Synthesis of 1,1,1-Tris(2-hydroxyethyl)amine-2-acylimide
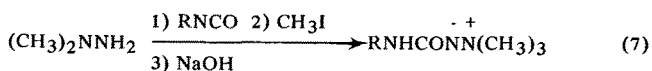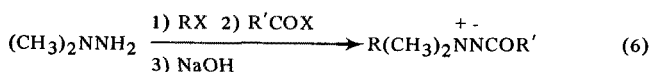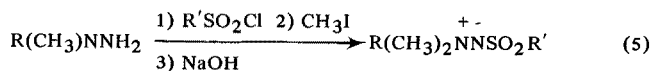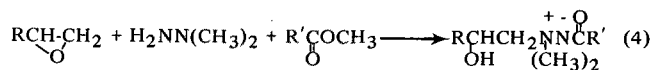
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ABSTRACT

1,1,1-Tris(2-hydroxyethyl)amine-2-acylimide (I) was prepared by the reaction of hydrazine hydrate, ethylene oxide, and fatty acid methyl ester. Reaction conditions such as solvent, reaction temperature, and molar ratio of reactants were investigated, and (I) was obtained in 73% yield by heating an isopropanol solution of hydrazine hydrate, methyl palmitate, and ethylene oxide in molar ratio of 1:6:6 at 80 C for 2 hr.
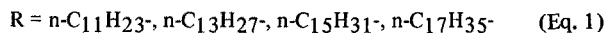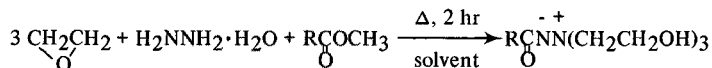
INTRODUCTION

Hitherto, aminimides have been prepared by Berry (1), Slagel (2), and Brown (3), and some surface active properties have also been investigated on the aminimides with long chain alkyl group shown in Scheme 1 (4-7):

$$RCH\text{-}CH_2 + H_2NN(CH_3)_2 + R'COCH_3 \longrightarrow R\overset{+}{CH}CH_2\overset{+}{N}N\overset{-}{C}R' \quad (4)$$
$$\overset{}{\underset{O}{\diagdown}} \qquad\qquad \underset{O}{\overset{}{\|}} \qquad \underset{OH}{} \underset{(CH_3)_2}{}$$

$$R(CH_3)NNH_2 \xrightarrow[\text{3) NaOH}]{\text{1) } R'SO_2Cl \text{ 2) } CH_3I} R(CH_3)_2\overset{+}{N}N\overset{-}{S}O_2R' \quad (5)$$

$$(CH_3)_2NNH_2 \xrightarrow[\text{3) NaOH}]{\text{1) } RX \text{ 2) } R'COX} R(CH_3)_2\overset{+}{N}N\overset{-}{C}OR' \quad (6)$$

$$(CH_3)_2NNH_2 \xrightarrow[\text{3) NaOH}]{\text{1) } RNCO \text{ 2) } CH_3I} RNHCON\overset{-}{N}\overset{+}{(}CH_3)_3 \quad (7)$$

SCHEME 1. Reported preparation methods of aminimides with long chain alkyl group.

In every case, however, the unsymmetrically substituted hydrazines, which were produced by rather complicated processes, were used as the starting material.

In this investigation, preparation of aminimide using the more accessible and inexpensive hydrazine hydrate was attempted. Thus, by heating a mixture of hydrazine hydrate, ethylene oxide, and fatty acid methyl ester, 1,1,1-tris(2-hydroxyethyl)amine-2-acylimide (I), which can be a new class of aminimide useful as surfactant, was obtained by one step (Eq. 1):

$$3\, CH_2CH_2 + H_2NNH_2\cdot H_2O + R\overset{}{C}OCH_3 \xrightarrow[\text{solvent}]{\Delta,\, 2\,hr} R\overset{-}{C}\overset{+}{N}N(CH_2CH_2OH)_3$$
$$\overset{}{\underset{O}{\diagdown}} \qquad\qquad\qquad \underset{O}{\overset{}{\|}} \qquad\qquad \underset{O}{\overset{}{\|}}$$

$$R = n\text{-}C_{11}H_{23}\text{-}, n\text{-}C_{13}H_{27}\text{-}, n\text{-}C_{15}H_{31}\text{-}, n\text{-}C_{17}H_{35}\text{-} \quad \text{(Eq. 1)}$$

Although it was reported by Slagel (2) that ethylene oxide reacted with 1,1-dimethylhydrazine and carboxylic acid ester in protic solvent to give aminimide quantitatively, quaternization of 1,1-bis(2-hydroxyethyl)hydrazine by ethylene oxide seemed to be a rather slow process owing to the steric hindrance.

To obtain the maximum yield of the aminimide (I), reaction conditions such as solvent, reaction temperature, and molar ratio of the reactants were investigated and the scope of the reaction was discussed.

EXPERIMENTAL PROCEDURES

Synthesis of 1,1,1-Tris(2-hydroxyethyl)amine-2-laurimide (Ia)

Ethylene oxide was condensed into an isopropanol solu-tion of hydrazine hydrate and methyl laurate cooled at -60~-70 C, and the mixture was heated at 80 C for 2 hr in a sealed tube. At the end of the reaction period, the solvent was removed in vacuo and the crude reaction product was recrystallized twice or three times from benzene to give Ia as white scales. Melting point 84-86 C; IR (KBr) 3378, 3135, and 1572 cm^{-1}; NMR (CDCl$_3$, δ) 0.88 (3 H, t), 1.27 (18 H, m), 2.03 (2 H, t), 3.99 (12 H, m), and 5.40 (3 H, br s). Anal. calcd. for C$_{18}$H$_{38}$N$_2$O$_4$:C, 62.39, H, 11.05; N, 8.08. Found: C, 62.28; H, 11.30; N, 7.96. Infrared spectra were recorded on Hitachi Infrared Grating Photometer Model 225.

The corresponding amine-myristimide (Ib) (mp 88.5-91 C. Anal. calcd. for C$_{20}$H$_{42}$N$_2$O$_4$:C, 64.13, H, 11.30; N, 7.48. Found: C, 64.17; H, 11.54; N, 7.45), amine-palmitimide (Ic) (mp 93-95 C. Anal. calcd. for C$_{22}$H$_{46}$N$_2$O$_4$:C, 65.63; H, 11.52; N, 6.96. Found: C, 65.51; H, 11.50; N, 6.76), and amine-stearimide (Id) (mp 95.5-97 C. Anal. calcd. for C$_{24}$H$_{50}$N$_2$O$_4$:C, 66.93; H, 11.70; N, 6.50. Found: C, 66.73; H, 12.05; N, 6.43) were synthesized by a similar procedure.

Synthesis of Authentic Compound (Ia)

A methylene chloride (25 ml) solution of mesitylenesul-fonylhydroxylamine (8) (2.57 g, 0.012 mol) was added to a stirred methylene chloride (25 ml) solution of tris(2-hydroxyethyl)amine (2.52 g, 0.017 mol) purified by distil-lation before use, under cooling in an ice bath. After the mixture was allowed to stand at room temperature for 10 min (9), the solvent was removed in vacuo. Potassium tert-butoxide (K: 0.5 g) in tert-butanol (15 ml) and methyl laurate (3.86 g, 0.018 mol) were added to a solution of crude product in tert-butanol (40 ml). After the mixture was stirred at room temperature for 27 hr, the solvent was removed in vacuo and the reaction mixture was dissolved in methylene chloride. Potassium mesitylenesulfonate, a white precipitate, was removed by filtration. Crude product was obtained by evaporating solvent in vacuo (4.18 g). Re-crystallization from methylene chloride gave Ia as white fine scales (1.14 g, 28%). Melting point 85-87.5 C; IR (KBr) 3378, 3135, and 1572 cm^{-1}; NMR (CDCl$_3$,δ) 0.88 (3 H, t), 1.26 (18 H, m), 2.00 (2 H, t), 3.97 (12 H, m), and 5.38 (3 H, br s). Anal. calcd. for C$_{18}$H$_{38}$N$_2$O$_4$: C, 62.39; H, 11.05; N, 8.08. Found: C, 62.00; H, 11.13; N, 8.20.

Synthesis of Laurohydrazide (II)

A methanol-isopropanol (50 ml, 50 ml) solution of methyl laurate (42.8 g, 0.2 mol) and hydrazine hydrate (10.0 g, 0.2 mol) was heated at 60 C for 5 hr. After evap-oration of solvent in vacuo, the crude product was recrys-tallized from hexane to give II as white scales (21.0 g, 49%). Melting point 106-107 C (104-105 C) (10); IR (KBr) 3320, 3200, 1630, and 1530 cm^{-1}. Anal. calcd. for C$_{12}$H$_{26}$N$_2$O: C, 67.24; H, 12.23; N, 13.07. Found: C, 67.30; H, 12.58; N, 12.99.

Synthesis of 2',2'-Bis(2-hydroxyethyl)laurohydrazide (III)

Ethylene oxide was bubbled into molten laurohydrazide (4.28 g, 0.04 mol) at 160 C till an increment of 1.76 g was obtained (ca. 1 hr). The reaction mixture was fractionated and purified by recrystallization with benzene to give III as white fine scales (3.58 g, 63%). Melting point 67.5-69 C; IR (KBr) 3280, 1660, and 1530 cm^{-1}; NMR (CDCl$_3$,δ) 0.88 (3 H, t), 1.25 (18 H, m), 2.16 (2 H, t), 2.95 (4 H, t), 3.60 (4 H, t), 4.28 (2 H, br s), and 7.67 (1 H, br s). Anal. calcd.
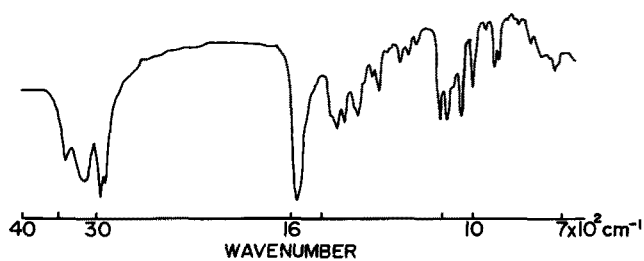
FIG. 1. IR spectrum of aminimide Ic.

TABLE I

Chemical Shifts of Oxyethylene Protons (CDCl$_3$, δ ppm)

Compound	C-CH$_2$-O	N-CH$_2$-C
RCONHN(CH$_2$CH$_2$OH)$_2$	3.60	2.95
RCONHNCH$_2$CH$_2$OH H	3.65	2.99
H$_2$NNCH$_2$CH$_2$OH H	3.70	2.87
HO(CH$_2$CH$_2$O)$_3$H	3.65 – 3.75	
Product of EO & HH[a]	3.62	2.75
Aminimide	3.99	

[a]3 $\underset{\diagdown O \diagup}{CH_2 CH_2}$ + H$_2$NNH$_2$·H$_2$O $\xrightarrow[\text{iso-PrOH}]{\text{80 C, 2 hr}}$; volatile component was evaporated in vacuo.
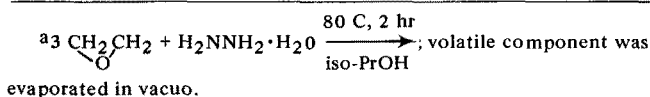
TABLE II

Effect of Alkyl Chain Length of Fatty Acid Methyl Ester on Yield of Aminimide I

Aminimide	Alkyl group	Aminimide (%)
Ia	n-C$_{11}$H$_{23}$-	36
Ib	n-C$_{13}$H$_{27}$-	40
Ic	n-C$_{15}$H$_{31}$-	36
Id	n-C$_{17}$H$_{35}$-	35

for C$_{16}$H$_{34}$N$_2$O$_3$: C, 63.54; H, 11.33; N, 9.26. Found: C, 63.65; H, 11.60; N, 9.50.

In the presence of sodium isopropoxide, an isopropanol solution of methyl laurate and 1,1-bis(2-hydroxyethyl) hydrazine was allowed to reflux for 5 hr. After evaporation of solvent in vacuo, starting materials were recovered and no objective compound was obtained.

Synthesis of 2'-(2-hydroxyethyl)laurohydrazide (IV)

An isopropanol solution of methyl laurate (4.28 g, 0.02 mol) and 2-hydroxyethylhydrazine (2.39 g, 0.04 mol) was allowed to reflux for 40 hr. After evaporation of solvent in vacuo, the crude product was recrystallized from carbon tetrachloride to give IV as white scales. Melting point 88.3-89.3 C; IR (KBr) 3300, 3250, and 1640 cm^{-1}; from the relationship of $\nu_{asym.}$ and $\nu_{sym.}$ the compound was identified to be C$_{11}$H$_{23}$CONNCH$_2$CH$_2$OH (11). NMR HH (CDCl$_3$,δ) 0.88 (3 H, t), 1.25 (18 H, m), 2.21 (2 H, t), 2.99 (2 H, t), and 3.65 (2 H, t). Anal. calcd. for C$_{14}$H$_{30}$N$_2$O$_2$: C, 65.07; H, 11.70; N, 10.84. Found: C, 64.93; H, 12.02; N, 10.83.

Synthesis of N,N,N-Tris(2-hydroxyethyl)hydrazinium Palmitate (V)

A solution of mesitylenesulfonylhydroxylamine (8) in

methylene chloride was added to a stirred methylene chloride solution of tris(2-hydroxyethyl)amine purified by distillation before use, under cooling in an ice bath. After the mixture was allowed to stand at room temperature for 10 min (9), the solvent was removed in vacuo. The crude N,N,N-tris(2-hydroxyethyl)hydrazinium mesitylenesulfonate were transformed to the corresponding palmitate by treatment with Amberlite IRA-400 ion-exchange resin (OH⁻ form) in deionized water followed by addition to palmitic acid in ethanol. After evaporation of solvent in vacuo, the crude product was purified by recrystallization from hexane or benzene to give V as white scales. IR (KBr) 3300 and 1560 cm^{-1}; NMR (CDCl$_3$, δ) 0.88 (3 H, t), 1.25 (26 H, m), 2.14 (2 H, t), 3.83 (6 H, br s), 4.05 (6 H, br s), and 6.51 (5 H, br s).

RESULTS AND DISCUSSION

Quaternization of dimethylalkylamine (11) and 1,1-dimethylhydrazine (2) with ethylene oxide has been reported to proceed successfully. Primary amine, however, gave N,N,N-tris(2-hydroxyethyl)alkylammonium salt less easily because of the steric hindrance (12).

The reaction of ethylene oxide with unsubstituted hydrazine has not been fully investigated (13,14), but it seemed interesting to make clear if the reaction between the unsubstituted hydrazine and ethylene oxide affords 1,1,1-tris(2-hydroxyethyl)aminimine, since it may be converted to aminimide by the reaction with carboxylic ester.[1]

The stoichiometric mixture of hydrazine hydrate, fatty acid methyl ester, and ethylene oxide in a specified solvent was allowed at specified temperature for 2 hr. After evaporation of solvent, the crude product was purified by recrystallization from benzene and was identified by IR, NMR, and elemental analysis to be 1,1,1-tris(2-hydroxyethyl)amine-2-acylimide (Eq. 1). For example, 1,1,1-tris(2-hydroxyethyl)amine-2-laurimide showed a hydroxyl stretching absorption at 3378 and 3135 cm^{-1}, the typical carbonyl stretching absorption at 1572 cm^{-1}, and complicated absorptions at 1000 - 1100 cm^{-1} (Fig. 1). The NMR spectrum (δ, CDCl$_3$) of aminimide showed 12 methylene protons of 2-hydroxyethyl group at 3.99 ppm. 2',2'-Bis(2-hydroxyethyl)acylhydrazide, formed as the main by-product, was isolated from reaction mixture and was identified by comparison of IR and NMR of authentic sample and elemental analysis.

Because of the difficulties of quaternization of 1,1-bis(2-hydroxyethyl)hydrazine with ethylene oxide, some by-products, such as diethanol hydrazide (III) which has almost similar properties to the desired aminimide, were inevitably formed in the reaction.

As the quantitative isolation of aminimide was unsuccessful, the content of aminimide in crude reaction product was determined by NMR spectrum analysis (JEOL JNM-PS-100).
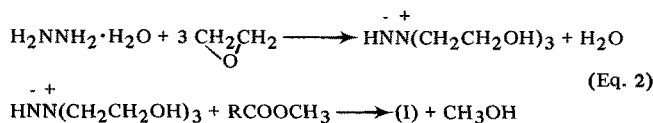
Chemical shifts of methylene protons of 2-hydroxyethyl group for hydrazides, hydrazines, and glycols which may be contained as by-products in crude product were shown in Table I together with that of aminimide. By comparing the number of oxyethylene protons of aminimide N-CH$_2$CH$_2$-O (3.99 ppm) with the total number of protons of alkyl group, the content of (I) was calculated.

To clarify the influence of alkyl chain length of fatty acid methyl ester, the stoichiometric mixture of hydrazine hydrate, fatty acid methyl ester, and ethylene oxide was heated at 80 C for 2 hr in isopropanol. The result is shown in Table II. The yield of the aminimide was 35-40%, and no

marked differences were observed in the range examined.

The failure in obtaining a high yield of aminimide I can be attributed to the slow formation of 1,1,1-tris(2-hydroxyethyl)aminimine, which may be the intermediate, due to steric hindrance of 2-hydroxyethyl groups as mentioned previously. Moreover, as shown in Equation 2, hydroxyl compounds such as water and methanol are released on formation of aminimide and may consume ethylene oxide.

$$H_2NNH_2 \cdot H_2O + 3 \; CH_2CH_2 \overset{\diagdown}{O} \longrightarrow HNN(CH_2CH_2OH)_3 + H_2O$$

(Eq. 2)

$$HNN(CH_2CH_2OH)_3 + RCOOCH_3 \longrightarrow (I) + CH_3OH$$

The reaction of excess amounts of ethylene oxide and ester at 80 C for 2 hr in isopropanol was attempted. Table III shows the results. The yield of aminimide has increased from 36 to 47% by increasing the amount of ethylene oxide, but in run 3 the yield has not increased any more, indicating that hydrazine may be consumed not giving aminimine. In runs 4 and 5, the yield of aminimide has increased to 62 and 73%, respectively, based on hydrazine hydrate.

The effect of solvent on the reaction of the stoichiometric mixture of each reactant at 80 C for 2 hr is shown in Table IV. Isopropanol gave 36% yield of aminimide Ic, while dimethyl formamide gave only 14% yield of Ic, indicating that protic solvent assists proton migration after quaternization of 1,1-bis(2-hydroxyethyl)hydrazine. However, methanol which is protic solvent not only decreased the yield of Ic to 17%, but also gave hydrazinium carboxylate (V). In cases of (1) and (2) in Table IV, the formation of hydrazinium carboxylate (V) was also observed from their IR spectra.

The effect of temperature on the reaction of the stoichiometric mixture of each reactant for 2 hr in isopropanol is shown in Table V. With increasing reaction temperature from 60 to 100 C, the yield of aminimide Ic increased to 41% (100 C); at approximately this temperature quaternization of amine with ethylene oxide was reported to be most favorable (15). The yield decreased at 120 C.

Figure 1 shows the IR spectrum of aminimide Ic. The IR spectrum showed the typical carbonyl absorption of aminimide at 1572 cm^{-1}, hydroxyl absorption at 3135 cm^{-1} indicating a strong hydrogen bond between the hydroxyl proton and the negative charge center (2), and another hydroxyl absorption at 3378 cm^{-1}.

In reaction path shown in Figure 2, 1,1,1-tris(2-hydroxyethyl)amine-2-acylimide (I) is produced by unsymmetrical addition of two ethylene oxide molecules to hydrazine (VI), quaternization (VII), proton migration to produce aminimine (VIII), and substitution reaction of ester. At the same time, 2',2'-bis(2-hydroxyethyl)acylhydrazide (III) and other acylhydrazides are formed as by-products by hydrazinolysis of ester with hydrazinium 1,1-bis-(2-hydroxyethyl)hydrazide (IX) and other hydrazinium hydrazides. Hydrazinium carboxylate (V), which was observed on using methanol as a solvent and on using hydrazine hydrate aqueous solution as a starting material, may form by hydrazinium hydroxide (X) from the reaction of hydrazinium alkoxide inner salt (VII) or aminimine (VIII) and water. This can be rationaized as follows. When a quantity of water in the reaction system became large, the hydroxide (X) increased, and when methanol was used, hydrazinium methoxide (XI) was generated before proton migration to aminimine (VIII) or substitution by ester to aminimide (I) could occur. The latter (generation of XI) occurs more easily in less acidic solvents. Methoxide (XI) converts to hydroxide (X) when water is present.

The formation of $RCONN((CH_2CH_2OH)_2)$ $CH_2CH_2OCH_2CH_2OH$ and higher molecular compounds

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TABLE III

Influence of Molar Ratio of Reactant on Yield of Aminimide Ic

Run number	Molar ratio (HH:MP:EO)[a]	Aminimide (%)[b]
1	1:1:3	36
2	1:1:4.5	47
3	1:1:6	48
4	1:2:6	62
5	1:6:6	73

[a]HH = hydrazine hydrate, MP = methyl palmitate, EO = ethylene oxide.

[b]Based upon hydrazine hydrate.

TABLE IV

Effect of Solvent on Yield of Aminimide Ic[a]

Solvent	Aminimide (%)
t-Butanol	35
Isopropanol	36
Ethanol	28
Methanol	17
Dimethyl formamide	14
Isopropanol (1)[b]	29
Isopropanol (2)[b]	24

[a]Methyl palmitate was used as ester.

[b]In (1) and (2), 70 and 50% hydrazine hydrate were used, respectively.

TABLE V

Effect of Reaction Temperature on Yield of Aminimide Ic[a]

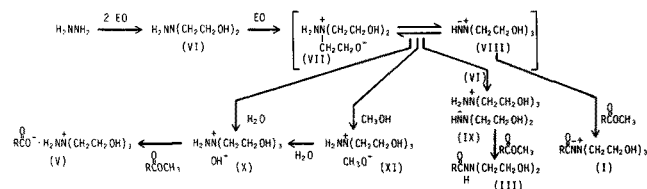| Reaction temperature (C)	Aminimide (%)
60	25
80	36
90	39
100	41
120	36

[a]Methyl palmitate was used as ester.

FIG. 2. Reaction path of hydrazine hydrate, ethylene oxide (EO), and fatty acid methyl ester.

could neither be confirmed nor denied. The properties of 1,1,1-tris(2-hydroxyethyl)amine-2-acylimide are under investigation.

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