✣New Amphoteric Surfactants Derived from Lysine. I. Preparation and Properties of N^{ϵ}-Acyllysine Derivatives

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ABSTRACT

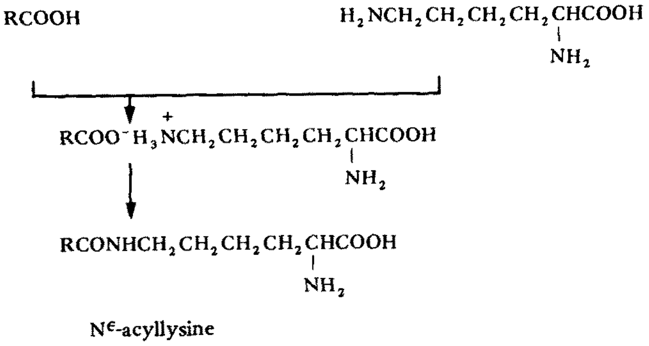
New amphoteric surfactants were prepared from N^{ϵ}-acyllysine which was obtained by the thermal dehydration of a higher fatty acid salt of lysine and was not soluble in water. N^{α},N^{α}-dimethyl-N^{ϵ}-acyllysine was prepared by the catalytic reductive condensation of N^{ϵ}-acyllysine ester with formaldehyde in good yield. N^{α},N^{α},N^{α}-trimethyl-N^{ϵ}-acyllysine was obtained from the reaction of N^{α},N^{α}-dimethyl-N^{ϵ}-acyllysine ester with methyl iodide. Confirmation of the structure of these derivatives was obtained by spectrometric and spectroscopic analyses.

The solubility of N^{ϵ}-acyllysine was improved significantly by the introduction of N^{α}-methyl groups. Physicochemical and surface active properties of the derivatives were investigated in terms of isoelectric points, dissolution temperatures, surface tensions, critical micelle concentrations (cmc), foaming properties and wetting powers. N^{α},N^{α},N^{α}-trimethyl-N^{ϵ}-acyllysine had lower dissolution temperatures than N^{α},N^{α}-dimethyl-N^{ϵ}-acyllysine. The latter showed lower surface tensions than the former at cmc. N^{α},N^{α}-dimethyl-N^{ϵ}-lauroyllysine was best in wetting power and foaming property.

INTRODUCTION

Amino acids are not only essential components of a living body but also interesting raw materials for surfactants. The presence of anionic and cationic moieties in the molecule of an amino acid makes it possible to prepare various kinds of surfactants by introducing a hydrophobic group into the molecule. The first research on introduction of a hydrophobic group was done by Bondi in 1909 to obtain N-acylglycine and N-acylalanine (1), which were anionic surfactants. A lot of N-acylamino acids were prepared and investigated by Abderhalden and Funk (2), Izar (3), Karrer (4), Staudinger and Becker (5), Naudet (6), Tsubone (7), Heitmann (8), Kester (9), Fieser (10), Komatsu (11), Takehara (12) and others. These N-acylamino acids also were anionic surfactants.

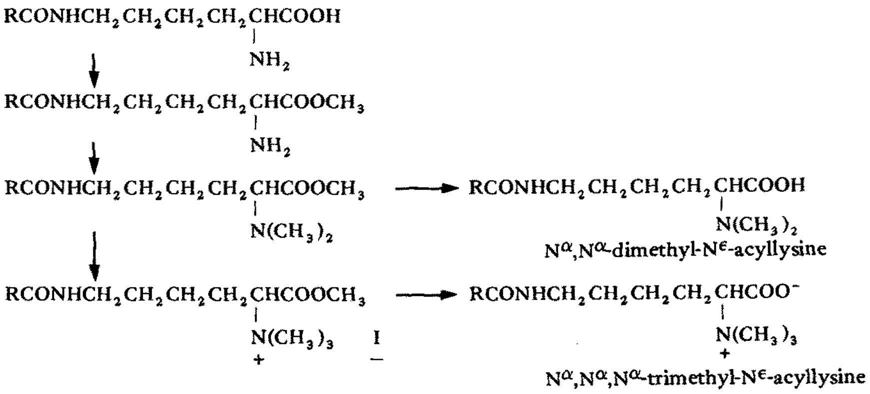
Studies on amphoteric surfactants derived from amino acids are rather few. In general, N-alkylation of amino groups has been adopted to prepare such surfactants (13, 14). Marumo obtained N-2-hydroxyalkylglutamic acid by the reaction of glutamic acid with 1,2-epoxyalkane (15). As to a basic amino acid, selective acylation of one of its basic amino groups is another way to prepare an amphoteric surfactant. Vogler prepared N^{ϵ}-acyllysine by acylating a copper complex of lysine with an acid halide (16). Takizawa obtained the same compound by a simple and unique method, in which neither acid halide nor protective treatment of lysine were needed in the selective mono-acylation of ε-amino group (17). Only the thermal dehydration of a fatty acid salt of lysine was necessary. The scheme is as follows:



SCHEME 1

However, the N^{ϵ}-acyllysine obtained was hardly soluble in water. It was regarded as a hydrophobic amino acid. Addition of ethylene oxide was tried to make N^{ϵ}-acyllysine soluble (18).

In this study, methylation of the α-amino group of N^{ϵ}-acyllysine was attempted to enhance solubility in water. N^{α},N^{α}-dimethyl and N^{α},N^{α},N^{α}-trimethyl derivatives of N^{ϵ}-acyllysine were prepared according to the following scheme:



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The solubility of N$^{\epsilon}$-acyllysine was improved significantly by the introduction of methyl groups into its α-amino group. These derivatives of N$^{\epsilon}$-acyllysine were confirmed in their structures and investigated on their physicochemical and surface-active properties.

EXPERIMENTAL PROCEDURES

Materials

N$^{\epsilon}$-acyllysine was prepared from DL-lysine by the procedure of Takizawa et al. (17).

Preparation of N$^{\epsilon}$-acyllysine Methyl Ester

N$^{\epsilon}$-lauroyllysine methyl ester (90 g) was prepared by the esterification of N$^{\epsilon}$-lauroyllysine (100 g) in methanol with sulfuric acid as catalyst and subsequent neutralization with sodium carbonate. The ester was recrystallized from a mixture of one part ethyl acetate and five parts petroleum ether.

Synthesis of N$^{\alpha}$,N$^{\alpha}$-dimethyl-N$^{\epsilon}$-acyllysine

N$^{\epsilon}$-lauroyllysine methyl ester (46.2 g, 0.135 mol) dissolved in 105 ml of methanol was reacted with formaldehyde (43.8 g, as 37% aqueous solution) and hydrogen (100 kg/cm^2) in a 300 ml volume autoclave in the presence of 10% palladium charcoal (6.75 g) at 30 C. The reaction was completed in ca three hr. The reaction mixture was filtered and concentrated into syrup under reduced pressure. The resulting syrup was cooled overnight to yield crystalline DMLL methyl ester (49.2 g, 98.3%).

The ester (15 g) was dissolved in 105 ml of methanol, and 81 ml of 1 N sodium hydroxide was added to hydrolyze it. Then the hydrolysis product was neutralized with 40.5 ml of 2 N hydrochloric acid concentrated (a small amount of n-butanol was added to prevent foaming) and dried under vacuum. Methanol (25 ml) was added to the product, and insolubles were removed by filtration. Then 150 ml of acetone was added slowly to the filtrate to yield 11.3 g of crystalline N$^{\alpha}$,N$^{\alpha}$-dimethyl-N$^{\epsilon}$-lauroyllysine (DMLL) (78.1%).

Synthesis of N$^{\alpha}$,N$^{\alpha}$,N$^{\alpha}$-trimethyl-N$^{\epsilon}$-acyllysine

DMLL methyl ester (10.0 g, 0.027 mol) was dissolved in 50 ml of methanol. Methyl iodide (7.7 g, 0.054 mol) was added to the solution drop by drop, reacted for three hr at room temperature and heated another two hr at 55 C. The mixture was concentrated and dried under vacuum, then recrystallized from a mixture of 30 ml methanol and 165 ml ether to yield yellowish crystalline N$^{\alpha}$,N$^{\alpha}$,N$^{\alpha}$-trimethyl-N$^{\epsilon}$-lauroyllysine (TMLL) methyl ester iodide (13.4 g, 96.8%).

This ester compound (12.3 g) was dissolved in 50 ml of methanol and hydrolyzed with 72.3 ml of 1 N sodium hydroxide at 60 C for 4 hr. The hydrolysis product was treated with strong cation-exchange resin using 2,000 ml of 3 N ammonia solution as an eluent. The eluate was condensed and dried, and the residue was crystallized from a mixed solvent of 20 ml methanol and 300 ml ether to yield crystalline TMLL (7.62 g, 85.4%).

PHYSICAL AND SURFACE ACTIVE PROPERTIES

Detection of Contained Water

Water content was measured with a Kyoto Electronics MK-AII Karl Fischer moisture meter. A release of the contained water by heating was observed with a Rigaku Thermoflex TG-DSC differential scanning calorimeter.

IR, NMR and Mass Spectrometric Analyses

Infrared spectra were obtained with a Digilab FTS-15E FT-IR spectrometer. Nuclear magnetic resonance spectra were run in CD_3OD on a JEOL GX-400 FT-NMR spectrometer (^{1}H, 400 MHz) with trimethylsilane (TMS) as the internal standard. Mass spectra were obtained with a JEOL JMS-DX300 mass spectrometer.

Isoelectric Points

A sample was dissolved at a concentration of 1.0×10^{-2} mol/l and titrated with 0.01 N HCl or 0.01 N NaOH. The pH was measured after each incremental addition of acid or base to give the titration curve for each derivative, from which the isoelectric point pI was determined.

Dissolution Temperatures

Dissolution temperatures were measured on isoelectric points at the concentration of 1×10^{-2} mol/l. The test samples initially were dissolved completely by heating. Then they were cooled to produce hydrated solids. Finally the test mixtures were warmed at a rate of 0.3-0.5 C/min with gentle agitation. Dissolution temperatures were determined from optical observation. When a liquid crystal phase appeared, the temperature at which double refraction in polarized light disappeared was regarded as the dissolution temperature. The reproducibility of each temperature was within ±0.2 C.

Surface Tensions and Critical Micelle Concentrations

Surface tensions were measured by Wilhelmy's vertical plate method with a Kyowa Kagaku A-3 tensiometer at various concentrations on the isoelectric points. N$^{\alpha}$,N$^{\alpha}$-dimethyl-N$^{\epsilon}$-palmitoyllysine (DMPL) was measured at 60 C and the others at 40 C. The cmc values were determined from the curves of surface tensions vs log concentrations.

Foaming Property

Foaming property was measured according to the Ross-Miles method (19). The foam heights of the derivatives of N$^{\epsilon}$-acyllysine were measured at concentrations of 0.025%, 0.1% and 0.25% at 40 C (except DMPL at 60 C).

Wetting Power

Wetting power of the derivatives of N$^{\epsilon}$-acyllysine was determined by a horizontal semimicro felt disk method (20). Each 50 ml of aqueous solution of a derivative of N$^{\epsilon}$-acyllysine was added to a beaker (42 mmϕ × 60 mm^h). A felt disk (Nikke's roller cloth 20 oz, 1 inch ϕ, 2 mm thick) was immersed in the solution with an inverted gooch filter funnel (34 mmϕ), and then it began to sink due to the permeation of the solution. Wetting time was established as the time elapsed between immersion and the beginning of sinking. A shorter time represents higher wetting power.

RESULTS AND DISCUSSION

Elemental analyses for the derivatives of N$^{\epsilon}$-acyllysine are shown in Table I. Each derivative was dried under vacuum at 80 C for eight hr, then submitted to the analysis. The experimental values for DMLL and DMPL were in good agreement with the calculated ones. Those of TMLL and TMPL, however, were not. The disagreement was due to water contained in TMLL and TMPL. A peak of thermal absorption derived from water release was observed above 100 C for TMLL and N$^{\alpha}$,N$^{\alpha}$,N$^{\alpha}$-trimethyl-N$^{\epsilon}$-palmitoyllysine (TMPL) (Fig. 1), whereas none was observed for DMLL and DMPL. The peak suggests that the contained

TABLE I

Elemental Analyses Result of N$^{\epsilon}$-acyllysine Derivatives

	Calculated			Found		
	C	H	N	C	H	N
DMLL calc for $C_{20}H_{40}N_2O_3$	67.37	11.37	7.86	67.00	11.42	7.86
DMPL calc for $C_{24}H_{48}N_2O_3$	69.85	11.73	6.79	69.70	11.59	6.83
TMLL calc for $C_{21}H_{42}N_2O_3$	68.07	11.42	7.56	66.19	11.32	7.30
	(66.36	11.42	7.37)			
TMPL calc for $C_{25}H_{50}N_2O_3$	70.37	11.81	6.57	68.57	11.94	6.42
	(68.89	11.80	6.43)			

Numbers in parentheses are corrected values according to water content.
2.5 wt% water in TMLL, and 2.1 wt% water in TMPL.

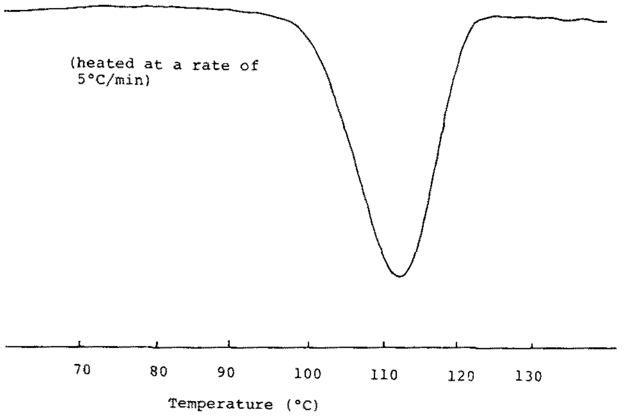

FIG. 1. A peak of thermal absorption observed for TMLL by DSC. The same peak was observed for TMPL.

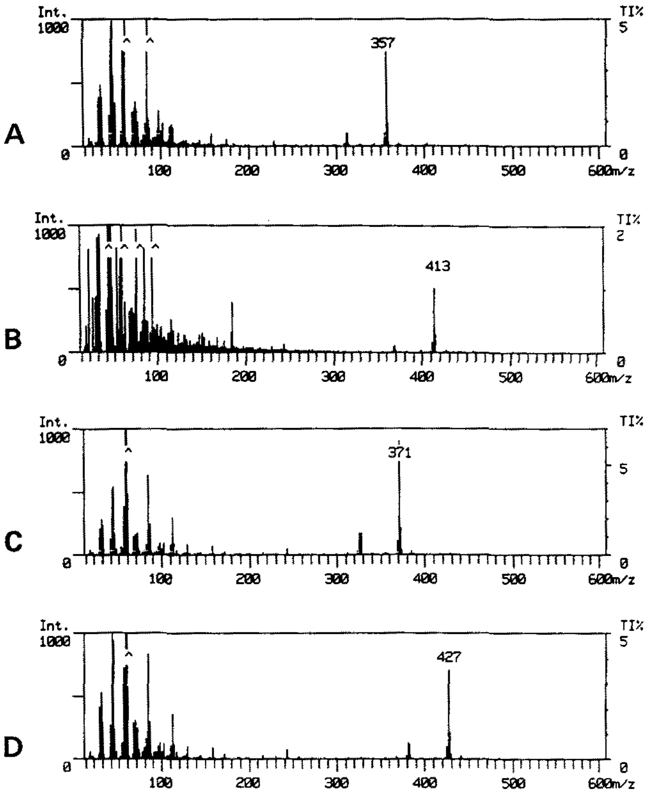

FIG. 2. A. Mass spectrum of DMLL. B. Mass spectrum of DMPL. C. Mass spectrum of TMLL. D. Mass spectrum of TMPL.

water was not adsorbed but bound water. The content of water was 2.5 wt% for TMLL and 2.1 wt% for TMPL. Corrected values, based on the water content and presented in parentheses, are in good agreement with the experimental values.

Mass, IR and NMR spectroscopic analyses were conducted to confirm the structure of the compounds. Figures 2a through 2d show the mass spectroscopic analyses. DMLL, DMPL, TMLL and TMPL displayed their molecular ion peaks as expected from their calculated molecular weights of 356, 412, 370 and 426, respectively. The existence of amide bonding in their molecules was confirmed by the IR spectrum band at 1645 cm^{-1}. Further confirmation of their structures was obtained from NMR spectroscopic analysis. The characteristic signal of N$^{\alpha}$,N$^{\alpha}$-dimethyl derivatives was observed at δ 2.85 ppm, whereas that of N$^{\alpha}$,N$^{\alpha}$,N$^{\alpha}$-trimethyl derivatives was observed at δ 3.18 ppm, right on the signal of the protons of ϵ-methylene units. These characteristic signals were attributed to the protons of methyl groups combined to α-nitrogen.

The titration curves of the derivatives are shown in Figure 3, and the pI values are listed in Table II. A shorter acyl group and a higher degree of N$^{\alpha}$-methylation resulted in higher pI values.

The dissolution temperature of N$^{\epsilon}$-acyllysine, which did not dissolve in water even at 100 C, was lowered greatly by the introduction of N$^{\alpha}$-methyl groups. The lowering effect was greater in N$^{\alpha}$,N$^{\alpha}$,N$^{\alpha}$-trimethyl derivatives than in N$^{\alpha}$,N$^{\alpha}$-dimethyl ones, as shown in Table II. TMPL was observed to show a simple change from a hydrated solid

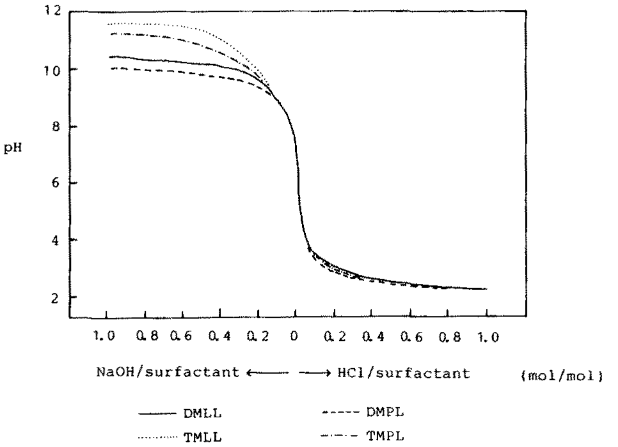

FIG. 3. Titration curves of N$^{\epsilon}$-acyllysine derivatives. ——, DMLL; - - - -, DMPL; . . . ., TMLL, and -·-·-·-, TMPL.

TABLE II

Solution Properties of N^{ϵ}-acyllysine Derivatives

	pI	Dissolution temperature (C)	cmc (mol/l) X 10^4	γ cmc (dyn/cm)
DMLL	6.3	39.4	7.0	33.3
DMPL	6.2	56.5	0.08	29.9
TMLL	6.8	0	8.9	38.4
TMPL	6.5	14.8	0.15	35.5

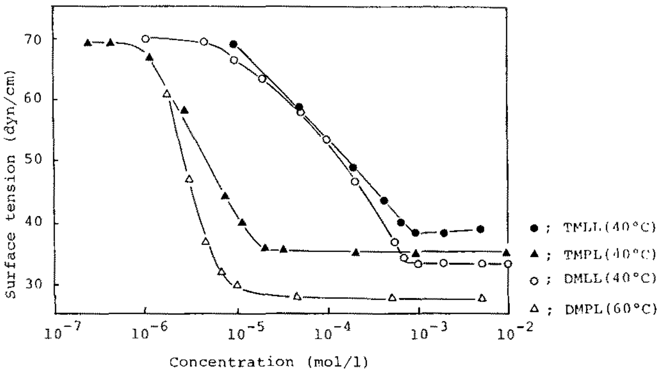

FIG. 4. Surface tension of N^{ϵ}-acyllysine derivatives on the isoelectric point.

phase into a micellar solution phase at the dissolution temperature. On the other hand, DMLL and DMPL showed complicated changes. The hydrated solid of DMLL first changed, with a rise in temperature, into an opaque, heterogeneous and viscous gel. Then it became a clear and homogeneous gel, which was regarded as liquid crystal because of the occurrence of double refraction in polarized light. As the temperature was raised further, the clear gel decreased in viscosity, lost birefringence in polarized light and changed into an isotropic and micellar solution at the dissolution temperature. DMPL showed the same changes as DMLL, although at higher temperatures.

The curves of surface tension vs concentration are shown in Figure 4, and the cmc values and surface tensions at cmc (γcmc) are listed in Table II. As expected, the cmc value and γcmc of each N^{α},N^{α}-dimethyl and N^{α},N^{α},N^{α}-trimethyl derivative decreased with an increase in hydrophobic moiety. But, as for γcmc, a larger effect was found to exist in the methylation degree of these compounds. N^{α},N^{α}-dimethyl derivatives had much lower γcmc than N^{α},N^{α},N^{α}-trimethyl derivatives, so that DMLL showed lower surface tensions above cmc than TMPL.

Foaming properties of these derivatives are shown in Table III. TMLL and TMPL were good in initial foaming but poor in foam retention, while DMLL had excellent initial foaming and foam retention even at a very low concentration.

Wetting powers obtained for DMLL, TMLL and TMPL are listed in Table IV. These derivatives showed good performances in wetting power. DMLL possessed an especially excellent wetting power, the quality of which was not obtained for the ethoxylated derivatives of N^{ϵ}-lauroyllysine (18).

TABLE III

Foaming Properties of N^{ϵ}-acyllysine Derivatives

		Foam height (mm)		
	Concn.	0 min	10 min	30 min
DMLL	0.025%	180	174	174
	0.10 %	185	168	162
	0.25 %	210	197	194
DMPL	0.025%	18	13	13
	0.10 %	165	82	38
	0.25 %	155	108	36
TMLL	0.025%	156	7	0
	0.10 %	190	8	0
	0.25 %	195	8	0
TMPL	0.025%	51	5	1
	0.10 %	159	15	5
	0.25 %	205	52	9

TABLE IV

Wetting Power of N^{ϵ}-acyllysine Derivatives

	Wetting time (sec)		
	0.025%	0.1%	0.25%
DMLL	27.5	5.6	1.8
TMLL	29.5	8.8	4.5
TMPL	28.7	13.2	7.4
Ethoxylated N^{ϵ}-acyllysine[a]			
(6-7 E.O.)	–	–	22
(30-32 E.O.)	–	–	101
(62-64 E.O.)	–	–	530

[a] Reference (18).

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