Mechanochemical Reaction of Calcium Alginate Hydrogel due to a Counterion Exchange

Kazuhiko Baba,† Masakatsu Yonese,* and Hiroshi Kishimoto
Faculty of Pharmaceutical Sciences, Nagoya City University,
Tanabe-dori, Mizuho-ku, Nagoya 467
† Pharmaceutical Research Laboratory, Taiho Pharmaceutical Co., Ltd.,
Kawauchi-cho, Tokushima 771-01

(Received June 14, 1991)

Stress relaxations of calcium alginate hydrogel (CaAlg gel) rods induced by adding other counterions were investigated by measuring their tensile stresses. The stress decreased upon adding Ba^{2+} and H^+, whereas it increased upon adding Pb^{2+}. The relaxation time, equilibrium elastic modulus and spontaneous elastic modulus were obtained. The relaxation times were analyzed using a theory involving counterion diffusion accompanied by an ion-exchange reaction under the assumption that the rate-determing step is the diffusion of added counterions (M^{2+} and M^+) in the gel. The relaxation time was found to be a function of the concentration and diffusivity of the added counterions, the radius of the gel rod, the concentration of carboxylate ions and the counterion-selectivity coefficient (K^{M}_{Ca}) of the alginate. By fitting the observed relaxation times with theoretical ones, the optimal values of K^{M}_{Ca} were obtained: $K^{Ba}_{Ca}=100$, $K^{Pb}_{Ca}=20$ and $K^{H}_{Ca}=3\times10^3$. The rate-determing step of stree relaxation was confirmed to be the counterion diffusion process in CaAlg gel.

Chemically induced mechanical reactions of hydrogels have been receiving considerable attention in recent years. Shurinking-swelling behavior due to changes in chemical environments (e.g., pH, ionic strength, and solvent composition) has been extensively studied on synthetic polymer hydrogels, such as polyacrylic acid and polyacrylamide derivatives.[1-3] However, the mechanochemical reactions of polysaccharide hydrogels were examined less because of their structural inhomogeneity and complex ion-binding properties.

Alginate (Alg) is a linear block copolymer of β-D-mannuronic acid (M) and α-L-guluronic acid (G). It forms hydrogels in the presence of divalent ions, except for Mg^{2+} and Hg^{2+}. The crosslinks are formed by a stacking of the G blocks due to the formation of chelate complexes between divalent ions and the carboxylate ions of G. Alg is an unusual polyelectrolyte in that it possesses pronounced divalent ion selective bindings.[4] The selectivities for metal ions depend on the M/G ratio and, particularly, on the amount of poly(G) block in the sample.

We previously investigated the tensile stress relaxation of Alg hydrogel rods formed in the presence of various counterions, and reported that the kind of metal ions greatly affected the elastic moduli of the gels.[5] The stress changes of Alg gels due to counterion exchanges are interesting mechanochemical reactions. The changes in the stiffness of the junctions and flexibility of the network structure are responsible for the stress changes. In the present study we investigated the stress relaxation of calcium alginate hydrogel (CaAlg gel) due to stepwise increments of Ba^{2+}, Pb^{2+}, and H^+ concentrations. The stress relaxation was analyzed by a theory of the counterion diffusion accompanied by a counterion exchange.

Experimental

Materials. Purified sodium alginate (NaAlg) was prepared from commercial NaAlg (Tokyo Kasei Kogyo Co., Ltd.) by dialyzing against distilled water for 3 d and by subsequent filtrating in order to remove any insoluble substances, as described in a previous paper.[5] The weight-average molar mass of NaAlg was determined to be $M_W=1.32\times10^5$ g mol^{-1} using a light-scattering photometer LS-8 (Toyo Soda Manufacturing Co., Ltd.). The composition of the NaAlg was analyzed by circular dichroism (CD)[6] and ^{1}H NMR.[7] The guluronate fraction (F_G) as well as the consecutive guluronate fraction F_{GG} were determined to be 0.37 and 0.28. All other reagents were of special grade. Distilled and deionized water was used for the preparation of all aqueous solutions.

Preparation of Algintate Gel Rod. NaAlg solutions (1.2 w/v%) in straight Teflon tubes (length: 6.0 cm, internal diameter: 0.4 cm) were gelled by immersing in a 0.3 mol dm^{-3} $CaCl_2$ solution. The gels are denoted by CaAlg gels. In the case of adding Pb^{2+}, a $Ca(NO_3)_2$ solution was used in all processes instead of a $CaCl_2$ solution so as to avoid the precipitation of $PbCl_2$. They had to be matured for at least 7 d in the solutions to attain an equilibrium swelling state. The gel rods were then removed from the tubes and kept at 4 °C in order to prevent rotting. They were equilibrated for 48 h at 25 °C before measuring their tensile stresses.

Measurement of the Tensile Stress of Gel Rod. A schematic diagram of the apparatus for measuring the tensile stress of the gels is shown in Fig. 1. A rod of CaAlg gel (length: 3 cm, diameter: 0.3 cm) was fixed by clamps A and B made of plastic plates with rough surfaces to prevent them from slipping. It was suspended in a 0.3 mol dm^{-3} $CaCl_2$ or $Ca(NO_3)_2$ solution at 25 °C. A strain was imposed by using a manupulater to raise clamp A, and the tensile stress σ was then measured by a strain gauge, SG (Shinkoh Communication Industry Co., Ltd.), connected to a constant direct current source, CC (Model 691B, Metronix Corp. Tokyo) and a microvolt meter, V (Model AM-1001, Ohkura Electric Co.). The apparatus was set up in an air-thermostated bath TB in order to eliminate any temperature effects on the strain gauge.

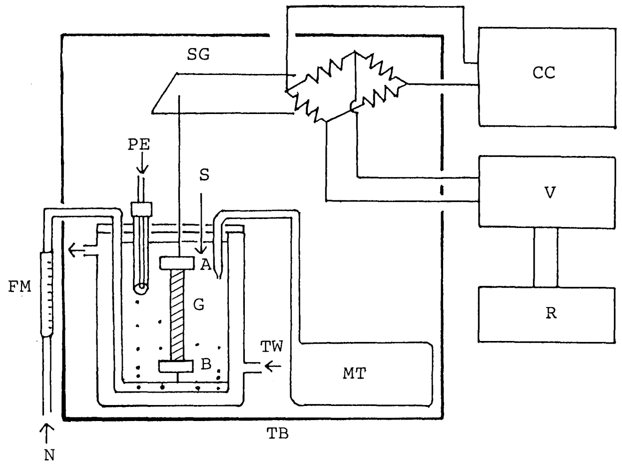

Fig. 1. Apparatus for measurement of gel tensile stress equipped with counterion solution adding system. A and B; clamp, G; gel rod, S; external solution, SG; strain gauge, TW; thermostated water (25 °C), MT; micro titrator, PE; pH electrode, FM; flow meter, N; N_2 gas, TB; thermostatic air bath, CC; constant direct current source, V; microvolt meter, R; recoder.

The stress relaxation of CaAlg gel due to counterion exchange was measured under a constant strain γ (=0.07) by adding $BaCl_2$ (0.5 mol dm^{-3}), $Pb(NO_3)_2$ (0.5 mol dm^{-3}) and HCl (0.1 mol dm^{-3}) solutions into the bulk solution with a microtitorator MT (Metrohm AG Herisau, No. E274). Ba^{2+}, Pb^{2+}, and H^+ concentrations (denoted by C_{Ba}, C_{Pb}, and C_H, respectively) were increased stepwise by 0.2—0.3 in their pBa (=$-\log C_{Ba}$), pPb (=$-\log C_{Pb}$), and pH (=$-\log C_H$), respectively. In the case adding H^+, the pH of the bulk solution was monitored with a pH electrode PE (Orion Research, Type 91-03). Bulk solutions were stirred by a nitrogen gas stream jetted out from small holes of a silicone tube surrounding the gel rod. The flow rate of the nitrogen gas was 8 cm^3 min^{-1}, at which rate the gel was not swinged.

Results

Stress Relaxation of CaAlg Gel under a Strain. The time course of the stress of CaAlg gel under a constant strain γ (=0.07) is shown in Fig. 2. The stress showed long relaxation and attained an equilibrium value after approximately 20 h, as reported in a previous paper.[5] The stress (σ) can be expressed by as a function of time t,

$$\sigma=\{G_e+G_r\exp(-t/\tau)\}\gamma, \qquad (1)$$

where G_e and (G_e+G_r) are the equilibrium elastic modulus and the spontaneous elastic modulus, respectively, and τ is the relaxation time. The values of G_e, G_r and τ were obtained by a curve-fitting method. The solid curve in Fig. 2 shows the stresses calculated from Eq. 1 using the best-fit values of G_e, G_r, and τ, which are indicated in the figure caption. The solid curve is in good agreement with the experimental results.

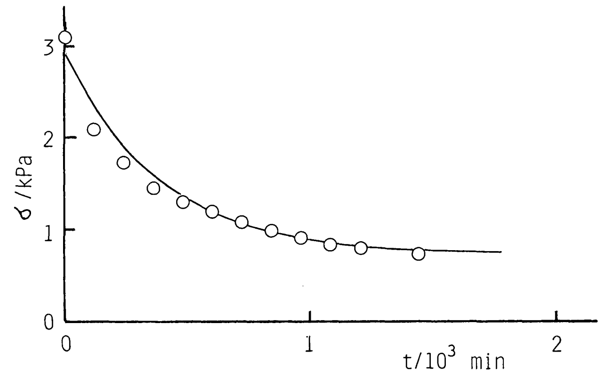

Fig. 2. Stress-relaxation curve of CaAlg gel under a constant tensile strain (γ=0.07). The solid curve shows the value calculated from Eq. 1 by a curve-fitting program. The parameter values used were G_e=10.0 kPa, G_r=30.4 kPa, and τ=23.9×10^3 s.

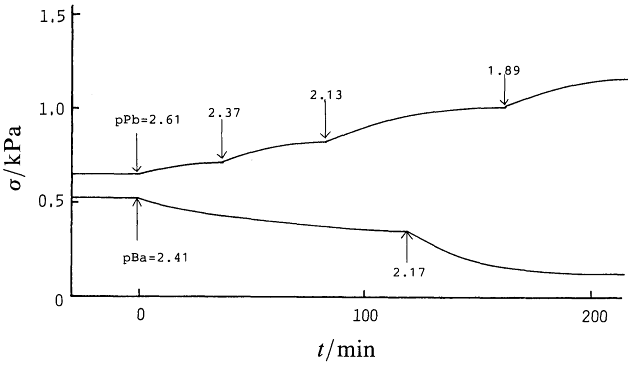

Fig. 3. Stress changes of CaAlg gel by stepwise addition of Ba^{2+} (lower curve) and Pb^{2+} (upper curve) ions. The Ba^{2+} and Pb^{2+} concentrations just before the concentration jumps ($C_{Ba,i-1}$ mol dm^{-3} and $C_{Pb,i-1}$ mol dm^{-3}) are indicated as pBa(=$-\log C_{Ba,i-1}$) and pPb(=$-\log C_{Pb,i-1}$).

Stress Relaxation of CaAlg Gel due to Counterion Exchange. After the stress of CaAlg gel attained an equilibrium value under γ=0.07, $BaCl_2$, $Pb(NO_3)_2$, and HCl were added into 0.3 mol dm^{-3} $CaCl_2$ or $Ca(NO_3)_2$ solutions. Figure 3 shows the stress relaxations of CaAlg gel upon adding Ba^{2+} and Pb^{2+} ions. Upon adding Ba^{2+} ions, the stress decreased with increasing time and attained equilibrium values after 60—120 min. On the other hand, upon adding Pb^{2+} ions, the stress increased with increasing time and attained equilibrium values after 30—60 min. As shown in Fig. 4, upon adding H^+ ions, the stress decreased in a similar manner as in the cases of Ba^{2+} ions.

Figure 5 shows the relationship between the added ion concentration just before the concentration jumps (C_M) and the equilibrium stress (σ_e). The abscissa is $-\log C_M$ (=pBa, pPb, or pH). The C_M at which the stress started to change depended on the kind of ions. When the Ba^{2+}

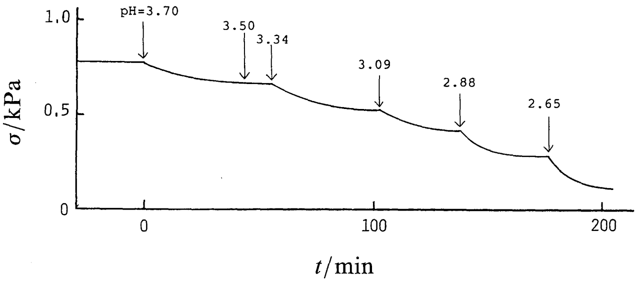

Fig. 4. Stress changes of CaAlg gel by stepwise addition of H^+ ions. The H^+ concentration just before the concentration jumps ($C_{H,i-1}$ mol dm^{-3}) is indicated as pH ($=-\log C_{H,i-1}$).

and Pb^{2+} concentrations were increased stepwise, the first stress change was observed at $-\log C_M=2.4$ and 2.6, respectively. In the case of adding H^+, the stress started to decrease at a much lower concentration ($-\log C_M=4.0$). In the case of adding Ba^{2+} and H^+, σ_e decreased almost linearly with decreasing $-\log C_M$ in the concentration region greater than these critical values, i.e. σ_e decreased with increasing C_M. On the other hand, σ_e increased almost linearly with decreasing $-\log C_M$ when Pb^{2+} was added. In the case of adding Ba^{2+} and H^+, the stress could not be measured by this apparatus due to an elongation of the gel rod in the range of $-\log C_M<2.1$ and 2.6, respectively.

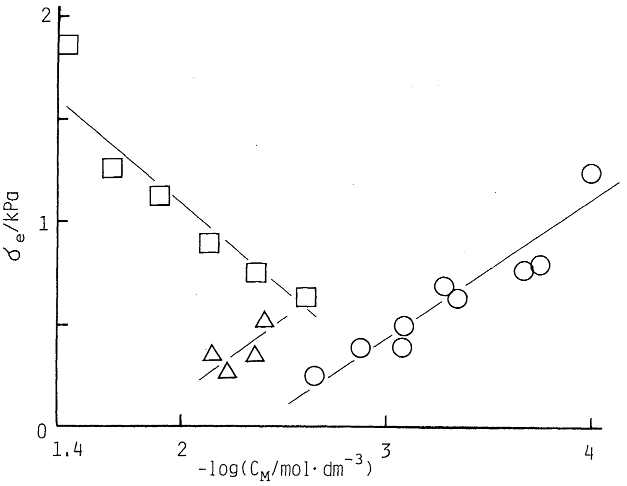

Fig. 5. Effect of added counterion concentration (C_M) on equilibrium stress (σ_e) of CaAlg gel. Added counterion: △; Ba^{2+}, □; Pb^{2+}, ○; H^+.

Each stress relaxation due to the addition of Ba^{2+}, Pb^{2+}, and H^+ ions can be also expressed by Eq. 1. Parameters G_e, G_r, and τ were determined by a curve-fitting method for each relaxation curve. The relaxation times τ of the stress changes upon the addition of Ba^{2+}, Pb^{2+}, and H^+ are shown in Fig. 6. We detail the results for τ in a later section.

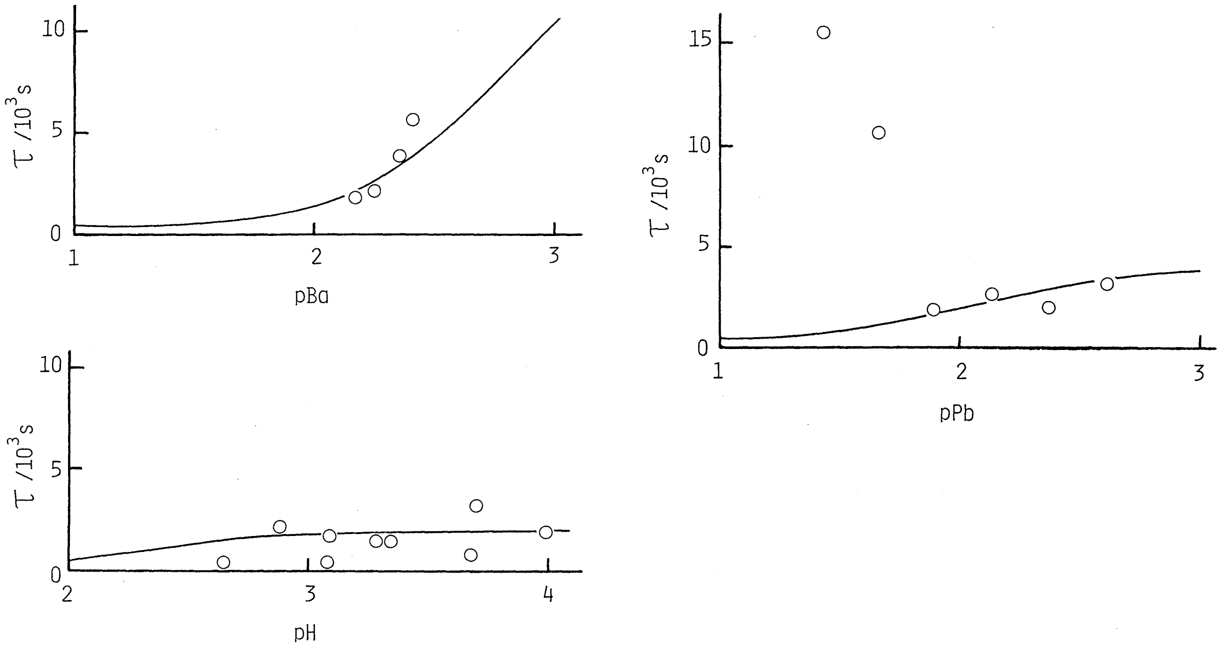

Fig. 6. Effect of added counterion concentration on experimental (circle) and theoretical (solid curve) time constants. (a) Added counterion: Ba^{2+} The theoretical values were calculated from Eq. 17 using $K_{Ca}^{Ba}=100$, $R=1.6\times10^{-3}$ m, $\bar{D}_{Ba}=1.1\times10^{-9}$ m^2 s^{-1}. (b) Added counterion: Pb^{2+} The theoretical values were calculated from Eq. 17 using $K_{Ca}^{Pb}=20$, $R=1.4\times10^{-3}$ m, $\bar{D}_{Pb}=0.79\times10^{-9}$ m^2 s^{-1}. (c) Added counterion: H^+ The theoretical values were calculated from Eq. 26 using $K_{Ca}^{H}=3\times10^3$, $R=1.5\times10^{-3}$ m, $\bar{D}_H=7.5\times10^{-9}$ m^2 s^{-1}. In all cases, C_t and $\bar{C}_{Ca}$ were fixed at 0.27 mol dm^{-3} and 0.3 mol dm^{-3}, respectively.

Discussion

The effects of the kind of counterions upon the viscoelastic properties of alginate gels have been studied by many reserchers.[5,8-10] Andersen and Smidsrød reported that when Ca^{2+} ions in CaAlg gel were partly exchanged for Pb^{2+} ions, the modulus of elasticity increased due to an increase in the internal energy.[8] They suggested that partly introduced Pb^{2+} ions into the junctions may lead the structure of junctions to become a more stable one than in the case of only Ca^{2+} ions. The stress enhancement of CaAlg gel upon adding Pb^{2+} ions in the present study is consistent with their result. Whereas the stress decreased upon the addition of Ba^{2+}. From the results of adding Ba^{2+} and Pb^{2+} ions, the kind of added counterion was found to affect both the structure and strength of the junctions of CaAlg gel. By adding Ba^{2+} ions, some reorganizations of the junction structure caused the gel strength to decrease, contrary to the case of adding Pb^{2+} ions. The decrease in the stress due to the addition of H^+ ions was attributable to a rupture of the junctions and a precipitation of the polymer due to the insolubility of the acid form of alginate.

Analysis on the Kinetics of Stress Relaxation. Nussbaum and Grodzinsky analyzed the stress changes of collagen membranes due to pH decrement using a diffusion reaction theory, under the assumption that the rate-determining step of the stress change is the diffusion of H^+ ions in the membrane.[11] The stress relaxation of CaAlg gel due to the addition of Ba^{2+}, Pb^{2+}, and H^+ ions is mainly attributed to changes in the strength and flexibility of the junctions, resulting from partial exchanges between the added ions and Ca^{2+} ions in the junctions. Assuming that the effect of unstirred boundary layers around the gel rod is negligible under our experimental conditions and that the rate of the ion-exchange reaction is very fast compared to counterion diffusion, the stress relaxations of CaAlg gel rods are discussed.

The addition of a counterion, M^{2+} (or M^+), induces an increment of its free concentrations ($\Delta\bar{C}_M(r)$) at position r which is the distance from the center of the gel rod. Assuming that the change of the tensile force ($\Delta F(r)$) is linearly propotional to $\Delta\bar{C}_M(r)$, according to Nussbaum and Grodzinsky the stress change of a gel rod ($\Delta\sigma$) is expressed by

$$\Delta\sigma=\frac{1}{\pi R^2}\left(\frac{\partial F}{\partial\bar{C}_M}\right)_{\bar{C}_M=\bar{C}_{M,\,i-1}}\int_0^R\Delta\bar{C}_M\,2\pi r\,\mathrm{d}r, \tag{2}$$

where R is the radius of the gel rod and $\left(\frac{\partial F}{\partial\bar{C}_M}\right)_{\bar{C}_M=\bar{C}_{M,i-1}}$ is a constant multiplier evaluated at the added ion concentration just before the ith concentration jump; $\bar{C}_M=\bar{C}_{M,i-1}$.

The case in which the divalent ion M^{2+} is added to the CaAlg gel is considered first. The counterion-exchange reaction of the carboxylate ions in CaAlg gel is

$$(RCOO)_2Ca+M^2\rightleftharpoons(RCOO)_2M+Ca^{2+}. \tag{3}$$

By approximating that the activity coefficients of M^{2+} and Ca^{2+} are unity, the counterion selectivity coefficient (K^M_{Ca}) can be expressed by

$$K^M_{Ca}=\frac{[(RCOO)_2M]\bar{C}_{Ca}}{[(RCOO)_2Ca]\bar{C}_M}. \tag{4}$$

Here, $\bar{C}_{Ca}$ and $\bar{C}_M$ are the free Ca^{2+} and M^{2+} concentrations in the gel, respectively, and $[(RCOO)_2M]$ and $[(RCOO)_2Ca]$ are the concentrations of the M^{2+} and Ca^{2+} ions bound to the carboxylate ions, respectively. The total carboxylate concentration (C_t) is expressed by

$$C_t=2[(RCOO)_2Ca]+2[(RCOO)_2M]+[RCOO^-]. \tag{5}$$

The concentration of the dissociated group $[RCOO^-]$ is negligibly small compared to the other concentrations.[13] $\bar{C}_{Ca}$ almost remains at the initial concentration in our experimental region. Then, $[(RCOO)_2M]$ can be expressed by

$$[(RCOO)_2M]=\frac{K^M_{Ca}C_t\bar{C}_M}{2(\bar{C}_{Ca}+K^M_{Ca}\bar{C}_M)}. \tag{6}$$

Since the changes in the water fraction of CaAlg gel were less than 0.5% in the range of $\bar{C}_M<10^{-2}$ mol dm^{-3}, the diffusion coefficient of the M^{2+} ions inside CaAlg gel, $\bar{D}_M$, is assumed to be constant throughout the experiment. The Fickian second equation of M^{2+} ions in the gel rod is expressed by

$$\frac{\partial}{\partial t}(\bar{C}_M+[(RCOO)_2M])=\frac{\bar{D}_M}{r}\frac{\partial}{\partial r}\left(r\cdot\frac{\partial\bar{C}_M}{\partial r}\right). \tag{7}$$

By adding M^{2+} ions, the concentration increases from $\bar{C}_{M,i-1}$ to $\bar{C}_{M,i}$. The concentration increment ($\tilde{C}_{M,i}$) is expressed by

$$\bar{C}_{M,i}=\bar{C}_{M,i-1}+\tilde{C}_{M,i}. \tag{8}$$

Assuming that $\tilde{C}_{M,i}\ll\bar{C}_{M,i-1}$, Eq. 7 can be linealized as follows by using Eqs. 6 and 8:

$$\frac{\partial\tilde{C}_{M,i}}{\partial t}=\frac{\bar{D}^*_M}{r}\frac{\partial}{\partial r}\left(r\cdot\frac{\partial\tilde{C}_{M,i}}{\partial r}\right). \tag{9}$$

Here, $\bar{D}^*_M$ is the diffusion coefficient of M^{2+} ions in a gel accompanied by an ion-exchange reaction. $\bar{D}^*_M$ is expressed by

$$\bar{D}^*_M=\bar{D}_M\left\{1+\frac{K^M_{Ca}C_t\bar{C}_{Ca}}{2(K^M_{Ca}\bar{C}_{M,i-1}+\bar{C}_{Ca})^2}\right\}^{-1}. \tag{10}$$

For $t=0$, the concentration of M^{2+} ions in the gel is

$\bar{C}_{M,i-1}$. At $t>0$, by adding M^{2+} ions to the solution, the concentration jumps from $\bar{C}_{M,i-1}$ to $\bar{C}_{M,i}$ at the gel surface, $r=R$:

$$\bar{C}_M = \bar{C}_{M,i-1} \qquad 0<r<R,\ t=0 \tag{11}$$

$$\bar{C}_M = \bar{C}_{M,i} \qquad r=R,\ t>0. \tag{12}$$

By solving Eq. 9 with these initial and boundary conditions, the concentration profile of M^{2+} ions inside the gel can be expressed by Eq. 13 as a function of t and r,[12)]

$$\frac{\bar{C}_M - \bar{C}_{M,i-1}}{\bar{C}_{M,i} - \bar{C}_{M,i-1}} = 1 - \frac{R}{2}\sum_{n=1}^{\infty} \frac{\exp(-\bar{D}_M^{*}\cdot\alpha_n^2\cdot t)J_0(r\cdot\alpha_n)}{\alpha_n\cdot J_1(R\cdot\alpha_n)}. \tag{13}$$

Here, $J_0(x)$ and $J_1(x)$ are Bessel functions of the first kind of order zero and one, respectively, and α_n is the root of Eq. 14,

$$J_0(R\cdot\alpha_n)=0. \tag{14}$$

The time constant (τ_n) is difined as

$$\tau_n = \frac{1}{\bar{D}_M^{*}\cdot\alpha_n^2}. \tag{15}$$

$\Delta\sigma$ of Eq. 2 is converted into Eq. 16 by using Eqs. 13 and 15,

$$\Delta\sigma = \left(\frac{\partial F}{\partial \bar{C}_M}\right)_{\bar{C}_M=\bar{C}_{M,i-1}} (\bar{C}_{M,i} - \bar{C}_{M,i-1}) \times\left\{1 - \frac{4}{R^2}\sum_{n=1}^{\infty}\frac{\exp(-t/\tau_n)}{\alpha_n^2}\right\}. \tag{16}$$

The time constant (τ_n) in Eq. 16 is considered to correspond to the relaxation time for the stress relaxation of a CaAlg gel due to a counterion exchange. The kinetics of Eq. 16 can be characterized by the first and longest time constant (τ_1). Using Eqs. 10 and 15, τ_{cal}=(τ_1) is expressed by

$$\tau_{cal} = \left\{1 + \frac{K_{Ca}^{M} C_t \bar{C}_{Ca}}{2(K_{Ca}^{M}\bar{C}_{M,i-1} + \bar{C}_{Ca})^2}\right\}(\bar{D}_M\cdot\alpha_1^2)^{-1}. \tag{17}$$

The equilibrated CaAlg gel is characterized by a uniform distribution of fixed ions ($RCOO^-$) and mobile ions (Ca^{2+}, Cl^-, and M^{2+}) inside the gel. The distribution satisfies the electroneutrality and the Donnan relationships:

$$2\bar{C}_{Ca} + 2\bar{C}_M - \bar{C}_{Cl} + \theta = 0, \tag{18}$$

$$\bar{C}_{Ca}(\bar{C}_{Cl})^2 = C_{Ca}(C_{Cl})^2, \tag{19}$$

and

$$\bar{C}_M(\bar{C}_{Cl})^2 = C_M(C_{Cl})^2, \tag{20}$$

where θ is the effective charge density of CaAlg gel and C_{Ca}, C_{Cl}, and C_M are the concentrations of the Ca^{2+}, Cl^-, and M^{2+} ions in the bulk solution, respectively. In order to obtain τ_{cal} from Eq. 20, the values $\bar{C}_M$ were calculated using Eq. 21, obtained from the simultanious solution of Eqs. 18—20,

$$4(1 + C_{Ca}/C_M)^2(\bar{C}_M)^3 + 4\theta(1 + C_{Ca}/C_M)(\bar{C}_M)^2 + \theta^2\bar{C}_M - (C_{Cl})^2 C_M = 0. \tag{21}$$

As θ of CaAlg gels, we used -7×10^{-3} mol dm^{-3} according to a previous report, which was determined by a membrane potential method.[13)] The τ_{cal} is found to be a function of R, $\bar{D}_M$, C_t, K_{Ca}^{M}, $\bar{C}_M$, and $\bar{C}_{Ca}$. Figure 7 shows the effects of these parameters on τ_{cal}.

The case in which monovalent ion M^+ is added to CaAlg gel can be derived in a similar manner to the case of adding divalent ions. The counterion-exchange reaction of the carboxylate ions is

$$(RCOO)_2Ca + 2M^+ \rightleftharpoons 2RCOOM + Ca^{2+}. \tag{22}$$

The selectivity coefficient (K_{Ca}^{M}) is expressed by

$$K_{Ca}^{M} = \frac{[(RCOOM]^2\bar{C}_{Ca}}{[(RCOO)_2Ca]\,(\bar{C}_M)^2}. \tag{23}$$

[RCOOM] can be expressed by

$$[(RCOOM] = \frac{2C_t\bar{C}_M}{A}\left(\sqrt{(\bar{C}_M)^2 + A} - \bar{C}_M\right), \tag{24}$$

where

$$A = \frac{8\bar{C}_{Ca}\cdot C_t}{K_{Ca}^{M}}. \tag{25}$$

Finally, the calculated time constant (τ_{cal}) of stress relaxation due to the addition of M^+ is obtained as

$$\tau_{cal} = \left[1 + \frac{2C_t}{A\sqrt{(\bar{C}_{M,i-1})^2 + A}}\left\{\sqrt{(\bar{C}_{M,i-1})^2 + A} - \bar{C}_{M,i-1}\right\}^2\right](\bar{D}_M\cdot\alpha_1^2)^{-1}. \tag{26}$$

Figure 8 shows some calculated results.

The solid curves in Fig. 7(a)—(e) show the values of τ_{cal} in the case adding divalent ions (e.g. Ba^{2+}) as a function of $-\log\bar{C}_M$ ($=-\log\bar{C}_{M,i-1}$), calculated from Eq. 17 by varying one parameter while fixing the other parameters. The values of the fixed parameters (shown in the figure captions) are determined either experimentally or

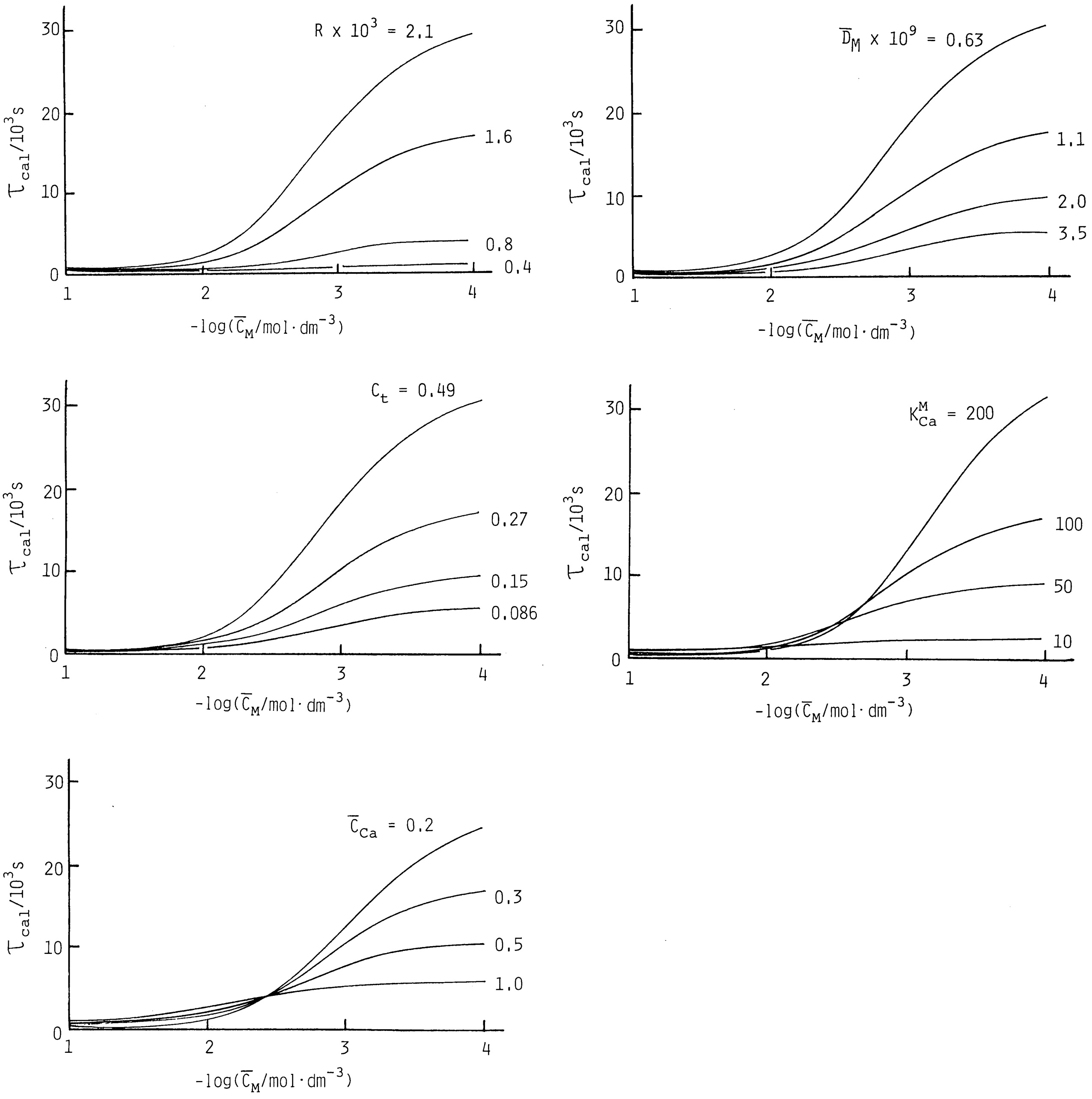

Fig. 7. Effect of added divalent ion concentration on τ_{cal} with a variation in the parameters. The solid curves show the theoretical values calculated using Eq. 17. (a) R is varied from 0.4 to 2.1×10^{-3} m. (b) $\overline{D}_{\mathrm{M}}$ is varied from 0.63 to 3.5×10^{-9} m^2 s^{-1}. (c) C_{t} is varied from 0.086 to 0.49 mol dm^{-3}. (d) $K^{\mathrm{M}}_{\mathrm{Ca}}$ is varied from 10 to 200. (e) $\overline{C}_{\mathrm{Ca}}$ is varied from 0.2 to 1.0 mol dm^{-3}. The other parameters in each variation were fixed at $R=1.6\times10^{-3}$ m, $\overline{D}_{\mathrm{M}}=1.1\times10^{-9}$ m^2 s^{-1}, $C_{\mathrm{t}}=0.27$ mol dm^{-3}, $K^{\mathrm{M}}_{\mathrm{Ca}}=100$, $\overline{C}_{\mathrm{Ca}}=0.3$ mol dm^{-3}.

theoretically. All of the relationships between τ_{cal} and $-\log \overline{C}_{\mathrm{M}}$ are expressed by sigmoidal curves. The values of τ_{cal} decrease with decreasing $-\log \overline{C}_{\mathrm{M}}$ and assymptote on the constant value $(\overline{D}_{\mathrm{M}}\alpha_1^2)^{-1}$, which is the characteristic diffusion time for M^{2+} ions across the cylinder (radius R) with no chemical reaction. τ_{cal} lengthens with increasing R and decreasing $\overline{D}_{\mathrm{M}}$ for any $\overline{C}_{\mathrm{M}}$ (Fig. 7(a) and (b)). With increasing C_{t}, the values of τ_{cal} increase and shift the point of inflection to a higher concentration (Fig. 7(c)). As shown in Figs. 7(d) and (e), the curves of τ_{cal} intersect the curves for other $K^{\mathrm{M}}_{\mathrm{Ca}}$ and $\overline{C}_{\mathrm{Ca}}$. These intersections are predicted from the two limits of Eq. 17. When $\overline{C}_{\mathrm{M},i-1} \ll \overline{C}_{\mathrm{Ca}}/K^{\mathrm{M}}_{\mathrm{Ca}}$, τ_{cal} is expressed by

$$\tau_{\mathrm{cal}} = \left(1 + \frac{K^{\mathrm{M}}_{\mathrm{Ca}} C_{\mathrm{t}}}{2\overline{C}_{\mathrm{Ca}}}\right)(\overline{D}_{\mathrm{M}}\cdot\alpha_1^2)^{-1}. \tag{27}$$

In this limit, τ_{cal} increases with increasing $K^{\mathrm{M}}_{\mathrm{Ca}}$ and

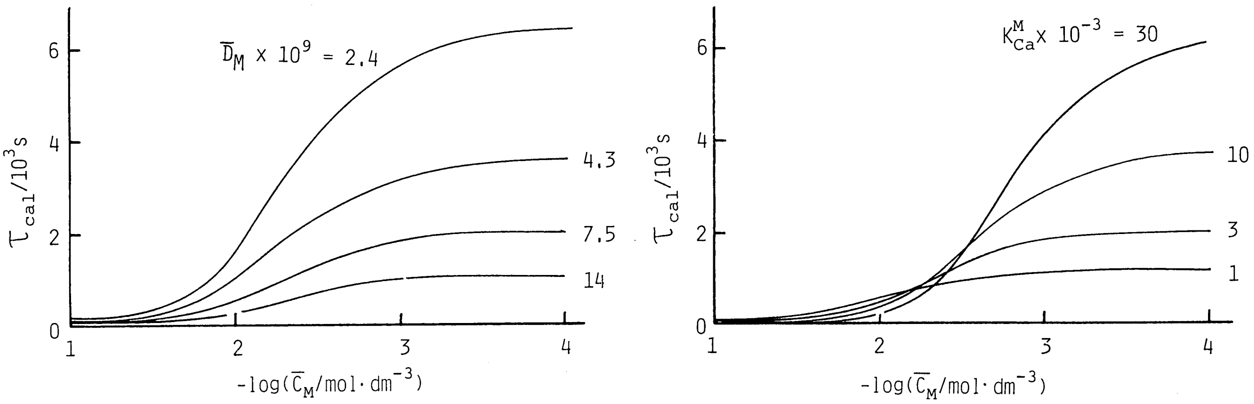

Fig. 8. Effect of added monovalent ion concentration on τ_{cal} with a variation in the parameters. The solid curves show the theoretical values calculated using Eq. 26. (a) $\bar{D}_M$ is varied from 2.4 to 14×10^{-9} m^2 s^{-1}. (b) K^M_{Ca} is varied from 1 to 30×10^3. The other parameters in each variation were fixed at $R=1.5\times10^{-3}$ m, $\bar{D}_M=7.5\times10^{-9}$ m^2 s^{-1}, $C_t=0.27$ mol dm^{-3}, $K^M_{Ca}=3\times10^3$, $\bar{C}_{Ca}=0.3$ mol dm^{-3}.

decreasing $\bar{C}_{Ca}$. When $\bar{C}_{M,i-1} \gg \bar{C}_{Ca}/K^M_{Ca}$, τ_{cal} is expressed by

$$\tau_{cal} = \left\{1 + \frac{\bar{C}_{Ca}C_t}{2K^M_{Ca}(\bar{C}_{M,i-1})^2}\right\}(\bar{D}_M\cdot\alpha_1^2)^{-1}. \tag{28}$$

In this limit, τ_{cal} decreases with increasing K^M_{Ca} and decreasing $\bar{C}_{Ca}$.

As regards to adding monovalent ions (e.g. H$^+$), Fig. 8 shows τ_{cal} as a function of $-\log \bar{C}_M$ ($=-\log \bar{C}_{M,i-1}$), calculated from Eq. 26 for various $\bar{D}_M$ and K^M_{Ca}. The feature of the curves is analogous to the cases of adding divalent ions. It should be noted that in the case adding monovalent ions, the values of τ_{cal} are obviously less sensitive to the variations of the parameters ($\bar{D}_M$ and K^M_{Ca}) than those in the cases adding divalent ions, as shown in Figs. 7(b) and (d). Although the results are not shown, the τ_{cal} values in the case adding monovalent ions are also less sensitive to variations in the other parameters (R, C_t, and $\bar{C}_{Ca}$) than those in the cases adding divalent ions.

Estimation of Alginate Ion-Selectivity Coefficients. From the relaxation times (τ) of stress relaxations of a CaAlg gel due to counterion exchanges, the values of K^M_{Ca} of the alginate were determined by fitting them with the values calculated from Eqs. 17 and 26. In the calculation, the radius of the CaAlg gel rod is assumed to remain constant ($=R$) throughout the experimental region. In fact, changes in the radius were within 2%. The total carboxylate concentration of CaAlg gel C_t and the diffusion coefficients of added ions in CaAlg gel $\bar{D}_M$ were determined as follows. The value C_t was obtained by

$$C_t = W_p \cdot \rho / M_u \tag{29}$$

where W_p, ρ, and M_u ($=195$ g mol^{-1}) are the the weight fraction of the polymer, the density of CaAlg gel, and the molar mass of uronate. C_t was calculated to be 0.27 mol dm^{-3} by using the values of W_p and ρ determined previously ($W_p=0.051$, $\rho=1.034\times10^3$ g dm^{-3}).5) $\bar{D}_M$ can be estimated from Eq. 30 derived by Mackie and Meares,14)

$$\bar{D}_M = D^0_M\left(\frac{V_w}{2-V_w}\right)^2. \tag{30}$$

Here, D^0_M is the diffusion coefficient of ion M in water and V_W is the volume fraction of water in a hydrogel. Using the values of D^0_M ($D^0_{Ba}=1.34\times10^{-9}$ m^2 s^{-1}, $D^0_{Pb}=0.98\times10^{-9}$ m^2 s^{-1} and $D^0_H=9.34\times10^{-9}$ m^2 s^{-1}),15) $\bar{D}_{Ba}$, $\bar{D}_{Pb}$, and $\bar{D}_H$ in CaAlg gel ($V_W=0.946$)5) were estimated to be 1.12×10^{-9} m^2 s^{-1} and 0.79×10^{-9} m^2 s^{-1} and 7.53×10^{-9} m^2 s^{-1}, respectively.15)

Figure 6 shows the observed values for stress relaxation due to the addition of Ba^{2+}, Pb^{2+}, and H$^+$. The values are in the range 10^3—10^4 s. They are 10—20 times greater than the time constants for the stress changes of collagen membranes due to the pH decrement reported by Nussbaum and Grodzinsky.11) The difference is attributed to a dimensional gap of the samples used, since the sample dimension considerably affects the time constant, as is shown in Fig. 7(a). We used a gel rod of 3 mm diameter, whereas they used a membrane of 0.1—0.2 mm thickness. The experimental values (τ) were compared with the τ_{cal} predicted from theory (Eqs. 17 and 26). By fitting τ with τ_{cal}, the optimum values of K^M_{Ca} were obtained, i.e. $K^{Ba}_{Ca}=100$, $K^{Pb}_{Ca}=20$, and $K^M_{Ca}=3\times10^3$, respectively. The solid curves in Fig. 6 show their calculated results. The ion-exchange reaction of the carboxylate ions in the junctions is considered to contribute primarily to stress changes of the CaAlg gel. On the other hand, that of carboxylate ions between the junctions is considered to contribute less. Therefore, the values of K^M_{Ca} obtained here are regarded as being the mean ion-selectivity coefficients without any distinction between them. We can calculate the degress of ion-exchange of the CaAlg gel using these ion-selectivity coefficients. When the first stress changes were observed (pBa=2.4, pPb=2.6, and pH=4.0), 57, 14, and 1.5% of the Ca^{2+} ions were replaced by Ba^{2+}, Pb^{2+}, and H^+ ions, respectively, and at a maximal addition of these counterions (pBa=2.1, pPb=1.4, and pH=2.6), 73, 73, and 39% of the Ca^{2+} ions were replaced by Ba^{2+}, Pb^{2+}, and H^+ ions, respectively. In the region of high Pb^{2+} concentration ($pPb<1.7$), the experimental results were considerably greater than the theoretical curve. One reason for this might be assigned to a reduced diffusivity of the Pb^{2+} ion. The water fraction (V_W) at pPb=1.4 was approximately 3% lower than that of initial CaAlg gel. The assumption that D_M, θ, C_t, and R do not change throughout is not considered to be appropriate in this case.

Haug and Smidsrφd studied the gel-formation and precipitation of a sodium alginate (guluronate fraction $F_G=0.08$) by adding various divalent ions.[16] They determined the ion-selectivity coefficients between divalent ions and sodium ions. The affinity for divalent metals decreased in the following order:

$$Ba^{2+}>Pb^{2+}>Sr^{2+}>Ca^{2+}. \tag{31}$$

The ion-selectivity coefficient between Ca^{2+} and Sr^{2+} (K^{Sr}_{Ca}) of an alginate ($F_G=0.4$) was estimated at approximately 2.[17] The estimated K^{Ba}_{Ca} and K^{Pb}_{Ca} in the present study are consistent with the order expressed by Eq. 31. The reciprocal of K^{H}_{Ca} is considered to be the dissociation constant of alginic acid including an ion-exchange reaction in the junctions. Haug reported that the dissociation constant of an alginic acid ($F_G=0.08$) was 3.8×10^{-4}.[18,19] Our result, $1/K^{H}_{Ca}(=3.3\times10^{-4})$, is close to the dissociation constant. Although a strict comparison of our results with those for other alginate samples might be difficult, reasonable ion-selectivity coefficients were found to be obtainable from stress relaxation measurements. Furthermore, we can say that the diffusion process of added counterions in CaAlg gel is the rate-determining step of the stress relaxation and that the following mechanical equilibration (e.g. molecular reconformation and osmotic swelling) occurs much faster.[11]

References

1) H. H. Hooper, J. P. Baker, H. W. Blanch, and J. P. Prausnitz, *Macromolecules,* **23**, 1096 (1990).

2) J. Ricka and T. Tanaka, *Macromolecules,* **17**, 2916 (1984).

3) P. E. Grimshaw, J. H. Nussbaum, A. J. Grodzinsky, and M. L. Yarmush, *J. Chem. Phys.,* **93**, 4462 (1990).

4) A. Haug and O. Smidsrφd, *Acta Chem. Scand.,* **24**, 843 (1970).

5) M. Yonese, K. Baba, and H. Kishimoto, *Bull. Chem. Soc. Jpn.,* **61**, 1857 (1988).

6) E. R. Morris, D. A. Rees, and D. Thom, *Carbohydr. Res.,* **81**, 305 (1980).

7) H. Grasdalen, B. Larsen, and O. Smidsrφd, *Carbohydr. Res.,* **68**, 23 (1979).

8) I. L. Andresen and O. Smidsrφd, *Carbohydr. Res.,* **58**, 271 (1977).

9) G. R. Seely and R. L. Hart, *Macromolecules,* **7**, 706 (1974).

10) O. Smidsrφd and A. Haug, *Acta Chem. Scand.,* **26**, 79 (1972).

11) J. H. Nussbaum and A. J. Grodzinsky, *J. Memb. Sci.,* **8**, 193 (1981).

12) J. Crank, "The Mathematics of Diffusion," 2nd ed, Clarendon Press, Oxford (1975), Chap. 5.

13) M. Yonese, K. Baba, and H. Kishimoto, *Bull. Chem. Soc. Jpn.,* **61**, 1077 (1988).

14) J. S. Mackie and P. Meares, *Proc. Roy. Soc. A,* **232**, 498 (1955).

15) R. Parsons, "Handbook of Electrochemical Constant," Butterworths Scientific Publications, London (1959), p. 79.

16) A. Haug and O. Smidsrφd, *Acta Chem. Scand.,* **19**, 341 (1965).

17) A. Haug and O. Smidsrφd, *Nature,* **215**, 757 (1967).

18) A. Haug, *Acta Chem. Scand.,* **15**, 950 (1961).

19) A. Haug, *Acta Chem. Scand.,* **15**, 1794 (1961).