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Poly(silyl ester)s: A New Family of Hydrolytically-Degradable Polymers with Attunable Stabilities

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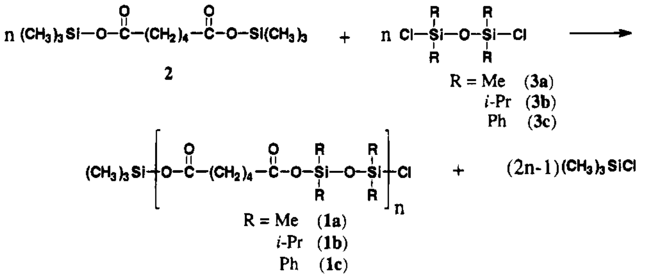
Polymers composed of nucleophilically-labile silyl ester bonds in the main chain are being investigated as a new class of degradable polymers with the potential for an extremely broad range of degradation behavior through variation in the functionalities attached to the silicon atoms. In initial studies, bis(trimethylsilyl) adipate underwent a transsilylation[1,2] reaction with dichloro tetrasubstituted disiloxanes to give a series of poly(silyl ester)s. The degradation time for a polymer containing isopropyl-substituted silicon atoms was found to be 30 times longer than for the methyl- and phenyl-substituted analogs.

The biomedical field[3] and environmental concerns[4] have been placing increasing demands on degradable materials. In the design of degradable materials, the physical and mechanical properties must be considered for performance in serving the expected function, while the degradation rate and degradation products are also very important. Much effort has been directed toward obtaining control and variability over the degradation rates and the degradation properties of hydrolytically-cleavable polymers, with concentration focusing to a large extent on aliphatic polyesters.[5] Poly(anhydride)s,[6] poly(ortho ester)s,[7] poly(organophosphazene)s,[8] and poly(silazane)s[9] have also received considerable attention as alternative labile functionalities employed to broaden the range of stabilities possible for polymeric materials.

Because the lability of a silyl ester linkage is dramatically affected by the substituents attached to the silicon atom,[10] poly(silyl ester)s would appear to be an ideal family of degradable polymers. It has been shown[10b] that silyl esters undergo S_N2 attack at the silicon atom with competing attack by the nucleophile at the carbonyl carbon. As substituents with increasing steric bulk or with increasing electron-donating capabilities are attached to the silicon atom, an increasing amount of the nucleophilic attack occurs at the carbonyl carbon.[11] This variable mechanism of cleavage for the silyl ester bond may allow for a much broader range of stabilities to be available with poly(silyl ester)s, than for structures composed of simply carbon−oxygen bonds, such as esters, anhydrides, etc.

Multifunctional silyl esters have found application as cross-linking agents that require only mild reaction conditions, especially for silicone elastomers.[12] However, few examples of polymers containing silyl ester bonds along their backbone can be found in the literature. Poly(siloxane)s bearing silyl ester end groups have been used as prepolymers, and trialkylsilyl ester side chain groups have been used for protection of reactive functionalities during anionic polymerization,[13] in photolithographic applications,[14] or for viscosity reduction.[15] Herein, we report the preparation, characterization, and degradative behavior of main-chain silyl ester polymers containing silyl ester bonds connecting each monomeric repeat unit, to allow for complete degradation of the material. In addition, versatile control over the rate of cleavage is demonstrated.

Scheme 1. Transsilylation Polymerization between Bis(trimethylsilyl) Adipate and 1,3-Dichloro tetrasubstituted Disiloxanes, Where R = Methyl (3a and 1a), Isopropyl (3b and 1b), and Phenyl (3c and 1c)



The syntheses of poly(silyl ester)s would seem to be straightforward, since silyl ester functionalities have been prepared by a number of routes in their use as protecting groups for carboxylic acids.[16] However, several of the most common approaches toward the formation of silyl esters were found to be inadequate for polymer syntheses, due to salt formation, byproduct side reactions, monomer insolubility, monomer impurity, and/or incomplete reaction. Therefore, the preparation of silyl esters by a transsilylation[1,2] reaction between a dichlorosilane and the trimethylsilyl ester of a diacid was investigated (Scheme 1). There are several benefits to this transsilylation approach: no base nor catalyst is required; the trimethylsilyl chloride byproduct is volatile; reaction between the growing poly(silyl ester) with the condensation byproduct, trimethylsilyl chloride, is nonterminating;[17] the polymerization can be performed at relatively low temperatures and without the addition of solvent; and the monomers can be readily purified.

A number of parameters are expected to affect the hydrolytic stability of polymers composed of silyl ester bonds along their backbones, including the substituents on silicon, the substituents attached to the carboxylate functionality, the hydrophobicity of the material, the crystallinity, etc. In this study, the composition of the difunctional trimethylsilyl ester monomer was held constant, while the effect of altering the silicon atom functionality was investigated. Therefore, as shown in Scheme 1, the poly(silyl ester)s, **1a−c**, were prepared by the transsilylation polymerization involving a ligand exchange reaction between bis(trimethylsilyl) adipate (**2**) and 1,3-dichlorotetramethyldisiloxane (**3a**), 1,3-dichlorotetraisopropyldisiloxane (**3b**), and 1,3-dichlorotetraphenyldisiloxane (**3c**), respectively. The preparation of **2** was by the reaction of adipic acid and 1,1,1,3,3,3-hexamethyldisilazane in THF heated at reflux under argon for 16 h, and distillation (86 °C at 0.13 mmHg, 99% yield) directly into the polymerization flask. The appropriate dichlorodisiloxane (freshly distilled) was then added *via* tared syringe, and the polymerization was allowed to proceed neat at 100−135 °C for 10−14 days.[18]

The polymerizations were monitored by both gel permeation chromatography (GPC) and ^{29}Si NMR using standard INEPT[19] (Insensitive Nuclei Enhanced by Polarization Transfer) experiments. Figure 1 shows the ^{29}Si (59.6 MHz) NMR INEPT spectrum of the reaction mixture taken after 3 days of reaction between **2** and **3a** at 65 °C, in which the resonances of the two monomers are observed at 23.02 and 7.07 ppm (referenced to tetramethylsilane at 0.0 ppm), respectively. Upon condensation, the 1-(acyloxy)-3-chlorotetrameth-

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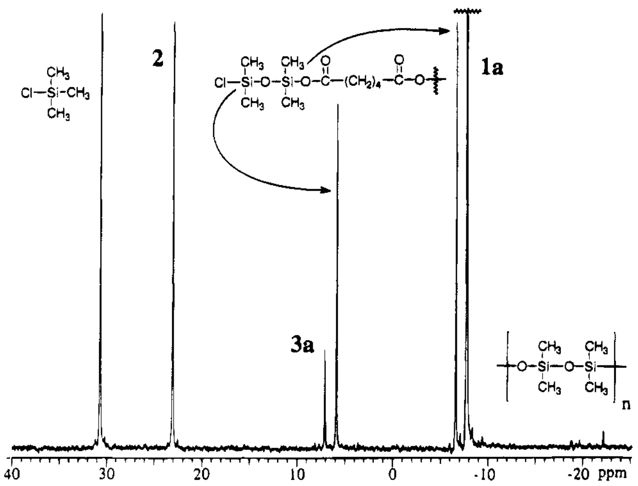

Figure 1. ^{29}Si NMR (60 MHz, $CDCl_3$) INEPT spectrum of the reaction mixture of **2** and **3a** at the oligomeric stage of the polymerization.

Table 1. Molecular Weight Data,[a] ^{29}Si NMR Resonances, and Glass Transition Temperatures (T_g) for Poly(silyl ester)s 1a–c

compd	M_w	PDI	DP_w	^{29}Si NMR (δ)	T_g (°C)
1a	2850	2.2	10	−7.74	−56
1b	2700	1.7	6.9	−11.38	−84
1c	2650	1.9	5.0	−36.99	3

[a] M_w is the weight average molecular weight, PDI is the polydispersity index or the molecular weight distribution, and DP_w is the calculated degree of polymerization.

yldisiloxane chain end of the oligomeric intermediates gives resonances at +5.86 and −6.64 ppm, trimethylsilyl chloride is observed at 30.63 ppm, and the silicon atoms of the 1,3-diacyloxy-substituted tetramethyldisiloxane repeat units of **1a** resonate at −7.74 ppm. As the reaction proceeds, all resonances due to the starting materials, intermediates, and trimethylsilyl chloride disappear and the single resonance at −7.74 ppm remains.

Due to the moisture sensitivity of **1a–c**, the crude polymers were characterized without purification.[20] The products were characterized by standard techniques, including infrared spectroscopy, ^{1}H NMR, ^{13}C NMR, and ^{29}Si NMR spectroscopy, gel permeation chromatography (GPC), and differential scanning calorimetry (DSC).

GPC with on-line viscometry and polystyrene standards was used for the determination of molecular weights and molecular weight distributions. Table 1 contains data for the molecular weights of polymers **1a–c**, with the distributions ranging from 500 to 15 000 amu.[20] In comparison to **1a**, the lower degree of polymerization for the isopropyl-substituted derivative (**1b**) may be due to steric effects, while viscosity problems plagued the polymerization of the phenyl derivative (**1c**).

Thermal analysis of the polymers by differential scanning calorimetry measured the glass transition temperatures (T_g) to be −56, −84, and +3 °C for **1a**, **1b**, and **1c**, respectively. The T_g's of the poly(silyl ester)s correlated well with the qualitative properties of each of the polymers, in which they were transparent viscous gels with the viscosity increasing in the order **1b** < **1a** < **1c**. This also agrees with the expected behavior, in which the isopropyl groups in **1b** introduce side chain branches and increase the free volume, resulting in a decrease in glass transition temperature. The incorporation of side chain aromatic rings causes a decrease in the flexibility of the polymer, either through interchain or intrachain π-stacking or perhaps simply due to the presence of the relatively high concentration of the rigid rings.

In addition to monitoring the polymerization, ^{29}Si NMR was invaluable in the characterization of the products. Each of the polymers gave a single ^{29}Si resonance (Table 1), and the expected[21] shifts to higher field when comparing **1a** to **1b** to **1c** were observed. ^{29}Si NMR also allowed for the detection and identification of any hydrolysis products. As mentioned above, the poly(silyl ester)s are readily hydrolyzed, and the reaction conditions required thorough exclusion of moisture. Trace amounts of water regenerate the diacid and give a dihydroxysilane, which can condense to form a poly(siloxane). The spectrum of Figure 1 was selected to illustrate this, in which a small amount of poly(dimethylsiloxane)[22] is observed at −22.1 ppm.

The hydrolysis and alcoholysis of **1a–c** were evaluated by GPC analyses of molecular weight loss with time for the polymers in THF solutions containing water, methanol, or *tert*-butyl alcohol (Table 2). The isopropyl-substituted polymer, **1b**, proved to be substantially more stable than the methyl- or phenyl-substituted polymers, which were found to have similar labilities, with **1c** degrading slightly faster than **1a**. This behavior is consistent with the half-life values measured for the desilylation of silyl ether-protected cyclohexane under the action of 5% sodium hydroxide in ethanol, where it was found that the rate of cleavage was *tert*-butyldiphenylsilyl > *tert*-butyldimethylsilyl > triisopropylsilyl.[10a] The isolation and characterization of the degradation products from reaction of **1a–c** with ^{18}O-labeled water, methanol, and *tert*-butyl alcohol are currently in progress to determine and compare the mechanisms of polymer degradation.

Table 2. Molecular Weight Data (M_w from GPC with On-Line Viscometry and Polystyrene Standards) for the Degradation Studies of Poly(silyl ester)s 1a–c as Solutions in 5% Water/THF, 1% Methanol/THF, or 1% *tert*-Butyl Alcohol/THF

	1a			1b			1c		
time	5% H_2O	1% MeOH	1% *t*-BuOH	5% H_2O	1% MeOH	1% *t*-BuOH	5% H_2O	1% MeOH	1% *t*-BuOH
0	2850	2850	2850	2700	2700	2700	2650	2650	2650
5 min	162	1520	2600	1480	2320	2390	170	880	1150
30 min	138	860	1410	1060	2230	2300	90	710	1010
1 h		840	1030	810	2220	2320		680	920
2 h		610	750	510	2040	2230		630	800
4 h		450	490	290	2030	2220		570	710
8 h				130	1930	2050		460	660
24 h					1320	1860		350	390
48 h					1090	1600			
96 h						1090			
120 h					300				
167 h						240			

In conclusion, poly(silyl ester)s have been prepared as a new class of organic/inorganic polymeric materials that are readily cleaved by nucleophilic attack. The substituents attached to the silicon atoms were varied and included methyl, isopropyl, and phenyl groups. The physical properties and, more importantly, the degradation properties of the materials were found to be dependent upon the silicon atom substituents. The susceptibility of the polymers toward hydrolysis and alcoholysis were found to increase in the order isopropyl $\ll$ methyl $<$ phenyl. Further modification of the silicon substituents (especially elimination of the electronegative oxygen of the siloxane repeat unit) and variation of the substituents attached to the acyloxy carbon atom are in progress. It is anticipated that a family of poly(silyl ester)s can be prepared with degradation properties ranging from rapid cleavage, such as that of **1a**, to more stable systems with degradation times similar to those typical for poly(ester)s.

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Supporting Information Available: Experimental procedures and characterization data for **1a**–**c** (2 pages). Ordering information is given on any current masthead page.

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(17) The reaction is an equilibrium, as determined from model studies and also ref 1.

(18) Because 1,3-dichlorotetramethyldisiloxane has a boiling point of 138 °C, the polymerization temperature was not raised above 125 °C, to prevent loss of a stoichiometric equivalence. In the case of 1,3-dichlorotetraphenyldisiloxane, which is a solid at room temperature, **2** was added via syringe to **3c**.

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(20) Although the product yield was 100%, a substantial amount of oligomeric products was present, which caused M_W to be quite low. The actual yield of polymer was less than 100%, and the percentage of product *vs* molecular weights was calculated from GPC cumulative molecular weight distributions, with the following weight fractions being obtained: **1a**, 75% > 1000, 32% > 3000, 11% > 5000 amu; **1b**, 79% > 1000, 29% > 3000, 8% > 5000 amu; **1c**, 72% > 1000, 26% > 3000, 6% > 5000 amu.

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(22) It is important to note that poly(dialkylsiloxane)s have refractive indices very close to the refractive index of THF, the solvent used with our GPC system, and the presence of a viscometry detector in combination with ^{29}Si NMR was fortuitous in the observation and characterization of any poly(siloxane) side products.

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