mony trioxide as catalysts. The temperature was gradually raised to 160 °C to 210 °C over a period of 18 h while the polymerization vessel was gradually evacuated to a final pressure of 10^{-2} mmHg.

Polymer VI was prepared by copolycondensation of the diol monomer with an equimolar mixture of thiophenol esters of oxalic acid and sebacic acid. The reaction procedure was the same as that for the preparation of V.

The molecular weight of each sample was estimated by a HLC-802UR gel permeation chromatograph (Toyo Soda Mfg. Co. Ltd.) calibrated for standard PS. To obtain samples of approximately equal molecular weight, polymers I, II, and V were fractionated.

Fluorescence Spectroscopy. A Hitachi MPF-4 spectrofluorometer was used. Spectrograde 1,2-dichloroethane (DCE) was further distilled immediately before use for spectroscopy. The monomer and exciplex intensities were determined at the maximum wavelengths, as already reported. No correction was made for the wavelength-dependent sensitivity of the spectrometer. The sample solution was deaerated by argon bubbling.

Registry No. I (copolymer), 76769-89-6; I (SRU), 91210-44-5; II (copolymer), 91210-52-5; II (SRU), 91210-45-6; III (copolymer), 91210-53-6; IV (copolymer), 91210-55-8; IV (SRU), 91210-46-7; V (copolymer), 91210-56-9; V (SRU), 91210-47-8; VI (copolymer), 91210-57-0.

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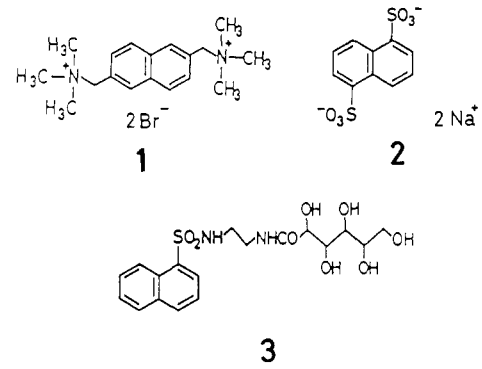
pH-Sensitive Permeation of Ionic Fluorescent Probes from Nylon Capsule Membranes[1,2]

The permeability of microcapsules has been investigated rather extensively because of its importance in designing and constructing sustained drug release devices and artificial cells.[3-6] However, these earlier studies dealt with the permeations of small, simple substances such as NaCl and glucose in the neutral-pH region.

Chart I



1 2 3

We report here that the permeation of ionic, water-soluble fluorescent probes (**1** and **2**, Chart I) from a large nylon capsule membrane is greatly affected by the ambient pH and is reversibly controlled by pH changes of the outer medium. This is the first example of pH-sensitive permeation control across capsule membranes. The permeability of NaCl or a nonionic probe **3** was not affected by the ambient pH.

Large, ultrathin nylon-2,12 capsules were prepared from ethylenediamine and 1,10-bis(chlorocarbonyl)decane by interfacial polymerization in the presence of a small amount of a cross-linking agent (trimesoyl chloride), by the method described in previous papers.[7-15] The presence of the cross-linking agent gave strong capsule membranes. The capsules (diameter: 2.5 mm, membrane thickness: 1 μm) were dialyzed against 0.01 mol dm^{-3} phosphate buffer (pH 7.0) containing a fluorescent probe (1.0×10^{-3} mol dm^{-3}) to give capsules with the trapped probe.

The permeability of the capsule toward the fluorescent probe was followed by detecting increases in the fluorescence intensity at 340 nm (excitation at 280 nm for **1** and at 290 nm for **2** and **3**) in the outer water phase. Permeation rates P were calculated from the following equation:[8,10,15]

$$P = \frac{kV}{AC} = \frac{1}{6}\frac{kd}{\Delta C} \qquad (1)$$

where k, V, and A are the slope of increases in fluorescence intensity with time (see Figure 1), the volume of the outer water phase, and the surface area of a capsule, respectively; C denotes the concentration of the probe trapped in the inner phase and can be substituted by ΔC (the change of the fluorescence intensity after crushing a capsule). P (cm s^{-1}) depends on the capsule diameter, d, the slope, k, and the fluorescence intensity after crushing a capsule, ΔC. The pH values of the outer medium were controlled by addition of HCl or NaOH.

Figure 1 shows reversible changes in the permeation of fluorescent probes from nylon capsules at different pH values of the outer medium. The permeability of NaCl was not affected by changing the ambient pH from 2 to 12. When the cationic probe **1** was employed as a permeant, the permeability was drastically reduced below that of NaCl at an ambient pH 2. When the pH of the outer medium was changed from 2 to 12, the permeability was immediately enhanced by a factor of ca. 100 and reduced again almost to the same slow rate by returning the ambient pH to 2. In the case of the permeation of the anionic probe **2**, the reverse occurred. The permeability was enhanced in the acidic medium (pH 2) and reduced in the basic medium (pH 12) by a factor of ca. 50. This pH-sensitive permeability regulation could be repeated over

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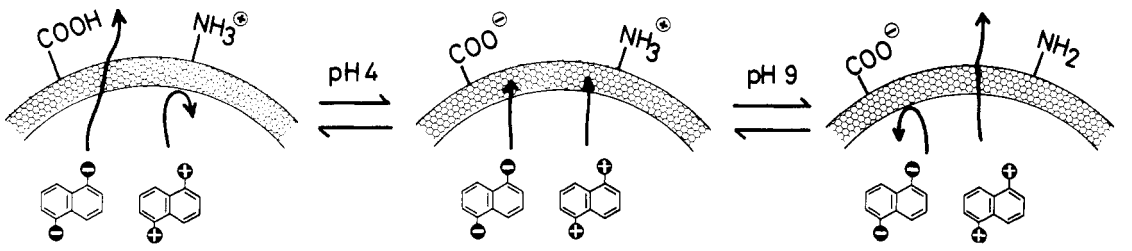
Scheme I



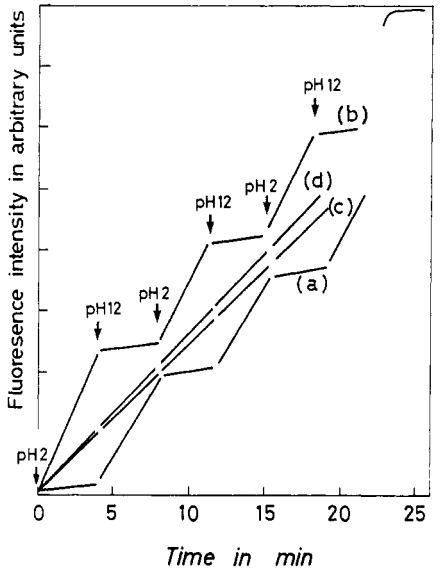


Figure 1. Reversible permeability control of fluorescent probes from a nylon capsule by pH changes of the outer medium at 25 °C: (a) cationic probe **1**; (b) anionic probe **2**; (c) nonionic probe **3**; (d) NaCl. The pH of the outer medium was changed by addition of HCl or NaOH at an arrow.

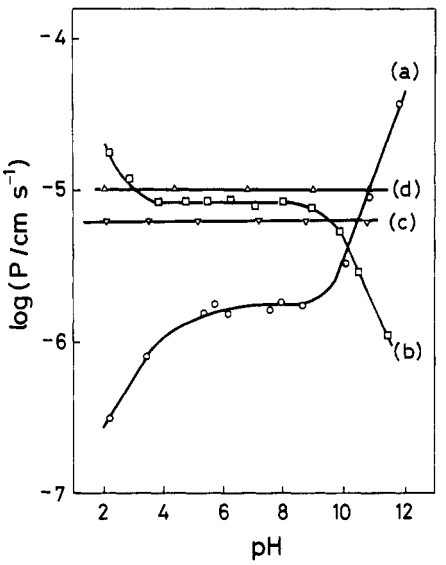


Figure 2. pH–rate profiles of the permeability of fluorescent probes from the nylon capsule at 25 °C: (a) cationic probe **1**; (b) anionic probe **2**; (c) nonionic probe **3**; (d) NaCl.

and over again. The permeation of the nonionic probe **3** was, however, not sensitive to pH.

Figure 2 shows pH–rate profiles of the permeation of fluorescent probes. The capsule membrane formed a high barrier to the permeation of the cationic probe **1** in the acidic medium (below pH 5) but not in the basic medium (above pH 9), relative to the neutral-pH region (pH 6–9). On the other hand, the anionic probe **2** permeated rapidly below pH 4 and very slowly above pH 9. In the case of the nonionic probe **3**, the permeability was nearly constant over the whole range of pH 2–12.

It is well-known that nylon membranes have a small amount of residual COOH and NH_2 end groups.[16-18] The pH–rate profiles indicate that ionizations of the residual amino and carboxyl end groups in nylon capsule membranes play an important role in the observed pH-sensitive permeation. The amino and carboxyl end-group contents of the capsule membrane were determined by acid–base titrations to be 1.4×10^{-4} and 1.5×10^{-4} equiv/g, respectively. These values are nearly equal to those of usual nylon films ($(0.5–5) \times 10^{-4}$ equiv/g[16,19,20]).

Since a small, hydrated electrolyte such as NaCl may diffuse through hydrated pores in the capsule membrane, the permeability is affected little by the ionization of end groups in the capsule membrane. The relatively hydrophobic fluorescent probes, however, will diffuse and permeate near the relatively hydrophobic region in the membrane and will be affected by the ionized end groups buried in the membrane. In the acidic medium, the capsule membrane is slightly charged positively (COOH and NH_3^+ end groups), and the permeation of the cationic probe **1** may be markedly reduced by the electric charge repulsion. On the other hand, the permeation of the negatively charged probe **2** is accelerated through the positively charged membrane at pH 2 (see the left-hand side of Scheme I). The opposite selectivity should be observed for the negatively charged membrane (COO^- and NH_2 end groups) at ambient pH 12 where the permeation of the cationic and anionic probes is accelerated and reduced, respectively (see the right-hand side of Scheme I). The permeation of the nonionic probe **3** is, as expected, not affected by the ionization of end groups.

In order to clarify the effect of end-group charges on the fluorescent probe permeation, we prepared two different types of nylon capsule membranes; partially hydrolyzed capsule membranes with a large (ca. 10 times) concentration of end groups (1.2×10^{-3} equiv/g) relative to that of the original one, and end-group-blocked ($COOCH_3$ and $NHCOCH_3$) capsule membranes having a few dissociative end groups (less than 1×10^{-5} equiv/g). When the partially hydrolyzed capsule was employed, the effect of pH on the probe permeation was enhanced 20 times over that of the original capsule. In the case of the capsule having blocked end groups, the permeability of neither cationic nor anionic probes was affected by ambient pH. these findings clearly indicate that the pH-sensitive permeation of ionic fluorescent probes across the capsule membrane can be attributed to ionization of residual end groups in nylon-2,12 capsule membranes.

The reversible permeability control across the capsule membrane, which responds to pH changes of the outer medium, is interesting for designing and constructing sustained drug release devices.

Registry No. **1**, 91606-37-0; **2**, 1655-29-4; **3**, 91606-38-1; NaCl, 7647-14-5; (ethylenediamine)·(1,10-bis(chlorocarbonyl)decane)·(trimesoyl chloride) (copolymer), 91606-39-2.

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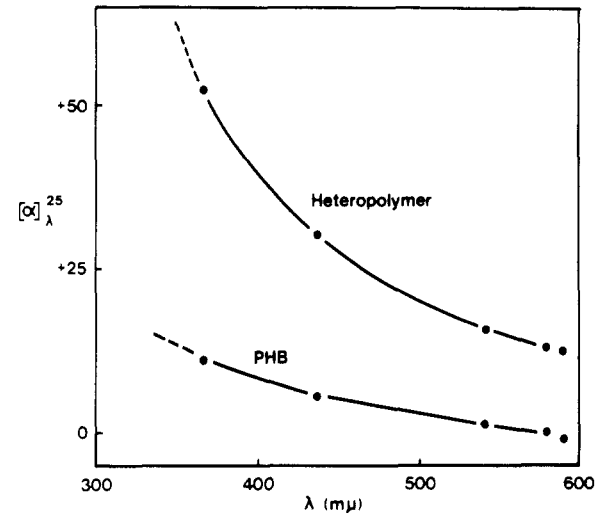

Figure 1. Optical rotatory dispersion curve for HV/HB heteropolymer and PHB in chloroform. The optical rotation of the heteropolymer (65 °C fraction) was recorded on a Perkin-Elmer 241 instrument. The results for PHB (M_n = 127 000) were taken from ref 9.

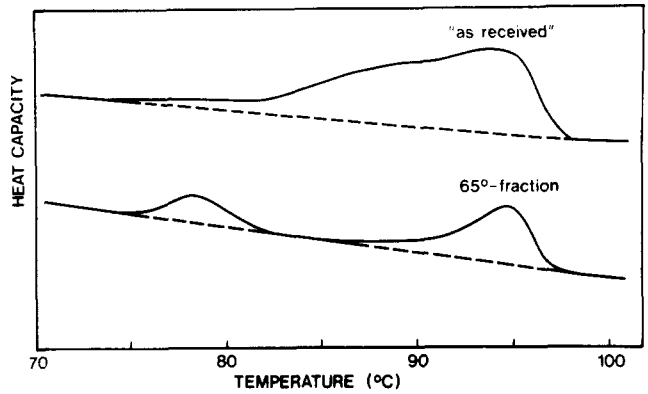

Figure 2. Differential scanning calorimeter trace for HV/HB heteropolymer. The heteropolymer "as received" and the 65 °C fraction were measured with a Perkin-Elmer 1B instrument at a scan rate of 10 °C/min.

Physical Properties of a Naturally Occurring Polyester: Poly(β-hydroxyvalerate)/Poly(β-hydroxybutyrate)

The chiral optical polyester poly(β-hydroxybutyrate) (PHB) is the first example of a true thermoplastic from biotechnology. Although it has been synthesized[1] it is clearly much more readily prepared by processes related to industrial microbiology.[2] In addition to being a thermoplastic with interesting biodegradable properties, it is also serving as a source of starting materials that serve as synthetic building blocks in both sophisticated and straightforward organic syntheses.[3] Recently, the availability of a family of polyesters of this type based on β-substituted β-hydroxypropionate derivatives had been reported. It was not clear whether true copolyesters were being obtained from the natural synthesis. The present communication is a detailed analysis of one such system containing PHB and poly(β-hydroxyvalerate) (PHV).

The heteropolymer sample was kindly provided by Dr. L. L. Wallen, Northern Regional Research Laboratory, Peoria, IL. This sample was used either "as received" or after partial fractionation in the following manner. The polymer was first purified by dissolving in boiling ethanol (0.05%), which dissolves only low molecular weight PHB (DP < 30), followed by crystallization at room temperature for 24 h. The recrystallized polymer was dissolved again in boiling ethanol, the solution was kept at 65 °C for 24 h, and the precipitate formed (65 °C fraction) was collected by filtration. From the resulting filtration lower temperature fractions (50 °C and room-temperature fractions) were prepared in a like manner.

On the basis of gas chromatography–mass spectroscopy of saponified heteropolymer, Wallen and Rohwedder[4] have shown that the ratio of β-hydroxyvalerate (HV) to β-hydroxybutyrate (HB) is 5:1. Pyrolysis studies[5] have shown that the heteropolymer is composed mainly of HV but contains a significant amount of HB. It seems, however, still open to question whether β-hydroxybutyrate is present as a comonomer or physically mixed as PHB in the "heteropolymer".

Infrared spectra of the heteropolymer[4] showed a strong band at 1465 cm^{-1}, which is absent in the spectrum of PHB. This band is assigned to the bending mode of the CH_2 (bonded to CH_3) group of the HV polymer. In the proton NMR spectrum,[4] signals characteristic of the protons on the methyl groups of HV and HB were observed at 0.89 and 1.27 ppm, respectively. In this study it was observed that the ratio of integrated intensities of these signals (HV/HB) change as a function of sample preparation. The ratios were 2.5, 4.9, 5.1, and 1.4 for the "as received", 65 °C, 50 °C, and room-temperature fractions, respectively.

The optical rotatory dispersion curve for the heteropolymer is shown in Figure 1. The heteropolymer has a higher specific rotation in chloroform than PHB. The $[\alpha]^{25}$ value was +12.5° for the former while a very small negative value is reported for the latter.[2,6]

In the differential scanning calorimeter trace (Figure 2)

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