Thermoresponsive Polymers

Synthesis of Thermoresponsive Polyurethane from 2-Methylaziridine and Supercritical Carbon Dioxide**

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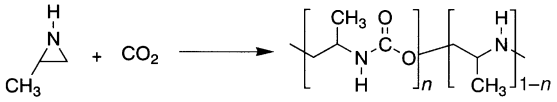
Utilization of CO_2 as an abundant C_1 feedstock is of environmental importance and a synthetic challenge.[1] Chemical fixation of CO_2 in functionalized polymers with long lifetimes is one of the most viable large-scale approaches.[2] Metal-catalyzed copolymerization of epoxides and CO_2 to give polycarbonates has been investigated as a potential method for CO_2 fixation.[3,4] Analogously, aziridines have been reported to react with CO_2 to give cyclic urethanes[5a] and polymers[5b] consisting of urethane and amine units (Scheme 1). However, the fraction of urethane linkages in the polymer products did not exceed 0.3, mainly because homopolymerization of aziridines competes with copolymerization with CO_2.[5b] The use of supercritical CO_2 ($scCO_2$) as reaction medium and reactant offers the opportunity to manipulate the outcome of reactions, including the polymer structure, this is thanks to the easy tunability of the properties of $scCO_2$ by means of pressure and temperature.[6,7] Herein we describe the reaction of 2-methylaziridine (**1**) and CO_2 under supercritical conditions to give polymer products with a high content of urethane units and unique temperature-sensitive phase transitions in water.



Scheme 1. Copolymerization of **1** with CO_2.

We examined the reactivity of **1** towards CO_2 under supercritical conditions by high-pressure NMR spectroscopy.[8] In the early stages of the reaction the aziridine was completely miscible with $scCO_2$ (Figure 1), but disappearance of the signals of **1** after 17 h suggested that CO_2-insoluble compounds would form under these conditions. Separate experiments showed that polymeric products were obtained by treatment of **1** with 3.0–22 MPa of CO_2 in a stainless steel

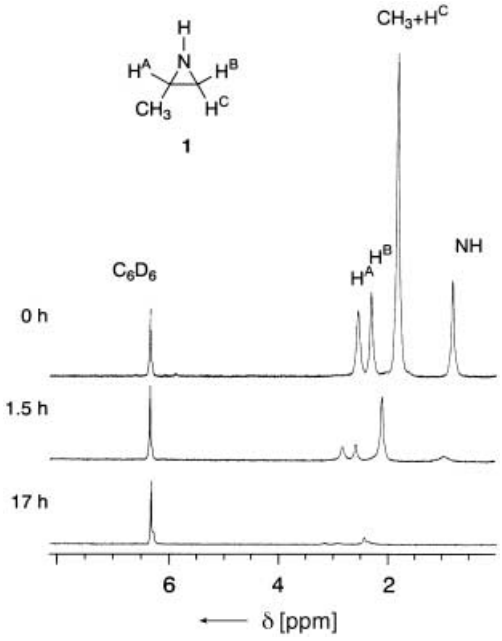


Figure 1. ^1H NMR spectra of **1** in $scCO_2$ (40 °C, 8.0 MPa). C_6D_6 in a sealed capillary tube was used as lock.

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autoclave at 100 °C, and **1** was completely consumed in the reaction. Reprecipitation by adding a solution of the reaction mixture in methanol to diethyl ether afforded a white powderlike material. The yields and properties of the obtained polymers **2**–**5** are listed in Table 1. In the absence of CO_2, no polymerized product was obtained, and the starting material was recovered completely. An increase in CO_2 pressure caused a marked improvement in the yield.

Table 1: Physical data on the product polymers prepared from **1** and CO_2.[a]

Entry	Product	p [MPa]	CO_2 density [g cm^{-3}]	Yield [%]	Urethane content[b] [unit ratio]	M_w
1		0	0.0	0.0	–	–
2	**2**	3	4.9×10^{-2}	14.2	0.32	6.5×10^{3}
3	**3**	10	2.0×10^{-1}	17.9	0.47	1.5×10^{5}
4	**4**	16	3.6×10^{-1}	22.1	0.53	1.4×10^{5}
5	**5**	22	5.2×10^{-1}	27.1	0.62	2.7×10^{4}

[a] 50-mL stainless autoclave, [**1**] = 8.8 mmol, 100 °C, 24 h. [b] Calculated on the basis of elemental analyses.

The ^{1}H and ^{13}C NMR spectra of the polymers showed signals arising from the NH protons and the carbonyl carbon atom of the urethane structure (−NHCOO−) at around δ = 4.0 and 158 ppm, respectively. Elemental analysis revealed that the urethane content of the products increased to 0.62 when the CO_2 pressure was increased to 22 MPa. An increase in the content of urethane units could also be confirmed by ^{1}H NMR spectroscopy. Analysis of **2**–**5** by size-exclusion chromatography coupled with multiangle laser light scattering (SEC-MALLS) revealed that the weight-average molecular weights M_w of the products obtained under supercritical conditions were significantly higher than that of **2** obtained at 3.0 MPa. The reaction of 2-ethylaziridine with $scCO_2$ at 22 MPa of CO_2 also gave the corresponding copolymer with a urethane content of 0.62, as observed in the reaction of **1**. These results indicate that the use of $scCO_2$ results in effective copolymerization of aziridines and CO_2 without any additives.

The outcome of the reaction proved to be strongly influenced by the phase behavior of the reaction system.[9] High-pressure NMR spectra of the reaction mixture indicated that the polymeric products formed an independent phase by precipitation from the reaction phase. Addition of appropriate co-solvents would allow easy manipulation of the rate of the reaction and the product properties by enhancing the solubility of the reaction mixture in $scCO_2$.[10] In fact, the reaction in the presence of *N*,*N*-dimethylacetamide (DMAc) at 22 MPa led to a marked improvement in the molecular weight of the polymers, and the urethane content of the product increased to 0.74 (Table 2). Visual inspection of the reaction mixture containing DMAc in a reactor equipped with a window confirmed that a homogeneous phase formed at 22 MPa. At lower CO_2 pressure, phase separation took place, and polymerization was strongly retarded. Thus, this phase behavior of the reaction mixture is a crucial factor in controlling the product properties.

Table 2: Effect of DMAc co-solvent on the polymerization of **1** and CO_2.[a]

p [MPa]	DMAc [wt%]	Phase	Yield [%]	Urethane content[b] [unit ratio]	M_w
12	7.2	biphasic	11.3	0.56	4.8×10^{3}
16	5.0	transient	22.0	0.63	2.8×10^{4}
22	3.6	homogeneous	30.7	0.74	2.1×10^{5}

[a] 50 mL stainless autoclave, [**1**] = 8.8 mmol, 100 °C, 24 h, 11 mmol DMAc. [b] Calculated on the basis of elemental analyses.

The copolymerization products of **1** and CO_2 exhibit thermally induced reversible transitions in water around the lower critical solution temperatures (LCSTs).[11] This unique thermal property of polymers, such as poly(*N*-isopropylacrylamide)s, in water has attracted increasing attention in the fields of drug-delivery systems,[12a] protein–ligand recognition,[12b] tissue-engineering applications,[12c] separation,[12d] and catalysis.[12e] Since the dissolution/precipitation transition in aqueous solution is attributed to the cleavage of the hydrogen-bonding network involving water and the polymers, as well as hydrophobic aggregation of the polymers, a suitable balance of hydrophilic and hydrophobic moieties in the polymer structure should essentially determine the thermoresponsive properties.[13]

Figure 2 shows the temperature dependence of the light transmittance of 2.0 wt% aqueous polymer solutions. The thermoresponsive properties of the products were delicately influenced by reaction conditions such as CO_2 pressure and the nature of the aziridine monomer. The transmittance of the solution of **2**, prepared at 3.0 MPa of CO_2, decreased gradually above 80 °C, while products **3**–**5**, obtained under supercritical conditions, exhibited a sharp drop in transmittance at their LCSTs. The effect of CO_2 pressure on the LCST is presumably due to the urethane content of the products. The increased urethane content of polymers obtained under supercritical conditions results in a decrease in their LCSTs, possibly because of the decreased hydrophilicity of the polymers. The molecular weight of the

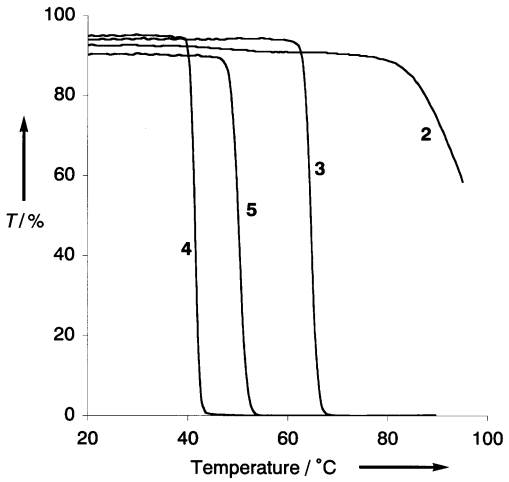

Figure 2. Temperature dependence of transmittance for aqueous solutions of **2**–**5** (LCSTs: **2**: 85 °C; **3**: 64 °C; **4**: 41 °C; **5**: 48 °C).

copolymer also influences the LCST, as was observed for copolymers **4** and **5** (Table 1 and Figure 2). An inverse dependence of LCST on molecular weight was reported in other polymer systems.[14] The copolymer obtained from 2-ethylaziridine and CO_2 under supercritical conditions was not sufficiently soluble in water and therefore showed no marked thermoresponsive behavior in water.

In conclusion, we have demonstrated a novel synthetic procedure for obtaining thermoresponsive polyurethanes from **1** and CO_2 under supercritical conditions. The copolymers exhibit LCST in aqueous solution, with a sharp phase transition over a wide range of 41–85 °C.

Experimental Section

Caution: Since high gas pressures are involved, appropriate safety precautions must be taken.

Typical procedure for copolymerization: The reaction was carried out in a 50-mL stainless steel autoclave. The autoclave was filled with argon gas, and **1** (8.8 mmol) was introduced by syringe. Then the vessel was charged with CO_2 through a cooling apparatus with an HPLC pump. After stirring at 100 °C for 24 h, the reaction was stopped by cooling the autoclave in a dry ice/methanol bath. CO_2 was vented and the autoclave was slowly warmed to room temperature. The crude reaction product was then dissolved in the methanol. The polymeric product was purified by reprecipitation by adding the methanol solution to diethyl ether to remove low-molecular-weight products and drying in vacuo.

The molar mass distributions of the products were determined by SEC-MALLS measurements, which were carried out at 40 °C on Shodex OHpak SB-804HQ and SB-806MHQ columns at a polymer concentration of 10 mg mL^{-1}. All samples were filtered through Millipore Milex-LG (0.20 μm) before analysis. An aqueous solution of 0.2 M Na_2SO_4/0.5 M CH_3COOH was used as eluent. The MALLS device was a DAWN model DSP-F (Wyatt Technology Co.) in which a laser beam of wavelength of 632.8 nm was focused on the flow cell. LCSTs of the polymers were measured by monitoring the absorbance at 500 nm at a heating rate of 2 °C min^{-1} with a variable-temperature Shimadzu UV-1600PC UV/Vis spectrometer.

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