

Preparation and Characterization of 2-Cyanoacrylate Copolymers

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SYNOPSIS

Butyl and ethoxyethyl 2-cyanoacrylate and mixtures thereof in different molar ratios were subjected to polymerization at pH 2.0, 3.0, 4.0, 5.5, and 6.9 and characterized by X-ray diffraction, hot-stage microscopy, and NMR analysis. The polymers were in an X-ray amorphous state. Their softening temperatures increased with ascending pH during polymerization. In all cases, the temperatures of the ethoxyethyl polymers were below those of the butyl polymers. Softening temperatures between those of the pure polymers could be achieved by copolymerization. The molar composition of the polymers was checked by NMR analysis. © 1992 John Wiley & Sons, Inc.

INTRODUCTION

2-Cyanoacrylates are widely used as "instant glues" in industry,¹ as biodegradable tissue adhesives in surgery,^{2,3} or—after polymerization—as drug carriers in the form of nanospheres in drug formulations.⁴ In medical application, the butyl ester is mainly used due to its good biological tolerance and degradability.^{5,6} A drawback of this substance is, however, that the polymer shows little flexibility, which sometimes limits its practical usefulness in bonding soft materials such as living tissues. It has been shown recently that another derivative, polymerized ethoxyethyl ester, exhibits low rigidity and high flexibility.⁷ The purpose of this study was, therefore, to investigate whether butyl and ethoxyethyl 2-cyanoacrylate can be copolymerized in order to yield mixed polymers with a plasticity greater than that of pure butyl ester.

The pure monomers and mixtures thereof in molar ratios ranging from 9 + 1 to 1 + 9 were polymerized at different pH values. The softening temperatures of the polymers were used as a measure of their plasticity and the molar composition of the copolymers was checked by NMR spectroscopy.

EXPERIMENTAL

Preparation of Polymer Samples

Monomeric 2-cyanoacrylate (0.4 mL pure butyl [BCA] or ethoxyethyl [ECA] ester received from Schering Bergkamen, Germany, or 0.4 mL of a mixture of BCA and ECA in molar ratios of 1 + 9, 3 + 7, 1 + 1, 7 + 3, and 9 + 1) was dispersed using ultrasound (Sonifier B15, Branson, Caronge-Genève, Switzerland) in 20 mL hydrochloric acid solution at pH 2.0, 3.0, 4.0, or 5.5 or in 20 mL phosphate buffer solution at pH 6.9. The resulting white, microparticulate polymer was centrifuged, washed with water, and dried in a drying chamber at 50°C for 24 h.

X-ray Diffraction

An aliquot of the polymer was put in a PW-1700 diffractometer (Philips, Eindhoven, Netherlands) and the diffraction pattern was recorded in an angle range of 4.02°–24.98° using CuK α radiation (voltage: 40 kV, current: 30 mA).

Hot-stage Microscopy

An aliquot of the polymer was placed between a slide and a coverglass and inserted in a hot stage 350

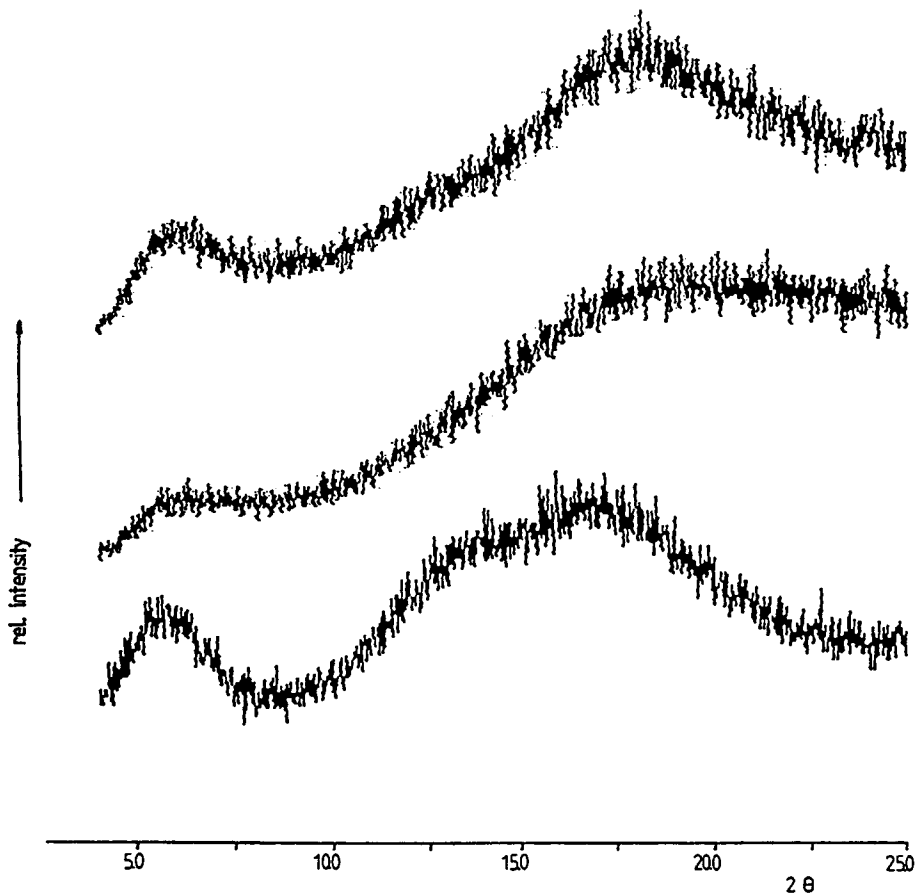


Figure 1 X-ray diffraction patterns of (top) polybutyl, (middle) polyethoxyethyl, and (bottom) polybutyl-ethoxyethyl-[1 + 1] 2-cyanoacrylate polymerized at pH 5.5.

(Leitz, Wetzlar, Germany) mounted on an Axioplan microscope (Zeiss, Oberkochen, Germany). Heating was performed at a rate of about 10 K/min using a

temperature control LR 40 (HWS, Mainz, Germany). Softening was observed using 320× magnification. The softening temperature was deter-

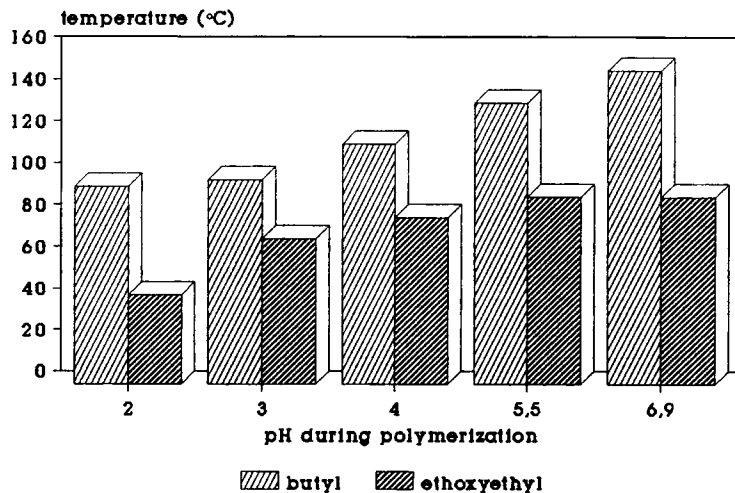


Figure 2 Softening temperatures of polybutyl and polyethoxyethyl 2-cyanoacrylate polymerized at different pH-values.

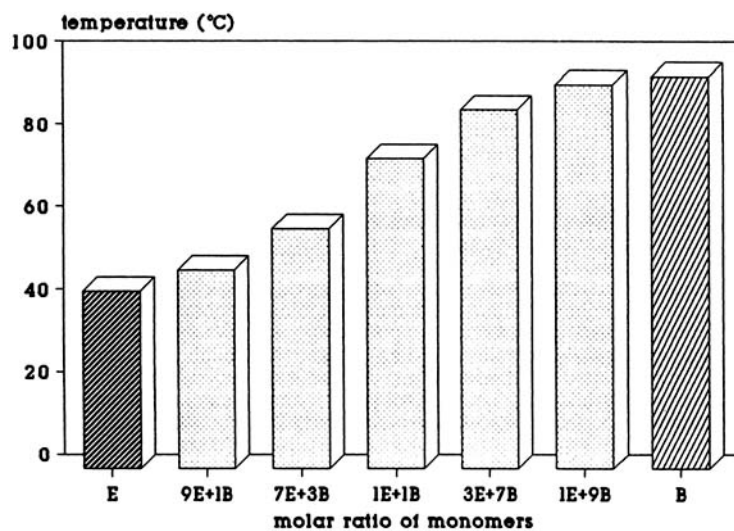


Figure 3 Softening temperatures of copolymers of (B) butyl and (E) ethoxyethyl 2-cyanoacrylate polymerized at pH 2.0.

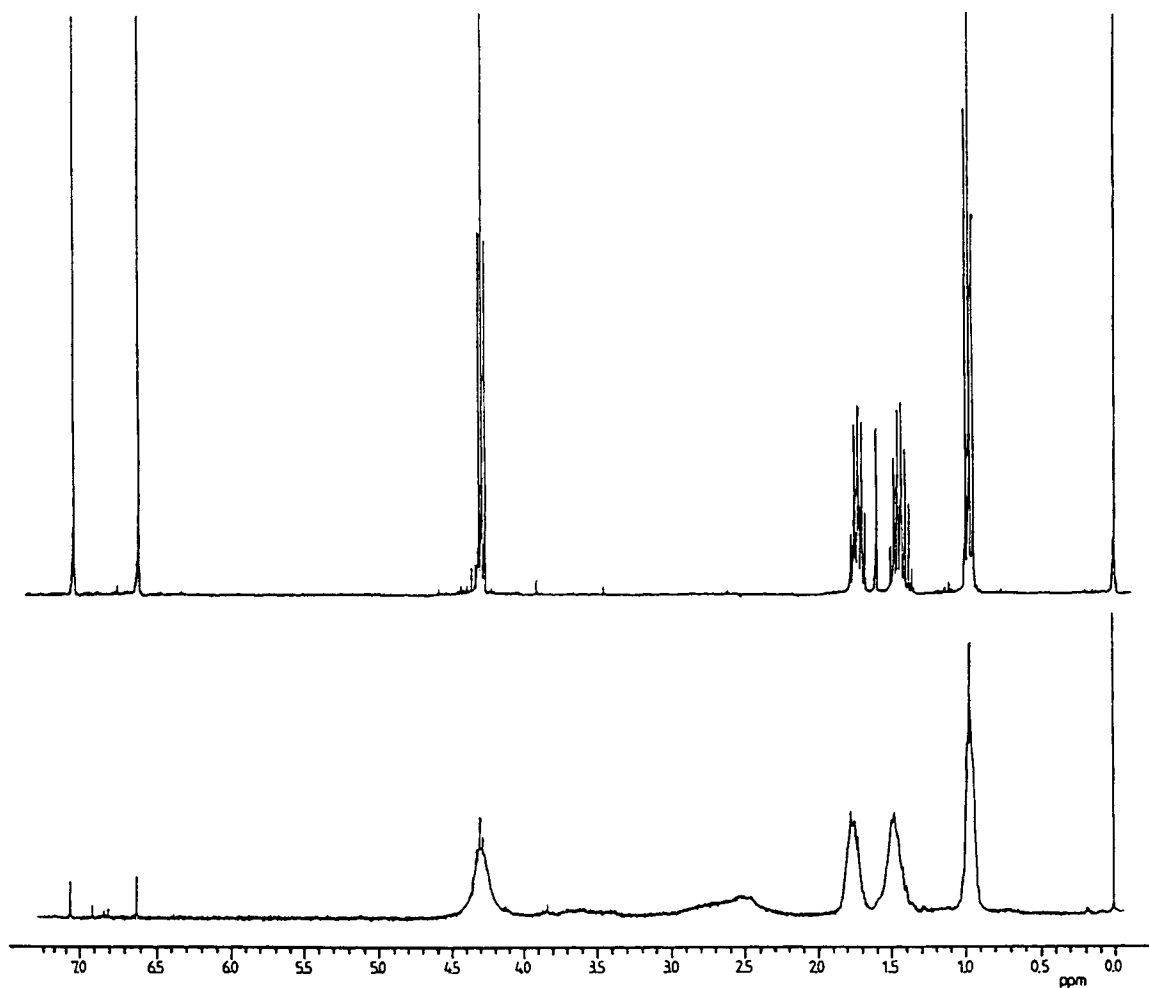


Figure 4 300 MHz NMR spectrum of butyl 2-cyanoacrylate dissolved in CDCl_3 : (top) monomer; (bottom) polymer.

mined as the mean of the temperature at which the softening started and that at which all particles had become transparent.

NMR Spectroscopy

An aliquot of the polymer was dissolved in CDCl_3 , and a 300 MHz NMR spectrum was recorded using a QE 300 (General Electric) with reference to tetramethylsilane singlet at 0 ppm.

RESULTS AND DISCUSSION

The diffraction pattern of polycyanoacrylates shows no crystalline peaks, only a diffuse halo, which in-

dicates that these polymers are in an X-ray amorphous state (Fig. 1). This may be the reason for the finding that no abrupt melting, only a gradual softening, was observed on heating the polymers on the hot stage. With decreasing viscosity of the molten polymer, the speed of spreading under the coverglass increased.

The softening temperatures of pure BCA and ECA, determined as described above, increased with ascending pH value during polymerization (Fig. 2). Softening of the pure ECA polymer occurred in all cases at temperatures below those of pure BCA, thus indicating a higher flexibility and lower rigidity of the long-chain ECA. This finding is consistent with the results of Tseng et al.⁷ After blending of BCA and ECA and subsequent polymerization, the re-

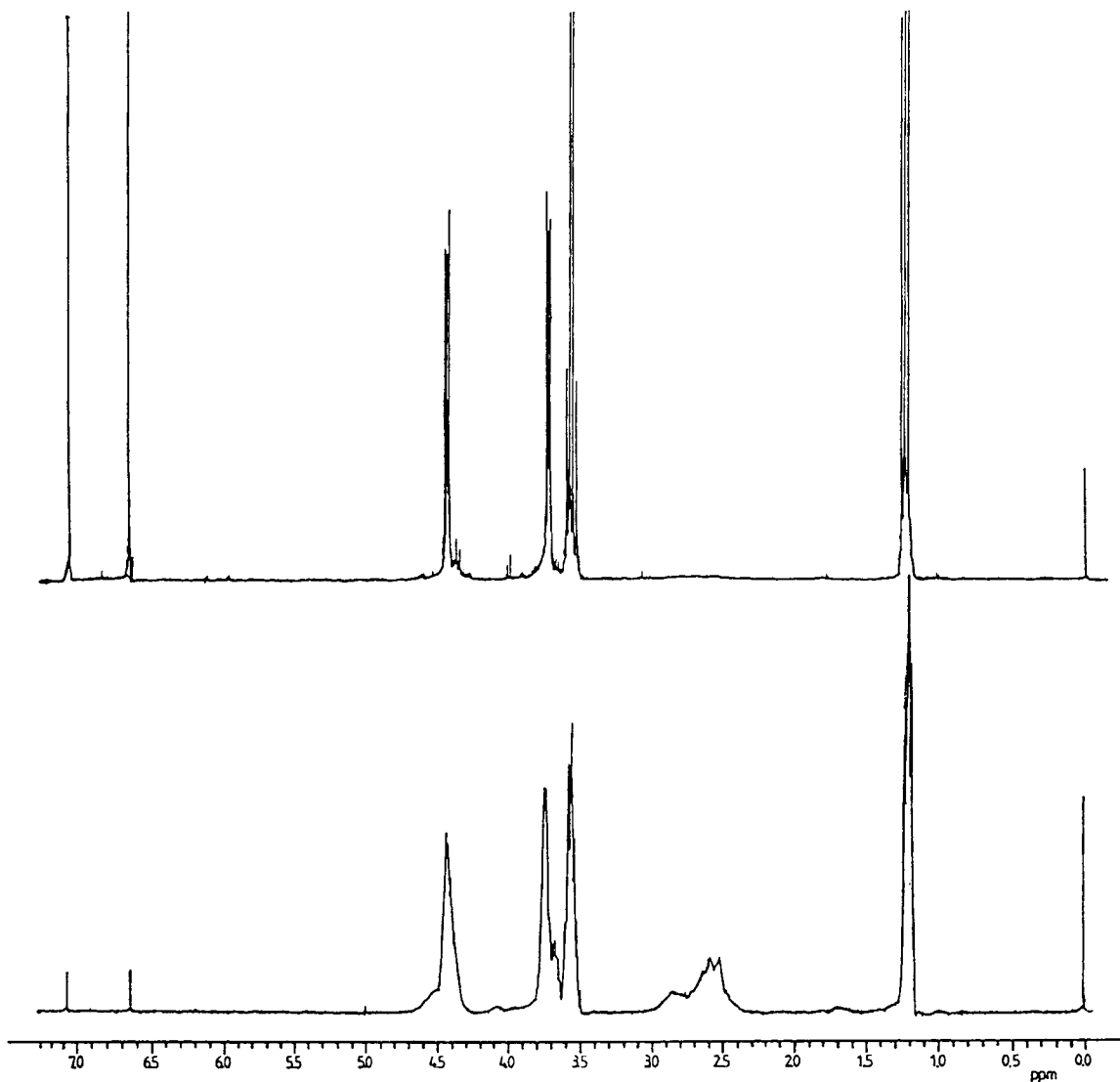


Figure 5 300 MHz NMR spectrum of ethoxyethyl 2-cyanoacrylate dissolved in CDCl_3 : (top) monomer; (bottom) polymer.

sulting copolymers exhibited softening temperatures between those of the pure polymers. Figure 3 shows, for example, the results obtained after polymerization at pH 2.0. Thus, the thermal properties of BCA could be modified by addition of ECA; the higher the content of ECA, the lower the softening temperature of the copolymer. It can be expected that such a copolymer will be more ductile at body temperature than will polymeric BCA, thereby improving the performance of this polymer in many applications.

The signals of the NMR spectra of the pure BCA and ECA polymers were broad and not split into multiplets as was the case in the spectra of the monomers (Figs. 4 and 5). Nevertheless, the signals

of the methyl and the methylene groups in each molecule could be clearly distinguished. The broadest signal, which ranged from 2.3 to 3.1 ppm, was caused by the methylene group of the polymer backbone. Trace amounts of monomer were found in both polymers as indicated by the single proton signals of the double bond at 6.6 and 7.1 ppm. The signals of ECA were shifted downfield compared to corresponding signals of BCA.

The spectra of the copolymers showed all signals of the single components. Figure 6 displays, for example, the spectra of the 1 + 1 and 7 + 3 copolymers. The molar composition of the copolymers could be derived from the spectra after integration of the peaks of the methyl protons at 1.20 ppm (ECA) and

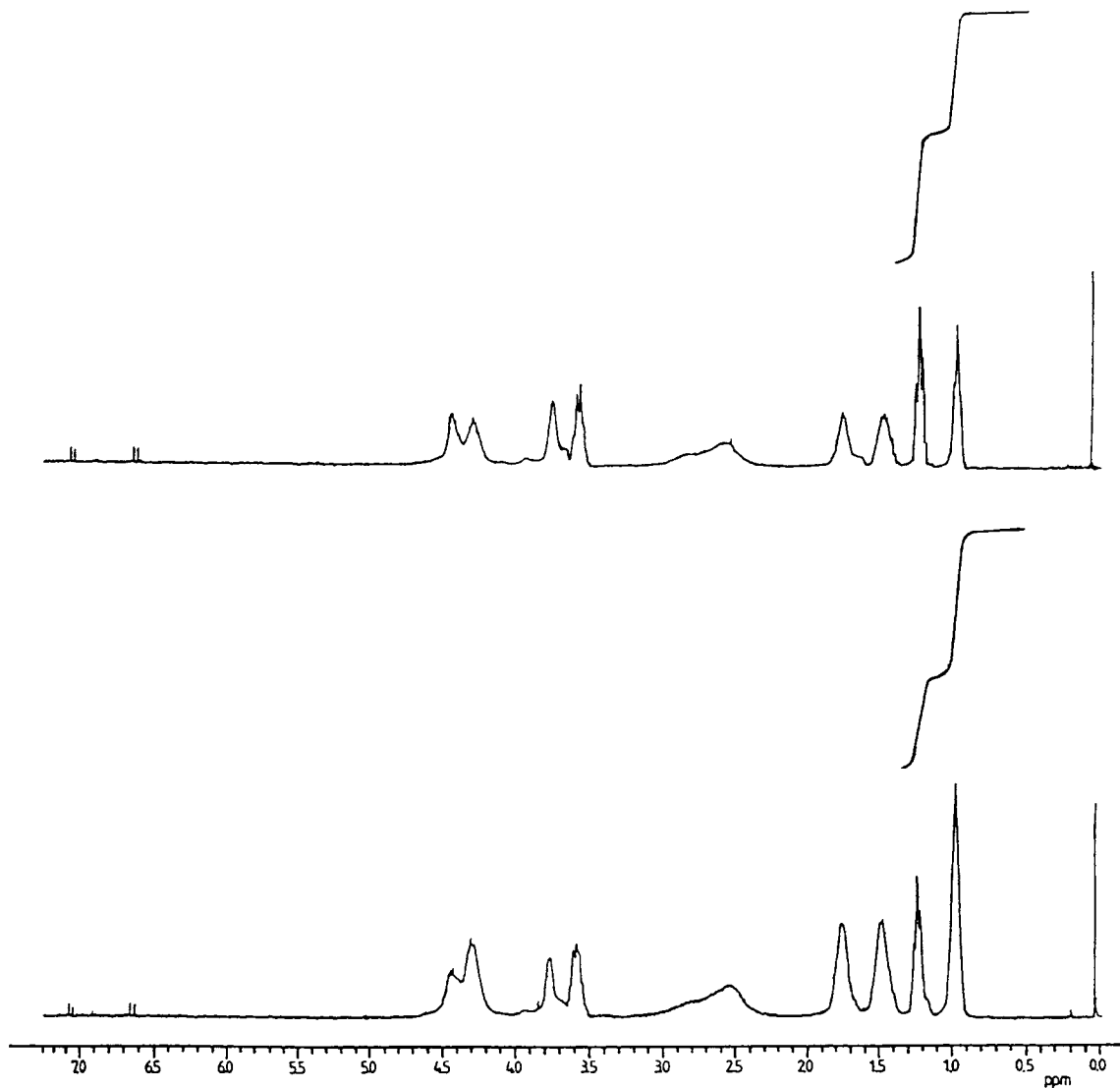


Figure 6 300 MHz NMR spectrum of polybutyl-ethoxyethyl 2-cyanoacrylates of different molar composition: (top) 1 + 1; (bottom) 7 + 3.

0.96 ppm (BCA). The ratio of these areas was in good accord with the molar ratio of the BCA and ECA monomers before polymerization.

CONCLUSION

It is obvious from this study that polybutyl and polyethoxyethyl 2-cyanoacrylates are not crystalline, but X-ray amorphous substances, and therefore show softening rather than sharp melting. The temperatures of this change in physical state can be influenced by the pH during polymerization and by copolymerization. The molar composition of the copolymers can be easily checked by NMR analysis. The use of butyl-ethoxyethyl ester copolymers instead of pure butyl ester may have advantages in medical applications when higher flexibility of the polymer is desired.

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