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Macroscopic and Microscopic Acid Dissociation of the 1:1 Copolymer of Acrylic Acid and 4-Vinylpyridine

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Acrylic acid and 4-vinylpyridine were copolymerized at 40 °C without any catalysts . The copolymer with 1:1 molar ratio of monomeric units was obtained over a wide range of the monomer ratios in the feed. Macroscopic and microscopic acid dissociation equilibria of the copolymer with 1:1 composition were determined in aqueous ethanol by potentiometric titration at 25 °C. The zwitterion and neutral molecule forms coexist over a wide range of pH, and the latter form is predominant. There exists only 10% of the zwitterion form in the neutral region.

One of the characteristic reaction of amphoteric compounds is the ability to give various forms which are dependent on pH. The acid-base chemistry of the amphoteric compounds is usually characterized in terms of macroscopic dissociation constants, which are composite of the microscopic constants for the individual groups. The chemical and biological activity of the amphoteric compounds is expected to vary with the degree of ionization. For this reason, microscopic acid dissociation constants of a number of pharmacologically and biologically active compounds (for example, amino acids,[1,2] oligopeptides,[3,4] pyridine derivatives,[5,6] drugs,[7,8] and so on) were determined. A number of papers and reviews on acid dissociation equilibria of polyelectrolytes have been published.[9] Particularly, poly(acrylic acid) was investigated in detail.[10] However, these works have been dealt only macroscopically with acid dissociation, and there are no reports on microscopic acid dissociation of amphoteric polymers. In regard to polyampholyte, Nagasawa and Holtzer presented macroscopic constant of poly(2-dimethylaminoethyl methacrylate-*co*-methacrylic acid).[11]

The copolymer of acrylic acid (AA) and 4-vinylpyridine (VP) is an amphoteric compound and a tautomer, in which a proton of the carboxyl group can migrate to nitrogen atom of the pyridine ring. The copolymer exists in protonated and deprotonated forms in the acidic and basic regions, respectively, while there is coexistence of zwitterion and neutral molecule forms in the neutral region. We present here the pH-metric determination of macroscopic and microscopic acid dissociation constants and tautomeric constant of the 1:1 copolymer of AA and VP. The copolymer with 1:1 molar ratio of monomeric units is hereinafter abbreviated PACP.

In the case of high concentration, mixing of AA and VP causes products to carbonize with a large

quantity of heat generated. However, on the mixing in the limited concentration range, the spontaneous copolymerization takes place without generation of heat. The copolymerization of AA and VP was carried out at 40 °C without any catalysts. The reaction was proceeded to conversion lower than 10%. After a given time, the copolymerization was stopped by pouring the reaction mixture into a large excess of ether. The composition of the copolymer was determined with a JEOL GX-400 NMR spectrometer. As can be seen from Fig. 1, the copolymer with 1:1 composition was obtained over a wide range of the monomer ratios in the feed. To obtain the sample for titration, the copolymerization of AA and VP ([AA]/[VP] = *ca.* 1) was carried out. Yield 39.5%. The copolymer obtained was purified by dialyzation and lyophilization. Number average molecular weight was determined as 3500 by a GPC method, relative to a polyethylene glycol. As described later, in order to determine microscopic constants of PACP, it is necessary to evaluate macroscopic constant of 1:1 copolymer of methyl acrylate (MA) and VP. The preliminary data for preparing the 1:1 copolymer of MA and VP are also shown in Fig. 1.

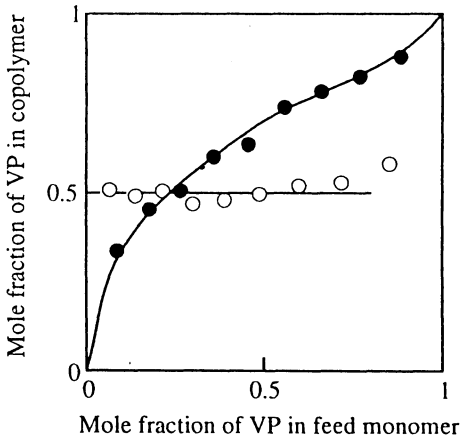

Fig. 1. Monomer-copolymer composition curves for the AA-VP (○) and MA-VP (●) systems.

Figure 2 gives a schematic representation of microscopic ionization equilibria of PACP, together with more familiar macroscopic stepwise acid distribution sequence. The relations between macroscopic

$$k_1 = \frac{[H^+][II]}{[I]} \qquad k_2 = \frac{[H^+][III]}{[I]} \qquad k_{12} = \frac{[H^+][IV]}{[II]} \qquad k_{21} = \frac{[H^+][IV]}{[III]}$$

$$K_1 = \frac{[H^+]\{[II] + [III]\}}{[I]} = k_1 + k_2 \qquad \frac{1}{K_2} = \frac{[II] + [III]}{[H^+][IV]} = \frac{1}{k_{12}} + \frac{1}{k_{21}}$$

$$K_1 \times K_2 = \frac{[H^+]^2[IV]}{[I]} = k_1 \times k_{12} = k_2 \times k_{21} \qquad K_t = \frac{[II]}{[III]} = \frac{k_1}{k_2} = \frac{k_{21}}{k_{12}}$$

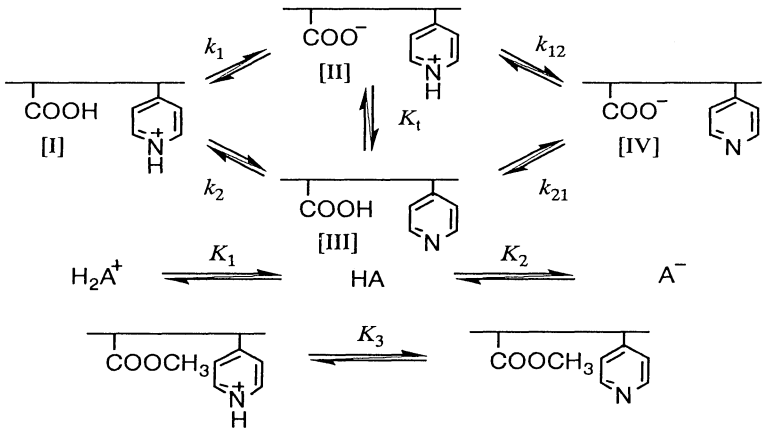

Fig.2. A schematic representation of macroscopic and microscopic ionization equilibria of PACP.

and microscopic dissociation constants are as follows.

To obtain macroscopic dissociation constants (pK_1 and pK_2), PACP was dissolved in the mixed solvent of ethanol and water (1:1 by volume). The concentration was 2.5×10^{-3} mol dm^{-3}. The calculated amount of nitric acid equivalent to the content of VP units in PACP was added to the solution, followed by potassium nitrate to keep the ion strength constant (μ = 0.1). The solution was then titrated with 0.02N potassium hydroxide. pH-Measurements were made at 25 °C with a TOA HM-60S pH meter equipped with an automatic titrator.

Figure 3 shows the titration curve of PACP, in which a sharp break is not observed. At α (degree of neutralization) = 1, a total amount of nitric acid added is neutralized. The values of pH at α = 0.5 and 1.5 correspond to macroscopic constants pK_1 and pK_2, respectively. There are equimolecules of H_2A^+ and HA at α = 0.5 and of HA and A^- at α = 1.5.

Copolymerization of MA and VP was performed at 60 °C with 2,2'-azobisisobutyronitrile as the initiator. Monomer reactivity ratios r_{MA} = 0.09 and r_{VP} = 1.13 were obtained by Kelen-Tüdös method,[12] on the basis of the copolymer composition determined by means of ^{1}H-NMR spectrometer. With reference to these values, the copolymer with 1:1 composition was prepared (Fig. 1). To obtain further information about acid dissociation of PACP, the 1:1 copolymer of MA and VP was titrated under the same conditions as in the

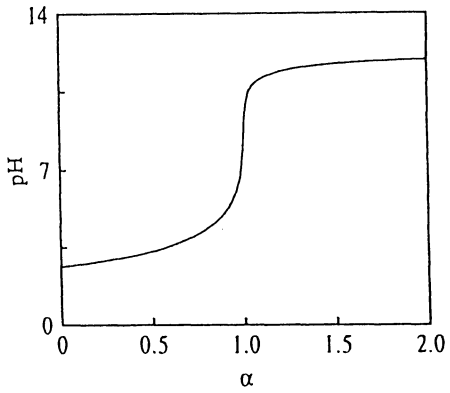

Fig. 3. pH-Titration of PACP. μ=0.1 (KNO_3), Temp. 25 °C

Table 1. Macroscopic microscopic acid dissociation constants of PACP

pK_1	3.31
pK_2	11.71
pk_1	4.37
pk_2	3.35
pk_{12}	10.65
pk_{21}	11.67
K_t	9.55×10^{-2}

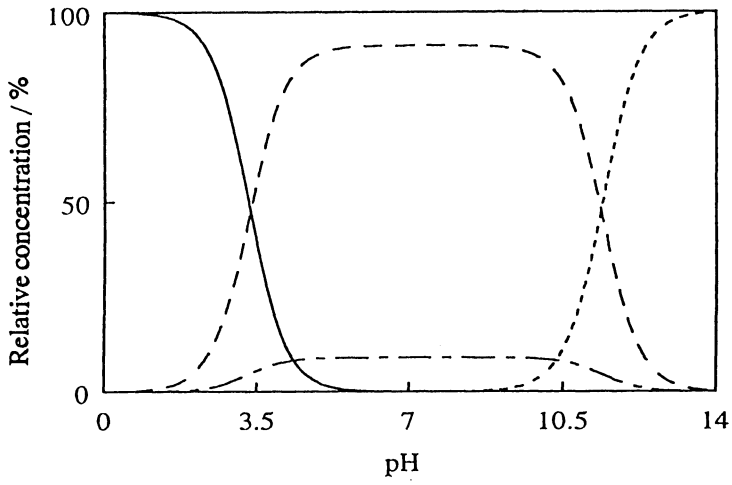

Fig. 4. pH Dependence of relative concentrations of the protonated (———), zwitterion (—·—), neutral molecule (– – – –) and deprotonated (·····) forms of PACP.

case of PACP and macroscopic constant $K_3 = 4.47 \times 10^{-4}$ was obtained. The microscopic constants of PACP were calculated by assuming $k_2 = K_3$. This assumption is generally accepted because the dissociation equilibria of the MA-VP copolymer are essentially attributed to deprotonation of pyridinium ion. Macroscopic and microscopic constants and tautomeric constant (K_t) of PACP are listed in Table 1. It is evident that neutral molecule type of PACP is more stable than the zwitterion type because of $K_t < 1$.

The distribution of the microscopic forms of PACP as a function of pH is of interest, in connection with pH-dependence of biologically and physiologically active amino acids and pyridine derivatives. Figure 4 shows the fractional concentrations of the respective forms of PACP. The relative concentrations were calculated using the relationship equations, which are shown above, of microscopic constants and hydrogen ion concentration. The fraction of the protonated form of PACP, which exists exclusively in the lower pH range, decreases with increasing pH value and fully vanishes at pH = *ca*. 5, while the deprotonated form begins to appear around pH = 9. The zwitterion and neutral molecule forms of PACP coexist over a wide range of pH, and the latter form is predominant regardless of pH value.

It is generally known in amino acids such as glycine[1] and lysine [2] that zwitterion form is more stable than neutral molecule form in neutral region. In PACP, however, the neutral molecule is the predominant form, contrary to amino acids. The reason for the preponderence of the neutral molecule type is not clear. A consistent explanation is that an increase in the hydrophobicity (an increase in aliphatic chain length) results in a depression in the dissociation. Incidentally, when two monomers (AA and VP) are mixed, about half of molecules changes to the ionic form. The ion pair or ion complex of AA^- and VP^+ may play an important role in the copolymerization. Though it is known that VP can be polymerized spontaneously, [13] there is no report on spontaneous copolymerization of AA and VP. Details of the spontaneous copolymerization will be reported elsewhere since the object of this letter is to explore the microscopic acid dissociation of the AA-VP copolymer.

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