ}$C and allowed to stir for 8 h. Excess thionyl chloride was evaporated under reduced pressure to give crude acid chloride which was then washed with petroleum ether to give pure product (79% yd) as a solid.

Reaction of EHMA with α-(4-phenylphenoxy)acetyl chloride

EHMA (0.52 g, 0.004 m), α-(4-phenylphenoxy)acetyl chloride (1.20 g, 0.005 m) and 20 ml of $CHCl_3$ were added to a 50 ml round bottom flask. The flask was placed in an ice bath and TEA (0.56 g, 0.0055 m) was added to the flask over 15 min. A nitrogen purge was used to remove evolved HCl gas. The mixture was stirred in the ice bath for

3 h. CHCl$_3$ was evaporated and the remaining solution was washed with water several times to remove salt. The solid was dried at room temperature under vacuum and washed with petroleum ether to give 92% pure product.

General Bulk Polymerization Procedure

Neat monomer containing AIBN (0.5 wt %) in a septum-sealed flask was subjected to three evacuate-freeze-thaw procedures and placed in a 60 °C oil bath. Polymers were purified by reprecipitation from CH$_2$Cl$_2$ into methanol.

Results and Discussion

Synthesis of ECAM and TBCAM

The first method for the preparation of ester-ether derivatives involved the synthesis of ethyl α-chloroacetoxymethacrylate and t-butyl α-chloroacetoxymethacrylate (Figure 1).

R= C$_2$H$_5$, C(CH$_3$)$_3$
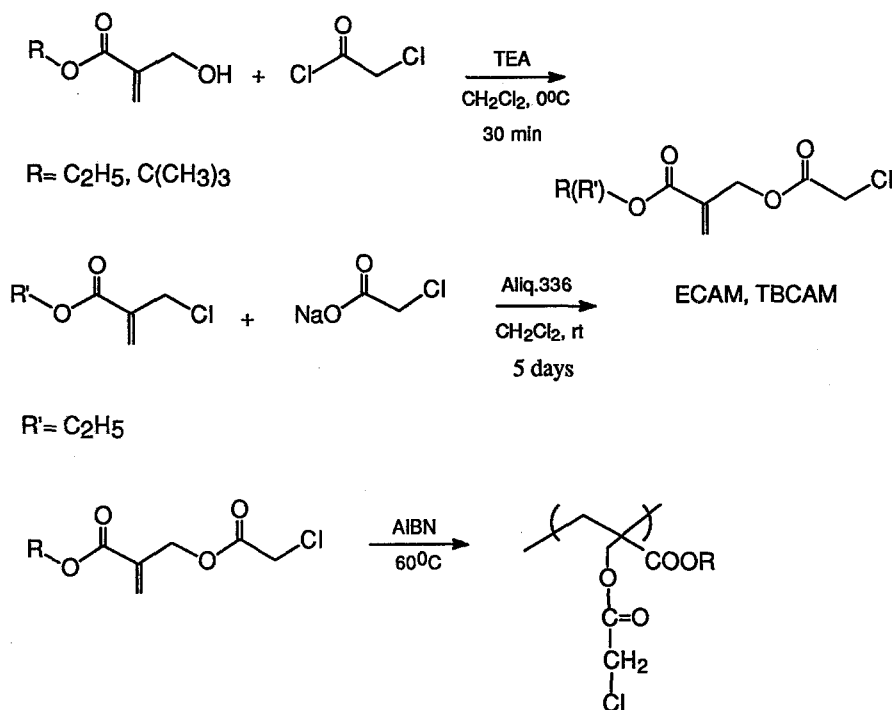
R'= C$_2$H$_5$

Figure 1. General acid chloride and sodium salt synthetic schemes with overall polymerization procedure for ECAM and TBCAM

These monomers and their polymers were expected to offer potential for synthesis of a wide variety of derivatives including derivatives with ether groups replacing the

chlorine. Two procedures were used for the synthesis of ethyl α-chloroacetoxymethacrylate. The first procedure involved reaction of EHMA with excess chloroacetyl chloride using TEA as catalyst and base. This procedure gave 98% pure product in 50% yield. The second procedure involved reaction of ECMA in CH_2Cl_2 with the sodium salt of chloroacetic acid in the presence of Aliquat 336, a quaternary ammonium chloride phase transfer catalyst. Yield of this procedure after distillation was very low (16%) due to side reactions, involving the reaction of the product (ECAM) with the salt or with itself to give glycolide dimer, trimer and oligomers through chain extension. The later opens up a novel pathway to reactive polyglycolide macromonomers. Due to low yields obtained from the phase transfer procedures, TBCAM was only synthesized by the acid chloride procedure, which gave 98% pure product in 40% yield.

Polymerization

ECAM and TBCAM were polymerized in bulk at 60 °C using AIBN. The polymerization rate was very fast (1-3 h) and gave polymers in yields of 70-76% after reprecipitation and drying. The Tg of the ECAM polymer was 66 °C as determined by DSC. The molecular weight of the ECAM polymer was very high as shown by SEC in THF (Mn= 1.15 million, Mw= 2 million). These values are comparable to other ester derivatives polymerized previously[4] and at least an order of magnitude higher than analogous ether derivatives. This polymer showed a higher peak molecular weight (Mp= 2.5 million) than weight average value due to autoacceleration during polymerization. Apparantly, chain transfer (which was expected at the chloroacetate group) did not occur. ECAM was also polymerized using 1 wt % photoinitiator at three different temperatures (30, 60, 80 °C). The conversion at about 80 seconds (which corresponds to the exotherm peak maximum) was 70-74%. SEC of polymer obtained from photopolymerization at 60 °C gave a very low number average molecular weight (18,600).

The ^{13}C NMR spectra of the ECAM monomer and polymer are given in Figure 2. They show disappearance of the monomer double bond carbons at 127 and 134 ppm and appearance of backbone carbons at 45 and 47.5 ppm in the polymer. Multiple peaks seen for the backbone carbons indicate tacticity similar to other ester derivatives.[4]

The molecular weights of the TBCAM polymer (Mn= 328,000, Mw= 820,000, PDI= 2.5, Mp= 970,000) were lower than for ECAM, indicating that the bulky t-butyl group inhibited propagation somewhat compared to the ethyl group. DSC analysis of poly-TBCAM showed a Tg at 118 °C. When the polymer was heated to 200 °C, an endotherm was observed at 190 °C due to loss of the t-butyl groups. The second DSC scan of this sample showed an increase in Tg (149 °C) due to acid-acid interactions and crosslinking reactions.

Reactions of ECAM

Reactions of ECAM with dodecanthiol and 4-cyano-4'-hydroxybiphenyl were carried out using TEA as catalyst and acid scavanger. A similar reaction of sodium formate with ECAM was done using phase transfer catalysis. The ^{13}C NMR spectra of the purified products did not show the expected monomers, but instead products due to Michael-like substitution by thiol, formate and alcohol moieties in which addition to the double bond is followed by loss of the chloroacetate group. This implies that the chloroacetate anion is an unexpectedly good leaving group for this substitution reaction (Figure 3).
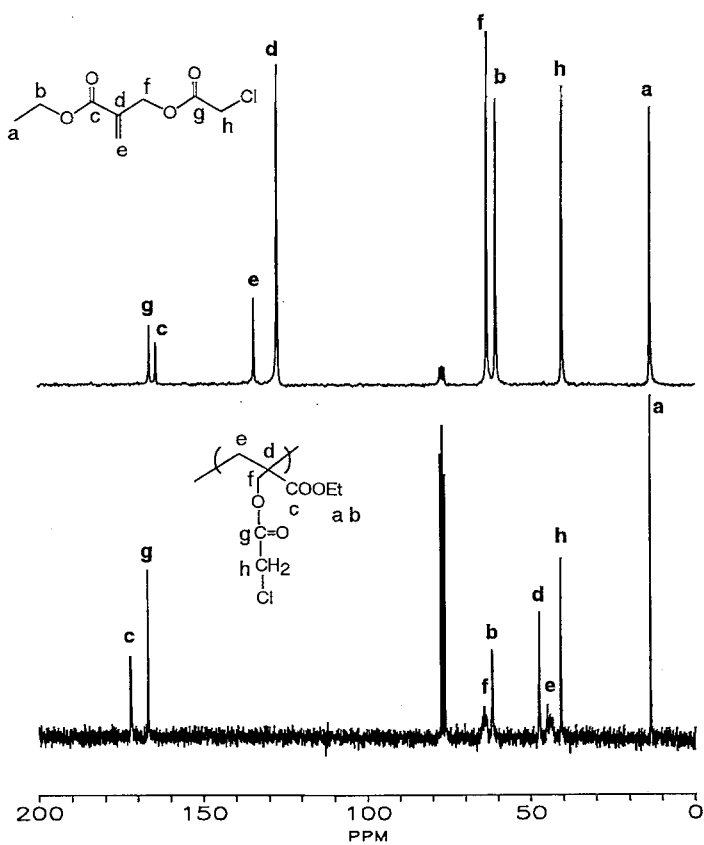
Figure 2. ^{13}C NMR spectra (CDCl$_3$) of ECAM monomer (upper trace) and polymer (lower trace)
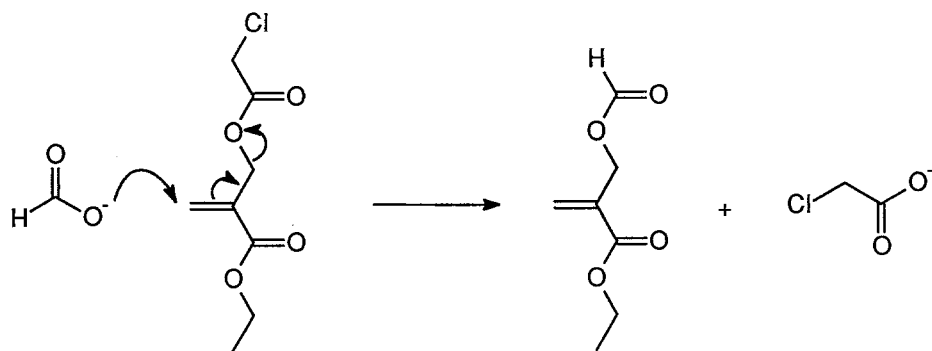

Figure 3. Reaction of ECAM with sodium formate

As a result of the unexpected failure of the attempted nucleophilic substitution reactions of ECAM, alternatives were explored. One alternative was to carry out reactions on poly-ECAM or poly-TBCAM to give polymers which were not available by direct polymerization of the desired monomers. Reactions of poly-ECAM and poly-TBCAM were done with 4-phenylphenol using K_2CO_3. Soluble polymers were obtained at room temperature (Figure 4).
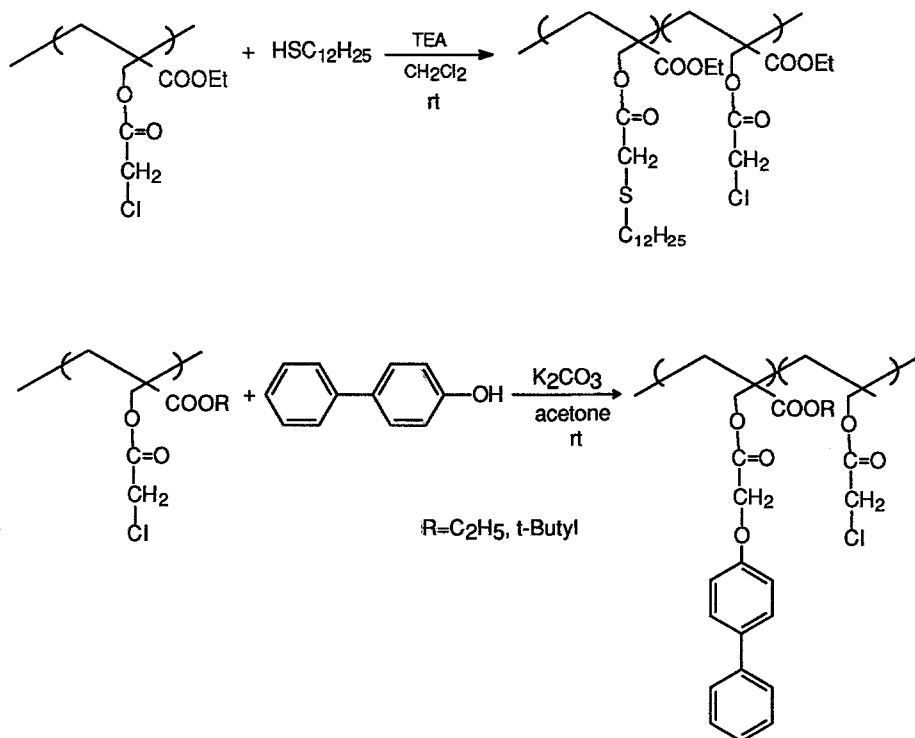

Figure 4. Reaction of poly-ECAM with dodecanthiol and 4-phenyl phenol

The ^{13}C-NMR spectrum of the substituted poly-ECAM was the same as that of the polymer obtained directly from its monomer (Figure 5) showing very high conversion of pendant groups. Altough high conversions were obtained from the poly-TBCAM reaction, the ^{13}C-NMR spectrum of the resulting polymer showed a third carbonyl peak due to unexpected hydrolysis of some of the t-butyl groups. Also, a small amount of crosslinking was observed when very high molecular weight starting polymers were used for this reaction.

The reaction of poly-ECAM with 1-dodecanthiol was also performed by displacement of the pendant chlorine with the alkyl thiol anion (Figure 4). This reaction was done in CH_2Cl_2 at room temperature using TEA as catalyst and base. A soluble polymer was obtained, although determination of its molecular weigth by SEC was not possible due to virtually no difference in refractive index of the polymer and solvent (THF). Its ^{13}C NMR spectrum showed new peaks due to the dodecyl side chains and a new carbonyl carbon. The pendant methylene carbon shifted upfield (to about 30 ppm) after reaction (chlorine replaced by sulfur). Comparison of peak heights of the three different

carbonyl carbons indicated ca 40% conversion. The Tg of the polymer (18 °C) was found to be considerably lower than that of the parent polymer (Tg= 66°C) which was expected due to the plasticizing effect of the pendant dodecane units.
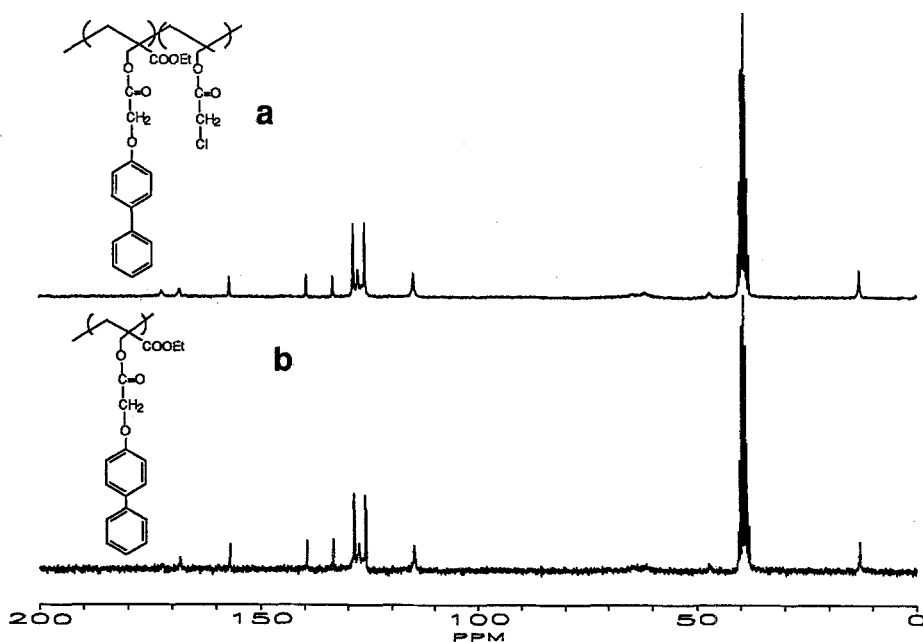

Figure 5. ^{13}C NMR spectrum (CDCl$_3$) of products from a) reaction of poly-ECAM with 4-phenylphenol b) polymerization of poly-ethyl 4-phenylphenoxyacetyl methacrylate

The second method for the preparation of ester-ether monomers involved reaction of ECMA with an α-ether of acetic acid sodium salt using PTC (Figure 6). The methoxyacetate derivative of EHMA was prepared by the reaction of ECMA with methoxyacetic acid sodium salt using Aliquat 336. Although this reaction gave high yields and clean products, the rate of reaction was very low; it took 31 days for all ECMA to be converted to product. This monomer was polymerized in bulk at 60 °C using AIBN (42% yd at 2.5 h). SEC in THF gave Mn=260,000, Mw=767,000, Mp=650,000, PDI=2.95. These values are comparable to other ester derivatives and much higher than those of ether derivatives; eg, the Mn for ethyl α-methoxymethacrylate was only 58,000.[3] The Tg of the polymer was found to be 40 °C. The lack of commercial availability of other ether derivatives of acetic acid limits the use of this method, and a third method for the synthesis of ester-ether derivatives was evaluated.

This third method involved polymerization of preformed monomer which obtained via a multistep synthesis. The first step involves the reaction of t-butyl chloroacetate with an alcohol to give an ether. The second step is the deprotection of the t-butylester group using either SOCl$_2$ or CF$_3$CO$_2$H. The last step is the reaction either of the acid chloride with EHMA or the acid with ECMA using phase transfer catalysis. Using this method, the 4-phenylphenol ether of ECMA was prepared; combined yields of the three steps was

70-80%, altough, the product contained 8% of residual acetic acid 4-phenylphenoxy ester. The product was polymerized at 60 °C in benzene using 0.5 wt % AIBN; the impurity was removed by precipitating the polymer solution into methanol. The polymer gave cloudy solutions in most solvents. ^{13}C NMR of the polymer (Figure 5) showed backbone carbons at 47 ppm, aromatic carbons between 115 and 157 ppm, and two different carbonyl carbons at 168 and 174 ppm. Tg of the polymer was 90-92 °C as determined by DSC. SEC traces of the polymer showed a bimodal distribution with Mn= 50,000, Mw= 300,000, Mp= 26,000, Pd= 6.6. These values are much higher than that of ethyl α-phenoxymethylacrylate which gave Mn= 5,900, Mw= 10,400 and Pd= 1.75.[7] The behavior of methyl α-phenoxymethacrylate was explained as due to a low ceiling temperature and a decrease in Mn by an addition-fragmentation reaction.[8,9]
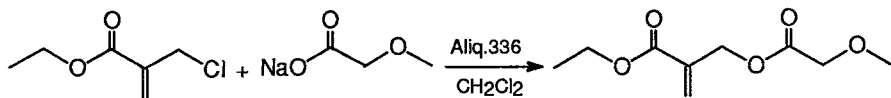

Figure 6. Synthesis scheme of ethyl α-methoxyacetylmethacrylate

      In conclusion, the approaches outlined here (except the unsucessful first one which involves ECAM or TBCAM) provide different ester-ether derivatives of α-hydroxymethylacrylates. While, the first route gave undesired Michael type substitution products, polymerization of the intermediates (ECAM and TBCAM) gave very high molecular weight polymers which were useful for substitution reactions. The other two monomer methods, involving preformed ether acids and ether acid chlorides of glycolic acid, allowed synthesis of the desired monomers and conversion to high molecular weight polymers. In comparison to ether derivatives, β ester linked ether derivatives are shown to give higher molecular weight polymers (ca ten times greater Mn values), clearly establishing the potential of this approach for general use in obtaining novel multifunctional polymers.

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