SURFACTANTS & DETERGENTS TECHNICAL

Syntheses of Sodium 2-(N-alkyl-N-methylamino)ethanephosphates and Their Physicochemical Properties

Kazuyuki Tsubone*, Noriko Uchida, Hideaki Niwase and **Keiichi Honda**
Kanebo, Ltd., Cosmetics Laboratory, 5-3-28 Kotobukicho, Odawara City, Kanagawa 250, Japan

A series of new amphoteric surfactants, sodium salts of 2-(N-alkyl-N-methylamino)ethanephosphates (alkyl: n-dodecyl, n-tetradecyl and n-hexadecyl) were prepared by reacting alkylbromides with N-methylaminoethanol, followed by addition of phosphoric acid groups and neutralization with sodium hydroxide. The structures of these compounds were confirmed by spectroscopy and elemental analysis. Physical properties such as Krafft point, isoelectric point, critical micelle concentration, occupation area of molecule at surface, foaming power and the effect of pH on surface activity were evaluated. These surfactants were found to exhibit zwitterionic characteristics in the pH range from approximately 5 to 9 and demonstrated good surface-active properties over a wide pH range (pH 4~10). Large occupation areas of the molecule at a surface in comparison with sodium dodecyl sulfate was noted as a characteristic feature of these surfactants.

Many surfactants have been developed and used as emulsifying agents, solubilizing agents, dispersing agents and detergents. To meet the need in the cosmetic industry for a surfactant with less damaging effects on the skin, Imokawa *et al.* (1) developed "monoalkyl phosphates" which possess good surface active properties and are safe for the skin in comparison with typical anionic surfactants. Krupin (2) has synthesized phosphate molecules incorporating polyoxyethylene or amide groups and tried to apply them as detergents. Okamoto *et al.* (3) have synthesized α-aminoalkylphosphoric acid, α-alkylaminoethyl phosphoric acid, alkoxymethylphosphoric acid and their derivatives. He has shown that the very poor water solubility of α-aminoalkylphosphoric acid was due to the formation of an intramolecular salt through the interaction of amino and phosphoric acid groups. On the other hand, phosphatidylcholine contains a phosphoryl choline group consisting of a quaternary ammonium group and a phosphoric acid group, which interact together to form a zwitterion structure.

No reports have yet been found in the literature on the preparation and properties of surfactants containing both a tertiary amino group and a phosphoric acid group as hydrophilic moieties. In this report, new alkyl phosphates, sodium 2-(N-alkyl-N-methylamino)ethanephosphates (alkyl:dodecyl, tetradecyl and hexadecyl), which incorporate a tertiary amino group in the middle of the

molecule and a phosphate group at the terminal, were synthesized and their physicochemical properties evaluated.

EXPERIMENTAL METHODS

The IR spectra were recorded with a Hitachi Model 270-30 infrared spectrometer. The NMR spectra were measured with a JEOL JNM-GX270 FTNMR (270 MHz) spectrometer. Chemical shifts are reported in parts per million (δ), using tetramethylsilane as an internal standard. Mass spectra were obtained with a JEOL JMX-DX-303 mass spectrometer. Elemental analyses were performed with a Yanagimoto Micro Analyzer Model MT-3.

The TLC was carried out on silica gel with Kieselgel 60 (Merck) as a stationary phase and chloroform-methanol-water (65:25:4) as a mobile phase. Column chromatography was performed on silica gel of Wakogel C-100 (Wako Pure Chemical Industries, Ltd., Japan).
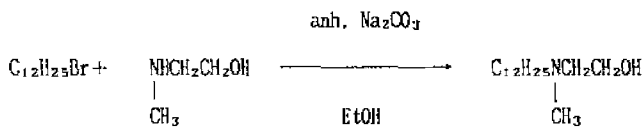
Synthesis of (N-dodecyl-N-methyl)ethanolamine (C_{12}-ME). C_{12}-ME was prepared by combining dodecylbromide (200 g, 0.8 mol) and 2-methylaminoethanol (60 g, 0.8 mol) in the presence of anhydrous sodium carbonate (90 g, 0.85 mol) in ethanol (400 ml) at reflux temperature for eight hr with stirring (Scheme 1). After removal of precipitated sodium bromide and residual sodium carbonate by centrifugation, ethanol was evaporated *in vacuo*. The crude product was purified by vacuum distillation to yield C_{12}-ME as a colorless liquid, 206 g yield 85%, b.p. 204~208°C/mm. IR (neat): 3420, 2925, 2850, 1465, 1380, 1040, 880, 720 cm^{-1}; ^{1}H-NMR(CDCl$_3$, δ): 0.88 [3H, t, $\underline{CH}_3$(CH$_2$)$_{10}$-], 1.27-1.49 [20H, m, CH$_3$($\underline{CH}_2$)$_{10}$-], 2.23 (3H, s, N $\underline{CH}_3$), 2.38 (2H, t, $\underline{CH}_2$N), 2.50 (2H, t, N $\underline{CH}_2$), 3.55 (1H, s, $\underline{OH}$), 3.57 (3H, t, $\underline{CH}_2$O); ^{13}C-NMR(CDCl$_3$, δ): 14.09 ($\underline{CH}_3$), 22.73 ($\underline{CH}_2$) 27.40 ($\underline{CH}_2$), 27.51 ($\underline{CH}_2$), 29.42 ~ 32.00 ($\underline{CH}_2$), 41.84 (N $\underline{CH}_3$), 58.10 (N $\underline{CH}_2$), 58.70 (N $\underline{CH}_2$), 59.24 ($\underline{CH}_2$OH); MS (70 eV) m/z (rel. int. %) 243 (M^r, 20), 212 (100), 88 (100); analysis calculated for $C_{15}H_{33}N_1O_1$: C, 75.21; H, 13.74; N, 5.20; found: C, 74.96; H, 13.55; N, 4.96.

C_{14}-ME and C_{16}-ME were prepared by similar procedures, and their NMR and IR spectra were consistent with the expected structures.
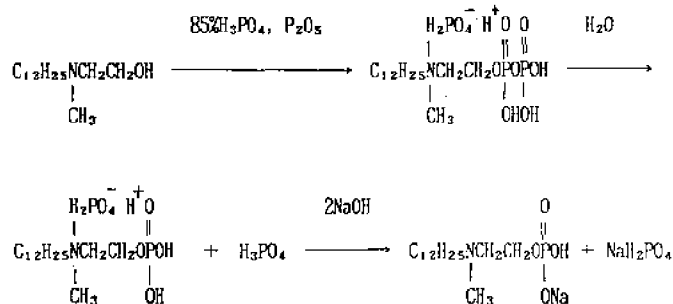
Synthesis of sodium 2-(N-dodecyl-N-methylamino)-ethanephosphate (C_{12}-MEP). C_{12}-ME (12.2 g, 0.05 mol) and 85% H$_3$PO$_4$ (5.8 g, 0.05 mol) were mixed in tetrahydrofuran (200 ml) and stirred for 20 min at room

---

anh. Na$_2$CO$_3$

$$C_{12}H_{25}Br + \quad \begin{matrix} NHCH_2CH_2OH \\ | \\ CH_3 \end{matrix} \quad \xrightarrow{\quad EtOH \quad} \quad \begin{matrix} C_{12}H_{25}NCH_2CH_2OH \\ | \\ CH_3 \end{matrix}$$

SCHEME 1. Preparation of (N-dodecyl-N-methyl)ethanolamine.

SCHEME 2. Preparation of 2-(N-dodecyl-N-methylamino)ethane-phosphate.

temperature followed by gradual addition of diphosphorous pentoxide (9.9 g, 0.07 mol) (Scheme 2). After dissolving diphosphorous pentoxide by stirring at room temperature, the solution was refluxed for 8 hr with stirring. The reaction mixture was cooled to room temperature, water (3.4 g, 0.19 mol) was added and the mixture was stirred for 30 min and NaOH (7.6 g, 0.19 mol) was then added, followed by stirring for 20 min. After removal of solvent, the residue was washed repeatedly with hot ethanol. A crude product was obtained upon evaporation. This product was purified by column chromatography using ethanol-water (1:1, vol/vol) as an eluent resulting in 11 g of sodium 2-(N-dodecyl-N-methylamino)ethanephosphate. The compound showed one spot on TLC (Rf: 0.7), yield 65%: IR: 3400, 2920, 1460, 1200, 1080, 930, 750 cm^{-1}; ^{1}H-NMR (CD$_3$OD, δ): 0.87 [3H, t, C$\underline{H}_3$(CH$_2$)$_{10}$-], 1.29-1.76 [20H, m, CH$_3$(C$\underline{H}_2$)$_{10}$-], 2.88 (3H, s, NC$\underline{H}_3$), 3.13 (2H, t, C$\underline{H}_2$N), 3.34 (2H, t, C$\underline{H}_2$N), 4.18 (2H, t, C$\underline{H}_2$O), 4.94 (1H, s, O$\underline{H}$); ^{13}C-NMR (CD$_3$OD, δ) 14.39 (C$\underline{C}$H$_3$), 23.65 ($\underline{C}$H$_2$), 25.00 ($\underline{C}$H$_2$), 27.69 ($\underline{C}$H$_2$), 30.24 $\sim$ 30.68 ($\underline{C}$H$_2$), 32.99 ($\underline{C}$H$_2$), 40.88 (N$\underline{C}$H$_3$), 57.82 (N$\underline{C}$H$_2$), 60.13 ($\underline{C}$H$_2$O); analysis calculated for C$_{15}$H$_{33}$N$_1$O$_4$P$_1$Na$_1$: C, 52.16; H, 9.63; N, 4.06. Found: C, 51.98; H, 9.07; N, 3.74.

Other MEP homologues, C$_{14}$-MEP and C$_{16}$-MEP, were prepared by similar procedures and showed one spot on TLC; yields and analytical data are as follows:

C$_{14}$-MEP: yield 70%; IR (neat): 3400, 2920, 1460, 1200, 1080, 930, 750 cm^{-1}; ^{1}H-NMR (CD$_3$OD, δ): 0.89 [3H, t, C$\underline{H}_3$(CH$_2$)$_{12}$-], 1.29-1.77 [24H, m, CH$_3$(C$\underline{H}_2$)$_{12}$-], 2.89 (3H, s, NC$\underline{H}_3$), 3.14 (2H, t, C$\underline{H}_2$N), 3.35 (2H, t, NC$\underline{H}_2$), 4.18 (2H, t, C$\underline{H}_2$O), 4.98 (1H, s, O$\underline{H}$); ^{13}C-NMR (CD$_3$OD, δ) 14.39 ($\underline{C}$H$_3$), 23.63 ($\underline{C}$H$_2$), 24.95 ($\underline{C}$H$_2$), 27.64 ($\underline{C}$H$_2$), 30.21 $\sim$ 30.70 ($\underline{C}$H$_2$), 32.97 ($\underline{C}$H$_2$), 40.85 (N$\underline{C}$H$_3$), 57.82 (N$\underline{C}$H$_2$), 60.17 ($\underline{C}$H$_2$O); analysis calculated for C$_{17}$H$_{37}$N$_1$O$_4$P$_1$Na$_1$: C, 54.68; H, 9.99; N, 3.75. Found: C, 54.08; H, 9.19; N, 3.66.

C$_{16}$-MEP: yield 68%; IR (neat): 3400, 2920, 1460, 1200, 1080, 930, 750 cm^{-1}; ^{1}H-NMR (CD$_3$OD, δ): 0.90 [3H, t, C$\underline{H}_3$(CH$_2$)$_{14}$-], 1.29-1.76 [28H, m, CH$_3$(C$\underline{H}_2$)$_{14}$-], 2.89 (3H, s, NC$\underline{H}$H$_3$), 3.14 (2H, t, C$\underline{H}_2$N), 3.35 (2H, t, C$\underline{H}_2$N), 4.18 (2H, t, C$\underline{H}_2$O), 4.85 (1H, s, O$\underline{H}$); ^{13}C-NMR (CD$_3$OD, δ) 14.39 ($\underline{C}$H$_3$), 23.66 ($\underline{C}$H$_2$), 25.05 (C$\underline{H}_2$), 27.68 ($\underline{C}$H$_2$), 30.25 $\sim$ 30.72 ($\underline{C}$H$_2$), 33.01 (C$\underline{H}_2$), 40.89 (N$\underline{C}$H$_3$), 57.87 (N$\underline{C}$H$_2$), 60.15 ($\underline{C}$H$_2$O); analysis calculated for C$_{19}$H$_{41}$N$_1$O$_4$P$_1$Na$_1$: C, 56.84; H, 10.29; N, 3.49. Found: C, 57.02; H, 10.15; N, 3.29.

Measurements of physicochemical properties. Krafft points were estimated from the temperature at which an abrupt change in electrical conductivity occurred. Isoelectric points (pHI) were determined by potentiometry. The titration was carried out with a Compact Titrator (Mettler DL20, Mettler Instruments AG, Switzerland). Samples were dissolved in a 0.1N HCl solution, and the titration was performed with a NaOH solution. Changes in the pH value were traced potentiometrically. The acid dissociation constant pK$_1$ and the base constant at pK$_2$ and pK$_3$ were determined from three minimal values on the differential curves and the value of pHI$_1$ and pH$_2$ calculated by the relationship pHI$_1$ = (pK$_1$ + pK$_2$)/2 and pHI$_2$ = (pK$_2$ + pK$_3$)/2 (4), respectively. With respect to the aqueous solution of compounds, surface tension was measured at 25°C with a du Noüy autotensiometer (Model 6801ES, Rigosha & Co., Ltd., Japan) at concentrations from 10^{-5} to 10^{-2} mol/l. The surface tension-concentration plots were used to determine critical micelle concentration (CMC, break points), surface tension lowering ability (γ cmc, surface tension at cmc) and occupation area of the molecule at the surface [A nm^2, from surface excess concentration calculated with Gibbs' equation (5)]. Foaming properties were measured according to the Ross-Miles method at 40°C (6).

Foaming height (mm) was recorded immediately (A) after dropping the test sample and after standing for five min (B). Foam stability was calculated as the ratio of B to A.
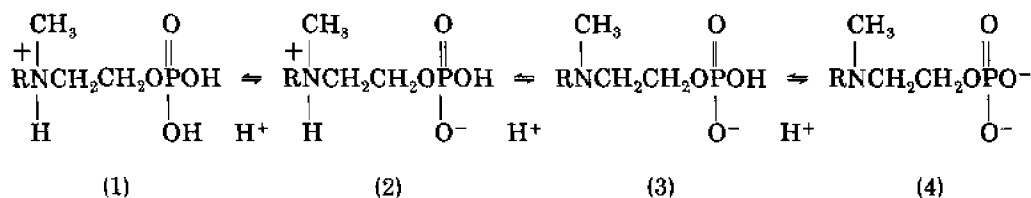
RESULTS AND DISCUSSION

Conductivity-temperature curves showed that Krafft points of MEP homologues were all below zero. These results indicate that these compounds are very strongly hydrophilic and clear water solutions can be obtained at room temperature. The pH values of their aqueous solutions (0.1 wt%) were within 5.8 $\sim$ 6.1.

With respect to solubility in organic solvents, they are soluble in ethanol, methanol and chloroform, but are almost insoluble in acetone and benzene.

In general, the amphoteric surfactants are classified into two types. Surfactants belonging to the first type behave practically as a cationic surfactant in an acid solution and act as an anionic surfactant in an alkaline solution. Surfactants of the second type exist as zwitterions over a wide pH range. Regarding MEP homologues, in order to determine the type of existence in aqueous solution, the consumption of HCl per unit pH was estimated on the basis of the titration curves.

The results of potentiometric titrations with the pH values of their aqueous solutions are shown in Table 1 together with other amphoteric surfactants (4,7). The differential curves show three maxima, which are due to the formation of quaternary ammonium salt from tertiary amine and to neutralizations of phosphate groups. The three minima of the curves correspond to pK$_1$ (4.7 $\sim$ 4.8), pK$_2$ (8.8 $\sim$ 8.9) and pK$_3$ (9.4 $\sim$ 9.5). The isoelectric points of MEP homologues first occurred at pH 6.8 $\sim$ 6.9. The pH values of aqueous solutions of MEP homologues were nearly equivalent to the isoelectric points. Thus, it is clear that they exist in four ionic forms, depending upon the pH values of aqueous solutions. These forms are shown in the following ion equilibrium.

$$\begin{array}{cccc}
\overset{CH_3}{\underset{H}{\overset{+}{R}NCH_2CH_2O\overset{O}{\overset{\|}{P}}OH}} & \overset{CH_3}{\underset{H}{\overset{+}{R}NCH_2CH_2O\overset{O}{\overset{\|}{P}}OH}} & \overset{CH_3}{\overset{|}{R}NCH_2CH_2O\overset{O}{\overset{\|}{P}}OH} & \overset{CH_3}{\overset{|}{R}NCH_2CH_2O\overset{O}{\overset{\|}{P}}O^-} \\
\overset{|}{OH} \; H^+ & \overset{|}{O^-} \; H^+ & \overset{|}{O^-} \; H^+ & \overset{|}{O^-} \\
(1) & (2) & (3) & (4)
\end{array}$$

The cationic structure (1) is formed predomdinatly in acidic solutions of pH below ca. 4.7. The zwitterion (2) exist in the range of pH ca. 4.7 ~ 8.8. The anionic form (3) and (4) is present mainly in alkaline solutions of pH above 8.9. Thus, it is clear that MEP homologues (first type) act as neutral electrolytes in a broader pH range (4.7 ~ 8.8) than those of amphoteric surfactants consisting of β-alanine (4,7).

The surface tension-log concentration plots for MEP homologues at pH 6.1 ~ 6.3 are shown in Figure 1. The formation of micelles in water was demosntrated by the clear evidence of a break point in each case. The cmc and γ cmc values are summarized in Table 2, and cmc values ranged from 0.1 ~ 0.36 mmol/l. The longer the alkyl chain, the lower the cmc values, which is the usual effect resulting from the hydrophobicity of long chain alkyl groups. The plot of logarithm of the cmc against alkyl chain carbon number (N) of Figure 2 gave the following equation:

TABLE 1

Isoelectric Points of Surfactants[a]

Surfactant	pK_1	pK_2	pK_3	pHI_1	pHI_2
C_{12}-MEP	4.7	8.8	9.4	6.8	9.1
C_{14}-MEP	4.7	8.9	9.4	6.8	9.2
C_{16}-MEP	4.8	8.9	9.4	6.9	9.1
N-dodecyl-β-alanine[b]	5.6	8.4		7.0	
Sodium N-(2-hydroxyethyl)-N-(2-hydroxydodecyl)-β-alanine[c]	5.1	8.5		6.9	

[a] Measured in water at 20°C.
[b] Ref. (4).
[c] Ref. (7).

$$Log(cmc) = -1.75-0.14N$$

The cmc value of C_{12}-MEP was found to be much lower than that of disodium dodecyl phosphate (1) and sodium dodecyl sulfate (10). This difference might be attributed to the effect of electric neutralization by amino groups upon the negative charge of phosphoric acid groups in MEP molecules in aqueous solutions. C_{12}-MEP showed a minimum surface tension of 39 dyne/cm.

TABLE 2

Interfacial Properties of Surfactants

Surfactant	CMC mmol/l (°C)	γ cmc dyne/cm	$A \times 10^2$ nm²
C_{12}-MEP	0.36 (25°C)	39.2	51.4
C_{14}-MEP	0.20 (25°C)	38.0	59.3
C_{16}-MEP	0.10 (25°C)	37.0	79.4
Sodium dodecyl sulfate[a]	7.2 (20°C)	35.0	40
Disodium dodecyl phosphate[b]	40 (20°C)	39.5	
N-dodecyl-β-alanine[c,d]	0.9 (30°C)	~35	45
N-dodecyl-β-amino dipropionic acid[e]	0.7 (25°C)		

[a] Ref. (10).
[b] Ref. (1).
[c] Ref. (4).
[d] Ref. (11).
[e] Ref. (12).
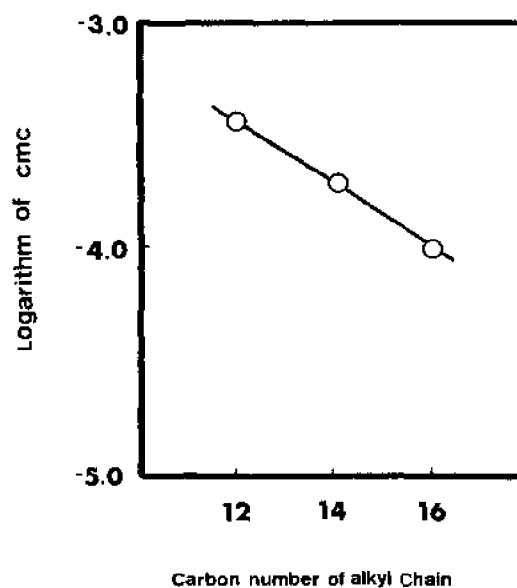

FIG. 1. Surface tension-concentration plots.

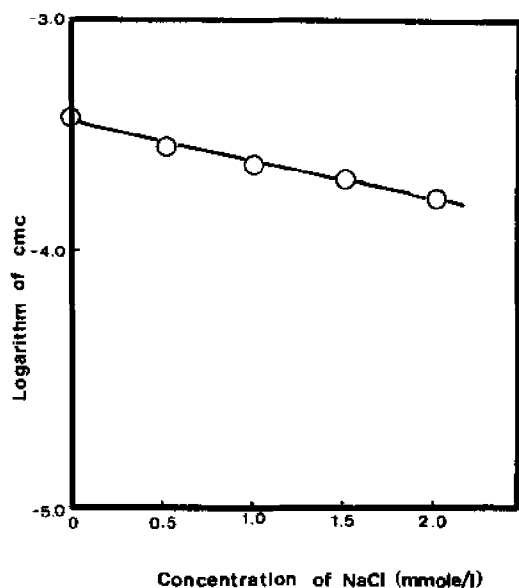FIG. 2. Plots of logarithm of cmc against the number of alkyl chain.

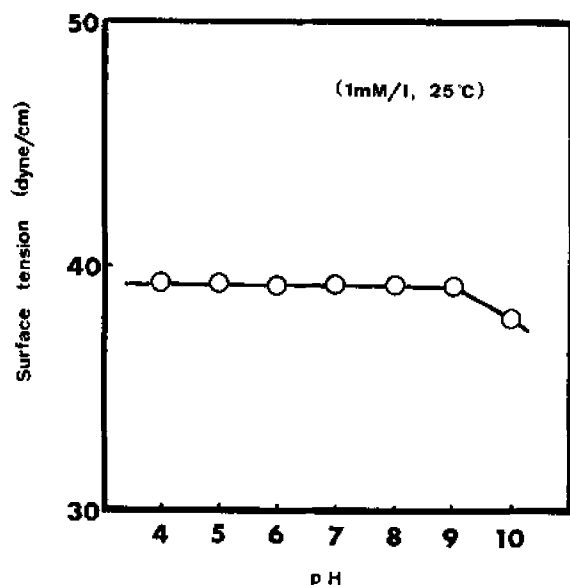FIG. 3. Effect of electrolyte (NaCl) on cmc value of C_{12}—MEP.

FIG. 5. Effect of pH on foaming power of surfactants.

FIG. 4. Effect of pH on surface tension of C_{12}-MEP.

TABLE 3

Foaming Power and Foam Stability of Surfactants

| | Foam height (mm) | | |
Surfactant	Immediately after test solutoin was dropped (A)	After standing 5 min (B)	Foam stability B/A
C_{12}-MEP	250	235	0.94
C_{14}-MEP	244	231	0.95
C_{16}-MEP	190	158	0.83
Sodium dodecanoate	255	243	0.95

The effect of electrolyte (NaCl) on cmc values of C_{12}-MEP in a nearly neutral aqueous solution (pH 6.3) is shown in Figure 3. Similar to nonionic surfactants (7), the logarithm of the cmc value decreases linearly with increasing concentration of NaCl, whereas for ionic surfactants a straight line is obtained by a logarithm-logarithm instead of semilogarithmic plot (8). This behavior is due to the zwitterionic nature of MEP in the first isoelectric region where the ionic charges in the molecule are neutralized. Therefore, MEP homologues are considered to be nonionic, as neutral electrolytes in this pH range.

Occupation area at the surface (A) was calculated from interfacial tension data using Gibbs' equation for nonionic surfactant (5) (Table 2). It should be noted that these values are comparatively large and longer alkyl chain analogues have larger A values; i.e., 51.4×10^{-2} nm² for C_{12}-MEP, 59.3×10^{-2} nm² for C_{14}-MEP and 79.4×10^{-2} nm² for C_{16}-MEP in contrast with 40×10^{-2} nm² for sodium dodecyl sulfate (9). This fact may arise from the large cross-sectional areas of phosphoric acid and amino groups. Figure 4 shows the effect of pH on surface tension of C_{12}-MEP at concentrations above the cmc value. Surface tension values fall within a narrow range from 39 to 37 dynes/cm over a wide pH range (4 ~ 10).

Foaming properties are shown in Table 3 in comparison with sodium dodecanoate (soap). Foaming property data revealed that C_{12} and C_{14}-MEP exhibited foaming power and foaming stability comparable to common anionic foaming agents. Figure 5 shows the effect of pH on foaming power of C_{12}-MEP together with those of other anionic surfactants. The foaming power of C_{12}-MEP at 40°C was within the range of 250 mm ~ 215 mm over a wide pH range due to its excellent solubility. This foaming power is superior to that of popular foaming agents,

such as sodium dodecanoate, sodium-N-lauroylglutamate and sodium dodecyl phosphate.

The amphoteric surfactants synthesized in this study, sodium 2-(N-alkyl-N-methylamino)ethanephosphates (alkyl = n-dodecyl, n-tetradecyl and n-hexadecyl) show good surface-active properties over a broad pH region (pH 4 ~ 10). These properties appear to result from the zwitterionic form present in the pH range ca. 5-9. This pH region is broader than those of amphoteric surfactants consisting of β-alanine (4,7). More detailed investigation on their characteristics as amphoteric surfactants will be presented in a future paper.

ACKNOWLEDGMENTS

REFERENCES

1. Imokawa, G., H. Tsutsumi and T. Kurosaki, *J. Am. Oil Chem. Soc. 55*:839 (1978).
2. Krupin, F., *Soap Chem. Spec. 45*:(5) 86 (1969).
3. Okamoto, Y., and H. Sakurai, *Kogyo Kagaku Zasshi 70*:52 (1967).
4. Okumura, T., K. Tajima and T. Sasaki, *Bull. Chem. Soc. Jpn. 47*:1067 (1974).
5. *Surfactants and Interfacial Phenomena*, Wiley-Interscience, New York, 1978, pp. 57-61.
6. Ross, T., and G. Miles, *Oil and Soap 18*:99 (1941).
7. Takai, M., H. Hidaka and M. Moriya, *J. Am. Oil Chem. Soc. 56*:914 (1979).
8. Shinoda, K., *Bull. Chem. Soc. Jpn. 34*:237 (1961).
9. Shinoda, K., *J. Phys. Chem. 59*:432 (1955). .
10. Nilson, G., *Ibid. 61*:1135 (1957).
11. Tokiwa, F., and K. Ohki, *Ibid. 66*:295 (1967).
12. Okumura, T., A. Nakamura, K. Tajima and T. Sasaki, *Bull. Chem. Soc. Jpn. 47*:2986 (1974).