

# New Amphoteric Surfactants Containing a Phosphoric Acid Group: I. Syntheses and Physicochemical Properties of Sodium 2-(N-2-hydroxyalkyl-N-methylamino)Ethyl Hydrogen Phosphate

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A series of new amphoteric surfactants having a phosphoric acid group, a tertiary amino group and a 2-hydroxyalkyl group, sodium 2-(N-2-hydroxyalkyl-N-methylamino)ethyl hydrogen phosphates (alkyl: n-tetradecyl, n-hexadecyl, n-octadecyl), were prepared by an addition reaction of 1,2-epoxyalkanes to N-methylaminoethanol, followed by the introduction of a phosphoric acid group and neutralization with sodium hydroxide. The structures of these compounds were confirmed by spectroscopy and elemental analysis. The solubility in solvents, Krafft point, surface tension, critical micelle concentration (CMC), occupation area of the molecule at the surface of aqueous solutions and foaming power were measured. It was shown that a 2-hydroxyethyl group in a long alkyl chain seemed to behave as a hydrophobic part.

Our previous paper described the preparation and basic physicochemical properties of the amphoteric surfactants, sodium 2-(N-alkyl-N-methylamino)ethyl hydrogen phosphates (1). One of the most important features of these surfactants is that they are very hydrophilic, because they have phosphoric acid groups and tertiary nitrogens.

Kanaya *et al.* (2) and Takai *et al.* (3) have synthesized 2-(hydroxyalkylamino)ethane sulfonic acids (2) and N-(2-hydroxyethyl)-N-(2-hydroxyalkyl)- $\beta$ -alanines (3), using 1,2-epoxyalkanes as starting materials, and evaluated their physicochemical properties. It seems that 1,2-epoxyalkanes are useful reagents for N-alkylation because of their high reactivity. When we use these reagents, the degree of contribution of a 2-hydroxyethyl group to hydrophobicity (or hydrophilicity) should be an interesting and important thesis to investigate concerning new products.

In this paper, a series of sodium 2-(N-2-hydroxyalkyl-N-methylamino)ethyl hydrogen phosphates (HMP) were synthesized, and their fundamental physicochemical properties were investigated in order to elucidate the effect of the 2-hydroxyethyl group in a long alkyl chain on surface-active properties in comparison with sodium 2-(N-alkyl-N-methylamino)ethyl hydrogen phosphates.

## EXPERIMENTAL METHODS

IR spectra were obtained with a Hitachi Model 270-30 infrared spectrometer. NMR spectra were measured with a JEOL JNM-GX270 FTNMR (270 MHz) spectrometer at 26°C or 40°C. Chemical shifts are reported in parts per million ( $\delta$ ), using tetramethylsilane as an internal standard. Mass spectra were obtained with a JEOL JMS-DX-303 mass spectrometer. Elemental analyses were performed with a Yanagimoto Micro Analyzer Model MT-3.

TLC was carried out on silica gel "Kieselgel 60" (Merck) as a stationary phase, and chloroform-methanol-water

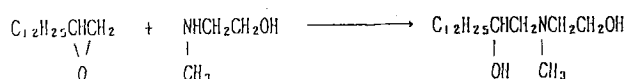
(65:25:4) as a mobile phase. Column chromatography was performed on silica gel of Wakogel C-100 (Wako Pure Chemical Industries, Ltd., Japan).

In this study, the following abbreviations are used: HMP for (N-2-hydroxyalkyl-N-methylamino)ethyl hydrogen phosphate; the notations, C<sub>14</sub>-, C<sub>16</sub>- and C<sub>18</sub>- in front of the abbreviations denote, respectively, the carbon numbers, 14, 16 and 18 in the long chain 2-hydroxyalkyl group. For example, C<sub>14</sub>-HMP presents sodium 2-(N-2-hydroxytetradecyl-N-methylamino)ethyl hydrogen phosphate.

*Synthesis of (N-2-hydroxytetradecyl-N-methylamino)-1-hydroxyethane (C<sub>14</sub>-HM).* C<sub>14</sub>-HM was prepared by combining 1,2-epoxytetradecane (170 g, 0.8 mole) and 2-methylaminoethanol (60 g, 0.8 mole) at 120°C for 8 hr with stirring (Scheme 1). The crude product was purified by vacuum distillation to yield C<sub>14</sub>-HM as a colorless liquid, 244 g yield, 85%, bp 180~185°C/1 mm. IR (neat): 3416, 2928, 2856, 1463, 1364, 1294, 1076, 1040, 944, 874, 794 cm<sup>-1</sup>; <sup>1</sup>H-NMR(CD<sub>3</sub>OD,  $\delta$ ): 0.89 (3H, t, CH<sub>3</sub>(CH<sub>2</sub>)<sub>11</sub>-), 1.29-1.39 (22H, m, CH<sub>2</sub>(CH<sub>2</sub>)<sub>11</sub>-), 2.29 (3H, s, NCH<sub>3</sub>), 2.33 (2H, t, CH<sub>2</sub>N), 2.55 (2H, t, NCH<sub>2</sub>), 3.59 (2H, t, CH<sub>2</sub>OH), 3.64 (1H, t, CHOH); <sup>13</sup>C-NMR(CD<sub>3</sub>OD,  $\delta$ ): 14.31 (CH<sub>3</sub>), 23.34 (CH<sub>2</sub>), 26.34 (CH<sub>2</sub>), 30.07 ~ 30.51 (CH<sub>2</sub>), 32.64 (CH<sub>2</sub>), 35.87 (CH<sub>2</sub>), 42.76 (NCH<sub>3</sub>), 59.63 (NCH<sub>2</sub>), 60.51 (NCH<sub>2</sub>), 65.10 (CH<sub>2</sub>OH), 68.64 (CHOH); MS (70 eV) *m/z* (rel int %) 287 (M<sup>+</sup>, 20), 256 (100); Analysis calculated for C<sub>17</sub>H<sub>37</sub>N<sub>1</sub>O<sub>2</sub>: C, 71.02; H, 12.97; N, 4.87, Found: C, 70.88; H, 13.19; N, 4.80.

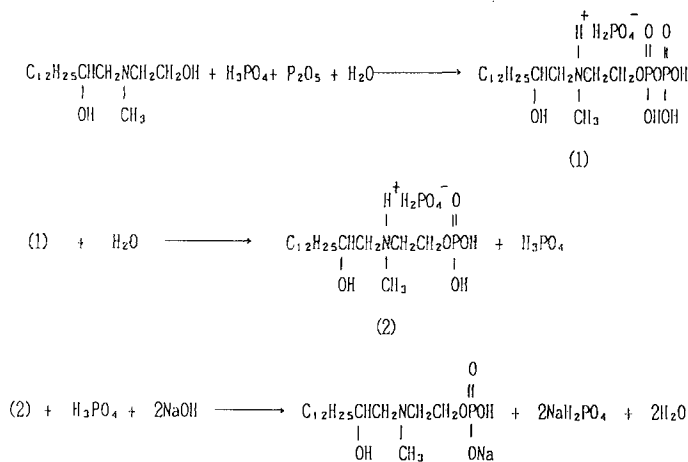
C<sub>16</sub>-HM and C<sub>18</sub>-HM were prepared by a similar procedure, and their spectral data and their elemental analysis data were consistent with expected structures.

*Synthesis of sodium 2-(N-2-hydroxytetradecyl-N-methylamino)ethyl hydrogen phosphate (C<sub>14</sub>-HMP).* C<sub>14</sub>-HMP was synthesized from C<sub>14</sub>-HM as shown in Scheme 2. C<sub>14</sub>-HM (14.4 g, 0.05 mole) and 85% H<sub>3</sub>PO<sub>4</sub> (6.3 g, 0.05 mole) were mixed in tetrahydrofuran (200 mL) and stirred for 20 min at room temperature followed by gradual addition of diphosphorous pentoxide (9.9 g, 0.07 mole). After dissolving the diphosphorous pentoxide by stirring it at room temperature, the solution was refluxed for 8 hr with stirring. The reaction mixture was cooled to room temperature, water (1.8 g, 0.10 mole) was added and the mixture was stirred for 30 min. Sodium hydroxide (7.6 g, 0.19 mole) was then added and the mixture was stirred for 20 min. After removal of solvent, the residue was washed repeatedly with hot ethanol with a Soxhlet-extraction apparatus. A crude product was obtained upon evaporation of the ethanol. This product was purified by



SCHEME 1. Preparation of (N-2-hydroxyalkyl-N-methylamino)-1-hydroxyethane (alkyl:tetradecyl).

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**SCHEME 2.** Preparation of sodium 2-(N-2-hydroxyalkyl-N-methylamino) ethyl hydrogen phosphate (alkyl:tetradecyl).

column chromatography using ethanol-water (1:1, v/v) as an eluent resulting in 14 g of sodium 2-(N-2-hydroxytetradecyl-N-methylamino)ethyl hydrogen phosphate. The compound showed one spot on TLC (Rf: 0.72), yield 70%: IR: 3248, 2924, 2852, 1464, 1376, 1178, 1074, 926, 754  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CD}_3\text{OD}$ ,  $\delta$ ): 0.87 (3H, t,  $\text{CH}_3(\text{CH}_2)_{10}$ ), 1.29–1.76 (20H, m,  $\text{CH}_3(\text{CH}_2)_{10}$ ), 2.88 (3H, s,  $\text{NCH}_3$ ), 3.13 (2H, t,  $\text{CH}_2\text{N}$ ), 3.34 (2H, t,  $\text{CH}_2\text{N}$ ), 4.18 (2H, t,  $\text{CH}_2\text{O}$ ), 4.94 (1H, s,  $\text{OH}$ );  $^{13}\text{C-NMR}$  ( $\text{CD}_3\text{OD}$ ,  $\delta$ ): 14.39 ( $\text{CH}_3$ ), 23.64 ( $\text{CH}_2$ ), 26.31 ( $\text{CH}_2$ ), 30.38 ~ 30.72 ( $\text{CH}_2$ ), 32.99 ( $\text{CH}_2$ ), 36.39 ( $\text{CH}_2$ ), 41.97 ( $\text{NCH}_3$ ), 58.59 ( $\text{NCH}_2$ ), 60.08 ( $\text{CH}_2\text{N}$ ), 63.17 ( $\text{CH}_2\text{O}$ ), 66.68 ( $\text{CHO}$ ); Analysis calculated for  $\text{C}_{17}\text{H}_{37}\text{N}_1\text{O}_5\text{P}_1\text{Na}_1$ : C, 52.43; H, 9.58; N, 3.60. Found: C, 52.54; H, 9.73; N, 3.53.

This surfactant is expected to have good stability, and indeed samples (35% aqueous solution) kept for a long period showed no pH change.

Other HMP homologues,  $\text{C}_{16}$ -HMP and  $\text{C}_{18}$ -HMP, were prepared by similar procedures and showed one spot on TLC; yields and analytical data are as follows:  $\text{C}_{16}$ -HMP: yields 70%; IR (neat): 3280, 2928, 2852, 1462, 1378, 1212, 1160, 932  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CD}_3\text{OD}$ ,  $\delta$ , 26°C): 0.90 (3H, t,  $\text{CH}_3(\text{CH}_2)_{10}$ ), 1.28–1.49 (20H, m,  $\text{CH}_3(\text{CH}_2)_{10}$ ), 2.97 (3H, s,  $\text{NCH}_3$ ), 3.17 (2H, t,  $\text{CH}_2\text{N}$ ), 3.43 (2H, t,  $\text{CH}_2\text{N}$ ), 4.18 (2H, t,  $\text{CH}_2\text{O}$ ), 5.08 (1H, s,  $\text{OH}$ );  $^{13}\text{C-NMR}$  ( $\text{CD}_3\text{OD}$ ,  $\delta$ ): 14.46 ( $\text{CH}_3$ ), 23.67 ( $\text{CH}_2$ ), 26.34 ( $\text{CH}_2$ ), 30.41~30.76 ( $\text{CH}_2$ ), 33.01 ( $\text{CH}_2$ ), 36.33 ( $\text{CH}_2$ ), 41.81 ( $\text{NCH}_3$ ), 58.49 ( $\text{NCH}_2$ ), 60.04 ( $\text{CH}_2\text{N}$ ), 63.01 ( $\text{CH}_2\text{O}$ ), 66.56 ( $\text{CHO}$ ); Analysis calculated for  $\text{C}_{17}\text{H}_{41}\text{N}_1\text{O}_5\text{P}_1\text{Na}_1$ : C, 54.66; H, 9.90; N, 3.35. Found: C, 54.79; H, 9.99; N, 3.40.

$\text{C}_{18}$ -HMP: yields 65%; IR (neat): 3296, 2916, 2848, 1460, 1380, 1202, 932  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CD}_3\text{OD}$ ,  $\delta$ , 26°C): 0.90 (3H, t,  $\text{CH}_3(\text{CH}_2)_{10}$ ), 1.28–1.49 (20H, m,  $\text{CH}_3(\text{CH}_2)_{10}$ ), 2.97 (3H, s,  $\text{NCH}_3$ ), 3.17 (2H, t,  $\text{CH}_2\text{N}$ ), 3.43 (2H, t,  $\text{CH}_2\text{N}$ ), 4.18 (2H, t,  $\text{CH}_2\text{O}$ ), 4.83 (1H, s,  $\text{OH}$ );  $^{13}\text{C-NMR}$  ( $\text{CD}_3\text{OD}$ ,  $\delta$ ): 14.41 ( $\text{CH}_3$ ), 23.66 ( $\text{CH}_2$ ), 26.30 ( $\text{CH}_2$ ), 30.40 ~ 30.74 ( $\text{CH}_2$ ), 33.02 ( $\text{CH}_2$ ), 36.41 ( $\text{CH}_2$ ), 42.00 ( $\text{NCH}_3$ ), 58.72 ( $\text{NCH}_2$ ), 60.13 ( $\text{CH}_2\text{N}$ ), 63.19 ( $\text{CH}_2\text{O}$ ), 66.70 ( $\text{CHO}$ ); Analysis calculated for  $\text{C}_{19}\text{H}_{45}\text{N}_1\text{O}_5\text{P}_1\text{Na}_1$ : C, 56.61; H, 10.18; N, 3.14. Found: C, 56.74; H, 10.27; N, 3.12.

*Measurements of physicochemical properties.* Krafft point was estimated from the temperature at which an

abrupt change in electric conductivity occurred. Isoelectric points (pHI) were determined by potentiometry, as described previously (1). The acid dissociation constant  $\text{pK}_1$  and the base constant at  $\text{pK}_2$  and  $\text{pK}_3$  were determined from three minima values on the differential curves and the values of  $\text{pHI}_1$  and  $\text{pHI}_2$  calculated by the relationship  $\text{pHI}_1 = (\text{pK}_1 - \text{pK}_2)/2$  and  $\text{pHI}_2 = (\text{pK}_2 + \text{pK}_3)/2$  (4), respectively.

With respect to the aqueous solution of the compounds, surface tension was measured at 25°C with a du Nöuy autotensiometer (Model 6801ES, RIGOSHA & CO. LTD, Japan) at concentrations from  $10^{-5}$  to  $10^{-2}$  mole/L. The surface tension-concentration plots were used to determine critical micelle concentration (CMC, break points), surface tension lowering ability ( $\gamma$  CMC, surface tension at CMC) and occupation area of the molecule at the surface ( $A$   $\text{nm}^2$ , from surface excess concentration calculated with Gibb's equation (5)). Foaming properties were measured according to the Ross and Miles method at 40°C (6). Foaming height (mm) was recorded immediately (A) after dropping the test sample and after standing for 5 min (B). Foam stability was calculated as the ratio of B to A.

## RESULTS AND DISCUSSION

### *Physicochemical properties of aqueous solution of HMP.*

HMP-homologues in this study were all white crystals. Their Krafft points were below zero. This result shows that these compounds are very strongly hydrophilic, because they have tertiary nitrogens and phosphoric acid groups in their molecules. Therefore, clear water solutions can be obtained at room temperature. The pH values of these aqueous solutions (0.1 wt%) were approx. 6.5. This might be attributed to hydroxyl group in the phosphoric acid group.

As for the solubility in organic solvents, these are soluble in ethanol and methanol but are almost insoluble in benzene, chloroform and acetone.

The results of potentiometric titrations with the pH values of their aqueous solutions are shown in Table 1. The differential curves indicate three maxima, which are due to the formation of quaternary ammonium salt from tertiary amine (protonated HMP cation) and to neutralization of phosphate group.

The three minima of the curves correspond to  $\text{pK}_1$  (4.7~4.8),  $\text{pK}_2$  (8.0) and  $\text{pK}_3$  (9.2~9.3). The isoelectric

**TABLE 1**

### Isoelectric Points of Surfactants\*

Surfactant	$\text{pK}_1$	$\text{pK}_2$	$\text{pK}_3$	$\text{pHI}_1$	$\text{pHI}_2$
$\text{C}_{14}$ -HMP	4.8	8.0	9.2	6.4	8.6
$\text{C}_{16}$ -HMP	4.7	8.0	9.3	6.4	8.7
$\text{C}_{18}$ -HMP	4.8	8.0	9.2	6.4	8.6
$\text{C}_{12}$ -MEP <sup>a</sup>	4.7	8.8	9.4	6.8	9.1
Sodium N-(2)hydroxyethyl-N-(2-hydroxydodecyl)- $\beta$ -alanine <sup>b</sup>	5.1	8.5		6.9	

\* Measured in water at 20°C.

<sup>a</sup> Reference (1).

<sup>b</sup> Reference (7).

## PHOSPHATE TYPE OF AMPHOTERICS

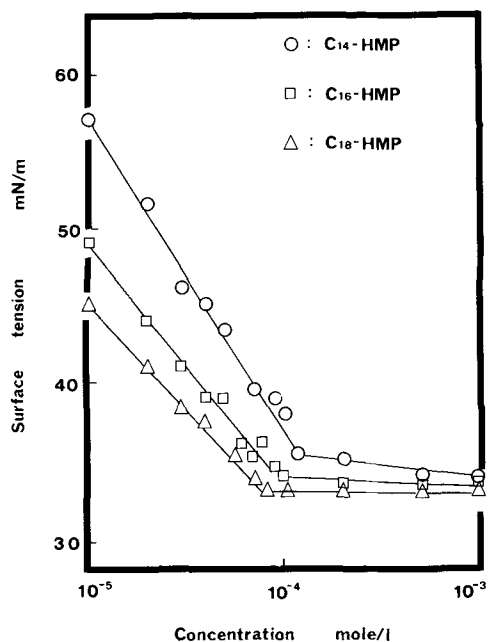


FIG. 1. Surface tension-concentration plot.

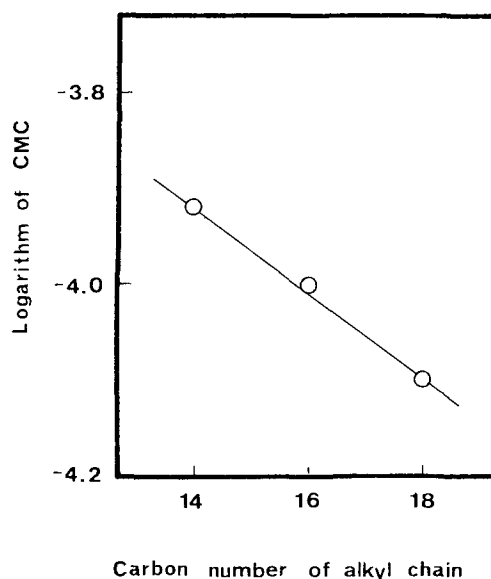


FIG. 2. Plots of logarithm of CMC against carbon number of alkyl chain.

TABLE 2

## Interfacial Properties of Surfactants

Surfactant	CMC mmole/L (°C)	$\gamma$ cmc mN/m	$A \times 10^2$ nm <sup>2</sup>
C <sub>14</sub> -HMP	0.12 (25)	35.5	47.5
C <sub>16</sub> -HMP	0.10 (25)	34.0	63.4
C <sub>18</sub> -HMP	0.08 (25)	33.0	71.5
C <sub>12</sub> -MEP <sup>a</sup>	0.36 (25)	39.2	51.4
C <sub>14</sub> -MEP <sup>a</sup>	0.20 (25)	38.0	59.4
C <sub>16</sub> -MEP <sup>a</sup>	0.10 (25)	37.0	79.4
N-dodecyl- $\beta$ -alanine <sup>b</sup>	0.9 (30)	35	45
Sodium dodecyl sulfate <sup>c</sup>	7.2 (20)	35.0	40

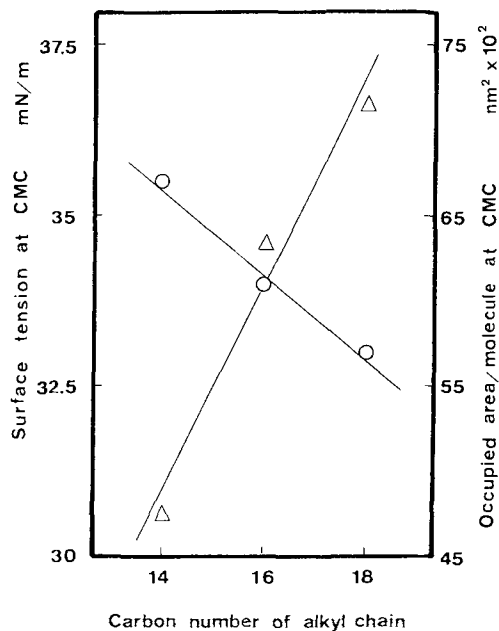
<sup>a</sup> Reference (1).<sup>b</sup> Reference (8).<sup>c</sup> Reference (9).

points of HMP-homologues, firstly, occurred at pH 6.4. The pH values of their aqueous solutions were nearly equivalent to the isoelectric points. Therefore, HMP is considered to be a zwitterion in the range of pH 4.7~8.0.

The formation of micelles was demonstrated by the presence of break points in the surface tension-log concentration plots for aqueous solution of HMP-homologues at pH 6.5 as shown in Figure 1. Their CMC and  $\gamma$  CMC values are summarized in Table 2, and CMC values are approx. 0.1 mmole/L. The longer the alkyl chain, the lower the CMC values from 0.12 mmole/L to 0.08 mmole/L. The relation of logarithm of the CMC values against the number (N) of carbon in alkyl chain is shown in Figure 2. The relation gave the following equation:

$$\text{Log}(\text{CMC}) = -3.38 - 0.045 N$$

The CMC values of HMP-homologues were found to be lower than those of corresponding sodium 2-(N-alkyl-N-

FIG. 3. Plots of surface tension (O) and occupied area per molecule at interface ( $\Delta$ ) against carbon number of alkyl chain.

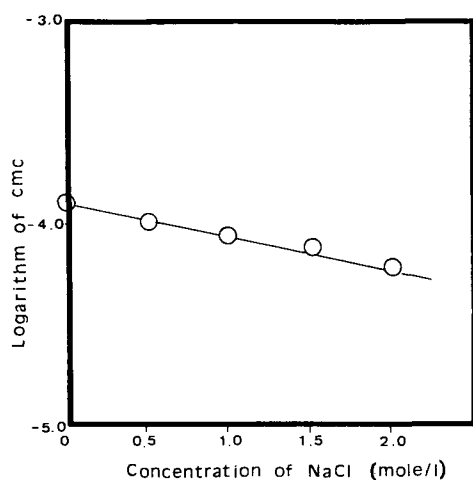
methylamino)ethyl hydrogen phosphates (1). This means that the 2-hydroxyethyl group in a long chain alkyl group has hydrophobic characteristics rather than hydrophilic. C<sub>18</sub>-HMP showed a minimum surface tension of 33.0 mN/m (Fig. 3).

The effect of electrolyte (NaCl) on CMC values (10) of C<sub>14</sub>-HMP in a nearly neutral aqueous solution (pH 6.5) is shown in Figure 4, representing the zwitterionic character. Thus, HMP homologues are considered to be nonionic at this pH. Occupation areas per molecule at the

**TABLE 3**  
**Foaming Power and Foam Stability of Surfactants**

Surfactant	Foam height (mm)		Foam stability (B/A)
	Immediately after the test solution was dropped (A)	After standing for 5 min (B)	
C <sub>14</sub> -HMP	250	245	0.98
C <sub>16</sub> -HMP	185	155	0.84
C <sub>18</sub> -HMP	152	110	0.72
C <sub>12</sub> -MEP <sup>a</sup>	250	235	0.94
Sodium dodecanoate	255	243	0.94

<sup>a</sup>Reference (1).



**FIG. 4.** Effect of electrolyte (NaCl) on CMC of C<sub>14</sub>-HMP.

air/water interface (A) were  $47.5 \times 10^{-2} \text{ nm}^2$  for C<sub>14</sub>-HMP,  $63.4 \times 10^{-2} \text{ nm}^2$  for C<sub>16</sub>-HMP and  $71.5 \times 10^{-2} \text{ nm}^2$  for C<sub>18</sub>-HMP, which was estimated by applying the Gibb's adsorption equation to the straight line immediately prior to the CMC as in the case of our previous study (1) (Table 2). These values increased linearly with the increase in the number of carbon atoms in the hydrophobic group (Fig. 2). This implies that adsorption of HMP molecules at the air/water interface is governed by steric factor of hydrophobic group. In addition, HMP homologues seemed to have conditions of more rigid adsorption at the interface than corresponding homologues of sodium 2-(N-alkyl-N-methylamino)ethyl hydrogen phosphates.

Foaming properties of HMP-homologues are shown in Table 3 in comparison with sodium dodecanoate (soap) and sodium 2-(N-dodecyl-N-methylamino) ethyl hydrogen phosphate (C<sub>12</sub>-MEP). The foaming power and foaming stability of C<sub>14</sub>-HMP, which was similar to those of soap, were superior to those of other homologues in this study. The foaming power of C<sub>14</sub>-HMP at 40°C was within the range of 250 mm ~ 220 mm over a wide pH range.

Moreover, as a result of investigations of the effects of pH on surface tension, it was found that they are almost constant in a broad pH range (4~10).

In addition, recently, Masuyama *et al.* (11) have reported that cyanoethyl group seemed to behave like a hydrophobic part. It is interesting that our studies have shown that even a hydroxyethyl group also seems to contribute as a hydrophobic part.

#### REFERENCES

1. Tsubone, K., N. Uchida, H. Niwase and K. Honda, *J. Am. Oil Chem. Soc.* 66:829 (1989).
2. Kanaya, F., T. Tanaka, S. Nakano and K. Negoro, *Nippon Kagaku Kaishi* 1982:824.
3. Takai, M., H. Hidaka and M. Moriya, *J. Am. Oil Chem. Soc.* 56:537 (1979).
4. Okumura, T., K. Tajima and T. Sasaki, *Bull. Chem. Soc. Jap.* 47:1067 (1974).
5. Rosen, M., *Surfactants and Interfacial Phenomena*, Wiley-Interscience, New York, 1978, pp. 57-61.
6. Ross, T., and G. Miles, *Oil Soap Specialties* 18:99 (1974).
7. Takai, M., H. Hidaka and M. Moriya, *J. Am. Oil Chem. Soc.* 56:914 (1979).
8. Tokiwa, F., and K. Ohki, *J. Phys. Chem.* 66:295 (1967).
9. Nilson, G., *Ibid.* 61:1135 (1957).
10. Mukerjee, P., *Ibid.* 69:4038 (1965).
11. Masuyama, A., T. Okuno and M. Okahara, *J. Am. Oil Chem. Soc.* 65:1830 (1987).

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