STUDIES ON SYNTHESIS AND PROPERTIES OF FUNCTIONAL COMPOUNDS CONTAINING OLIGO(OXYETHYLENE) GROUPS

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ARAKI MASUYAMA

Department of Applied Chemistry

Faculty of Engineering

Osaka University

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（オリゴオキシエチレン基を有する機能性化合物の合成と物性に関する研究）

大阪大学工学部

益　山　新　樹

PREFACE

The work in this thesis was performed under the guidance by Professor Mitsuo Okahara at the Department of Applied Chemistry, Faculty of Engineering, Osaka University.

The object of this thesis is to synthesize functional compounds containing oligo(oxyethylene) groups and to study their properties and application. The author hopes that this basic work described in this thesis stimulates further research on such new kinds of functional compounds.

Araki Masuyama

Suita, Osaka, Japan

CONTENTS

GENERAL INTRODUCTION

An oligo- or poly(oxyethylene) group is widely used not only as an important component of macrocyclic ligands such as crown ethers but also as a hydrophilic part of nonionic surfactants or as a structural unit of synthetic polymers.

Many researchers have recently grappled with the molecular design of crown compounds to improve the complexing ability and/or selectivity of ligands toward a specific cation, to construct biomimetic systems in which crown compounds play an important role, or to apply crown compounds to "multi-functional" amphipathic materials. Lariat ethers, which are crown ether derivatives having an electron-donating sidearm, have become of major interest because their complexing ability or selectivity toward various cations can be finely adjusted by changing the structure of sidearm.[1] Crown compounds having a lipophilic group such as a long-chain alkyl group act as amphipathic materials of which properties can be controlled by changing the kind of coexisting cation.[2] They are considered a sort of "multi-functional" surfactants which can be applied to phase transfer catalysts or reagents for cation transport systems.

Poly(oxyethylene) compounds are also used in some kinds of "biocompatible" polymer materials which are called "biomedical" materials. Nowadays substitute products (artificial organs) have been developed for almost all organs except brain, stomach and intestines. Both mechanical strength and biocompatibility are indispensable to "biomedical" materials. There are many

researches on antithrombogenic polymers for an artificial heart or blood circulation systems for which blood compatibility is required.[3] Among them, urethane polymers with the micro-phase separation structure [segmented poly(ether-urethane)s; SPU], which are prepared from polyetherdiols, commercially available aryl diisocyanates, and alkylene diamines, have shown excellent antithrombogenicity.[4] The investigation of a new type of SPU polymers is important for the improvement of SPU polymers to enhance their utilization.

By the way, so-called "multi-functional" surfactants, which have additional extra functions such as chemical reactivity, complexing ability with metal cations, catalytic activity, vesicle-forming property, and so on, besides basic surface active properties, have attracted special interest. Long-chain alkyl poly(oxyethylene) monoethers (alcohol ethoxylates) are very useful as a building block of "multi-functional" surfactants because their preparation is very easy, various types of alcohol ethoxylates are commercially available, and the HLB (hydrophile-lipophile balance) of alcohol ethoxylates can be finely adjusted by changing the number of oxyethylene units.[5]

In this study, the author synthesized various compounds containing oligo(oxyethylene) groups and related compounds, and investigated their properties or application with a view to develop new types of "functional" compounds having oligo-(oxyethylene) groups.

In Chapter 1, N-oligo(oxyethylene) monoaza crown ether derivatives were synthesized, and the effect of oxygen atoms in

the sidearm on their complexation with metal cations was clarified. In the case of monoaza crown compounds having a long-chain alkyl group, their water solubility and the evaluation method of their complexing ability with metal cations in water were discussed. Furthermore, the facile synthetic method of urethane types of crown ethers, which were analogues to model compounds of natural ionophores, was investigated.

In Chapter 2, the author paid attention to N-ammonioamidates as a new building block of biomedical urethane polymers. Various types of N-ammonioamidates having a hydroxyl group in an acyl moiety were prepared, and the effect of their structure on the types of urethane compounds which were formed by the thermolysis of the N-ammonioamidates was discussed.

From Chapter 3 to Chapter 6, the author prepared a series of "multi-functional" surfactants by the modification of the terminal group of alcohol ethoxylates and clarified their various properties. First, terminal hydroxamic acid types of alcohol ethoxylates were synthesized, and their water solubility, complexation with iron(III) ion, surface active properties under various conditions, and micellar catalytic activity were discussed. (Chapter 3) Second, terminal ketone or oxime types of alcohol ethoxylates were prepared and some features about their hydrophilicity and foaming properties were studied. (Chapter 4) Third, surface active properties of alcohol ethoxylates with an amide oxime terminal group were synthesized and measured under various pH conditions with a view to apply them to ion-flotation systems. (Chapter 5) Finally, surface active properties of

terminal amide types of alcohol ethoxylates were determined both in pure water and in hard water, and their lime-soap dispersing ability was also checked. (Chapter 6)

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The contents of this thesis are composed of the following papers:

1. Complexing Ability of N-Oligoethylene Glycol Monoaza Crown Ethers with Sodium and Potassium Cations
   A.Masuyama, Y.Nakatsuji, I.Ikeda, and M.Okahara,
   Tetrahedron Lett., **22**(46), 4665(1981).
2. Complexing Abilities of N-[ω-(Long-chain alkyl)oligo(oxyethylene)] Monoaza Crown Ethers with Metal Cations in Water and in Methanol
   A.Masuyama, P.-L.Kuo, I.Ikeda, and M.Okahara,
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3. Preparation of Urethane-type Crown Ethers by Thermolytic Reaction of Aminimides
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A.Masuyama, A.Shindoh, D.Ono, and M.Okahara,
J.Am.Oil Chem.Soc., in contribution.

CHAPTER 1 SYNTHESIS AND PROPERTIES OF MONOAZA CROWN ETHER DERIVATIVES AND URETHANE TYPES OF CROWN ETHERS

1-1 Introduction

Recently, various kinds of crown ethers with functional groups have been prepared and many studies have been reported on their application to phase transfer catalysts or cation transport systems on their selective complexation abilities with inorganic or organic cations.[1,2] Especially, up-to-date molecular design of crown compounds has been attempted to improve the complexing abilities with specific cations or to develop a novel selectivity for cations.

It is expected that the complexing abilities of crown compounds which contain a side chain including donor atoms will be higher than that of normal crown ethers when the three dimensional coordination with a spherical metal cation is possible as observed in cryptates. Both Gokel[3] and Okahara[4] have reported the synthesis and enhanced complexing abilities of so-called "lariat ethers" which have an oxyethylene chain in the side arm of crown ethers.

Crown compounds having a suitable lipophilic group can act as surface active agents which can exhibit additional functions besides basic surface active properties attributed to their complexing abilities with metal cations. Le Moigne,[5] Moroi,[6] and Kuwamura[7] have reported surface active properties of these types of crown ethers. Okahara also has reported the preparation of "typical" long-chain alkyl crown ethers and N-(long-chain

alkyl) monoaza crown ethers[8] and investigated their surface active properties in the absence or presence of metal cations.[9]

In this chapter, the author synthesized new types of "aza lariat ethers" -- N-oligo(oxyethylene) monoaza crown ethers and N-[ω-alkyloligo(oxyethylene)] monoaza crown ethers -- and measured both their complexing stability constants with Na^+ and K^+ in methanol or in water/methanol and their cloud point of aqueous solutions in the absence or presence of metal salts. From these results, the author clarified the effect of oxyethylene oxygen atoms in the side chain on the complexation with metal cations. (Section 2)

Furthermore, amide types of crown ethers have become of interest as model compounds for natural ionophores,[10] and it is said that urethane types of crown compounds are analogues of amide type crown ethers. But there are only few reports on the synthesis of urethane types of crown ethers except the formation of crown compounds with a bis-urethane linkage by the intermolecular cyclization.[11] Our research group has investigated the facile synthesis of many crown compounds by the intramolecular cyclization of oligo(oxyethylene) derivatives.[8,12] In view of the synthesis of the urethane compounds, N-ammonio-amidates (aminimides) seem to be useful as precursors of urethane compounds because they are generally stable under ordinary conditions but easily rearrange to isocyanates on heating.[13]

In this chapter, the author described the preparation of some compounds which had a hydroxyl group and an N-ammonioamidate group at both ends of oligo(oxyethylene) derivatives, and the formation of new types of crown ethers with a urethane unit in the ring by

the thermolysis of those N-ammonioamidates. (Section 3)

1-2 Synthesis and Complexing Abilities with Metal Cations of N-Oligo(oxyethylene) Monoaza Crown Ether Derivatives

1-2-1 Experimental

The ^1H NMR spectra were measured with a JEOL JMN-PS-100 spectrometer using TMS as an internal standard. The IR and mass spectra were measured on a Hitachi 260 spectrometer and a Hitachi RMU-6E mass spectrometer at an ionization potential of 70 eV, respectively.

Materials. Commercially available alkyl bromides and oligoethylene glycol derivatives were used without further purification. N-Unsubstituted monoaza crown ethers [**IIa**; Abbreviation: N15, **IIb**; N18 ("15" and "18" mean the ring size of crown ether, see Scheme 1-1)] were synthesized and purified by the previously reported method.[14] N-(Long-chain alkyl) monoaza crown ethers [**IVa-d**; C_x-N(15 or 18) ("x" means the number of carbon atoms of alkyl group in the side chain)] were prepared by the reaction of **IIa,b** with alkyl bromides in the presence of Na_2CO_3 and purified by Kugelrohr distillation.[8a] Hexa(oxyethylene) dodecyl ether (**V**; $C_{12}E6$) was the commercial product of guaranteed reagent grade (Nikko Chemicals Co., Tokyo) and used after Kugelrohr distillation.

*Synthesis of N-oligo(oxyethylene) monoaza crown ethers [**IIIa-c,j-l**; E(m+1)-N(15 or 18)] and N-[ω-alkyloligo(oxyethylene)]*

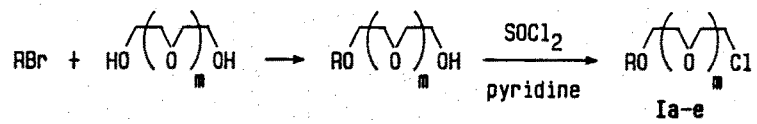
*monoaza crown ethers [**IIId-i,m-r**; $C_xE(m+1)$-N(15 or 18)].* (See Scheme 1-1) Compounds (**IIIa,j**) were prepared by the reaction of **IIa,b** with ethylene oxide at 170°C.[15] Compounds (**IIIb-d,k-m**) were prepared by the reaction of **IIa,b** with corresponding commercially available oligoethylene glycol monochlorides at 120°C for 12 hr in the presence of Na_2CO_3. Remaining compounds (**IIIe-i,n-r**) were similarly obtained from **IIa,b** and chlorides (**Ia-e**) which were derived from alkyl bromides and oligoethylene glycols. All crown ethers (**IIIa-r**) were isolated by Kugelrohr distillation and their purity was checked by GLC, IR, ^1H NMR, mass, and elemental analyses. The synthetic results and some physical properties are summarized in Table 1-1.

Metal chlorides (Na, K, Mg, Ca, Ba, and Sr) were commercial guaranteed-grade reagents, and were dried at 80°C under reduced pressure. Water was deionized by passing through an ion-exchange resin column.

Measurement. The stability constants (log K_1') for crown compounds with Na^+ and K^+ were measured by the Frensdorff's method[16] at 25°C in methanol or in a water/methanol mixture (1:9 v/v). The cloud point (T_{cp}) of each aqueous solution of samples was determined by observation with naked eyes, using a solution of 10 mg or 50 mg of sample in 1 ml of water or the salt solution of specific concentration (0.1, 0.5, 1.0, 2.0, 3.0, 4.0, and 5.0 molality) in a test tube of 10 mm of inner diameter under heating or cooling with a rate of ca. 0.5°C/min. From these results, the difference of cloud point between the values in the absence and presence of metal chlorides (ΔT_{cp}) was calculated as follows:

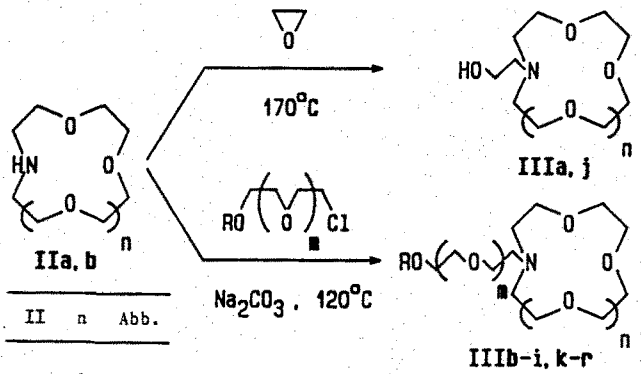
$$\Delta T_{cp} = T_{cp(m)} - T_{cp}$$

where the subscript letter "m" means a salt concentration in molality unit.

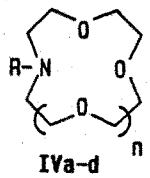


Ia-e

I	R	m
a	C_8H_{17}	0
b	C_8H_{17}	1
c	C_8H_{17}	2
d	$C_{12}H_{25}$	0
e	$C_{12}H_{25}$	1



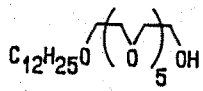
II	n	Abb.
a	2	N15
b	3	N18



IVa-d

IV	R	n	Abb.
a	C_8H_{17}	2	C_8-N15
b	$C_{12}H_{25}$	2	C_{12}-N15
c	C_8H_{17}	3	C_8-N18
d	$C_{12}H_{25}$	3	C_{12}-N18

III	R	m	n	Abb.	III	R	m	n	Abb.
a	H	0	2	E1-N15	j	H	0	3	E1-N18
b	H	1	2	E2-N15	k	H	1	3	E2-N18
c	H	2	2	E3-N15	l	H	2	3	E3-N18
d	CH_3	2	2	C_1E3-N15	m	CH_3	2	3	C_1E3-N18
e	C_8H_{17}	0	2	C_8E1-N15	n	C_8H_{17}	0	3	C_8E1-N18
f	C_8H_{17}	1	2	C_8E2-N15	o	C_8H_{17}	1	3	C_8E2-N18
g	C_8H_{17}	2	2	C_8E3-N15	p	C_8H_{17}	2	3	C_8E3-N18
h	$C_{12}H_{25}$	0	2	C_{12}E1-N15	q	$C_{12}H_{25}$	0	3	C_{12}E1-N18
i	$C_{12}H_{25}$	1	2	C_{12}E2-N15	r	$C_{12}H_{25}$	1	3	C_{12}E2-N18



V (C_{12}E6)

Scheme 1-1 Synthesis of monoaza crown ether derivatives (III) and formula of reference compounds for comparison.

Table 1-1 Synthesis and characterization of monoaza crown ether derivatives (III)[a].

Compd	Yield (%)	bp[b] (°C/Torr)	mass (M^+)/(base peak)	^1H NMR ($CDCl_3$) (δ, ppm)
IIIa	45	80/0.005	263/232	2.75(m,6H), 3.5-3.7(m,19H)
IIIb	43	140/0.01	307/232	2.78(m,6H), 3.5-3.8(m,23H)
IIIc	50	150/0.005	351/232	2.78(m,6H), 3.37(s,1H), 3.5-3.8(m,26H)
IIId	57	145/0.005	365/232	2.80(m,6H), 3.35(s,3H), 3.5-3.8(m,26H)
IIIe	71	180/0.01	375/232	0.87(t,3H), 1.1-1.6(m,12H), 2.80(m,6H), 3.3-3.8(m,20H)
IIIf	60	180/0.01	419/232	0.87(t,3H), 1.1-1.6(m,12H), 2.80(m,6H), 3.3-3.8(m,24H)
IIIg	61	200/0.005	463/232	0.87(t,3H), 1.2-1.7(m,12H), 2.80(m,6H), 3.4-3.8(m,28H)
IIIh	60	200/0.01	431/232	0.87(t,3H), 1.2/1.6(m,20H), 2.75(m,6H), 3.3-3.8(m,20H)
IIIi	63	220/0.005	475/232	0.87(t,3H), 1.2-1.6(m,20H), 2.80(m,6H), 3.4-3.8(m,24H)
IIIj	52	140/0.005	307/276	2.75(m,6H), 3.5-3.7(m,23H)
IIIk	58	145/0.005	351/276	2.78(m,6H), 3.5-3.8(m,27H)
IIIl	47	175/0.01	395/276	2.78(m,6H), 3.35(s,1H), 3.5-3.8(m,30H)
IIIm	55	190/0.01	409/276	2.78(m,6H), 3.35(s,3H), 3.5-3.7(m,30H)
IIIn	68	180/0.01	419/276	0.87(t,3H), 1.4-1.6(m,12H), 2.80(m,6H), 3.3-3.8(m,24H)
IIIo	52	200/0.03	463/276	0.87(t,3H), 1.2-1.7(m,12H), 2.80(m,6H), 3.4-3.8(m,28H)
IIIp	62	220/0.005	507/276	0.87(t,3H), 1.2-1.7(m,12H), 2.80(m,6H), 3.4-3.8(m,32H)
IIIq	55	180/0.01	475/276	0.87(t,3H), 1.2-1.6(m,20H), 2.80(m,6H), 3.3-3.8(m,24H)
IIIr	63	220/0.005	519/276	0.87(t,3H), 1.2-1.6(m,20H), 2.80(m,6H), 3.3-3.8(m,28H)

a) Satisfactory microanalyses (C,H,N; $\leq \pm$ 0.4 %) for all compounds were obtained. Following compounds showed the same IR spectra: IIIa-c,j-l; 3350, 2950, 1470, 1350, 1300, 1250, 1110, 980, and 940 cm^{-1} (neat), IIId-i,m-r; 2950, 1470, 1350, 1300, 1250, 1110, 980, and 940 cm^{-1} (neat).

b) Kugelrohr distillation.

1-2-2 Results and Discussion

Effect of the side chain on log K_1' for crown compounds with Na^+ and K^+. The results of log K_1' in methanol or in water/methanol are listed in Table 1-2.

Table 1-2 Stability constants[a] (log K_1') for **II**, **III**, and **IV** with Na^+ and K^+.

Compound (15-CR-5)		Solv.[b]	log K_1'		Compound (18-CR-6)		Solv.[b]	log K_1'	
			Na^+	K^+				Na^+	K^+
IIa	N15	M	2.06	2.72	**IIb**	N18	M	2.77	4.18
IVa	C_8-N15	M	3.08	2.82	**IVc**	C_8-N18	M	3.59	4.87
IVb	C_{12}-N15	M	3.06	2.86	**IVd**	C_{12}-N18	M	3.61	4.98
"	"	W/M	2.6	2.3	"	"	W/M	2.9	3.5
IIIa	E1-N15	M	3.92	3.67	**IIIj**	E1-N18	M	4.75	5.49
IIIb	E2-N15	M	4.68	4.42	**IIIk**	E2-N18	M	4.34	5.88
IIIc	E3-N15	M	4.34	4.77	**IIIl**	E3-N18	M	4.26	5.69
IIId	C_1E3-N15	M	4.32	4.85	**IIIm**	C_1E3-N18	M	4.28	5.96
IIIe	C_8E1-N15	M	3.83	3.58	**IIIn**	C_8E1-N18	M	4.21	5.73
IIIf	C_8E2-N15	M	4.26	4.57	**IIIo**	C_8E2-N18	M	4.27	5.74
IIIg	C_8E3-N15	M	4.36	4.74	**IIIp**	C_8E3-N18	M	4.33	5.75
IIIh	C_{12}E1-N15	M	3.76	3.55	**IIIq**	C_{12}E1-N18	M	4.23	5.62
"	"	W/M	3.2	2.9	"	"	W/M	3.4	3.8
IIIi	C_{12}E2-N15	M	4.21	4.46	**IIIr**	C_{12}E2-N18	M	4.27	5.70
"	"	W/M	3.5	3.4	"	"	W/M	3.4	3.9

a) At 25°C.

b) M: Methanol, W/M: Water/methanol (1:9 v/v).

It was observed that the stability constants in methanol were enhanced by the introduction of an oligo(oxyethylene) side chain on the nitrogen atom of monoaza crown ether. The complexing abilities for N-oligo(oxyethylene) monoaza crown ethers (**IIIa-c,j-l**) with both Na^+ and K^+ were superior to those for not only N-unsubstituted compounds (**IIa,b**) but also N-alkyl monoaza crown ethers (**IVa-d**). From these results, it is clear that oxyethylene oxygen atoms in the side chain make a remarkable contribution to the complexation with metal cations.

Compounds having a methoxy group in the terminal of the side chain (**IIId,m**) indicated the similar or better complexing abilities compared with the corresponding compounds having a hydroxyl group (**IIIc,l**), due to the inductive effect of methyl group. The stability constants for crown ethers containing an octyl or dodecyl group (**IIIe-i,n-r**) were slightly lower than those for the corresponding N-oligo(oxyethylene) monoaza crown compounds (**IIIa-c,j-l**) probably because of steric hindrance of long-chain alkyl group.

As a whole, the log K_1' values for both monoaza 15-crown-5 and monoaza 18-crown-6 derivatives with Na^+ seemed to converge on those for compounds containing two oxygen atoms in the side chain. In the case of the complexation of monoaza 18-crown-6 derivatives with K^+, the first oxygen atom in the side chain made a remarkable contribution to the complex formation. On the other hand, the log K_1' values for monoaza 15-crown-5 derivatives with K^+ increased with an increase in the number of oxygen atoms in the side chain.

From the facts described above, it is reasonable to conclude

that the complexing abilities for a series of N-oligo(oxyethylene) monoaza crown ether derivatives become optimum in case the cation size fits a three dimensional cavity composed of the monoaza crown ring and the side oligo(oxyethylene) chain. It seems that the oligo(oxyethylene) chain can easily participate in the complexation because the side chain is flexible.

Evaluation of the contribution of the oligo(oxyethylene) group in the side chain to the hydrophilicity of the molecule by the measurement of cloud point (T_{cp}). Since the crown ring consists of a limited number of oxyethylene units and has no hydroxyl group, the hydrophilicity of this sort of surfactants is low compared with that of the usual nonionic surfactants.[9e] Improvement of the hydrophilicity by enlarging the crown ring may affect the complexing ability with metal cations. It is expected that the hydrophilicity of $C_xE(m+1)$-N(15 or 18) (**IIIe-i,n-r**) containing an oxyethylene group in the side chain is higher than that of the corresponding C_x-N(15 or 18) (**IVa-d**). The increase of hydrophilicity was confirmed by the measurement of cloud point. The results of T_{cp} of 1 wt% aq solutions of monoaza crown ethers with a long-chain alkyl group and a reference typical nonionic compound (**V**) are listed in Table 1-3.

Table 1-3 Cloud points (T_{CP})[a] of C_x E(m+1)-N(15, 18) and the reference compounds

Sample	T_{CP}(℃)	Sample	T_{CP}(℃)
C_8-N 15	23.0	C_8-N 18	33.5
C_8 E 1-N 15	30.0	C_8 E 1-N 18	43.5
C_8 E 2-N 15	37.5	C_8 E 2-N 18	50.0
C_8 E 3-N 15	49.5	C_8 E 3-N 18	57.5
C_{12}-N 15	13.0	C_{12}-N 18	29.0
C_{12} E 1-N 15	20.5	C_{12} E 1-N 18	38.5
C_{12} E 2-N 15	30.5	C_{12} E 2-N 18	46.0
		C_{12} E 6	51.5

a) 1 wt% of sample solution.

When the size of crown ring and the length of alkyl chain were the same, the T_{cp} values of crown derivatives increased almost linearly with an increase of the number of oxyethylene oxygen atoms in the side chain. The T_{cp} values of 5 wt% aq solutions were the same to those of 1 wt% aq solutions.

Difference of cloud point between the values in the absence and presence of metal chlorides (ΔT_{cp}). Figures 1-1 and 1-2 show the correlations of the salt/sample molar ratio and the ΔT_{cp} values using 5 wt% aq solutions of dodecyl derivatives (**IIIh,i,q,r** and **IVb,d**). And Table 1-4 summarizes the ΔT_{cp} values of 2 molality salt solutions including a 1 wt% of sample (ΔT_{cp}= $T_{cp(2)} - T_{cp}$).

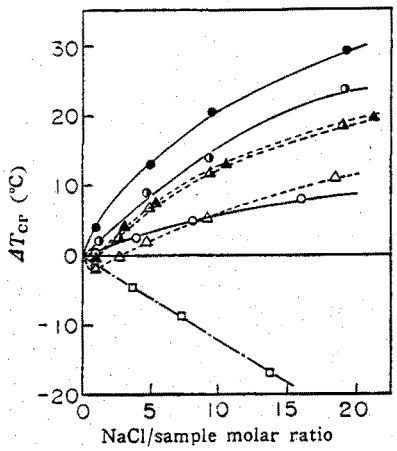


Fig. 1-1 ΔT_{CP} as a function of NaCl/sample molar ratio (5 wt% of sample soln.)

—○— : C_{12}-N 15, —◑— : C_{12} E 1-N 15,
—●— : C_{12} E 2-N 15, --△-- : C_{12}-N 18,
--▲-- : C_{12}-E 1-N 18, --▲-- : C_{12} E 2-N 18,
--□-- : C_{12} E 6

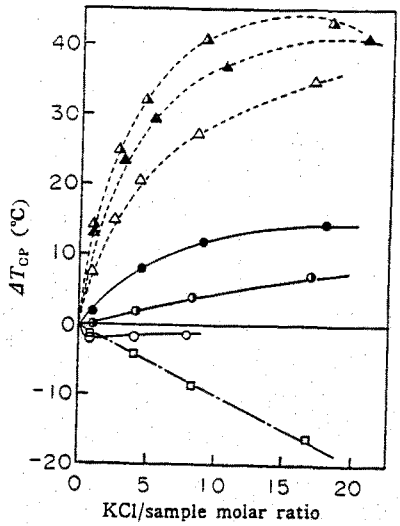


Fig. 1-2 ΔT_{CP} as a function of KCl/sample molar ratio (5 wt% of sample soln.)

—○— : C_{12}-N 15, —◑— : C_{12} E 1-N 15,
—●— : C_{12} E 2-N 15, --△-- : C_{12}-N 18,
--▲-- : C_{12} E 1-N 18, --▲-- : C_{12} E 2-N 18,
--□-- : C_{12} E 6

Table 1-4 Cloud point changes between the absence and the presence of metal chlorides[a)]

Sample	ΔT_{CP} (°C)[b)]					
	NaCl	KCl	$MgCl_2$	$CaCl_2$	$SrCl_2$	$BaCl_2$
C_{12}-N 15	5.5	−6.0	15.0	25.5	39.0	32.0
C_{12} E 1-N 15	19.0	1.5	4.5	30.0	56.5	49.5
C_{12} E 2-N 15	21.5	11.5	7.0	38.5	*c*)	64.5
C_{12}-N 18	14.5	38.0	22.0	27.0	*c*)	*c*)
C_{12} E 1-N 18	19.5	41.5	7.5	28.0	*c*)	*c*)
C_{12} E 2-N 18	19.0	40.5	12.0	31.0	*c*)	*c*)
C_{12}-E 6	−22.5	−20.5	*d*)	*d*)	*d*)	*d*)

a) 2 Molal salt solutions including 1 wt% of sample.
b) $\Delta T_{CP} = T_{CP(2)} - T_{CP}$ *c*) $T_{CP(2)} > 100$°C.
d) No measurement.

Many studies about the effect of added inorganic electrolytes on the cloud point of open chain poly(oxyethylene) type nonionics have been reported.[17] In the presence of metal salts except ones containing a counter anion of water-destructuring type, such as SCN^-, NO_3^-, and so on, the T_{cp} values of these open chain type nonionics usually fall down because of the salting-out effect. In the case of crown ethers, however, the salting-in effect based on the complexation of crown ring with metal cations causes a rise in T_{cp} values compared with the cases in the absence of metal salts.[9a,f] From Figures 1-1 and 1-2, it was clarified that the ΔT_{cp} values of almost all monoaza crown derivatives were positive contrary to the trend in open chain $C_{12}E6$ (**V**). And from Table 1-4, it was found that the ΔT_{cp} values depended on both the number of oxyethylene oxygen atoms in the side chain and kinds of metal chlorides.

Relationship between ΔT_{cp} and log K_1'. Though the log K_1' values for dodecyl derivatives (**IIIh,i,q,r** and **IVb,d**) in water/methanol were smaller than the values in methanol, no confusion in the order of log K_1' values was found between any two crown compounds in both solution systems. (Table 1-2) Gokel measured the log K_1' values for 15-crown-5 and 18-crown-6 with Na^+ in the mixture of methanol and water, and reported that the log K_1' values enhanced proportionally to the ratio of methanol in the mixture and that the solvent composition didn't affect the relative order of log K_1' values.[18] The relative order of the stability constants for a series of these monoaza crown ethers in water therefore seems similar to that in methanol or in water/methanol. In this work, the comparison of the ΔT_{cp} with the

log K_1' was carried out under controlled conditions [at MCl (M= Na or K)/sample= 5.0 (molar ratio)]. The relationship between the number of oxygen atoms in the side chain and either the ΔT_{cp} or the log K_1' in the water/methanol mixture at MCl/crown= 5.0 (molar ratio) is shown in Fig. 1-3.

Figure 1-3 clearly shows the correlation between the ΔT_{cp} and the log K_1': both the ΔT_{cp} and the log K_1' of crown compounds containing an oxyethylene group in the side chain are higher than those of the corresponding N-dodecyl monoaza crown ethers. So it becomes clear that the complexing abilities of a series of monoaza crown derivatives with metal cations in water can be evaluated indirectly by the measurement of the ΔT_{cp} values, like simple alkyl crown ethers previously reported.[9a,f] It is said that $C_{12}E(m+1)$-N(15 or 18) (**IIIh,i,q,r**) and C_{12}-N(15 or 18) (**IVb,d**) can strongly complex with alkali and alkaline earth metal cations, especially with K^+, Sr^{2+}, and Ba^{2+}, even in water as shown in Table 1-4.

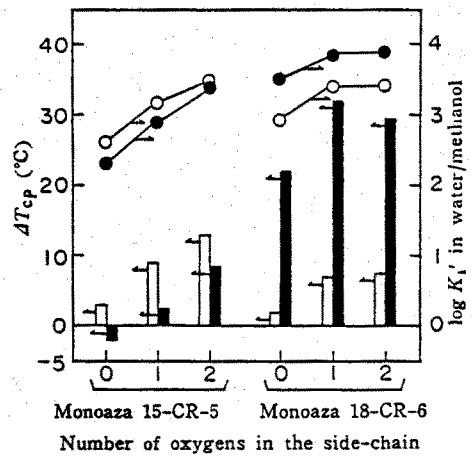
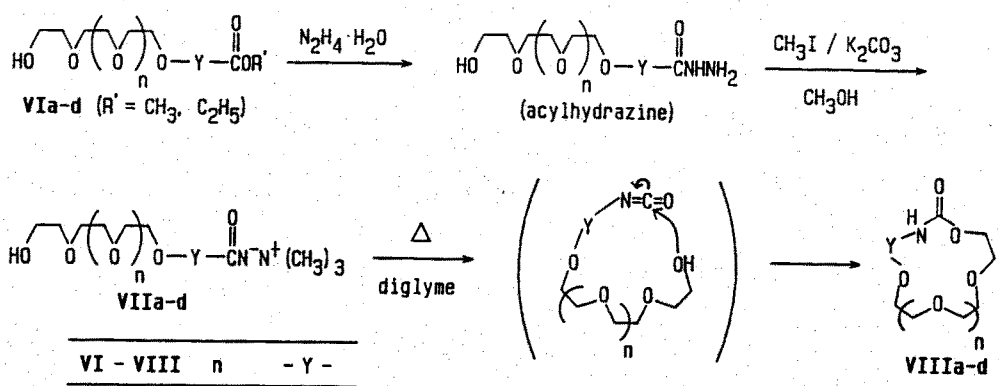


Fig. 1-3 Relationship between ΔT_{CP} at MCl/crown molar ratio=5.0 and log K_1' in water/methanol (10 : 90 v/v) mixture

□ (ΔT_{CP}) and ○ (log K_1') : NaCl
■ (ΔT_{CP}) and ● (log K_1') : KCl

1-3 Synthesis of Urethane Types of Crown Ethers by Thermolysis of N-Ammonioamidates

1-3-1 Experimental



VI - VIII	n	- Y -
a	2	$-CH_2-$
b	3	
c	1	
d	2	

Scheme 1-2 Synthesis of urethane types of crown ethers (**VIII**) from N-ammonioamidates (**VII**).

Preparation of N-ammonioamidates (VII): Typical procedure. A mixture of the methyl ester (**VIa**; 8.0 g, 0.03 mol) and hydrazine hydrate (80 %) (5.6 g, 0.09 mol) was stirred at 60°C for 2 hr. After evaporation of the unreacted hydrazine, methyl iodide (41.5 g, 0.3 mol) was dropped at 20°C to the suspension of the crude acylhydrazine and K_2CO_3 (13.8 g, 0.1 mol) in methanol. The reaction mixture was stirred for 10 hr at reflux temperature, and then insoluble solids were separated by filtration. Excess methyl iodide and the solvent were evaporated off, and extraction of the residue with acetone several times followed by a silica-gel column chromatography with an acetone : methanol (= 5:1) eluent gave a

7.1 g (79 %) of N-ammonioamidate (**VIIa**) as a slightly yellowish liquid. Using the similar procedure, **VIIb-d** were also obtained as a slightly yellowish liquid in each case. The synthetic results and some physical properties of **VIIa-d** are summarized in Table 1-5.

Table 1-5 Characterization of N-ammonioamidates (**VII**).

Compd	Yield (%)	IR (neat) (cm^{-1})	mass (M^+)/(base peak)	^1H NMR ($CDCl_3$) (δ, ppm)
VIIa	79	3360, 1600, 1120	308/59	3.47(s,9H+1H), 3.6-3.8(m,16H), 3.86(s,2H)
VIIb	77	3400, 1610, 1110	352/45	3.50(s,9H+1H), 3.6-3.8(m,20H), 3.86(s,2H)
VIIc	65	3400, 1600, 1580, 1130	326/45	3.4-3.9(m,9H+10H+1H), 4.16(d,2H), 6.95(dd,2H), 7.23(d,1H), 7.39(d,1H)
VIId	74	3300, 1600, 1580, 1120	370/45	3.4-3.9(m,9H+14H+1H), 4.16(d,2H), 6.90(dd,2H), 7.17(d,1H), 7.35(d,1H)

Preparation of urethane types of crown ethers (VIII): Typical procedure. A solution of N-ammonioamidate (**VIIa**) in diglyme (150 ml) was heated at 160°C for 2 hr with stirring in nitrogen atmosphere. The solvent was evaporated off and the residue (0.8 g, semi-solid) was distilled by a Kugelrohr apparatus (130°C/0.01 Torr) to give a 0.4 g (49 %) of urethane type of crown ether (**VIIIa**) as a colorless liquid. Crown ethers (**VIIIb-d**) were also obtained as a colorless liquid in each case according to this procedure. The preparation results and some physical properties are listed in Table 1-6.

Table 1-6 Characterization of urethane types of crown ethers (**VIII**).

Compd	Yield (%)	bp[a] (°C/Torr)	IR (neat) (cm^{-1})	mass (M^+)/(base peak)	^1H NMR ($CDCl_3$) (δ, ppm)
VIIIa	49	130/0.01	3350, 1720, 1100	249/45	3.6-3.8(m,14H), 4.27(t,2H), 4.70(d,2H), 6.7(br,1H)
VIIIb	58	145/0.03	3320, 1720, 1110	293/45	3.6-3.8(m,18H), 4.23(t,2H), 4.69(d,2H), 6.7(br,1H)
VIIIc	35	130/0.05	3200, 1720, 1600, 1100	267/267	3.4-3.8(m,8H), 4.20(m,2H), 4.32(m,2H), 7.00(m,3H), 7.58(s,1H), 7.70(m,1H)
VIIId	50	140/0.03	3200, 1720, 1600, 1150	311/311	3.6-3.9(m,12H), 4.15(m,2H), 4.30(m,2H), 6.92(m,3H), 7.9-8.1(m,1H+1H)

a) Kugelrohr distillation.

Measurement. The stability constants (log K_1') were measured in methanol at 25°C as mentioned in this chapter, Section 2. The number-average molecular weight was measured with a Hitachi Perkin Elmer 115 type vapor pressure osomometer in chloroform solutions at 25°C.

1-3-2 Results and Discussion

Treatment of methyl ester having oxyethylene units (**VIa**)[12e] with hydrazine hydrate afforded the corresponding acylhydrazine (IR: $\nu_{C=O}$ 1670 cm^{-1}). The crude acylhydrazine was treated with excess methyl iodide in the presence of K_2CO_3 in methanol to give N-ammonioamidate (**VIIIa**; IR: $\nu_{C=O}$ 1600 cm^{-1}) as a liquid in 79 %

yield after purification on a silica-gel column. N-Ammonioamidate (**VIIIb**) was similarly prepared from **VIb** in 77 % yield.

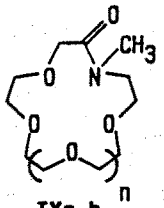
A dilute solution of N-ammonioamidate (**VIIa**) in diglyme was heated at 160°C. Distillation of the product by a Kugelrohr apparatus gave the distillate (IR: $\nu_{C=O}$ 1720 cm^{-1}) which showed one main peak in GLC (5 % Silicone OV-1 on Uniport KP, 1 m, 180°C). Its molecular weight was determined as 250 by a vapor-pressure osomometer, and from these results and its spectral data (see experimental section, Table 1-6), it was identified as the urethane type of crown ether (**VIIIa**; 49 % yield). Urethane crown (**VIIIa**) may be formed by the intramolecular addition of ω-hydroxyl group to isocyanato group which is formed by the thermolytic rearrangement of N-ammonioamidate (**VIIIa**). (See Scheme 1-2) And the residue which showed similar IR and ^1H NMR spectra to the distillate was recognized as urethane oligomers formed via intermolecular reaction. Crown ether (**VIIIb**) was also prepared from **VIIb** in 58 % yield. The addition of a template salt such as $NaBF_4$ and KBF_4 in the thermolysis showed no remarkable effect in yield of urethane types of crown ethers.

Furthermore, urethane type benzocrown compounds (**VIIIc,d**) which were possible to introduce an additional functional group into an aryl ring[19] were analogously synthesized from ethyl o-oligo(oxyethylene)oxy-benzoates (**VIIc,d**). (See Scheme 1-2)

As one of the properties of urethane types of crown ethers, the stability constants (log K_1') for **VIIIa,b** with Na^+ and K^+ in methanol at 25°C were measured. These results are listed in Table 1-7 together with the results for monoamide types of crown ethers (**IXa,b**).[12h]

Table 1-7 Stability constants (log K_1') for **VIIIa,b** and **IXa,b**[a] with Na^+ and K^+ in methanol at 25°C.

Compound	log K_1'	
	Na^+	K^+
VIIIa (16-membered ring)	1.4	1.8
VIIIb (19-membered ring)	2.2	2.9
IXa (15-membered ring)	<0.5	0.8
IXb (18-membered ring)	1.8	1.9



IXa, b
a : n= 1
b : n= 2

a) Ref. 12h.

It was expected that the complexing properties of urethane types of crown ethers toward these cations were not so good because of their strained structures suggested by a C.P.K. model demonstration. But the complexing abilities of **VIIIa,b** were superior to those of amide types of crown ethers (**IXa,b**) and some selectivity of **VIIIb** toward K^+ was observed.

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CHAPTER 2 SYNTHESIS AND THERMOLYSIS OF N-AMMONIOAMIDATES CONTAINING OLIGO(OXYETHYLENE) GROUP AND/OR HYDROXYL GROUP IN ACYL MOIETY

2-1 Introduction

Segmented poly(ether-urethane)s (SPU) have recently become of major interest as "biomedical" polymer materials for artificial hearts or blood circulation systems for which blood compatibility is required.[1)] There are many reports from every point of view on the preparation of modified SPU,[2)] the morphology or the structure effect,[3)] and evaluation of antithrombogenicities[1a,4)] of them. But, to our knowledge, most of the studied SPU polymers result from polyetherdiols, commercially available aryl diisocyanates, and alkylene diamines as chain extender. The investigation of a new type of SPU precursor seems to be important for the improvement of SPU polymers to enhance their utilization.

As one type of urethane precursors, the so-called "AB type" was reported,[5)] which has both a hydroxyl- and a functional group convertible into an isocyanato group, such as an azide group, in the same molecule. N-Ammonioamidates (aminimides) also seem to be useful as urethane precursors, because they are generally stable and easy to deal with under ordinary conditions, but readily rearrange to isocyanates upon heating.[6)]

The author described the synthesis of urethane types of crown ethers by the thermolytic reaction of N-ammonioamidates containing an ω-hydroxyoligo(oxyethylene)oxy group in Chapter 1, Section 3.

In this chapter, the author described the preparation and properties of N-ammonioamidates with a hydroxyl group in an acyl moiety from commercially available lactones or α-hydroxy carboxylates and discussed the effect of structure of those N-ammonioamidates and the solution concentration on types of urethane compounds that were formed by the thermolysis of N-ammonioamidates in mesitylene. (Section 2)

Furthermore, the author synthesized N-ammonioamidates containing a hydroxyl group, oxyalkylene units (as a "soft" part), and an alkylene chain or a phenylene group (as a "hard" part) in the same molecule, as model compounds of new types of SPU precursors, and clarified the relation between the structure of N-ammonioamidates and the products obtained by their thermolysis. (Section 3)

2-2 Synthesis and Thermolysis of N-Ammonioamidates Containing Hydroxyl Group in Acyl Moiety

2-2-1 Experimental

The ^{1}H NMR and IR spectra were taken on a JEOL JNM-PS-100 spectrometer and a Hitachi 260 spectrometer, respectively. The mass spectra were measured with a Hitachi RMU-6E mass spectrometer at an ionization potential of 70 eV. GLC analyses were performed on a Shimadzu gas chromatograph GC-4CPT using a 1 m x 3 mm column packed with 10 % Silicone OV-1 on Uniport KS. The number-average

molecular weight was measured with a Hitachi Perkin Elmer 115-type vapor-pressure osmometer in a chloroform solution at 25°C. The starting materials were commercial products of analytical reagent grade. Their purities were checked by GLC and IR, and they were purified by distillation when necessary. N,N,N-Trimethylhydrazinium iodide (III) was obtained as white solids by the interaction of equivalent N,N-dimethylhydrazine and methyl iodide in diethyl ether at 20°C and used without further purification. Mesitylene was distilled under reduced pressure before use.

*Preparation of N-Trimethylammonio-4-hydroxybutanamidate (**IVb**) by the hydrazinium iodide-method.* Potassium metal (4.7 g, 0.12 mol) was dissolved in 300 ml of t-BuOH, and then III (20.2 g, 0.10 mol) and 4-butanolide (**Ib**, 8.6 g, 0.10 mol) were slowly added, in turn, to the solution. After 5 hr of stirring at 50°C and subsequent neutralization by hydrochloric acid (to pH 8.0), the reaction mixture was filtered. Precipitates were washed with dichloromethane, and the solvent was removed from a combined solution of filtrate and washings. Solid-liquid extraction of the residue with dichloromethane several times was followed by the filtration and evaporation of the extracts. This afforded a 12.8 g of crude N-ammonioamidate, as white solids (80 %). The pure **IVb** was obtained by recrystallization from acetone as fine white needles (9.9 g, 62 %). Crude ammonioamidate showed a similar IR spectrum to the corresponding pure one. Using a similar procedure, N-(trimethylammonio)hydroxyalkanamidates (**IVc-f**; see Scheme 2-1) were also obtained.

Preparation of N-trimethylammonio-3-hydroxypropanamidate

(IVa) by the hydrazine-method. A mixture of 3-propanolide (**Ia**, 7.2 g, 0.10 mol) and hydrazine hydrate (80 %) (9.4 g, 0.15 mol) was stirred at 60°C for 5 hr. After evaporation of the unreacted hydrazine, methyl iodide (85.2 g, 0.60 mol) was dropped into the suspension of crude 3-hydroxypropanohydrazide (**VIa**, 10.9 g, about 0.1 mol) and potassium carbonate (27.6 g, 0.20 mol) in 300 ml of methanol at 20°C. The reaction mixture was stirred for 8 hr at reflux temperature, and then insoluble solids were separated by filtration. Excess methyl iodide and the solvent of the filtrate were evaporated off. The residue was extracted with acetone several times followed by filtration and evaporation of the extracts. This afforded a 11.0 g of crude N-ammonioamidate as white solids (75 %). The pure **IVa** was obtained by recrystallization from acetone as fine white needles (7.7 g, 53 %). Using a similar procedure, N-ammonioamidates (**IVb,g,h**) were also obtained. A characterization of the N-ammonioamidates (**IVa-h**) and the isolated acylhydrazines (**VIa,b**) (recrystallization from ethanol) was accomplished by standard methods (Table 2-1). Elemental analyses of **IVa-h** are shown in Table 2-2.

Thermolysis of IVa under dilute conditions. Dry mesitylene (100 ml) was heated at 160°C in a 200-ml separable reaction flask under a nitrogen atmosphere. After addition of **IVa** (1.00 g, 6.84 mmol) to hot mesitylene, the solution was stirred until the absorption peak (based on the carbonyl group in the IR spectrum of aliquot) completely shifted to about 1700 cm^{-1} (6 hr). Then, the solvent was evaporated off and the residue (0.57 g, solids), which was entirely dissolved in chloroform and showed one

main peak in GLC, was distilled using a Kugelrohr apparatus (120°C/0.02 Torr) to give a 0.55 g of 2-oxazolidinone (**VIIa**) as fine white needles (92 % yield based on **IVa**). A very small amount of residue was observed. The thermolysis and work-up of the thermolytic products of **IVb**, **IVc**, or **IVd** under dilute conditions were undertaken in the same way as above since the crude product in each case was also wholly dissolved in chloroform. Perhydro-1,3-oxazin-2-one (**VIIb**, 86 %), 6-methylperhydro-1,3-oxazin-2-one (**VIIc**, 95 %), and 6-pentylperhydro-1,3-oxazin-2-one (**VIId**, 90 %) were obtained from **IVb**, **IVc**, and **IVd**, respectively.

*Thermolysis of **IVe** under dilute conditions.* A solution of **IVe** (1.00 g, 5.74 mmol) in dry mesitylene (100 ml) was heated as described above. The solvent was evaporated off and the residue (0.56 g, semi-solid) was extracted with chloroform (100 ml) and filtered. The insoluble solids were washed with chloroform and dried in vacuo (pale-brown; 0.17 g after drying). The chloroform extracts were combined, the solvent was evaporated off, and the residue (0.39 g) was distilled using a Kugelrohr apparatus at 120°C (0.02 Torr) to separate a distillate (0.18 g) as fine white needles and a residue (0.21 g) as pale-brown solids. The distillate was identified as perhydro-1,3-oxazepin-2-one (**VIIe**, 27 % yield based on **IVe**). Perhydro-1,3-oxazocin-2-one (**VIIf**, 0.06 g, 8 % yield based on **IVf**) as a distillate, a 0.37 g of residue, and a 0.14 g of chloroform-insoluble solid were obtained from **IVf** using a similar procedure.

Elemental analyses of **VIIa-f** are shown in Table 2-2.

Table 2-1 Characterization of N-ammonioamidates (IV) and acylhydrazines (VI).

Compound	IR (KBr pellet)	^{1}H NMR ($CDCl_3$)	MS (70eV)
	ν/cm^{-1}	δ	m/z (rel. intensity)
IVa	3200, 1580	2.21(t, 2H), 3.33(s, 9H), 3.72(t, 2H), 4.7(br, 1H)	146(M^+, 3), 101(14), 59(100), 58(47)
IVb	3300, 1580	1.77(m, 2H), 2.25(t, 2H), 3.35(s, 9H), 3.65(t, 2H), 5.4—5.9(br, 1H)	160(M^+, 2), 116(27), 101(39), 59(100), 58(62)
IVc	3350, 1580	1.16(d, 3H), 1.65(m, 2H), 2.25(m, 2H), 3.37(s, 9H), 3.80(m, 1H), 5.5(br, 1H)	174(M^+, 3), 116(18), 101(36), 59(100), 58(56)
IVd	3350, 1580	0.87(t, 3H), 1.1—1.6(m, 8H), 1.70(m, 2H), 2.28(m, 2H), 3.36(s, 9H), 3.70(m, 1H), 4.6—5.8(br, 1H)	230(M^+, 2), 159(42), 116(24), 101(40), 59(100), 58(71)
IVe	3350, 1580	1.4—1.9(m, 4H), 2.06(t, 2H), 3.38(s, 9H), 3.60(t, 2H), 4.3(s, 1H)	174(M^+, 1), 116(14), 101(39), 59(100), 58(61)
IVf	3300, 1580	1.2—1.8(m, 6H), 2.05(t, 2H), 3.40(s, 9H), 3.62(t+s, 2H+1H)	188(M^+, 2), 116(28), 101(34), 59(100), 58(54)
IVg	3300, 1600	1.29(d, 3H), 3.40(s, 9H), 3.7—4.1(br, 1H), 4.00(q, 1H)	146(M^+, 1), 101(42), 59(100), 58(74)
IVh	3330, 1600	3.22(s, 9H), 4.63(s+s, 1H+1H), 7.1—7.6(m, 5H)	149(M^+—59, 3), 106(66), 101(16), 77(72), 59(58), 58(100)
VIa[a)]	3300, 1630	2.16(t, 2H), 3.58(t, 2H), 4.6(br, 3H), 8—10(br, 1H)	104(M^+, 1) 73(20), 43(28), 32(100)
VIb[b)]	3300, 1640	1.63(m, 2H), 2.02(m, 2H), 3.40(t, 2H), 4.15(s, 2H), 4.47(t, 1H), 8.9(s, 1H)	118(M^+, 3), 87(10), 43(14), 32(100)

a) Mp; 95—97°C. b) Mp; 94—96°C.

Table 2-2 Elemental analysis of N-ammonioamidates (IV) and cyclic urethanes (VII).

Compound	Molecular formula	Found (Calcd)/%		
		H	C	N
IVa	$C_6H_{14}N_2O_2$	9.61 (9.65)	49.25 (49.30)	19.12 (19.16)
IVb	$C_7H_{16}N_2O_2$	9.94 (10.07)	52.39 (52.48)	17.23 (17.48)
IVc	$C_8H_{18}N_2O_2$	10.35 (10.41)	55.01 (55.15)	15.99 (16.08)
IVd	$C_{12}H_{26}N_2O_2$	11.27 (11.38)	62.33 (62.57)	12.04 (12.16)
IVe	$C_8H_{18}N_2O_2$	10.32 (10.41)	55.21 (55.15)	15.91 (16.08)
IVf	$C_9H_{20}N_2O_2$	10.61 (10.71)	57.53 (57.42)	14.85 (14.88)
IVg	$C_6H_{14}N_2O_2$	9.55 (9.65)	49.54 (49.30)	19.32 (19.16)
IVh	$C_{11}H_{16}N_2O_2$	7.75 (7.74)	63.42 (63.44)	13.37 (13.45)
VIIa	$C_3H_5NO_2$	5.85 (5.79)	41.51 (41.38)	16.08 (16.09)
VIIb	$C_4H_7NO_2$	6.96 (6.98)	47.23 (47.52)	13.80 (13.85)
VIIc	$C_5H_9NO_2$	7.88 (7.88)	52.10 (52.16)	12.10 (12.17)
VIId	$C_9H_{17}NO_2$	9.97 (10.01)	63.00 (63.13)	8.20 (8.18)
VIIe	$C_5H_9NO_2$	7.95 (7.88)	52.22 (52.16)	12.14 (12.17)
VIIf	$C_6H_{11}NO_2$	8.59 (8.58)	55.62 (55.80)	10.85 (10.84)

*Thermolysis of **IVa** under Concentrated Conditions.*

A solution of **IVa** (1.00 g, 6.84 mmol) in dry mesitylene (10 ml) in a 50-ml separable reaction flask was heated at 160°C for 3 hr with stirring under a nitrogen atmosphere. Work-up of the reaction product was performed in the same way as the case of the thermolysis of **IVe** under dilute conditions. Cyclic urethane (**VIIa**, 0.22 g, 37 % yield based on **IVa**) as a distillate, a 0.31 g of residue, and a 0.02 g of chloroform-insoluble solids were afforded. The thermolysis of N-ammonioamidates (**IVb-f**) under concentrated conditions was carried out using a similar procedure. The results of thermolytic reactions, including α-hydroxyl type N-ammonioamidates (**IVg,h**), are presented in Table 2-4.

2-2-2 Results and Discussion

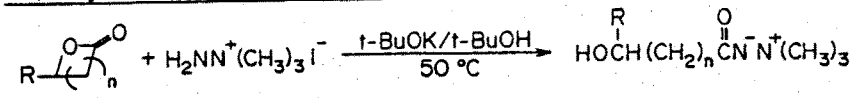
N-Ammonioamidates (**IV**) were prepared from lactones (**I**) or α-hydroxy carboxylates (**II**) by the following two methods. (Scheme 2-1)

(A) Hydrazinium iodide-method. N-Ammonioamidates were obtained by a one-step reaction between **I** and N,N,N-trimethylhydrazinium iodide (**III**), which was formed in quantitative yield from N,N-dimethylhydrazine and methyl iodide, in t-BuOH in the presence of t-BuOK.[7)]

(B) Hydrazine-method. This method consisted of two-steps reactions. The preparation of acylhydrazines (**VI**) from **I** or **II** and excess hydrazine hydrate (80 %) (**V**) followed by the reaction with a large excess of methyl iodide (more than six folds to **I**) in methanol in the presence of potassium carbonate yielded N-ammonioamidates.

After reactions involving both methods, crude products of N-ammonioamidates were separated by extraction with dichloromethane and pure compounds were obtained by recrystallization from acetone or ethyl acetate. The isolated products were characterized by spectral and elemental analyses (Tables 2-1 and 2-2). The yields and melting points of **IV** are listed on Table 2-3. Difference in yield of N-trimethylammonio-4-hydroxybutanamidate (**IVb**) from 4-butanolide (**Ib**) was not observed between both methods, and **IVb** was obtained in good yield (above 80 %) by each method. By the hydrazinium iodide-method, however, N-ammonioamidates were hardly obtained from 3-propanolide (**Ia**) and α-hydroxy carboxylates (**II**).

A ; Hydrazinium iodide - method



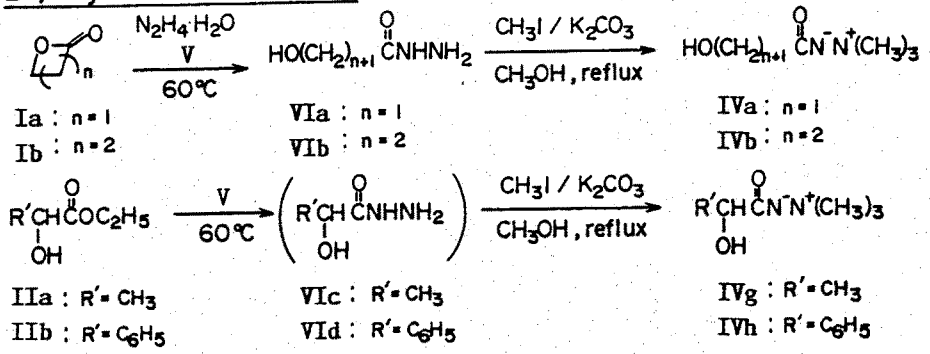
Ib–f III IVb–f

I,IVb : n = 2 , R = H I,IVe : n = 3 , R = H

I,IVc : n = 2 , R = CH_3 I,IVf : n = 4 , R = H

I,IVd : n = 2 , R = C_5H_{11}

B ; Hydrazine - method



Ia : n = 1 VIa : n = 1 IVa : n = 1

Ib : n = 2 VIb : n = 2 IVb : n = 2

IIa : R′ = CH_3 VIc : R′ = CH_3 IVg : R′ = CH_3

IIb : R′ = C_6H_5 VId : R′ = C_6H_5 IVh : R′ = C_6H_5

Scheme 2-1

Table 2-3 Yield and melting point of N-ammonioamidates (IV).

N-Ammonioamidate	Method[a)]	Yield[b,c)] %	Mp θ_m/°C
IVa	B	75 (53)	125—126
IVb	A	80 (62)	107—108
IVb	B	82	
IVc	A	93 (69)	92—94
IVd	A	85 (63)	86—88
IVe	A	94 (61)	95—96
IVf	A	85 (68)	116—117
IVg	B	86 (55)	108—109
IVh	B	81 (59)	140(dec)

a) A; Hydrazinium iodide method, B; Hydrazine method. b) Crude yields based on I or II . c) Values in parentheses are yields after recrystallization.

The hydrazine-method has some advantages as follows: using an inexpensive hydrazine hydrate (**V**) instead of N,N,N-trimethylhydrazinium iodide and being applicable to both lactones and α-hydroxy carboxylates. Intermediates, 3-hydroxypropanohydrazide (**VIa**) and 4-hydroxybutanohydrazide (**VIb**), obtained from **Ia** and **Ib**, respectively, were isolated by recrystallization from ethanol and identified by spectral analyses (Table 2-1). However, there was no difference in yield when a crude acylhydrazine was used in a following reaction without further purification.

The thermolysis of prepared N-ammonioamidates (**IVa-h**) was carried out in mesitylene as an inert and high-boiling-point solvent. The N-ammonioamidate was stirred at 160°C in mesitylene under a nitrogen atmosphere until the carbonyl absorption in the IR spectrum shifted to about 1700 cm^{-1} due to the formation of a urethane bond. The solvent was evaporated off and the residue (solids or semi-solids) was extracted with chloroform to separate the soluble- and insoluble portions (insoluble one; Fraction 3). The chloroform-soluble portion was further separated into the distillate (Fraction 1) and the residue (Fraction 2) by distillation at 120°C/0.02 Torr using a Kugelrohr apparatus.

The thermolysis was carried out in both dilute- (1.00 g of N-ammonioamidate/100 ml of mesitylene) and concentrated- (1.00 g of N-ammonioamidate/10 ml of mesitylene) conditions. The yields of reaction products and the weight percentage of each fraction are shown in Table 2-4.

Table 2–4 Thermolysis of N-ammonioamidates (IVa–h).

Run	N-Ammonioamidate	Reaction system[a)]	Reaction time/h	Yield[b)]	Fraction ratio/wt %		
				g	Fr.1[c)]	Fr.2[d,e)]	Fr.3[f)]
1	IVa	Dilute	6	0.57	≅100	Trace	0
2	IVa	Concd	3	0.55	40	55 (157)	5
3	IVb	Dilute	2	0.55	≅100	Trace	0
4	IVb	Concd	3	0.52	30	65 (255)	5
5	IVc	Dilute	3	0.65	≅100	Trace	0
6	IVc	Concd	3	0.60	70	27 (270)	3
7	IVd	Dilute	3	0.68	≅100	Trace	0
8	IVd	Concd	3	0.69	55	45 (242)	0
9	IVe	Dilute	3	0.56	32	38 (416)	30
10	IVe	Concd	3	0.51	0	15 (425)	85
11	IVf	Dilute	3	0.57	10	65 (555)	25
12	IVf	Concd	3	0.54	0	10 (520)	90
13	IVg	Dilute	5	0.61	37	18 (271)	45
14	IVg	Concd	5	0.59	0	21 (285)	79
15	IVh	Dilute	5	0.70	31	28 (354)	41
16	IVh	Concd	5	0.68	0	17 (339)	83

a) Dilute system: 1.0g(IV)/100 ml (mesitylene); concd system: 1.0g(IV)/10 ml (mesitylene). b) Yield of the residue after removal of mesitylene. c) The distillate of chloroform-soluble portion using a Kugelrohr apparatus (120°C/0.02Torr) d) The residue of chloroform-soluble portion by Kugelrohr-distillation. e) Values in parentheses are number-average molecular weights ($\overline{Mn}$) measured by a VPO in a chloroform at 25°C. f) The chloroform-insoluble portion.

In the thermolysis of **IVa-f**, the distillates (Fraction 1) were white solids which showed one peak in GLC. Also, needle-like crystals were obtained by recrystallization from ethyl acetate. From their spectral data and elemental analyses, these fractions were identified as cyclic urethanes (**VIIa-f**). These compounds may be formed by the intramolecular addition of a hydroxyl group to an isocyanato group which was introduced by the thermolytic rearrangement of the N-ammonioamidates. The properties and elemental analyses of **VIIa-f** are shown in Tables 2-5 and 2-2, respectively.

The residual compounds in the distillation (Fraction 2) were semi-solids which showed some peaks for longer retention times than that of the corresponding Fraction 1 in GLC. But their IR spectra and both the chemical shift and the integral ratio in their ^{1}H NMR were similar to those of the corresponding Fraction 1. Their molecular weights were determined by the VPO method (Table 2-4) and they were considered as urethane oligomers with low molecular weights which might be formed by the intermolecular reaction between hydroxyl and isocyanato groups. It is probable that Fraction 2 was for the most part cyclic oligomers since their molecular weights were not so large and the existence of expected terminal groups in linear structures were not observed in the ^{1}H NMR spectra.

The chloroform-insoluble matter (Fraction 3) was white or pale-brown solids and showed the same IR spectra to the corresponding Fraction 2. Thus, Fraction 3 could be considered as a linear or cyclic urethane polymer with a higher molecular weight

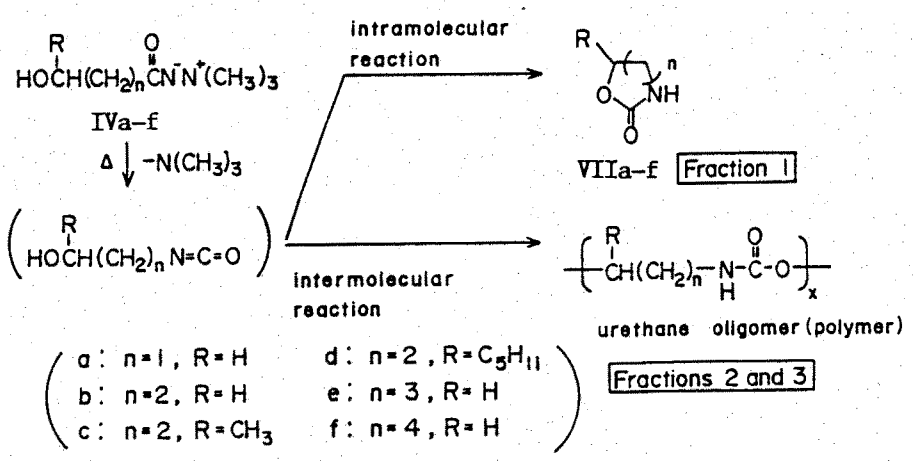
Table 2-5 Characterization of cyclic urethanes (**VIIa-f**).

Compound	Starting N-Ammonioamidate	Mp θ_m/°C	IR (KBr pellet) ν/cm^{-1}	^{1}H NMR ($CDCl_3$) δ	MS (70 eV) m/z(rel. intensity)
VIIa	**IVa**	88—89	3370, 1730	3.62(t, 2H), 4.44(t, 2H), 6.55(s, 1H)	87(M^+, 100), 59(49), 42(23), 28(43)
VIIb	**IVb**	83—84	3275, 1690	1.96(q, 2H), 3.35(t, 2H), 4.30(t, 2H), 6.6—7.2(br, 1H)	101(M^+, 100), 56(39), 33(16), 29(23), 28(77)
VIIc	**IVc**	98—99	3260, 1720	1.38(d, 3H), 1.75(m, 2H), 3.35(q, 2H), 4.41(m, 1H), 6.88(s, 1H)	115(M^+, 40), 71(21), 56(45), 43(66), 42(70), 30(100), 28(99)
VIId	**IVd**	102—103	3265, 1700	0.88(t, 3H), 1.1—2.1(m, 10H), 3.35(m, 2H), 4.25(m, 1H), 6.75(s, 1H)	171(M^+, 1), 100(88), 82(23), 74(41), 55(69), 43(30), 30(100)
VIIe	**IVe**	61—62	3345, 1710	1.6—2.0(m, 4H), 3.15(q, 2H), 4.16(t, 2H), 6.47(s, 1H)	115(M^+, 77), 70(11), 56(21), 42(100), 30(60)
VIIf	**IVf**	75—76	3350, 1700	1.5—2.0(m, 6H), 3.30(m, 2H), 4.20(t, 2H), 6.05(s, 1H)	129(M^+, 11), 68(40), 56(99), 43(82), 30(100)

than Fraction 2. Their molecular weights and ^{1}H NMR spectra were not measured, however, since they were only slightly soluble in water, alcohols, tetrachloromethane or other organic solvents.

The mechanism of the formation of urethane compounds mentioned above is shown in Scheme 2-2.

In the thermolysis of α-hydroxyl type N-ammonioamidates (**IVg,h**), Fraction 1 was obtained as a pale-yellow liquid which showed some peaks in GLC and absorption peaks at 1830 and 1760 cm^{-1}, besides 1710 cm^{-1} in IR spectra. But the formation of compound **VII** type cyclic urethane was not detected by mass spectra. And their ^{1}H NMR spectra were complicated, so that their ingredients could not be identified. The IR spectra of Fraction 2 was similar to that of Fraction 1. Fraction 3 was white solids which showed a strong absorption peak at 1740 cm^{-1}.



Scheme 2-2

As shown in Table 2-4, the formation ratio of cyclic urethanes (**VII**), urethane oligomers with low molecular weights, and urethane polymers was considerably affected by both the chain length (defined as the number of carbons between carbonyl- and hydroxyl group of **IV**) and the concentration of the solution. In the case of dilute conditions, five-membered (**VIIa**) and six-membered rings (**VIIb-d**) of cyclic urethanes were quantitatively formed from **IVa** (chain length= 2) and **IVb-d** (chain length= 3), respectively, and the formation of oligomer and polymer was not observed (Table 2-4, Runs 1, 3, 5, and 7). On the other hand, oligomers were mainly obtained in the thermolysis of **IVe** and **IVf**. It seemed reasonable that the intermolecular reaction took place prior to the intramolecular reaction in which a seven- (**VIIe**) or eight-membered ring (**VIIf**) compound was formed (Runs 9 and 11). Under concentrated conditions, an oligomer was also formed in the reaction of **IVa-d** (Runs 2, 4, 6, and 8) and a polymer was obtained (for the most part) in the case of **IVe** and **IVf** (Runs 10 and 12).

2-3 Synthesis and Thermolysis of N-Ammonioamidates as Model Precursors of New Types of Segmented Poly(ether-urethane)s

2-3-1 Experimental

The GPC analyses were carried out with a JAI LC-07 liquid chromatograph apparatus [column: JAIGEL GPC column (porous polystyrene gel; exclusion limit: (1-1.5) x 10^3 for linear polystyrenes); eluent: chloroform; flow rate: 3.3 ml/min]. The thermolytic temperature was measured with a DTA-TG (Rigaku Thermoflex) apparatus.

Diglyme (2,5,8-trioxanonane) was distilled under reduced pressure before use. The purity of commercial products was checked by GLC and IR, and they were purified by distillation when necessary.

Preparations of the esters. Methyl esters having oxyethylene units and an alkylene chain (**VIIIa-e**) were prepared from oligo(alkylene glycol)s and ω-haloalkanecarboxylic acids by the previously reported method[8]. Ethyl esters containing oxyethylene units and a phenylene group (**VIIIf-i**) were obtained according to the method reported by Hiratani[9].

Preparations of the N-ammonioamidates. N-Ammonioamidates containing a hydroxyl group, oxyalkylene units, and an alkylene chain or a phenylene group (**IXa-i**; see Scheme 2-2) were prepared from the corresponding esters (**VIIIa-i**) using similar procedures to those described in Chapter 1, Section 3. Yields and properties of **IXf** and **IXg** were also described in there. All compounds,

except **IXi**, were obtained as a pale-yellow liquid. Synthetic yield, spectral and elemental analytical data are listed in Table 2-6.

Thermolysis of the N-ammonioamidates: Typical procedure. Dry diglyme (10 ml) was heated at 160°C in a 50 ml separable reaction flask under a nitrogen flow. After addition of **IXa**

Table 2-6 Synthesis and characterization of N-ammonioamidates (**IX**).

Compd	Yield (%)	IR (neat) (cm^{-1})	mass m/e	^1H NMR ($CDCl_3$) (δ, ppm)	Anal. Found(Calcd)
IXa	62	3350, 1580, 1120	278(M^+), 101, 59	2.30(t,2H), 3.40(s,9H), 3.5-3.9(m,14H), 4.0-4.4(br,1H)	C, 51.26(51.78) H, 9.54 (9.41) N, 10.16(10.06)
IXb	84	3400, 1580, 1100	292(M^+), 159, 101, 59, 45	1.7-1.9(m,2H), 2.0-2.1(m,2H), 3.42(s,9H), 3.5-3.9(m,14H+1H)	C, 53.32(53.41) H, 9.92 (9.65) N, 9.66 (9.58)
IXc	72	3450, 1610, 1100	306(M^+), 101, 59, 45	1.4-1.8(m,4H), 2.2-2.4(m,2H), 3.50(s,9H), 3.6-4.2(m,14H+1H)	C, 54.57(54.88) H, 10.10 (9.89) N, 9.48 (9.14)
IXd	55	3350, 1600, 1120	248(M^+), 101, 59	1.10(d,6H), 3.2-3.7(m,6H+1H), 3.40(s,9H), 3.85(s,2H)	C, 53.11(53.21) H, 9.89 (9.74) N, 11.35(11.28)
IXe	60	3300, 1600, 1120	306(M^+), 101, 59	1.16(d,9H), 3.45(s,9H), 3.4-3.7(m,9H+1H), 3.83(s,2H)	C, 54.67(54.88) H, 10.06 (9.87) N, 9.13 (9.14)
IXh	65	3400, 1600, 1580, 1130	326(M^+), 59, 58, 45	2.9-3.2(br,1H), 3.40(s,9H), 3.5-3.9(m,10H), 4.18(t,2H), 6.92(d,1H), 7.21(t,1H), 7.5-7.6(m,2H)	C, 58.46(58.88) H, 8.02 (8.03) N, 8.84 (8.58)
IXi[a)]	72	3400, 1600, 1560, 1130	326(M^+), 59, 58, 45	2.4-2.8(br,1H), 3.42(s,9H), 3.5-3.9(m,10H), 4.15(t,2H), 6.83(d,2H), 7.83(d,2H)	C, 59.17(58.88) H, 8.08 (8.03) N, 8.55 (8.58)

a) Mp: 79-81°C, the IR spectrum was measured in KBr pellet.

(1.00 g; 3.59 mmol) to hot diglyme, the solution was stirred for 3 hr. Then, the solvent was evaporated and the residue (0.79 g; greasy) was separated into distillate (0.16 g; liquid) and residue (0.63 g; brown greasy) by distillation at 140°C/0.02 Torr, using a Kugelrohr apparatus. The distillate was identified as 14-oxo-1,4,7,10-tetraoxa-13-azacyclotetradecane (**Xa**; yield: 20%) and the residue was oligo(1,4,7,10-tetraoxa-13-aza-14-oxotetradeca-methylene) (**XIa**) according to the chemical analyses and physical data. Thermolysis of **IXb-i** was carried out using a similar procedure. In the cases of **IXd**, **IXe**, **IXh**, and **IXi**, no distillates were obtained when using a Kugelrohr apparatus at 160°C (0.02 Torr), and the presence of intramolecular cyclization products could not be confirmed by GPC analyses of the residues. Characterization of thermolytic products of N-ammonioamidates is summarized in Table 2-7. Properties of **Xf** and **Xg** were described in Chapter 1, Section 3.

2-3-2 Results and discussion

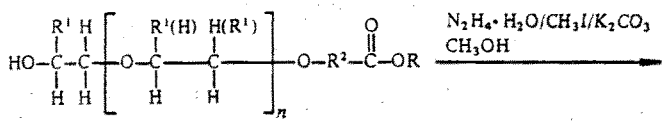
N-Ammonioamidates (**IXa-i**) were prepared from methyl or ethyl esters (**VIIIa-i**), containing a hydroxyl group and oxyalkylene units, via acylhydrazines according to the method described in Chapter 1, Section 3. (Scheme 2-3) Their purification was carried out by a silica-gel column chromatography with acetone/methanol (5:1 v/v) as an eluent, and their structures and compositions were confirmed by spectral and elemental analyses. Though pure **IXa-h** were obtained as a pale yellow liquid at room temperature, **IXi** was

obtained as white, fine needles by recrystallization from benzene.

Table 2-7 Characterization of thermolytic products (**X** and **XI**) of N-ammonioamidates (**IX**).

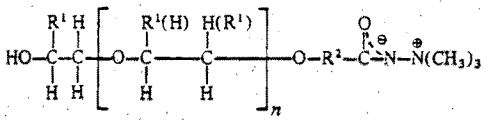
Compd	State	IR (neat) (cm^{-1})	^1H NMR ($CDCl_3$) (δ, ppm)	Anal.	Found(Calcd)
Xa[a]	viscous liquid (bp: 130°C/0.03 Torr)[b]	3350, 1725, 1110	3.3-3.4(m,2H), 3.5-3.9(m,12H), 4.30(t,2H), 4.30(t,2H), 4.8-5.6(br,1H)	calcd for $C_9H_{17}NO_5$	C, 49.02(49.31) H, 7.99 (7.82) N, 6.52 (6.39)
Xb[c]	viscous liquid (bp: 140°C/0.03 Torr)[b]	3300, 1730, 1110	1.78(tt,2H), 3.34(t,2H), 3.5-3.8(m,12H), 4.21(t,2H), 4.8-5.8(br,1H)	calcd for $C_{10}H_{19}NO_5$	C, 51.32(51.49) H, 8.19 (8.21) N, 6.00 (6.01)
Xc[d]	viscous liquid (bp: 140°C/0.02 Torr)[b]	3350, 1725, 1120	1.4-1.9(m,4H), 3.1-3.3(m,2H), 3.4-3.9(m,12H), 4.23(t,2H), 5.7-6.2(br,1H)	calcd for $C_{11}H_{21}NO_5$	C, 53.71(53.43) H, 8.84 (8.56) N, 5.88 (5.66)
XIa	pale-brown, greasy	3300, 1720, 1120	3.3-3.4(m,2H), 3.5-4.0(m,12H), 4.3(t,2H), 5.0-6.0(br,1H)	calcd for $(C_9H_{17}NO_5)_n$	C, 48.73(49.31) H, 7.74 (7.82) N, 6.06 (6.39)
XIb	pale-brown, greasy	3250, 1710, 1110	1.76(tt,2H), 3.32(t,2H), 3.5-3.8(m,12H), 4.20(t,2H), 5.2-5.7(br,1H)	calcd for $(C_{10}H_{19}NO_5)_n$	C, 50.32(51.49) H, 8.27 (8.21) N, 6.05 (6.01)
XIc[e]	pale-brown, solid	3300, 1710, 1100	1.4-2.0(m,4H), 3.0-3.3(m,2H), 3.4-3.9(m,12H), 4.25(t,2H), 5.5-6.5(br,1H)	calcd for $(C_{11}H_{21}NO_5)_n$	C, 52.38(53.43) H, 8.39 (8.56) N, 5.74 (5.66)
XId	brown, semi-solid	3350, 1720, 1100	1.0-1.4(m,6H), 3.2-4.2(m,6H), 4.6-5.3(m,2H), 5.9-6.6(br,1H)	calcd for $(C_8H_{15}NO_4)_n$	C, 50.78(49.51) H, 7.81 (7.99) N, 7.70 (7.40)
XIe	brown, semi-solid	3320, 1720, 1100	1.0-1.4(m,9H), 3.2-4.2(m,9H), 4.6-5.2(m,2H), 5.8-6.6(br,1H)	calcd for $(C_{11}H_{21}NO_5)_n$	C, 52.51(53.43) H, 7.95 (8.56) N, 5.73 (5.66)
XIf	pale-brown, semi-solid	3400, 1720, 1600, 1110	3.6-4.0(m,8H), 4.0-4.2(m,2H), 6.7-7.1(m,3H), 7.7-7.9(br,1H), 8.0-8.2(m,1H)	calcd for $(C_{13}H_{17}NO_5)_n$	C, 57.48(58.42) H, 6.46 (6.41) N, 5.51 (5.24)
XIg	pale-brown, semi-solid	3350, 1720, 1600, 1110	3.4-3.9(m,8H), 4.20(t,2H), 4.4-4.5(m,2H), 7.0-8.0(m,4H+1H)	calcd for $(C_{15}H_{21}NO_6)_n$	C, 57.38(57.87) H, 6.93 (6.80) N, 4.65 (4.50)
XIh	pale-brown, semi-solid	3300, 1710, 1600, 1100	3.4-4.0(m,8H), 4.1-4.3(m,2H), 4.3-4.5(m,2H), 6.8-7.6(m,4H+1H)	calcd for $(C_{13}H_{17}NO_5)_n$	C, 57.55(58.42) H, 6.87 (6.41) N, 6.20 (5.24)
XIi[e]	pale-brown, solid	3300, 1720, 1600, 1110	3.5-3.9(m,8H), 4.0-4.2(m,2H), 4.2-4.4(m,2H), 6.7-6.9(m,2H), 7.1-7.4(m,2H+1H)	calcd for $(C_{13}H_{17}NO_5)_n$	C, 57.81(58.42) H, 6.49 (6.41) N, 5.30 (5.24)

a) The mass spectrum (m/e): 219(M^+), 176, and 45. b) Kugelrohr distillation.
c) The mass spectrum (m/e): 233(M^+), 190, and 45. d) The mass spectrum (m/e): 247(M^+), 189, and 45.
e) The IR spectrum was measured in KBr pellet.

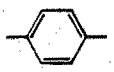


VIII

(R = CH_3 or C_2H_5)



IX

	VIIIa,IXa	b	c	d	e	f	g	h	i
R^1	H	H	H	CH_3	CH_3	H	H	H	H
$-R^2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	$-CH_2-$	$-CH-$				
n	2	2	2	1	2	2	3	2	2

Scheme 2-3

Before the thermolytic reaction, DTA and TG analyses of **IXe**, **IXg**, and **IXi** were performed to investigate the thermal decomposition temperature of those N-ammonioamidates. Exothermic changes, accompanying the decrease of weight, were observed in all cases between 150 and 160°C, so that the thermolytic reactions were carried out at 160°C. N-Ammonioamidates were dried at 70°C for 2 hr in vacuo using a Kugelrohr apparatus just before the next reaction.

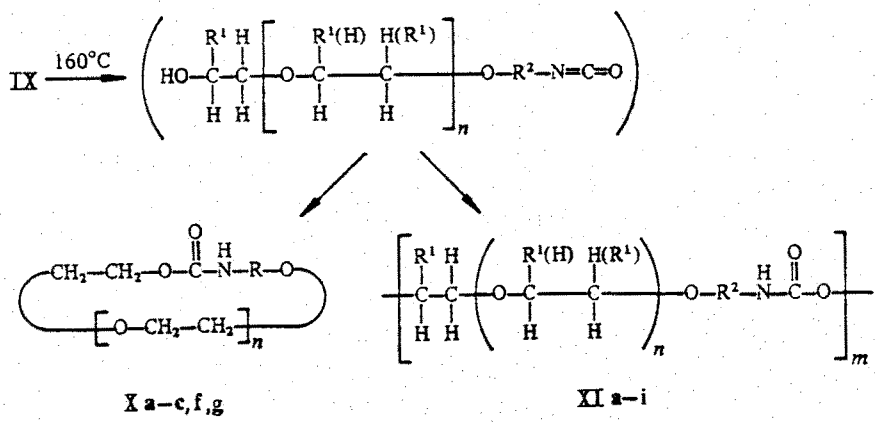
N-Ammonioamidate (1.0 g) was stirred at 160°C in diglyme (10 ml) in a dry nitrogen atmosphere until the carbonyl absorption in the IR spectrum completely shifted from about 1600 cm^{-1} (N-ammonioamidate) to about 1700 cm^{-1}, due to the formation of a urethane bond (3 hr in each case). The solvent was evaporated off and the residue (brown semi-solids) was distilled, using a

Kugelrohr apparatus under reduced pressure to separate the low-boiling products.

No volatile products were obtained under these conditions in the thermolysis of N-ammonioamidates containing oxypropylene units (**IXd,e**), a 1,3-phenylene (**IXh**) or a 1,4-phenylene group (**IXi**). In other cases, the distilled products were a clear or pale-yellow liquid which showed one peak in gas chromatography (GLC) and were identified as urethane types of crown ethers (**X**) from their spectral data and elemental analyses. These compounds are formed by the intramolecular addition of an ω-hydroxyl group to an isocyanato group.

The residues of the distillations were brown solids or greases. From the results of their IR, ^{1}H NMR, and number-average molecular weight determinations, they were considered as linear or cyclic oligo(ether-urethane)s (**XI**) formed by the intermolecular or intramolecular reactions respectively, between hydroxyl and isocyanato groups. (Scheme 2-4) The results of the thermolysis of **IX** are listed in Table 2-8.

It was observed that the ratios of products **X** : **XI**, formed from **IX**, were influenced significantly by the structure of N-ammonioamidates. Reactions of **IXa-c** having an alkylene chain (-R^2-= ethylene, trimethylene, or tetramethylene, respectively) gave the intramolecular cyclization products **Xa-c** in resembling yields. Although **IXf** and **IXg** had similar structures, except one oxyethylene unit, the product ratio of **Xg** (17-crown type) : **XIg** was much higher than that of **Xf** (14-crown type) : **XIf**. In the case of N-ammonioamidates containing oxypropylene units (**IXd,e**),



X a–c,f,g　　XI a–i

R_1, $-R^2-$, n: see VIIIa–i

Scheme 2–4

Table 2–8 Results of the thermolysis of N-ammonioamidates (IX).

Starting compd	Product ratio in wt% cyclic product (X) : oligomer (XI)	$\overline{Mn}$ of XI[a)]	Degree of oligomerization of XI
IXa	20 : 80	1060	4.8
IXb	11 : 89	1520	6.5
IXc	15 : 85	2510	10.2
IXd	0 : 100	1420	7.5
IXe	0 : 100	1500	6.1
IXf	22 : 78	1520	5.7
IXg	57 : 43	1080	3.5
IXh	0 : 100	1170	4.4
IXi	0 : 100	3350	12.5

a) Measured by the VPO in chloroform at 25°C.

a 1,3-phenylene (**IXh**), and a 1,4-phenylene group (**IXi**), no intramolecular cyclization products could be detected by GPC analyses of the thermolytic products.

An excess of isocyanates as compared to diols is commonly used in preparations of polyurethanes, considering the hydrolysis of isocyanates. The degree of oligomerization of **XIa-i** was rather small, probably due to the fact that the number of isocyanato groups resulting from the corresponding N-ammonioamidates was equal to that of hydroxyl groups. In the range of this study, however, the degree of oligomerization of **XIc** and **XIi** was higher than that of others. In addition, a great difference in the degree of oligomerization was observed between oligomers (**XIh**) with a 1,3-phenylene group and (**XIi**) with a 1,4-phenylene group (cf. GPC analyses, Figure 2-1). From the ^{1}H NMR and mass spectral analyses of the major GPC fractions, a fair part of the fraction containing **XIh** was considered to have a cyclic structure with low degree of oligomerization. But most of the fraction containing **XIi** included oligomers with higher molecular weight than the exclusion limit of the column. Compound (**IXi**) has a rigid structure due to the 1,4-phenylene group, so that the formation of cyclic oligomers with low molecular weight is not probable. Although the degree of oligomerization of **XIa**, **XIb**, and **XIc** was increasing in this order, more detailed examination is needed to clarify the correlation between the degree of oligomerization and the lengths of their alkylene chains.

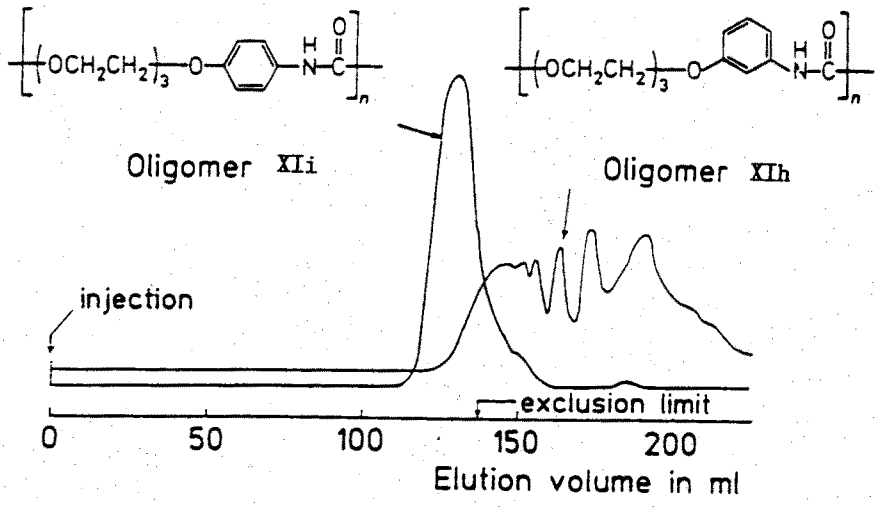


Fig. 2-1 GPC of oligomers **XIh** and **XIi**.

Poly(ether-urethane)s reported in this section are new SPU models consisting of "soft" parts only, or of "soft" and "hard" parts directly connected without a urethane bond. N-ammonio-amidate (**IXi**) may be an especially adequate precursor of SPU, because its thermolysis leads to oligomers with high molecular weight without the formation of low-molecular-weight cyclic products.

2-4 References

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CHAPTER 3 SYNTHESIS AND PROPERTIES OF SURFACE ACTIVE HYDROXAMIC ACIDS

3-1 Introduction

By the modification of the terminal OH-group of poly(oxyethylene) types of nonionics (alcohol ethoxylates), the improvement of surface active properties compared with parent compounds and the appearance of new functions have been expected. There have been many reports on the introduction of additional functional group into the end of the hydrophilic part of alcohol ethoxylates.[1] Among them, surface active properties of ether sulfates[2] and ether carboxylates[2a,3] have been investigated in detail.

Recently, hydroxamic acids have been studied with respect to chelates with iron(III) ion for medical use and as siderophore models,[4] the application to metal separation process,[5] and so on. Because most synthetic alkyl- or arylhydroxamic acids have poor water solubility, their use in aqueous media is limited. Some trials have been undertaken to increase the water solubility of hydroxamic acids. For example, Katzhendler et al. reported the preparation of a hydroxamic acid type of micellar catalyst containing a quaternary ammonium group.[6] Yamada et al. synthesized telomeric hydroxamic acids and found some interesting properties in aqueous media.[7]

In this chapter, Section 2, the author prepared some compounds with a hydroxamic acid group at the end of the

hydrophilic part of oxyethylene types of nonionic surfactants for the purpose of both the development of water soluble long-chain alkyl hydroxamic acids and their application to surfactants which can interact with metal cations. The author described their properties such as the water solubility, the pKa values, the complexation with iron(III) ion, and the possibility of their micelle formation from the results of the surface tension of aq solutions under various conditions.

In Section 3, the author reported the comparison of surface active properties of hydroxamic acids with ketones and methyl esters containing the similar hydrophilic and lipophilic structure, and typical monodisperse oligo(oxyethylene) nonionics under neutral conditions to investigate the effect of the terminal hydroxamic acid group on surface active properties as nonionics.

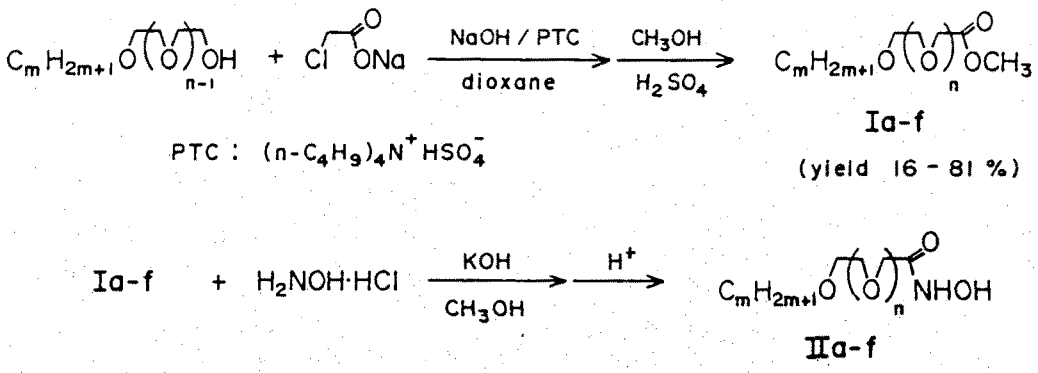
By the way, hydroxamic acids are often used as the nucleophiles in the model system of protease such as α-chymotrypsin. It is a conventional strategy that the model reaction is carried out in the micellar system in order to mimic the functions of enzyme, such as the reaction specificity, selectivity, and acceleration effects.[8] The catalytic activities of a variety of hydroxamic acids for the hydrolysis of ester substrates have been investigated under the micellar conditions organized by additional surfactants.[9] And the micellar catalytic effect of cationic surfactants containing a hydroxamic acid group for the similar reaction was reported by some groups.[10] But many factors, such as the influence of additional surfactants or the complex structure of catalysts, must be considered to analyze

those micellar catalytic reactions. By the use of micelle-formable hydroxamic acids with a simple structure as the "functional" micelles, the hydrophobic interaction between substrates and nucleophiles, which is one of the important effect on the micellar catalytic systems, will become clear directly. In Section 4, the author investigated the deacylation of some p-nitrophenyl carboxylates (substrates) in the micellar system composed of surface active hydroxamic acids containing an oligo(oxyethylene) group only, and clarified the influence of combination of the substrate and the nucleophile on the deacylation rate.

3-2 Synthesis and Properties of [α-Alkyloligo(oxyethylene)-ω-yloxy]acetohydroxamic Acids

3-2-1 Experimental

Materials. Starting materials, alcohol ethoxylates, were synthesized from n-alkylbromides and oligo(ethylene glycol)s (50-65 %). [α-Alkyloligo(oxyethylene)-ω-yloxy]acetohydroxamic acids (II) were prepared according to the equation given in Scheme 3-1. Their purity was confirmed by spectral (IR, mass, and ^{1}H NMR) and elemental analyses ($<\pm 0.4\%$). The results of their preparation are summarized in Table 3-1 with their abbreviations.



Scheme 3-1

Table 3-1 Synthesis and characterization of hydroxamic acids (II)[a].

Compound (m,n)	Abbreviation symbol	Yield[b] (%)	Mp (C)	^{1}H-NMR[c] ($CDCl_3$) (δ)	MS (70 eV) m/z (rel. intens.)	% N[d] calcd	% N[d] found
IIa (8,1)	C_8E1HA	76	29.5-30.5	0.90 (t,3H), 1.3-1.6(m,12H), 3.4-3.7 (m,6H), 4.10(s,2H),9.0(br,1H), 10.0(br,1H)	247(M$^+$, Amp), 57(100), 45(74)	5.66	5.50
IIb (8,2)	C_8E2HA	82	34.5-35.0	0.90 (t,3H), 1.2-1.7(m,12H), 3.4-3.7(m,10H), 4.10(s,2H), 9.1(br,1H), 9.9(br,1H)	291(M$^+$, Amp), 57(100), 45(93)	4.81	4.94
IIc (8,3)	C_8E3HA	96	—[e]	0.90(t,3H), 1.2-1.7(m,12H), 3.4-3.7(m,14H), 4.10(s,2H), 7.0(br,1H), 10.2(br,1H)	335(M$^+$, Amp), 57(100), 45(62)	4.18	3.92
IId (8,4)	C_8E4HA	81	—[e]	0.90(t,3H), 1.2-1.7(m,12H), 3.4-3.7(m,18H), 4.10(s,2H), 7.0(br,1H), 10.2(br,1H)	379(M$^+$, Amp), 57(79), 45(100)	3.69	3.61
IIe (10,4)	C_{10}E4HA	69	35.0-36.0	0.90(t,3H), 1.2-1.7(m,16H), 3.4-3.7(m,18H), 4.10(s,2H), 9.0(br,1H), 10.0(br,1H)	407(M$^+$, Amp), 57(95), 45(100)	3.44	3.38
IIf (12,4)	C_{12}E4HA	70	38.0-39.0	0.90(t,3H), 1.2-1.7(m,20H), 3.4-3.8(m,18H), 4.10(s,2H), 9.0-11.0(br,2H)	435(M$^+$, Amp), 57(80), 45(100)	3.22	3.20

[a] All compounds showed the same IR spectra: 3500, 3200, 2930, 2870, 1680, 1470, 1350, 1300, 1250, 1120, 940 and 850 cm^{-1} (neat).
[b] Based on I.
[c] 100 MHz.
[d] Satisfactory microanalyses were obtained (C, H ±0.4%).
[e] Viscous liquid.

Methyl [α-long-chain alkyloligo(oxyethylene)-ω-yloxy]acetate (I): Typical Procedure. Sodium chloroacetate (35.0 g, 0.3 mol) and tetra(n-butyl)ammonium hydrogensulfate (3.7 g, 0.01 mol) were added slowly, in turn, to a suspension of n-octyl tetra(oxyethylene) monoether (m= 8, n= 4; 30.6 g, 0.1 mol) and powdered sodium hydroxide (21.5 g, 0.5 mol) in dioxane (50 ml) with mechanically stirring. After 27 hr of stirring at 50°C, the reaction mixture was added to water (300 ml), and the unreacted materials were removed by extraction with ether. The aqueous phase was acidified with hydrochloric acid followed by extraction several times with ether. After the extracts were combined and dried with $MgSO_4$, evaporation of the solvent gave a residue (33.2 g; crude free acid) as a viscous liquid.

This residue was dissolved to methanol (300 ml) and stirred in the presence of sulfuric acid (2 ml) at the reflux temperature for 15 hr. After cooling and neutralization by K_2CO_3, the reaction mixture was filtered. The precipitates were washed with methanol, and evaporation of the solvent gave a methyl ester (36.6 g). The GLC-pure **Id** was obtained by distillation using a Kugelrohr apparatus. (bp 170°C/0.03 Torr; 29.4 g, 78 % yield)

[α-Alkyloligo(oxyethylene)-ω-yloxy]acetohydroxamic acids (II): Typical procedure. Methyl ester (**Id**; m= 8, n= 4; 6.80 g, 18 mmol) was dropped into a mixture of potassium hydroxide (3.54 g, 54 mmol) and hydroxylamine hydrochloride (2.49 g, 36 mmol) in methanol (60 ml) over a 10-min period at ca. 0°C. After 18 hr of stirring at room temperature and subsequent neutralization by hydrochloric acid (to pH 5), insoluble solids

were separated by filtration. Evaporation of the solvent from the filtrate gave a crude product (8.16 g). The pure hydroxamic acid (**IId**) confirmed by its spectral data was obtained by the silica-gel column chromatography with a methylene chloride : acetone (= 97:3) eluent as a pale-yellow viscous liquid (5.53 g, 81 %).

For solid hydroxamic acids, recrystallization from hexane was carried out.

Methods. The pKa values were measured either in a water-ethanol mixture (50:50 v/v) or in water at 20°C under a nitrogen flow according to the reported method.[11)]

The evaluation of complexation of **II** with iron(III) ion was attained by the general molar ratio method to determine the composition of the complex using a UV spectrometer. The measurement was carried out both in ethanol [**IIa-e** and nonanehydroxamic acid (C_8HA)] and in water (**IId**) under pH 1.5-2.0 conditions at 20°C using $FeCl_3.6H_2O$.

The surface tension was measured with a Wilhelmy tensiometer (Shimadzu ST-1) under various conditions at 20°C. Water was ion-exchanged and distilled twice from an alkaline permanganate solution in the presence of sodium hydroxide.

3-2-2 Results and Discussion

Preparations of methyl esters (I) and hydroxamic acids (II). Carboxymethylation of alcohol ethoxylates was heterogeneous reaction (solid-solid-liquid), so the use of phase transfer catalyst (PTC) was attempted in this reaction. Isolating yields

of I under these conditions are as follows: **Ia** (m,n= 8,1) 16 %, **Ib** (8,2) 53 %, **Ic** (8,3) 52 %, **Id** (8,4) 78 %, **Ie** (10,4) 81 %, and **If** (12,4) 70 %. From those results, it is probable that the influence of the number of oxyethylene units of substrates on yield was larger than that of PTC. The low yield of compound (**Ia**) may be due to the low solubility of intermediate alcoholate in the reaction media of carboxymethylation.

The preparation of hydroxamic acid (**II**) from methyl ester (**I**) was very easy and the purification of **II** could be carried out by the silica-gel column chromatography or, in the case of solids, recrystallization.

Properties of hydroxamic acids (II). The water solubility and the pKa value of hydroxamic acids are shown in Table 3-2.

Table 3-2 Physical properties of hydroxamic acids (II).

Hydroxamic acid		Water solubility[a]	pKa[b]
C_8E1HA	(IIa)	not soluble	10.2
C_8E2HA	(IIb)	slightly soluble	10.2
C_8E3HA	(IIc)	partially soluble	10.3
C_8E4HA	(IId)	soluble	10.3 (9.5)
$C_{10}E4HA$	(IIe)	soluble	10.4 (9.6)
$C_{12}E4HA$	(IIf)	soluble	10.5 (9.9)
C_8HA		not soluble	10.2

[a]Measured at 25°C. Slightly soluble, ca. 0.01 mol/l; partially soluble, ca. 0.1 mol/l; soluble, freely soluble at least to 1.0 mol/l.
[b]Measured in ethanol-water (50:50, v/v) at 20°C. Values in parentheses were measured in water. Acetohydroxamic acid = pKa 9.4 in water

It became clear that long-chain alkyl hydroxamic acids could be readily soluble in water with the introduction of oxyethylene units into a molecule. In the range of this study, four oxyethylene units were found to be enough to dissolve the hydroxamic acids with a C_8-C_{12} alkyl group in water. Little difference in pKa values was observed between **IIa-d** containing oxyethylene units and nonanehydroxamic acid, and the measured pKa values in water for **IId-f** were closer to that of acetohydroxamic acid [= pKa 9.4][12].

Complexation of hydroxamic acids (II) with iron(III) ion. The interaction of hydroxamic acids (**IIa-e**) with iron(III) ion in ethanol (pH 1.5-2.0) was evaluated by the molar ratio method using a UV spectrum ($FeCl_3.6H_2O$= 2.5 x 10^{-4} mol.l^{-1} constant). The absorption maximum due to the complex formation was found at 490-510 nm, and a similar relation between absorbance at λ_{max} and molar ratio of hydroxamic acid to iron(III) ion was obtained in each case. The measurement of water soluble C_8E4HA (**IId**) in dilute hydrochloric acid (pH 2.0) was also carried out in the same manner, changing the molar ratio of **IId** to iron(III) ion. Though precipitations were formed at the ratio above five, the absorption maximum of the water soluble complex was observed at 470 nm until the ratio reached five. These results are shown in Fig. 3-1. Since both the clear break point and the plateau part were not recognized in each curve, the equilibrium between some kinds of complexes which had different compositions might exist both in ethanol and in water.[13] Each complex of C_{10}E4HA and C_{12}E4HA with iron(III), however, was only partially soluble in water under

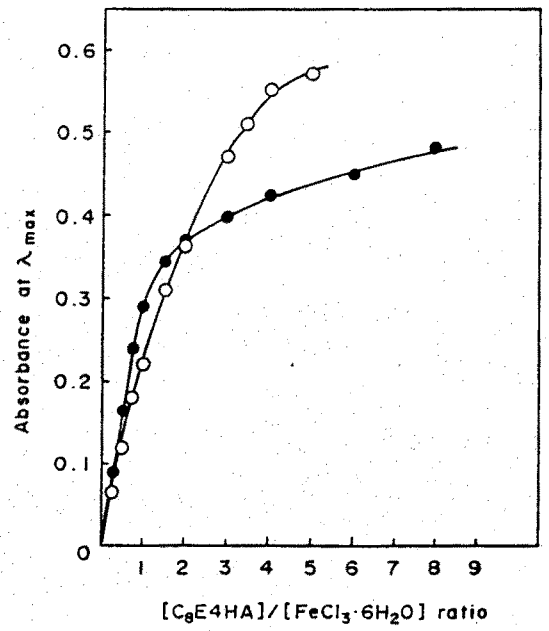


Fig. 3-1 **Absorbance at λ_{max} vs. $[C_8E4HA]/[Fe^{3+}]$ ratio for hydroxamic acid (IId) solutions at 20°C. ○, in H_2O ($[FeCl_3 \cdot 6H_2O] = 6.0 \times 10^{-3}$ mol/l); ●, in EtOH ($[FeCl_3 \cdot 6H_2O] = 2.5 \times 10^{-4}$ mol/l).**

those concentration conditions.

Surface tension of aqueous solution of water soluble hydroxamic acids (IId-f) under various conditions.

Since it was observed that C_8E4HA, C_{10}E4HA, and C_{12}E4HA could be freely miscible with water, these types of compounds were expected to be useful as surfactants. The surface tension - concentration plots of these hydroxamic acids are shown in Fig. 3-2. It was proved that these three hydroxamic acids could form micelles in water because the break point was clearly noticed in each case.

Furthermore, to investigate the effect of the terminal hydroxamic acid group on surface active properties, the surface

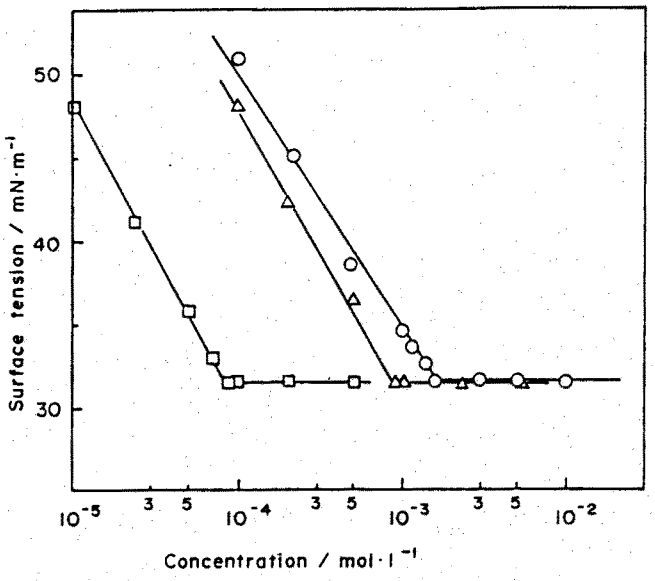


Fig. 3–2 Surface tension-concentration plots of aq. hydroxamic acid solutions at 20°C (pH 5.5). ○, C_8E4HA (IId); △,C_{10}E4HA (IIe); □, C_{12}E4HA (IIf).

tension of C_8E4HA solutions was measured under various pH conditions; pH 2.20, 3.82 (adjustment by HCl), 5.50 (neutral aqueous solution), 7.10, 8.95 (tris buffer), and 11.50 ($NaHCO_3$-NaOH buffer). Two types of surface tension-concentration curves were found. (Fig. 3-3) One was obtained under acidic and neutral conditions, while the other was in a basic solution. In the basic region, the hydrophilicity of the molecule might increase by the dissociation of hydroxamic acid to its anion form, so that the break in the curve (CMC) shifted to a higher concentration than that in neutral conditions. On the other hand, because similar curves were found in acidic and neutral conditions, it was considered that this compound could act as a kind of end-blocked

nonionic surfactants. To clarify the structural change of hydroxamic acid molecules between pH 7 and pH 9 in detail, the surface tension of this hydroxamic acid at a fixed concentration (2×10^{-3} mol.l^{-1}) was measured under some pH conditions (adjustment by tris buffer). The relation between the surface tension and pH value is shown in Fig. 3-4. The surface tension changed linearly from pH 7 to pH 9. It was considered that the dissociation of this hydroxamic acid to its anion form could occur above pH 7 from the calculation of the degree of dissociation using the pKa value. So those experimental facts seemed to agree with the calculation results.

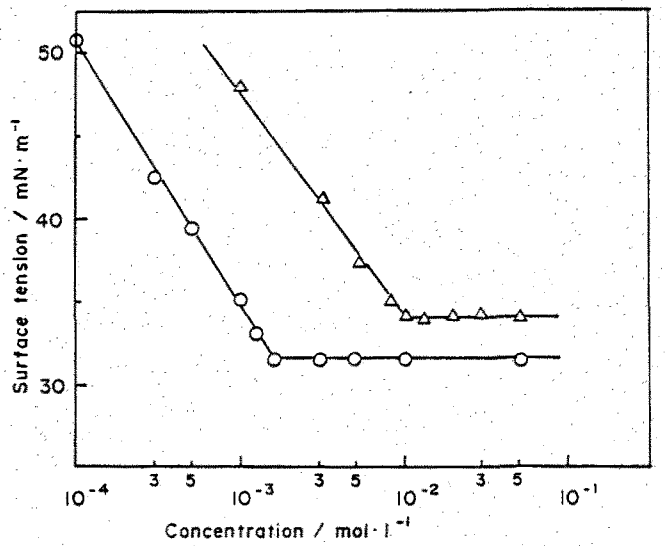


Fig. 3-3 Surface tension-concentration plots of aq. C_8E4HA (IId) solutions under various pH conditons at 20°C. ○, pH 2.20, 3.82, 5.50, and 7.10 (acidic and neutral conditions); △, pH 8.95 and 11.50 (basic conditions).

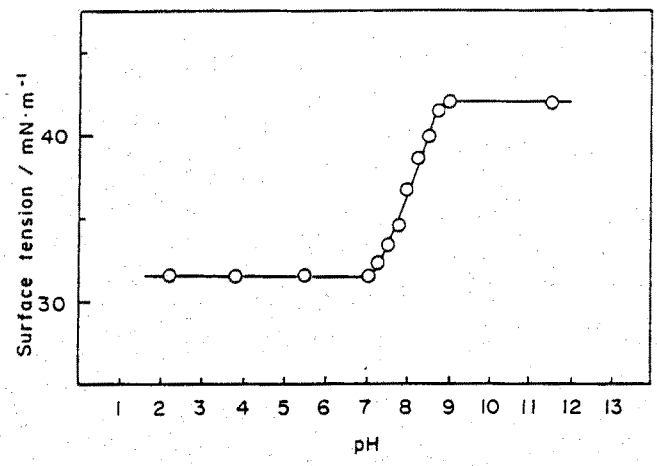


Fig. 3–4 Surface tension vs. pH for aq. C_8E4HA (IId) solutions (2×10^{-3} mol/l) at 20°C.

Because the surface tension of some alkyl ethylenediamine-chelates has been reported[14] as one of the important surface active properties of metal chelate surfactants, the surface tension of solutions of C_8E4HA, which could form the water soluble complex with iron(III) ion, was measured in the presence of iron(III) ion. Similar surface tension - concentration curves were obtained for the three solution systems in which the molar ratio of hydroxamic acid to iron(III) ion was constantly kept at one, two, and three respectively. (Fig. 3-5) The CMC shifted to a lower concentration as compared to C_8E4HA only, and no precipitation was observed in the range of this measurement.

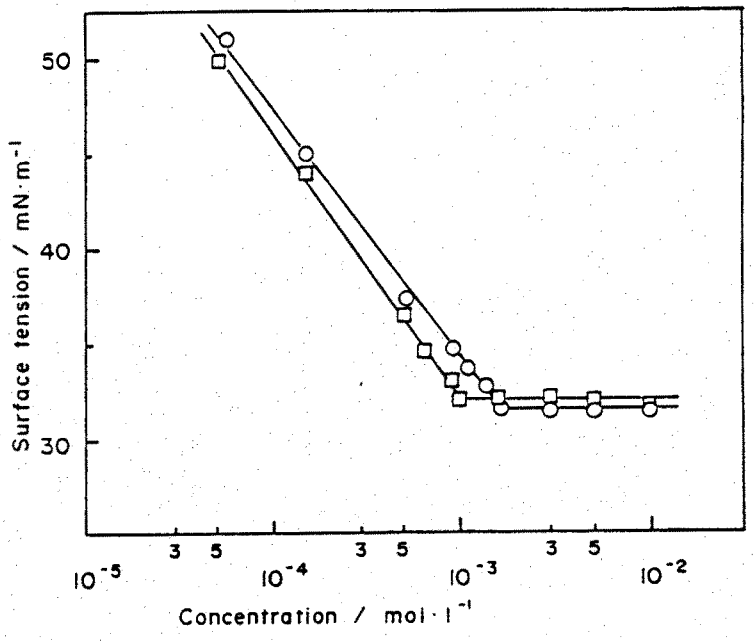


Fig. 3–5 Surface tension-concentration plots of aq. C_nE4HA (IId) solutions in the presence of (□) and in the absence of (○) ferric ion at 20°C (pH 2.0, $[C_nE4HA]:[Fe^{3+}]$ = 1:1, 2:1, and 3:1).

3-3 Comparison of Surface Active Properties of Hydroxamic Acids with Ketones and Methyl Esters with Similar Hydrophilic and Lipophilic Structure

3-3-1 Experimental

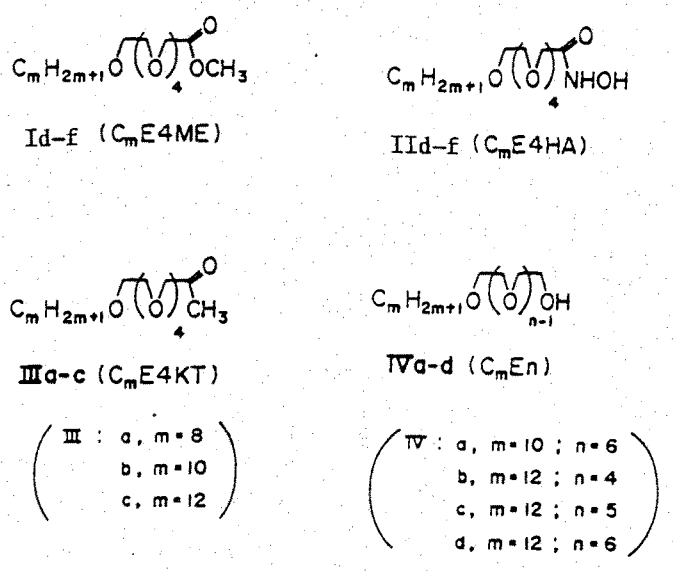


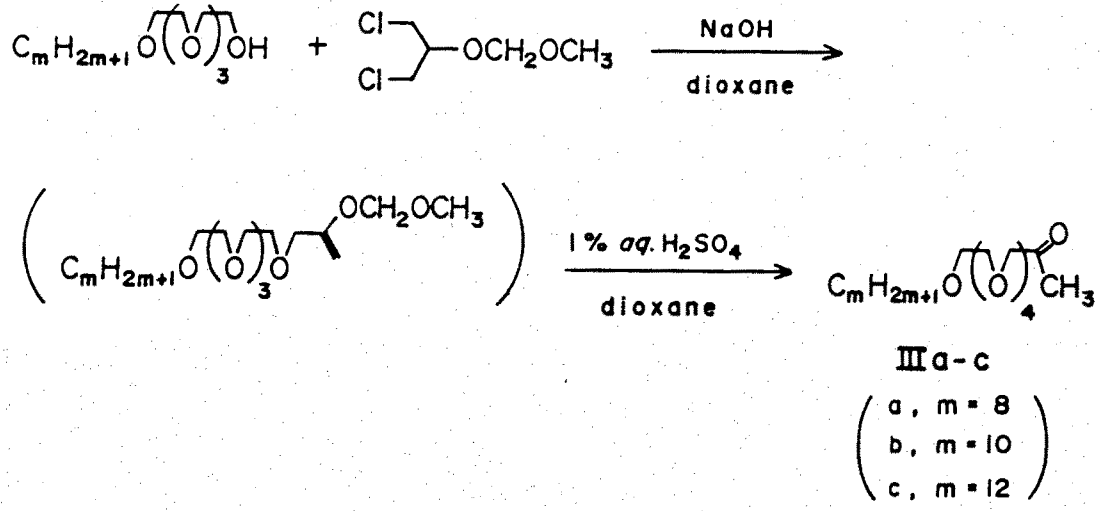
Fig. 3-6 Surface active compounds investigated in this section.

Materials. (See Fig. 3-6) The preparation of [α-long-chain alkyltetra(oxyethylene)-ω-yloxy]acetohydroxamic acids (**IId-f**) and methyl [α-long-chain alkyltetra(oxyethylene)-ω-yloxy]-acetates (**Id-f**) were mentioned in this chapter, Section 2. Long-chain alkyl[tetra(oxyethylene)]oxymethyl methyl ketones (**IIIa-c**) was prepared by the acetonylation of the corresponding alcohols according to the equation given in Scheme 3-2.[15] Purification of

I and III was done by Kugelrohr distillation. Their purity was ascertained by gas-liquid chromatography (GLC), spectral (IR, mass, and ^{1}H NMR), and elemental analyses (within $\pm$0.4%). It was also assessed from the observed sharp break in surface tension - concentration curves. Their properties are summarized in Table 3-3 with their abbreviations. Dodecyl hexa(oxyethylene) monoether (**IVd**; $C_{12}E6$) as a typical monodisperse nonionic surfactant was the commercial product of guaranteed reagent grade (Nikko Chemicals Co., Tokyo).

Long-chain alkyl[tetra(oxyethylene)]oxymethyl methyl ketone (III): Typical procedure. A mixture of tetra(ethylene glycol) monodecyl ether (m= 10; 7.0 g, 21 mmol), 1,3-dichloroprop-2-yl methoxymethyl ether (6.7 g, 42 mmol),[16] and NaOH (pellet; 3.5 g, 84 mmol) in dioxane (20 ml) was stirred vigorously at 60°C. The reaction was continued until the GLC peak based on the alcohol disappeared (24 hr). After insoluble solids were removed by a short column filtration (silica gel), evaporation of the eluent gave residue (8.3 g, intermediate olefin) as a liquid. A mixed solution of 1% aq H_2SO_4 (30 ml) and dioxane (30 ml) was added to the residue. After 2 hr of stirring at room temperature and subsequent extraction of the reaction mixture with ether (100 ml, 3 times), crude ketone (7.7 g) was obtained as a residue after evaporation of the solvent. Distillation of the crude product under reduced pressure using a Kugelrohr apparatus (bp: 160°C/0.05 Torr) gave pure **IIIb** (6.8 g, 83%).

Methods. The cloud point (T_{cp}) was determined by the naked eyes with a 1% aqueous solution of surfactant. The surface



Scheme 3-2

Table 3-3 Synthesis and characterization of ketones (III) and methyl esters (I)[a].

Compound (m)	Abbreviation symbol	Yield[b] %	Bp[c] °C/Torr	^{1}H-NMR[d] ($CDCl_3$) δ	MS (70 eV) m/z (rel.intens.)	Anal. found(calcd)
IIIa (8)	C_8E4KT	77	150/0.05	0.90(t,3H), 1.2-1.6(m,12H), 2.20(s,3H), 3.4-3.7(m,18H), 4.20(s,2H)	362(M^+, 10), 101(97), 57(100)	C, 63.19(62.95) H, 10.29(10.57)
IIIb (10)	C_{10}E4KT	83	160/0.05	0.90(t,3H), 1.2-1.6(m,16H), 2.20(s,3H), 3.4-3.7(m,18H), 4.20(s,2H)	390(M^+, 8), 101(100), 57(87)	C, 64.19(64.58) H, 10.98(10.84)
IIIc (12)	C_{12}E4KT	84	175/0.04	0.90(t,3H), 1.2-1.7(m,20H), 2.20(s,3H), 3.4-3.7(m,18H), 4.20(s,2H)	418(M^+, 15), 101(100), 57(83)	C, 65.92(65.99) H, 11.22(11.08)
Id (8)	C_8E4ME	73	130/0.05	0.90(t,3H), 1.2-1.6(m,12H), 3.4-3.8(m,20H), 4.20(s,3H)	378(M^+, Amp), 117(100), 59(45)	C, 60.00(60.29) H, 10.24(10.12)
Ie (10)	C_{10}E4ME	81	165/0.05	0.90(t,3H), 1.2-1.6(m,16H), 3.4-3.8(m,20H), 4.20(s,3H)	406(M^+, Amp), 117(100), 59(61)	C, 61.83(62.04) H, 10.48(10.41)
If (12)	C_{12}E4ME	70	170/0.05	0.90(t,3H), 1.2-1.7(m,20H), 3.4-3.8(m,20H), 4.20(s,3H)	434(M^+, Amp), 117(100), 59(48)	C, 63.59(63.56) H, 10.75(10.67)

[a] IR spectra: ketones: 2950, 2870, 1720, 1470, 1360, 1300, 1250, 1130, 940, and 870 cm^{-1} (neat), esters: 2950, 2870, 1760, 1460, 1440, 1350, 1290, 1220, 1130, 950, and 850 cm^{-1} (neat).

[b] Based on parent alcohol ethoxylates.

[c] Kugelrohr distillation.

[d] 100 MHz.

tension of a surfactant solution below T_{cp} (20°C, ordinarily) was measured with a Wilhelmy tensiometer using a series of aqueous solutions at various concentrations. The foaming properties were evaluated by the semi-micro TK method[17] with a 1% aqueous solution of surfactant below T_{cp} (20°C, ordinarily). All surface active properties were measured at pH 5.5 (neutral condition). The data of surface active properties of general nonionics (**IVa-c**) were quoted from the literature.[18]

3-3-2 Results and Discussion

The surface tension - concentration curves of aqueous solutions of hydroxamic acids (**IId-f**), ketones (**IIIa-c**), and methyl esters (**Id-f**) are shown in Fig. 3-7.

The CMC was determined from the break point of each curve. The adsorption area/molecule at the air-water interface (A) was calculated from the plot of the surface tension - logarithm concentration below CMC using the Gibbs' adsorption isotherm.[19] Those results and T_{cp} are summarized in Table 3-4 with data of some typical nonionics (**IV**). The results of foaming properties are given in Table 3-5.

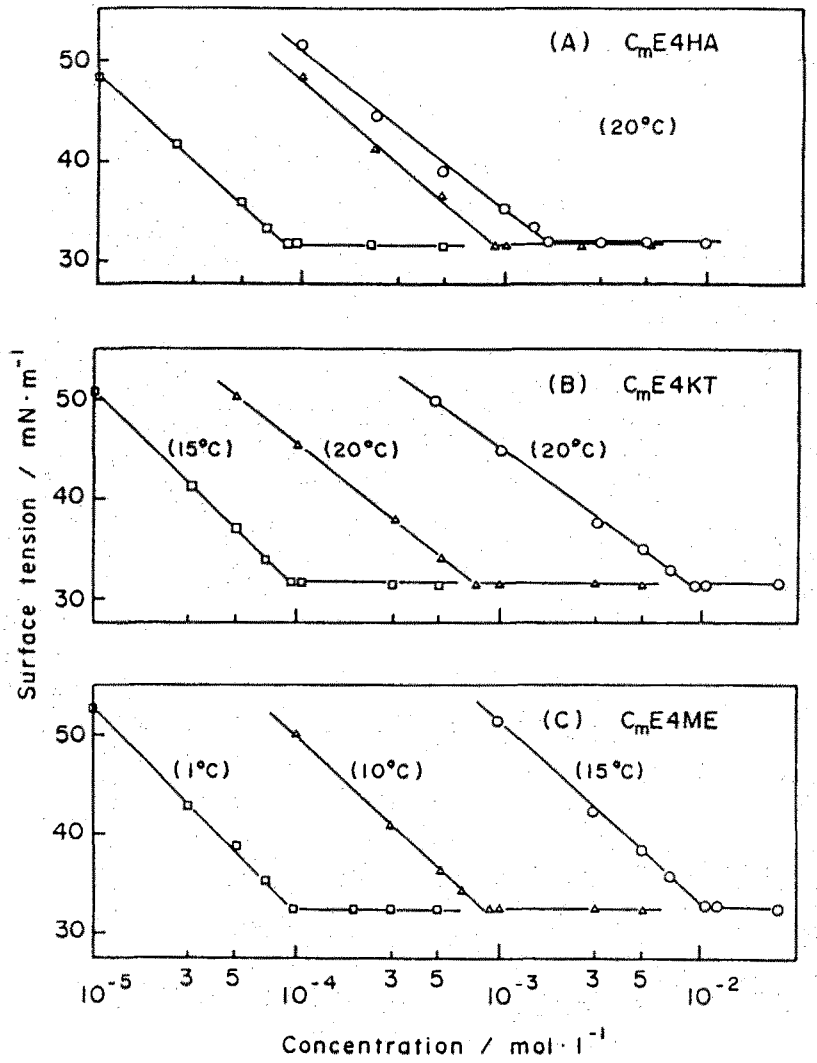


Fig. 3–7 Surface tension-concentration plots of aqueous surfactant solutions. (A), hydroxamic acid; (B), ketone; (C), methyl ester; ○, C_8; △, C_{10}; □, C_{12}.

Table 3–4 Surface active properties of II, III, I, and IV (20°C).

Compound	T_{cp} (°C)	10^4CMC (mol.l^{-1})	γ_{CMC} (mN.m^{-1})	10^2A (nm^2)
Hydroxamic Acid				
C_8E4HA (**IId**)	>75[a]	17	31.5	58
C_{10}E4HA (**IIe**)	72.0	8.7	31.5	48
C_{12}E4HA (**IIf**)	42.0	0.85	31.5	42
Ketone				
C_8E4KT (**IIIa**)	38.5	91	31.5	64
C_{10}E4KT (**IIIb**)	27.5	8.7	31.5	56
C_{12}E4KT (**IIIc**)	18.5	0.94[b]	31.5[b]	47[b]
Methyl Ester				
C_8E4ME (**Id**)	18.3	120[b]	32.5[b]	52[b]
C_{10}E4ME (**Ie**)	11.7	7.8[c]	32.5[c]	49[c]
C_{12}E4ME (**If**)	5.0	0.97[d]	32.5[d]	45[d]
Typical Nonionic				
C_{10}E6[e] (**IVa**)	60.0	----	----	--
C_{12}E4[e] (**IVb**)	7.0	----	----	--
C_{12}E5[e] (**IVc**)	25.0	0.40	----	--
C_{12}E6 (**IVd**)	49.0	0.85	32.0	52

a) Decomposition. b) At 15°C. c) At 10°C.
d) At 1°C. e) Ref.(18).

Table 3-5 Foaming properties of II, III, I, and IV.

Compound	Temp. (°C)	Foaming Volume (ml) 0"	30"	1'	1'30"	2'	5'
Hydroxamic Acid							
C_8E4HA (IId)	20	40	0	--	--	--	--
C_{10}E4HA (IIe)	20	140	100	70	30	0	--
C_{12}E4HA (IIf)[a]	20	260	260	260	260	260	200
Ketone							
C_8E4KT (IIIa)	20	80	10	0	--	--	--
C_{10}E4KT (IIIb)	20	160	80	20	0	--	--
C_{12}E4KT (IIIc)	15	260	260	160	80	20	0
Methyl Ester							
C_8E4ME (Id)	10	30	0	--	--	--	--
C_{10}E4ME (Ie)	10	100	20	0	--	--	--
C_{12}E4ME (If)	1	180	100	60	20	0	--
Typical Nonionic							
C_{12}E6 (IVd)	20	250	220	160	140	100	0

a) 20', 120 ml; 30', 70 ml; 40', 0 ml.

The T_{cp} values of hydroxamic acids (II) were much higher than both the corresponding ketones (III) and methyl esters (I). On comparing C_{12}E4HA (IIf) with nonionic surfactants (IVc,d) (Table 3-4), the T_{cp} value of IIf was 17°C higher than that of C_{12}E5 (IVc) having the same number of ether oxygens, and the contribution of the terminal $-CH_2C(=O)NHOH$ group to the hydrophilicity was similar to that of one oxyethylene unit of nonionics (IV) in the rough estimation. The solution of C_8E4HA (IId) and other hydroxamic acids (IIe,f) irreversibly turned pale yellow above 75°C, probably because of hydrolysis. It was found that the hydrophilicity of ketones (III) was better than that of

methyl esters (I).

The CMC of three corresponding types of surfactants showed similar values except C_8E4HA (IId). Although precise comparison was difficult since the measurement was carried out at different temperatures, a linear relation between the alkyl chain length (m) of both ketones (III) and methyl esters (I) and log CMC was observed. But a similar relation was not found in the case of hydroxamic acids (II) in this study.

The γ_{CMC} values were almost the same among three types of compounds and were by no means inferior to the typical nonionic surfactant C_{12}E6 (IVd). The adsorption area/molecule at the surface (A) decreased with an increase in the number of carbon atoms in the lipophilic group in each type of compound. This tendency is similar to that of general nonionic surfactants.[19]

The foaming ability and foam stability of surfactants with a dodecyl group are superior to those having an octyl or decyl group. A feature of end-blocked nonionics is low foaming or antifoaming properties,[20] but C_{12}E4HA (IIf) especially showed good foaming ability and foam stability.

From the above facts, it might be concluded that hydroxamic acids (II) had better hydrophilicity and showed better surface active properties than the corresponding ketones (III), methyl esters (I) or typical nonionics (IV). Those hydroxamic acids seem to be applicable to new types of "functional" surface active agents because hydroxamic acids can foam chelates with transition metals, and can be transformed into isocyanates by Lossen rearrangement.

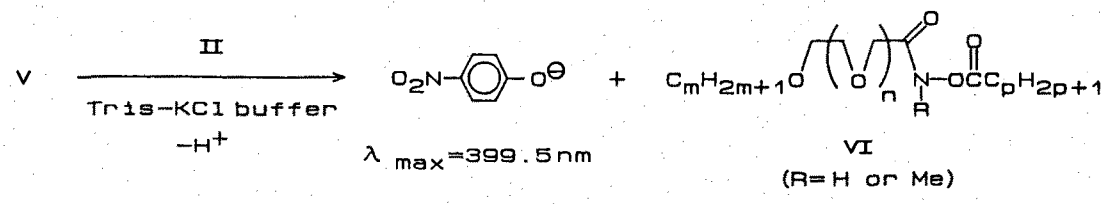
3-4 Micellar Catalytic Activity of Water Soluble [α-Alkyloligo-(oxyethylene)-ω-yloxy]acetohydroxamic Acids for Deacylation of p-Nitrophenyl Carboxylates

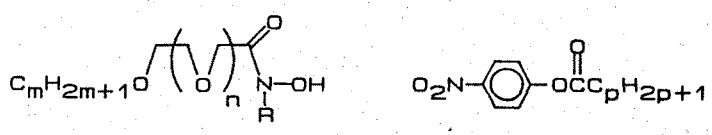
3-4-1 Experimental

The ^1H NMR spectra were measured with a JEOL JNM-PS-100 spectrometer using TMS as an internal standard. The IR and mass spectra were recorded on a Hitachi 260 spectrometer and a Hitachi RMU-6E mass spectrometer at an ionization potential of 70 eV, respectively. The UV spectra were obtained with a Shimadzu UV-200 spectrometer equipped with a thermostated cell-holder.

Methods. The pKa values and surface active properties were measured by the methods described in this chapter, Sections 2 and 3 under various conditions.

Each kinetic measurement was initiated by adding an aqueous buffer solution of hydroxamic acid to an acetonitrile (MeCN) solution of substrate in a thermostated UV cell. The following standard conditions were chosen: 30(±0.2)°C, 5×10^{-5} M substrate, 5×10^{-4} or 5×10^{-3} M hydroxamic acid, pH 8.80 [5×10^{-2} M Tris and 5×10^{-2} M KCl in water-acetonitrile (MeCN) (97:3, v/v)]. The reaction proceeding was checked by tracing the absorbance of p-nitrophenolate anion which was one of the reaction products at 399.5 nm with a UV spectrophotometer. (Fig. 3-8) The kinetic measurement was carried out at least three times, and the pseudo-first-order kinetics were simulated by a micro-computer (NEC PC-9801) system.





Hydroxamic Acid (II)

II	m	n	R
d	8	4	H
e	10	4	H
f	12	4	H
g	14	4	H
h	8	4	Me
i	10	4	Me
j	12	4	Me
k	1	3	H

Substrate (V)

V	p
a	1
b	7
c	8
d	9
e	11

Fig. 3-8 Reaction and structure of hydroxamic acids (II) and substrates (V).

Materials. p-Nitrophenyl acetate (**Va**) was obtained by recrystallization of the commercial product (guaranteed grade) from cyclohexane. p-Nitrophenyl octanoate (**Vb**), nonanoate (**Vc**), decanoate (**Vd**), and dodecanoate (**Ve**) were prepared and purified according to the literature.[21] Their purity was checked by GLC, spectral data, and elemental analyses (C,H,N; $<\pm 0.4$ %).

Properties of **IIg-k** which were newly obtained are summarized in Table 3-6.

Table 3-6 Synthesis and characterization of hydroxamic acids (**IIg-k**)[a].

Compd (m,n,R)	Yield (%)	mass m/e	^{1}H NMR ($CDCl_3$) (δ, ppm)	Anal. Found(Calcd)
IIg[b] (14,4,H)	57	404(M^+-59), 103, 89, 71, 57, 45	0.90(t,3H), 1.2-1.7(m,24H), 3.50(t,2H), 3.6-3.8(m,16H), 4.10(s,2H), 9.0(br,1H), 10.0(br,1H)	C, 62.08(62.17) H, 10.78(10.65) N, 2.97 (3.02)
IIh (8,4,CH_3)	67	393(M^+), 375, 116, 71, 57, 45	0.90(t,3H), 1.2-1.7(m,12H), 3.20(s,3H), 3.50(t,2H), 3.6-3.8(m,16H), 4.40(s,2H), 9.20(s,1H)	C, 57.85(57.99) H, 10.06 (9.99) N, 3.75 (3.56)
IIi (10,4,CH_3)	65	421(M^+), 403, 116, 71, 57, 45	0.90(t,3H), 1.2-1.7(m,16H), 3.20(s,3H), 3.40(t,2H), 3.6-3.8(m,16H), 4.36(s,2H), 8.90(s,1H)	C, 59.91(59.83) H, 10.38(10.28) N, 3.49 (3.32)
IIj (12,4,CH_3)	70	449(M^+), 431, 116, 72, 57, 45	0.90(t,3H), 1.2-1.7(m,20H), 3.20(s,3H), 3.40(t,2H), 3.6-3.8(m,16H), 4.38(s,2H), 8.70(s,1H)	C, 61.10(61.43) H, 10.54(10.54) N, 3.37 (3.12)
IIk (1,3,H)	51	237(M^+), 219, 103, 89, 59, 45	3.24(s,3H), 3.3-3.7(m,12H), 3.90(s,2H), 8.7(br,1H), 10.4(br,1H)	C, 45.47(45.56) H, 8.33 (8.07) N, 5.48 (5.90)

a) All compounds showed the similar IR spectra: 3300, 2900, 1670, 1450, 1320, 1280, 1100, and 970 cm^{-1} (neat).
b) Mp: 44.0-45.0°C.

3-4-2 Results and Discussion

Hydroxamic acids (**IId-k**) were prepared and purified according to the method described in Section 2. All of those were soluble in water at room temperature. The pKa values of those compounds in water were almost same (9.1-9.9) and were closer to that of acetohydroxamic acid (= pKa 9.4).[12] And all hydroxamic acids

except **IIk** showed good surface active properties in water under various pH conditions as follows: the cloud point (T_{cp}, 1 wt%); 26-75°C, the critical micelle concentration (CMC, at 20°C); 0.012-2.5 mM (at pH 2.0 and 5.5) and 0.022-23 mM (at pH 11.5), the lowering ability of surface tension (γ_{CMC}, at 20°C); 31.5-32.0 $mN.m^{-1}$ (at pH 2.0 and 5.5) and 34.0-34.5 $mN.m^{-1}$ (at pH 11.5).

The reactions of both micelle-formable **IId-j** and unformable **IIk** with p-nitrophenyl carboxylates (**V**) in an aqueous tris(hydroxymethyl)aminomethane (Tris)-KCl buffer solution were investigated at 30°C.

The liberation rate of p-nitrophenolate anion (Fig. 3-8) obeyed the pseudo-first-order rate equation until about 80 % conversion in each case, and the apparent second-order rate constant ($k_{a.obs}$) for the deacylation of a substrate (i.e. the acylation of a hydroxamic acid) was estimated by equation (1).

$$k_{a.obs} = (k_{total} - k_{spont})/[II] \qquad (1)$$

where k_{total} and k_{spont} refer to the observed first-order rate constants for the deacylation of **V** in the presence and the absence of **II**, respectively, and [**II**] signifies the initial concentration of **II**. The k_{spont} values were as follows (at pH 8.80, [**V**]= 5×10^{-5} M): **Va**; 3.53×10^{-4} s^{-1}, **Vb**; 1.40×10^{-4} s^{-1}, **Vc**; 1.42×10^{-5} s^{-1}, **Vd**; 9.62×10^{-6} s^{-1}, **Ve**; 6.21×10^{-6} s^{-1}. And it was examined according to the previous method[9c] that the deacylation rate of the acylated hydroxamic acid (**VI**) formed along with the p-nitrophenolate anion was much slower than the

liberation rate of phenolate anion under those conditions. A mixture of water and MeCN (97:3 v/v) was used as the reaction solvent since substrates (**V**) were not soluble easily in water. Furthermore, it was confirmed that dodecanehydroxamic acid, which contained no oxyethylene group, was insoluble in this reaction solvent. So the introduction of oligo(oxyethylene) group affords long-chain alkylhydroxamic acids good water solubility. Then, the CMC of hydroxamic acids under the kinetic-studied conditions was also determined: **IId**; 1.8×10^{-3} M, **IIe**; 5.0×10^{-4} M, **IIf**; 5.0×10^{-5} M, **IIg**; 1.0×10^{-5} M, **IIh**; 4.8×10^{-3} M, **IIi**; 5.5×10^{-4} M, **IIj**; 6.7×10^{-5} M.

The $k_{a.obs}$ values of **II** for each substrate are illustrated graphically in Fig. 3-9. From the comparison of micelle-unformable **IIk** with others, it was noticed that the reaction was promoted by the micelle formation in the case of hydroxamic acids (**IIe-g,i,j**) with a C_{10-14} alkyl group. Since the standard concentration of hydroxamic acid (0.5 mM; see Experimental) was lower than the CMC values of **IId,h** with a C_8 alkyl group, the $k_{a.obs}$ values of **IId,h** for each substrate were similar to those of micelle-unformable **IIk**. Although the measurement was carried out at 5 mM of **IId,h** (above their CMC values), the difference in the $k_{a.obs}$ values was small between 0.5 mM and 5 mM of surfactant. The $k_{a.obs}$ values of **IIf,g,j** for hydrophobic substrates (**Vb-e**) were markedly larger than those of other hydroxamic acids for **Vb-e**, while the $k_{a.obs}$ values of all hydroxamic acids for hydrophilic **Va** were the same order. Hydroxamic acid (**IIg**) having a C_{14} alkyl group showed higher $k_{a.obs}$ values for **Va-e** than **IIf** having a C_{12}

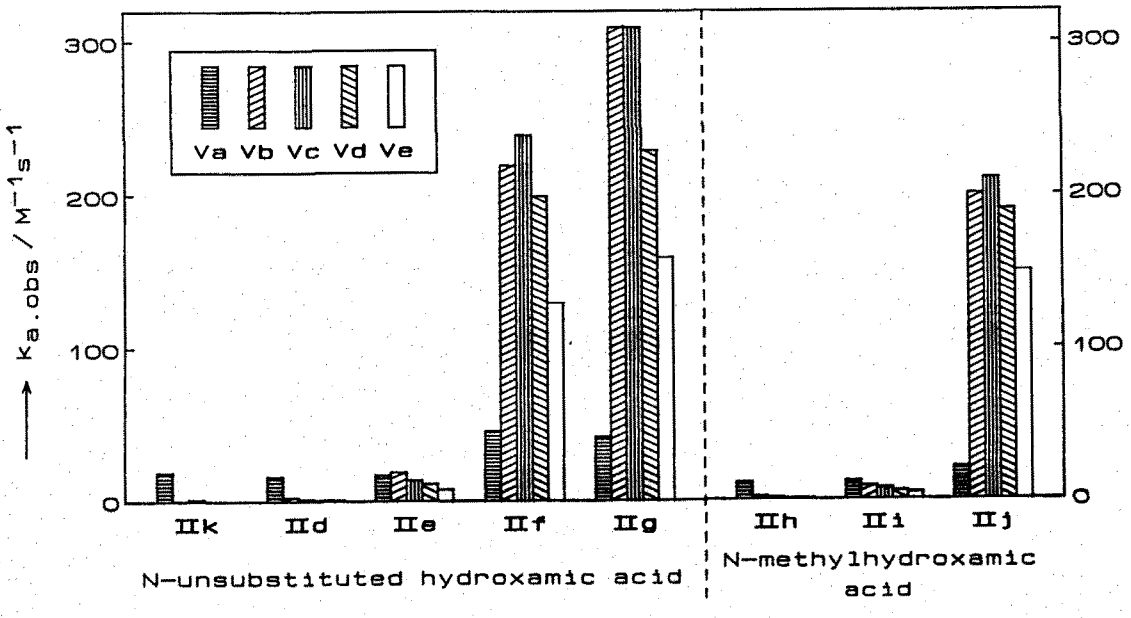


Fig. 3-9 Rate constants for the reaction of p-nitrophenyl carboxylates (**V**) with hydroxamic acids (II) at 30°C and pH 8.80 in H_2O-MeCN (97:3 v/v) solution (5 x 10^{-2} M Tris, 5 x 10^{-2} M KCl, 5 x 10^{-4} M II, 5 x 10^{-5} M **V**).

alkyl group for **Va-e**. But the difference in the $k_{a.obs}$ values between **IIf** and **IIg** was smaller than that between **IIf** and **IIe** having a C_{10} alkyl group.

It was previously reported about the similar reaction of a series of p-nitrophenyl carboxylates with decanehydroxamic acid in the absence of additional surfactants that the deacylation rate decreased in order as the hydrophilicity of the substrate increased.[9d] This tendency was also found about hydroxamic acids (**IId,e,h,i,k**) through our measurement. But the reaction rates of hydroxamic acids (**IIf,g,h**) having a C_{12} or C_{14} alkyl group took a

maximum value for **Vb** or **Vc**. So it is considered that the hydrophobic interaction between substrates and surface active hydroxamic acids, which also act as nucleophiles, is a major factor of this micellar catalytic activity. And the formation of mixed micelles composed of hydroxamic acids and substrates with the moderate size of hydrophobic part is suggested.

The rate constants of N-methylhydroxamic acids (**IIh-j**) and the corresponding N-unsubstituted hydroxamic acids (**IId-f**) were not the same, but the tendency of $k_{a.obs}$ values of **IIh-j** for each substrate was similar to those of **IId-f**.

Reactions of **IIf** with **Va** or **Vb** were examined at various ion strengths as shown in Fig. 3-10. When the deacylation of p-nitrophenyl carboxylates by hydroxamic acids as nucleophiles was carried out in the presence of cationic micelles such as hexadecyltrimethylammonium bromide, the rate constant decreased as the ion strength increased because the nucleophilicity of hydroxamic acids was lowered by the adsorption of inorganic anions on the micellar surface of the cationic surfactant.[9d] But in this work, the $k_{a.obs}$ values for each substrate increased in proportion to the concentration of potassium chloride. Our system doesn't contain cationic micelles and it is said that the influence of electrolytes is somewhat less predictable in the micellar catalytic reaction.[8a] Rosen mentioned that the addition of neutral electrolyte to an aqueous solution of ionic surfactants caused an increase in the micellar aggregation number because of compression of the electrical double layer surrounding the ionic heads.[22] Although the reason of our results is not clear yet, it

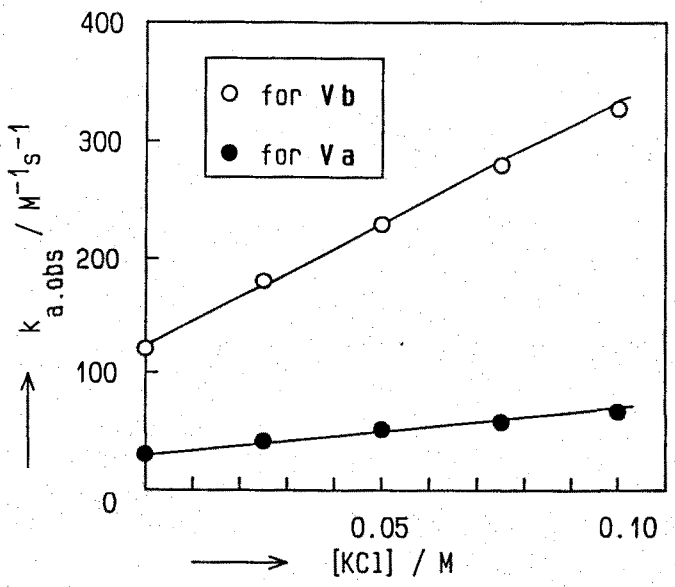


Fig. 3-10 Plots of $k_{a.obs}$ of IIf for **Va** and **Vb** vs. the concentration of KCl at 30°C and pH 8.80 in H_2O-MeCN (97:3 v/v) solution (5×10^{-2} M Tris, 5×10^{-4} M IIf, 5×10^{-5} M V).

is considered that the increase in the aggregation number may be one of the possible reason.

Then, the influence of the pH on the $k_{a.obs}$ values was investigated in both **IIf-Va** and **IIf-Vb** systems. (Fig. 3-11) The rate constants for each substrate increased suddenly at about pH 8. It has been clarified that this type of hydroxamic acid began to dissociate to its anion form at about pH 7.5 from our measurement of surface tension of an aqueous this hydroxamic acid under various pH conditions. (see Section 2, Fig. 3-4) So it is also ascertained in our micellar system that the deacylation of

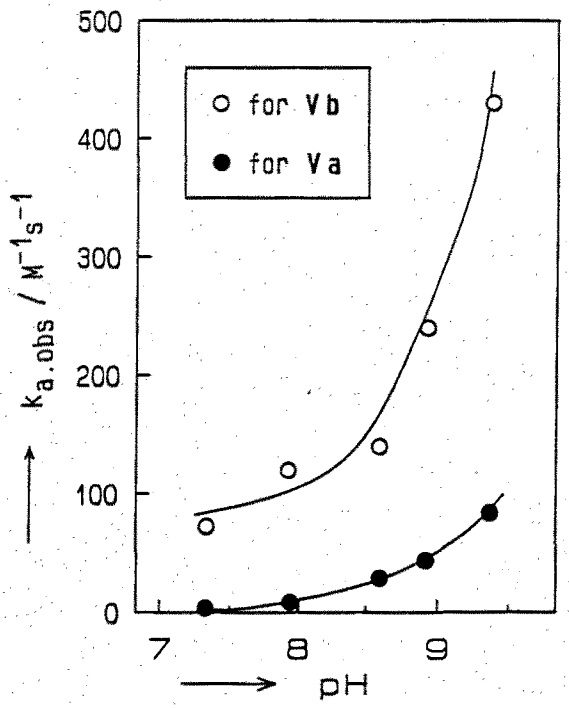


Fig. 3-11 Plots of $k_{a.obs}$ of IIf for **Va** and **Vb** vs. the pH at 30°C in H_2O-MeCN (97:3 v/v) solution (5 x 10^{-2} M KCl, 5 x 10^{-4} M IIf, 5 x 10^{-5} M V).

esters is extremely promoted by the increase in the amount of hydroxamate anions.[9a,10] Unfortunately the rate constant for **Vb** at above pH 9.5 couldn't be determined because the reaction was too fast to trace in our equipments.

The following hydrophobic interaction becomes clear through this work: the deacylation of both hydrophilic and hydrophobic substrates is enormously promoted by hydroxamic acids having a hydrophobic part more than C_{12} alkyl group, but the reaction rates of these hydroxamic acids take a maximum value for the substrate with a C_7 or C_8 alkyl group. The latter result is different from

the previous result about decanehydroxamic acid in the similar system. The main effect of oligo(oxyethylene) group is to bring water solubility to alkylhydroxamic acids, so that this type of hydroxamic acids can be applied to micellar catalysts for various reactions in an aqueous solution without other surfactants or organic additives.

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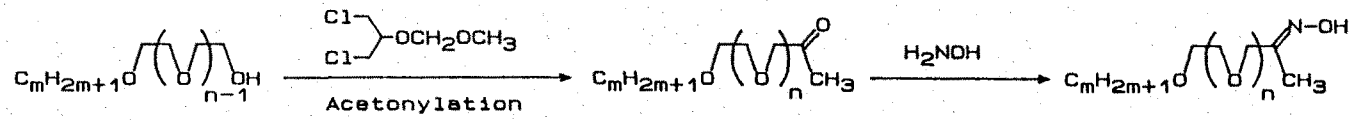
CHAPTER 4 SYNTHESIS AND PROPERTIES OF SURFACE ACTIVE KETONES AND OXIMES

4-1 Introduction

The author prepared novel surface active hydroxamic acids by the modification of the terminal OH-group of alcohol ethoxylate types of nonionics and clarified their surface active properties under various conditions. (Chapter 3)

This time, the author synthesized some compounds with an oxime group at the end of the hydrophilic part of alcohol ethoxylate, as part of our studies on "functional" surfactants. The oxime group has the complexing ability toward various metal ions,[1] and besides, oximes can be transformed into amides by Beckmann rearrangement.[2] In order that many functions of surfactants which can interact with metal ions may be exhibited most effective in aqueous media, these surfactants are necessary to have the water solubility and good surface active properties under a wide range of conditions (pH, temperature, concentration, etc.). Long-chain alkyloximes have poor water solubility, and hence the author attempted to introduce a hydrophilic part to long-chain oximes and have chosen alcohol ethoxylates as the building block. It is an advantage that the HLB values of alcohol ethoxylates can be finely adjusted by changing the number of oxyethylene units.[3]



Ia–m; C_mEn IIa–m; C_mEnKT IIIa–l; C_mEnOX

I	m	n	I	m	n
a	8	4	g	12	4
b	8	5	h	12	7
c	8	6	i	12	8
d	8	7	j	14	7
e	10	4	k	14	8
f	10	7	l	16	8
			m	12	$\bar{9}$

II	m	n	II	m	n
a	8	4	g	12	4
b	8	5	h	12	7
c	8	6	i	12	8
d	8	7	j	14	7
e	10	4	k	14	8
f	10	7	l	16	8
			m	12	$\bar{9}$

III	m	n	III	m	n
a	8	4	g	12	7
b	8	5	h	12	8
c	8	6	i	14	7
d	8	7	j	14	8
e	10	4	k	16	8
f	10	7	l	12	$\bar{9}$

Scheme 4-1 Alcohol ethoxylate types of ketones (II) and oximes (III) with their abbreviations.

In this chapter, the author described the preparation of oximes with monodispersed oxyethylene group (**IIIa-k**; C_mEnOX), and discussed various surface active properties of these oximes, ketones (**IIa-l**; C_mEnKT) which were precursors of these oximes, and other reference compounds. Furthermore, the author mentioned the preparation and surface active properties of both ketone (**IIm**; $C_{12}E\bar{9}KT$) and oxime (**IIIl**; $C_{12}E\bar{9}OX$) from dispersed alcohol ethoxylate for the practical application of these compounds. Prepared compounds in this chapter are summarized in Scheme 4-1.

4-2 Experimental

Materials. Alcohol ethoxylates (**Ia-l**) were synthesized from n-alkylbromides and oligo(ethylene glycol)s. (50-70 %) Poly(ethylene glycol) dodecyl ether (**Im**; $C_{12}E\bar{9}$, nine average oxyethylene units) was the commercial product of specially prepared reagent grade (Nakarai Chemicals LTD., Kyoto). 3-Alkyl-[oligo(oxyethylene)]oxy-2-propanones (ketones; II) were prepared by the reaction of alcohol ethoxylates with acetonylating reagent, 2-chloro-1-(chloromethyl)ethyl methoxymethyl ether,[4] according to the method described in Chapter 3, Section 3. Purification of II except **IIm** was done by Kugelrohr distillation or recrystallization from hexane.

3-Dodecyl[oligo(oxyethylene)]oxy-2-propanone with dispersed oxyethylene group (IIm). A mixture of poly(ethylene glycol) dodecyl ether (**Im**; $C_{12}E\bar{9}$, 12.0 g), 2-chloro-1-(chloromethyl)ethyl

methoxymethyl ether (7.1 g) and NaOH (pellet; 4.3 g) in dioxane (50 ml) was stirred vigorously at 100°C for 47 hr. After insoluble solids were removed by a silica-gel short column filtration, evaporation of the eluent gave 14.9 g of residue as a liquid. A mixed solution of 1 % aq H_2SO_4 (30 ml) and dioxane (30 ml) was added to the residue. After 2 hr of stirring at 60°C, the reaction mixture was extracted with methylene chloride. (200 ml, 3 times) After the extracts were combined and dried with $MgSO_4$, evaporation of the solvent gave a 13.1 g of ketone (**IIm**; $C_{12}E\bar{9}KT$) as a colorless liquid.

*3-Alkyl[oligo(oxyethylene)]oxy-2-propanone oxime with monodispersed oxyethylene group (**IIIa-k**): Typical procedure.* 3-Tetradecyl[hepta(oxyethylene)]oxy-2-propanone (**IIj**; $C_{14}E7KT$; 2.50 g, 4.3 mmol) was added dropwise into a mixture of sodium hydroxide (0.73 g, 17 mmol) and hydroxylamine hydrochloride (1.20 g, 17 mmol) in methanol (50 ml) over a 10-min period at 0°C. After 48 hr of stirring at room temperature, insoluble solids were separated by filtration. Methylene chloride (50 ml) was added to the residue and insoluble solids were filtered off again. Crude product (2.68 g) was obtained by evaporation of the filtrate. Pure 3-tetradecyl[hepta(oxyethylene)]oxy-2-propanone oxime (**IIIi**; $C_{14}E7OX$), confirmed by its spectral data, was obtained by a silica-gel column chromatography with a benzene : 2-propanol (9:1 v/v) eluent as a colorless liquid. (2.22 g, 87 % yield)

*3-Dodecyl[oligo(oxyethylene)]oxy-2-propanone oxime with dispersed oxyethylene group (**III1**).* The reaction of **IIm** (5.0 g) with hydroxylamine hydrochloride (2.8 g)/NaOH (1.7 g) was

carried out in the same way as described above. After a silica-gel column filtration with a benzene : 2-propanol (3:7 v/v) eluent, a 4.9 g of oxime (**IIIl**) was obtained as a pale-yellow liquid.

The structures of **II** and **III** were confirmed by their IR (Hitachi 260 spectrometer), ^{1}H NMR (JEOL JNM-PS-100), mass (Hitachi RMU-6E) spectra and elemental analyses. IR (neat): ketones; 2950, 2870, 1720, 1470, 1360, 1300, 1250, 1130, 940, and 870 cm^{-1}, oximes; 3300, 2950, 2870, 1460, 1360, 1120, 940, and 860 cm^{-1}. ^{1}H NMR ($CDCl_3$): ketones; δ= 0.88 (t, 3H, CH_3-C-C), 1.1-1.8 (m, -CH_2- in alkyl chain), 2.14 [s, 3H, CH_3-C(=O)-C-], 3.3-3.9 (m, -O-CH_2CH_2-O-) and 4.12 [s, 2H, C-C(=O)-CH_2-O-], oximes; δ= 0.88 (t, 3H), 1.1-1.8 (m), 1.90 [s, 3H, CH_3-C(=N-O)-C-], 3.3-3.9 (m), 4.04 and 4.40 [s,s, 2H, C-C(=N-O)-CH_2-O-, the former is attributed to E-isomer, the latter is attributed to Z-isomer],[5] and 6.0-8.5 [br, 1H, -C(=N-OH)-; disappeared by addition of D_2O]. The molecular ion peak of each compound except **IIm** and **IIIl** was observed in its mass spectrum. The results of newly obtained compounds are summarized in Table 4-1 with the data of elemental analyses.

Methods. The pKa values were determined either in a water-ethanol mixture (1:1 v/v) at 25°C or in water ordinarily at 20°C under a nitrogen flow, according to the method in references.[6] The cloud point (T_{cp}) and other surface active properties of aqueous solutions of those compounds were measured at pH 5.5 (neutral condition) by the methods described in Chapter 3, Sections 2 and 3. The T_{cp} and foaming properties were

Table 4-1 Properties of ketones (II) and oximes (III).

Compound (m,n)	Abbreviation Symbol	Yield[a] (%)	Bp[b] or Mp (°C/Torr) or (°C)	Anal. Found(Calcd)
Ketone				
IIb (8,5)	C_8E5KT	92	155/0.005	C, 61.86(62.04) H, 10.42(10.41)
IIc (8,6)	C_8E6KT	89	160/0.01	C, 61.44 61.31) H, 10.26(10.29)
IId (8,7)	C_8E7KT	90	175/0.02	C, 60.33(60.70) H, 10.15(10.19)
IIf (10,7)	$C_{10}E7KT$	94	205/0.05	C, 61.76(62.04) H, 10.41(10.41)
IIh (12,7)	$C_{12}E7KT$	84	205/0.04	C, 63.33(63.24) H, 10.61(10.61)
IIi (12,8)	$C_{12}E8KT$	89	33.0-34.2	C, 62.41(62.60) H, 10.48(10.51)
IIj (14,7)	$C_{14}E7KT$	68	37.0-37.5	C, 64.22(64.33) H, 10.84(10.80)
IIk (14,8)	$C_{14}E8KT$	78	38.5-39.0	C, 63.61(63.63) H, 10.68(10.68)
III (16,8)	$C_{16}E8KT$	59	43.0-43.2	C, 64.11(64.58) H, 10.82(10.84)
IIm (12,9)	$C_{12}E\bar{9}KT$	>95[c]	(oily)	C, 61.11(62.17)[d] H, 10.29(10.44)[d]
Oxime				
IIIa (8,4)	C_8E4OX	63	(oily)	C, 60.08(60.45) H, 10.50(10.41) N, 3.74 (3.71)
IIIb (8,5)	C_8E5OX	90	(oily)	C, 59.62(59.83) H, 10.32(10.28) N, 3.31 (3.32)
IIIc (8,6)	C_8E6OX	87	(oily)	C, 58.79(59.33) H, 10.04(10.17) N, 2.93 (3.01)

(To be continued on the next page)

(Table 4-1; continued)

IIId (8,7)	C_8E7OX	79	(oily)	C, 58.64(58.91) H, 9.99(10.09) N, 2.78 (2.75)
IIIe (10,4)	$C_{10}E4OX$	76	(oily)	C, 61.75(62.19) H, 10.71(10.69) N, 3.36 (3.45)
IIIf (10,7)	$C_{10}E7OX$	80	(oily)	C, 59.89(60.31) H, 10.36(10.31) N, 2.82 (2.60)
IIIg (12,7)	$C_{12}E7OX$	70	(oily)	C, 61.72(61.56) H, 10.52(10.51) N, 2.64 (2.48)
IIIh (12,8)	$C_{12}E8OX$	44	(oily)	C, 61.00(61.06) H, 10.39(10.41) N, 2.38 (2.30)
IIIi (14,7)	$C_{14}E7OX$	87	(oily)	C, 62.39(62.70) H, 10.87(10.69) N, 2.71 (2.36)
IIIj (14,8)	$C_{14}E8OX$	89	(waxy)	C, 61.90(62.14) H, 10.53(10.59) N, 2.33 (2.20)
IIIk (16,8)	$C_{16}E8OX$	41	(waxy)	C, 63.16(63.13) H, 10.79(10.75) N, 1.87 (2.10)
IIIl (12,9)	$C_{12}E\bar{9}OX$	>95[c]	(oily)	C, 60.92(60.72)[d] H, 10.38(10.34)[d] N, 2.40 (2.18)[d]

a) GLC- or IR-pure. Based on parent alcohol ethoxylates (in the case of ketones) or ketones (in the case of oximes).

b) Kugelrohr distillation.

c) Crude.

d) Calculated from the found values of Ir (C, 61.97; H, 10.83).

measured with a 1 wt% aqueous surfactant solution at 20°C, unless otherwise described.

4-3 Results and Discussion

The preparation of oximes (III) from alcohol ethoxylates (I) with a monodispersed or dispersed oxyethylene group was easy and these compounds were obtained in good yields.

Karabatsos et al. have reported on the chemical shifts of oxime isomers (E and Z isomers) in ^{1}H NMR spectrum in detail.[5)] They have clarified that α-methylene protons of E isomers of alkylketoximes resonanced at higher magnetic field than that of Z isomers.[5b)] In all purified oximes, two singlet signals attributed to α-methylene protons were found at about δ 4.04 and 4.40, and the former was identified as an E isomer based on the investigation by Karabatsos et al. From the integration values of those two signals, the ratio of E isomer to Z isomer was about six in each compound.

The pKa values of III were measured by the general acid-base titration method (Table 4-2). Oximes (III) were pKa≃ 12 in water, so that they would act as nonionic surfactants in the range of practical use (~pH 12).

The surface tension - concentration curves of aqueous solutions of ketones (C_mE7KT and C_mE8KT) and oximes (C_mE7OX and C_mE8OX) are shown in Fig. 4-1. The CMC and the adsorption area/molecule at the surface (A) were determined by the methods

Table 4-2 pKa values[a] of oximes (III).

Compound	pKa	
C_8E4OX (IIIa)	---	(12.7)
C_8E5OX (IIIb)	---	(12.4)
C_8E6OX (IIIc)	12.0[b]	(12.9)
C_8E7OX (IIId)	11.6	
$C_{10}E4OX$ (IIIe)	---	(12.7)
$C_{10}E7OX$ (IIIf)	11.8	
$C_{12}E7OX$ (IIIg)	11.6	
$C_{12}E8OX$ (IIIh)	11.7	
$C_{14}E7OX$ (IIIi)	12.2[b]	
$C_{14}E8OX$ (IIIj)	11.7	
$C_{16}E8OX$ (IIIk)	11.5	

a) Measured in water at 20°C. Values in parentheses were measured in ethanol-water (1:1 v/v) at 25°C.

b) At 15°C.

mentioned in Chapter 3. Those results and the T_{cp} values are summarized in Table 4-3.

The T_{cp} values varied depending on the structure of terminal group. The relation between the T_{cp} and the number of carbon atoms in the alkyl group (m) for ketones (II) and oximes (III) containing a series of oxyethylene groups is illustrated in Fig. 4-2 with the data of some alcohol ethoxylates (I).[7] Oximes (III) showed much lower T_{cp} than the corresponding ketones (II) and alcohol ethoxylates (I). Above a hepta(oxyethylene) group as a hydrophilic part is required for the use of this type of oxime above room temperature. For compounds II and III containing a long oligo(oxyethylene) chain (n= 7 or 8), the decrease of T_{cp}

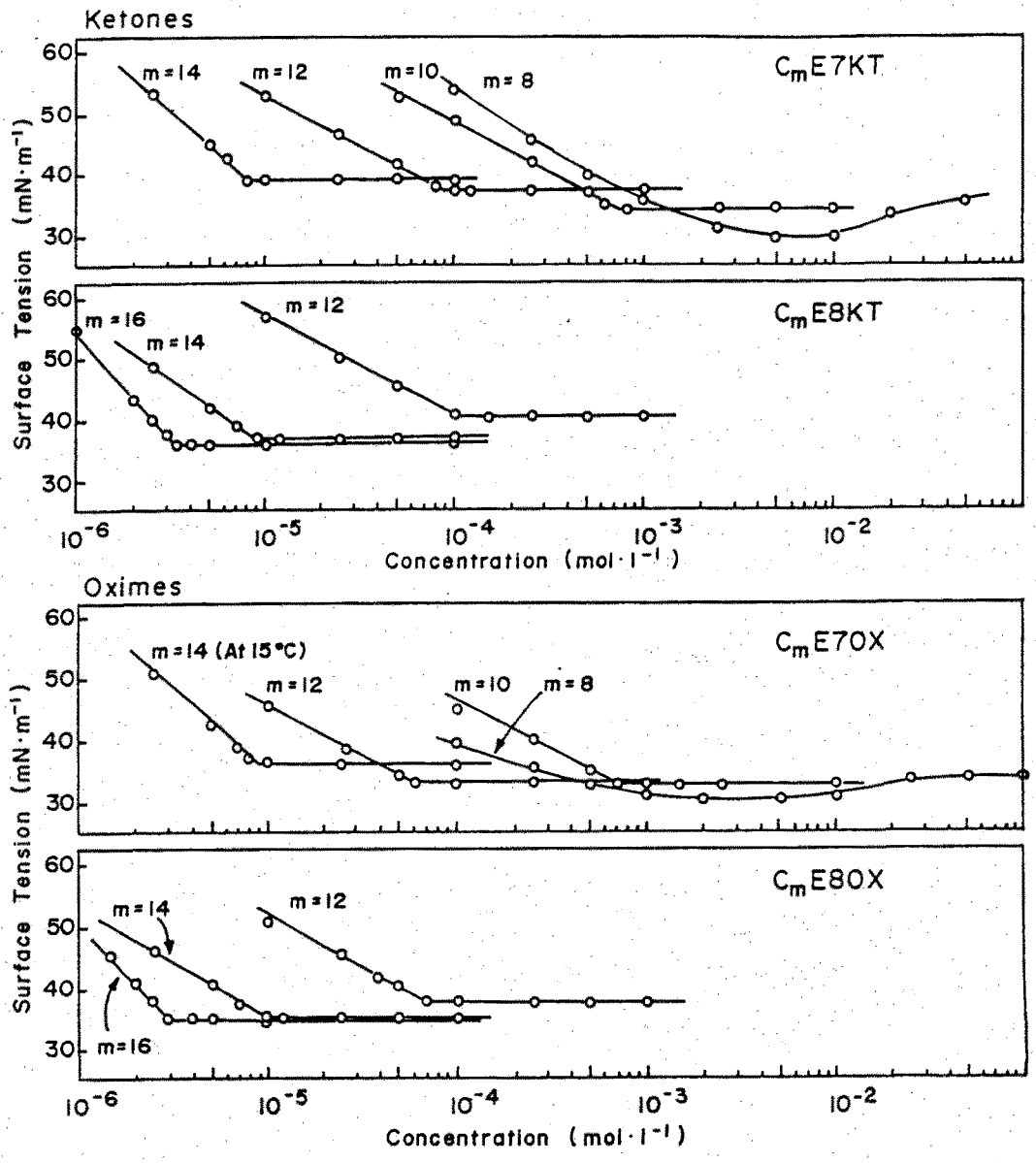


Fig. 4-1 Surface tension - concentration plots of aqueous surfactant solutions at 20°C.

Table 4–3 Surface active properties of ketones (II), oximes (III), and alcohol ethoxylate (Im) (20°C, neutral condition).

Compound	T_{cp}(1wt%) (°C)	10^4CMC (mol.l^{-1})	γ_{CMC} (mN.m^{-1})	10^2A (nm^2)
Ketone				
C_8E4KT (IIa)[a]	38.5	91	31.5	64
C_8E5KT (IIb)	50.5	---[b]	---[b]	--[b]
C_8E6KT (IIc)	55.6	---[b]	---[b]	--[b]
C_8E7KT (IId)	63.0	---[c]	29.5[d]	--[c]
$C_{10}E4KT$ (IIe)[a]	27.5	8.7	31.5	56
$C_{10}E7KT$ (IIf)	61.3	6.8	34.0	57
$C_{12}E4KT$ (IIg)[a]	18.5	0.94[e]	31.5[e]	47[e]
$C_{12}E7KT$ (IIh)	61.0	0.90	37.2	58
$C_{12}E8KT$ (IIi)	69.5	1.0	40.0	55
$C_{14}E7KT$ (IIj)	56.0	0.080	39.0	32
$C_{14}E8KT$ (IIk)	66.0	0.085	36.8	41
$C_{16}E8KT$ (IIl)	61.0	0.032	36.0	25
$C_{12}E\bar{9}KT$ (IIm)	70.5	0.80	31.0	40
Oxime				
C_8E4OX (IIIa)	<0.0	---[b]	---[b]	--[b]
C_8E5OX (IIIb)	<0.0	---[b]	---[b]	--[b]
C_8E6OX (IIIc)	21.5	28	33.5	61
C_8E7OX (IIId)	27.8	---[c]	30.0[d]	--[c]
$C_{10}E4OX$ (IIIe)	<0.0	---[b]	---[b]	--[b]
$C_{10}E7OX$ (IIIf)	27.0	7.0	32.5	58
$C_{12}E7OX$ (IIIg)	23.5	0.60	32.8	57
$C_{12}E8OX$ (IIIh)	32.5	0.70	37.4	56
$C_{14}E7OX$ (IIIi)	18.5	0.086[e]	36.2[e]	32[e]
$C_{14}E8OX$ (IIIj)	30.9	0.10	35.0	51
$C_{16}E8OX$ (IIIk)	30.0	0.030	34.5	28
$C_{12}E\bar{9}OX$ (IIIl)	39.8	0.66	30.2	61
Alcohol Ethoxylate				
$C_{12}E\bar{9}$ (Im)	76.7	0.80	30.5	34

a) Data cited from Chapter 3, Section 3.

b) Not determined.

c) Clear break point was not observed in the surface tension – log (concentration) plots.

d) The minimum value of surface tension.

e) At 15°C.

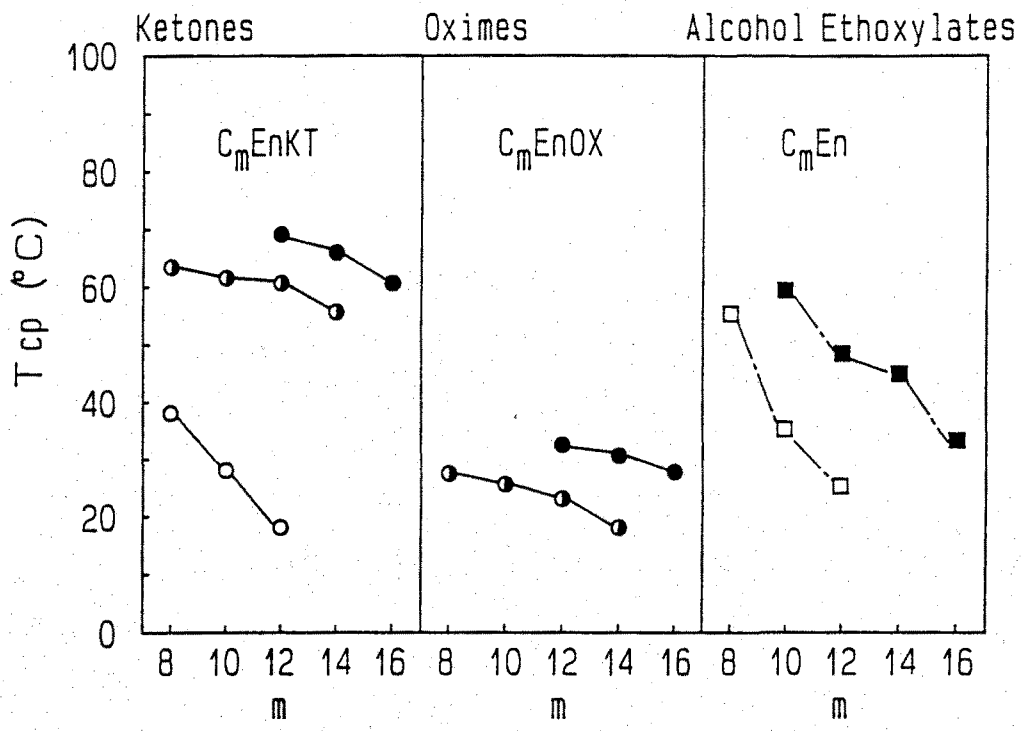


Fig. 4-2 T_{cp} vs. the number of carbon atoms in the alkyl group (m) for ketones (II; C_mEnKT), oximes (III; C_mEnOX), and alcohol ethoxylates [I; C_mEn, ref.(7)],
○ ; E4, □ ; E5, ■ ; E6, ◑ ; E7, ● ; E8.

with an increase in the number of carbon atoms (m) is somewhat smaller than that for II and I containing a short oligo(oxyethylene) chain (n= 4 or 5). The T_{cp} values of ketones (II) were relatively high. The cloud point of oxime with a dispersed oxyethylene group (IIIl) was also much lower than the corresponding ketone (IIm) and the parent alcohol ethoxylate (Im).

The author reported surface active properties of both hydroxamic acids (IV; C_mEnHA) and methyl esters (V; C_mEnME) in Chapter 3. From the T_{cp} values of our developed alcohol

ethoxylate types of nonionics ($C_{12}H_{25}(OCH_2CH_2)_4O$-Z; Z is a terminal functional group), the degree of contribution of terminal functional groups to the improvement of hydrophilicity can be evaluated as follows: (Z=) $-CH_2C(=O)NHOH$ (C_{12}E4HA; T_{cp}= 42.0°C) > $-CH_2CH_2OH$ (C_{12}E5; 25.0°C) > $-CH_2C(=O)CH_3$ (C_{12}E4KT; 18.5°C) > $-CH_2C(=O)OCH_3$ (C_{12}E4ME; 5.0°C) > $-CH_2C(=N-OH)CH_3$ (C_{12}E4OX; insoluble).

As shown in Fig. 4-1, the clear break point was not recognized in surface tension - concentration curves of C_8E7KT (IId) and C_8E7OX (IIId) probably because the hydrophilic part of those compounds was too large compared with the lipophilic part.

The relation between log CMC and the number of carbon atoms in the alkyl chain of II, III and I [cited from (8)] is shown in Fig. 4-3. Similar log CMC values were found for the corresponding II, III and I with the same number of carbon atoms (m), and a linear relationship was established between the log CMC and m in each case where $m \leq 14$. The log CMC values of ketones and oximes didn't change remarkably with the number of oxyethylene units. These tendencies coincide with the reported results about alcohol ethoxylates.[9)]

The γ_{CMC} values of II and III varied from 30 to 40 $mN.m^{-1}$, but the value of II was larger than that of the corresponding III. The adsorption area/molecule at the surface (A) decreased with an increase in the number of carbon atoms in the lipophilic group (m). Especially, the value for II and III with a tetra- or hexadecyl group is fairly small.

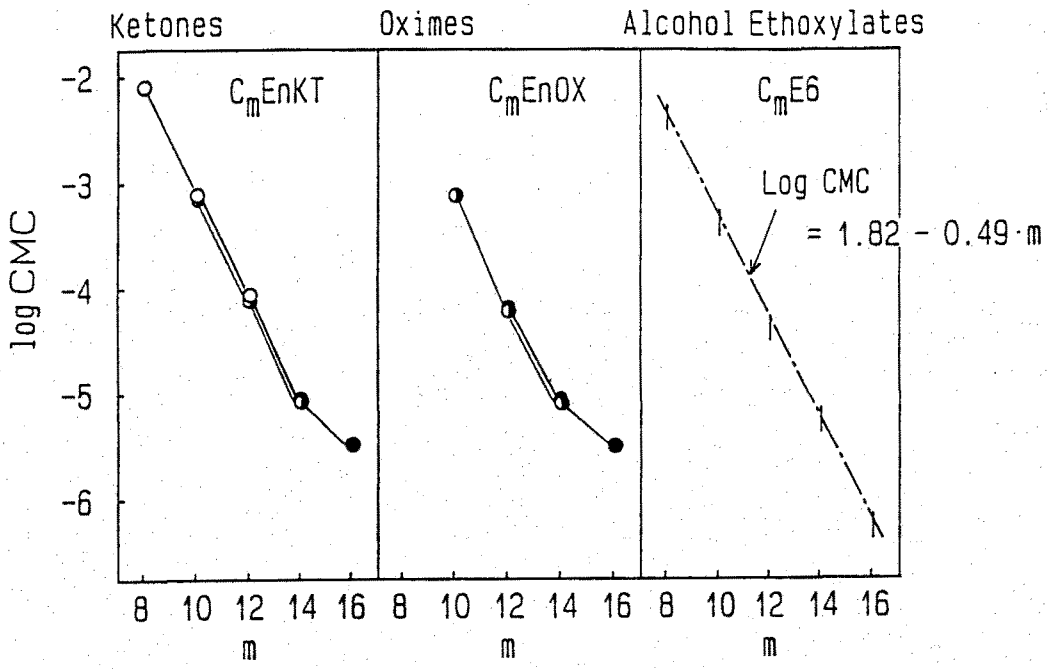


Fig. 4-3 Log CMC vs. the number of carbon atoms in the alkyl group (m) for ketones (II, 20°C), oximes (III, 20°C), and alcohol ethoxylates [I, 25°C, ref.(8)], ○ ; E4, ◑ ; E7, ● ; E8.

The foaming properties measured by the semi-micro TK method[10] are given in Table 4-4. Ketones (II) showed low foaming ability compared with the corresponding alcohol ethoxylates (I) as demonstrated in Chapter 3. Moreover, the foaming properties of oximes (III) were extraordinarily low compared with ketones. Compounds (III) seem to function as a kind of end-blocked nonionics which has the low foaming or antifoaming property,[11] because the hydrophilicity of the terminal oxime group is very low judging from the results of T_{cp} as discussed in this chapter.

Table 4–4 Foaming properties of ketones (II), oximes (III), and alcohol ethoxylate (Im) (20°C, neutral condition, 1 wt%).

Compound	Foam Volume (ml)					
	0'	30"	1'	1'30"	2'	5'
Ketone						
C_8E4KT (IIa)[a]	80	10	0			
C_8E6KT (IIc)	40	10	0			
C_8E7KT (IId)	70	10	0			
$C_{10}E4KT$ (IIe)[a]	160	80	20	0		
$C_{10}E7KT$ (IIf)	100	20	0			
$C_{12}E4KT$ (IIg)[a]	260	260	160	80	20	0
$C_{12}E7KT$ (IIh)	200	110	40	20	20	0
$C_{12}E8KT$ (IIi)	170	40	20	10	0	
$C_{14}E7KT$ (IIj)[b]	260	250	210	150	110	0
$C_{14}E8KT$ (IIk)	160	110	70	40	30	0
$C_{16}E8KT$ (IIl)	250	220	150	90	60	0
$C_{12}E\overline{9}KT$ (IIm)	260	240	230	200	170	70[c]
Oxime						
C_8E7OX (IIId)	10	0				
$C_{10}E7OX$ (IIIf)	15	0				
$C_{12}E7OX$ (IIIg)	30	0				
$C_{12}E8OX$ (IIIh)	30	0				
$C_{14}E7OX$ (IIIi)[b]	120	30	10	0		
$C_{14}E8OX$ (IIIj)	90	10	0			
$C_{16}E8OX$ (IIIk)	210	70	10	10	10	0
$C_{12}E\overline{9}OX$ (IIIl)	260	250	210	100	50	0
Alcohol Ethoxylate						
$C_{12}E\overline{9}$ (Im)	260	240	210	190	170	140[c]

a) Data cited from Chapter 3, Section 3.

b) At 15°C.

c) 30', 0 ml.

4-4 References

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CHAPTER 5 SYNTHESIS AND PROPERTIES OF SURFACE ACTIVE AMIDE OXIMES

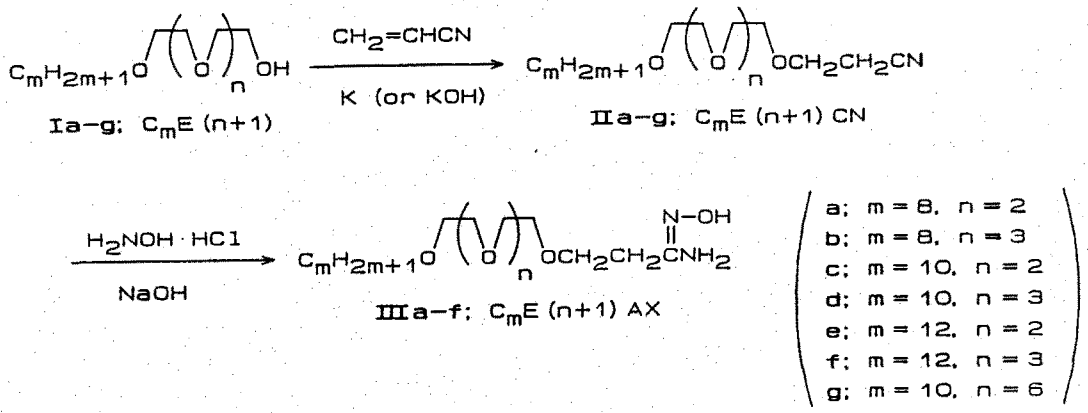
5-1 Introduction

It is known that amide oxime compounds can complex with various metal ions[1] and many reports on the application of this property to practical uses are available. Especially, the application of amide oximes to the separation, concentration or recovery process for valuable metals such as uranium or gallium and harmful metals such as mercury or cadmium has become of major interest recently. There are some reports on the recovery of uranium from seawater by amide oxime polymers,[2] the separation of various transition metals by telomer type of surface active amide oximes in ion-flotation systems,[3] or the concentration of gallium from the Bayer's solution by amide oximes.[4]

The author prepared novel surface active hydroxamic acids (Chapter 3), ketones and oximes (Chapters 3 and 4) by the modification of the terminal hydroxyl group of alcohol ethoxylates and clarified their surface active properties or the effect of the terminal functional groups on interfacial properties under various conditions.

In this chapter, the author prepared a new type of surface active amide oximes [**IIIa-f**; $C_mE(n+1)AX$] from alcohol ethoxylates having a monodispersed oligo(oxyethylene) group [**Ia-g**; $C_mE(n+1)$] to make some functions of amide oxime group exhibit as molecular aggregations in aqueous media under various conditions. The author determined surface active properties of these amide oximes

and compared with other alcohol ethoxylate types of functional surfactants developed by us. The synthetic route for amide oximes and abbreviations of compounds are shown in Scheme 5-1.



Scheme 5-1 Preparation of amide oximes (III) and abbreviations of compounds (I-III).

5-2 Experimental

Materials. Alcohol ethoxylates (Ia-g) were prepared from n-alkylbromides and monodispersed oligo(ethylene glycol)s. (50-70 %) 3-Alkyl[oligo(oxyethylene)]oxy-2-propionamide oximes (III) were obtained from nitriles [II; $C_mE(n+1)CN$] which were prepared by the cyanoethylation of the corresponding alcohol ethoxylates.[5] Amide oximes were purified by the silica-gel (metal free) column chromatography or recrystallization from hexane.

3-Alkyl[oligo(oxyethylene)]oxypropionenitrile (II): Typical procedure. After metallic potassium (0.2 g, 5 mmol) was dissolved in decyl tetra(oxyethylene) monoether (**Id**; $C_{10}E4$; 16.7 g, 50 mmol), acrylonitrile (3.0 g, 57 mmol) was dropped carefully at 30°C and the mixture was stirred at this temperature for 24 hr. After neutralization by hydrochloric acid, water (100 ml) was added and the reaction mixture was extracted with methylene chloride (100 ml, 4 times). After the extracts were combined and dried with $MgSO_4$, evaporation of the solvent gave a crude product. (12.0 g; crude nitrile) The gas-liquid chromatography (GLC)-pure 4,7,10,13,16-pentaoxahexacosanenitrile (**IId**; $C_{10}E4CN$) was obtained by Kugelrohr distillation. (bp: 150°C/0.05 Torr; 10.9 g, 64 % yield)

3-Alkyl[oligo(oxyethylene)]oxypropionamide oxime (III): Typical procedure. Hydroxylamine hydrochloride (3.50 g, 51 mmol) in methanol (30 ml) was added to sodium hydroxide (2.11 g, 50 mmol) in methanol (30 ml) at 0°C, and insoluble solids were separated off by filtration. Compound (**IId**) (7.74 g, 20 mmol) in methanol (40 ml) was dropped into this filtrate and the mixture was stirred at room temperature for 24 hr (pH 5-7 under these conditions). After filtration and subsequent evaporation of the filtrate, methylene chloride (50 ml) was added to the residue. Insoluble solids were filtered off again, and a 7.98 g of crude product was obtained by evaporation of the filtrate. The pure 4,7,10,13,16-pentaoxahexacosanamide oxime (**IIId**; $C_{10}E4AX$), confirmed by its spectral data, was obtained by a silica-gel column chromatography with a hexane : 2-propanol (4:1

v/v) eluent as colorless solids. (mp: 29.5-30.0°C, 7.82 g, 93 % yield)

The structures of II and III were confirmed by their IR (Hitachi 260 spectrometer), ^{1}H NMR (JEOL JNM-PS-100), mass (Hitachi RMU-6E) spectra and elemental analyses. IR (neat): nitriles; 2950, 2870, 2250, 1480, 1350, 1120, 950, and 850 cm^{-1}, amide oximes; 3300, 2950, 2870, 1660, 1580, 1470, 1380, 1120, 940, and 860 cm^{-1}. ^{1}H NMR ($CDCl_3$): nitriles; δ= 0.88 (t, 3H, CH_3-C-C), 1.2-1.8 (m, -CH_2- in alkyl chain), 2.55 (t, 2H, O-C-CH_2-CN), 3.39 (t, 2H, O-CH_2-C-CN) and 3.5-3.8 [m, O-CH_2CH_2-O and (alkyl chain)-CH_2-O], amide oximes; δ= 0.88 (t, 3H), 1.1-1.8 (m), 2.35 [t, 2H, -C-CH_2-C(=N-O)-N], 3.44 [t, 2H, O-CH_2-C-C(=N-O)], 3.5-3.8 (m) and 4.0-5.5 [br, 3H, C-C(=N-OH)-NH_2; disappeared by addition of D_2O]. The molecular ion peak of each compound was observed in its mass spectrum. The synthetic results of **IIg** and **IIIa-f**, which are the objects of this investigation about surface active properties, are summarized in Table 5-1 with the data of elemental analyses.

Methods. The pKa values were determined either in water ordinarily at 20°C or in a water-ethanol mixture (1:1 v/v) at 25°C under a nitrogen flow, according to the potentiometric method. The cloud point (T_{cp}) and other surface active properties of aqueous solutions of those compounds were measured by the previously reported methods. (Chapters 3 and 4) The T_{cp} and foaming properties (at 20°C) were measured with a 1 wt% aqueous surfactant solution, according to the usual procedure. The pH of aqueous solutions was adjusted by addition of hydrochloric acid or sodium hydroxide.

Table 5-1 Properties of nitrile (IIg) and amide oximes (IIIa-f).

Compound (m,n)	Abbreviation Symbol	Yield[a] (%)	bp[b] or mp (°C/Torr) or (°C)	Anal. Found(Calcd)
IIg (10,6)	$C_{10}E7CN$	82	195/0.06	C, 61.86(62.40) H, 10.37(10.28) N, 2.86 (2.69)
IIIa (8,2)	C_8E3AX	89	(oily)	C, 58.12(58.59) H, 10.53(10.41) N, 7.83 (8.04)
IIIb (8,3)	C_8E4AX	92	(oily)	C, 58.15(58.14) H, 10.31(10.27) N, 7.14 (7.14)
IIIc (10,2)	$C_{10}E3AX$	90	(oily)	C, 60.52(60.61) H, 10.78(10.71) N, 7.29 (7.44)
IIId (10,3)	$C_{10}E4AX$	93	29.5-30.0	C, 59.98(59.97) H, 10.62(10.54) N, 6.62 (6.66)
IIIe (12,2)	$C_{12}E3AX$	89	30.5-31.0	C, 62.33(62.34) H, 10.96(10.96) N, 6.29 (6.92)
IIIf (12,3)	$C_{12}E4AX$	80	32.0-33.0	C, 62.13(61.57) H, 10.73(10.78) N, 5.70 (6.24)

a) GLC- or IR-pure. Based on parent alcohol ethoxylate (in the case of nitrile) or nitriles (in the case of amide oximes).

b) Kugelrohr distillation.

5-3 Results and Discussion

While the cyanoethylation of **Ia-f** was carried out in the presence of a catalytic amount of potassium without solvent, the reaction medium became solid in the case of **Ig**. Thus, potassium hydroxide and dioxane were used as a base and a solvent, respectively, for the preparation of nitrile (**IIg**). The preparation of amide oximes was very easy, and they were obtained in good yield.

The pKa values of **III** were measured by the general acid-base titration method. Amide oximes generally have two dissociation constants (Ka_1 and Ka_2),[1a] but only pKa_1 was found in each amide oxime (**III**) by this method. (Table 5-2) From the pKa_1 values, compounds (**III**) were expected to act as both cationic surfactants under acidic conditions and nonionic ones under neutral and basic conditions.

Table 5-2 pKa_1 values[a] of amide oximes (**IIIa-f**).

Compound	pKa_1	Compound	pKa_1
C_8E3AX (**IIIa**)	4.9	C_{10}E4AX (**IIId**)	5.1 (5.5)
C_8E4AX (**IIIb**)	5.1	C_{12}E3AX (**IIIe**)	4.9[b] (5.3)
C_{10}E3AX (**IIIc**)	4.8	C_{12}E4AX (**IIIf**)	4.9 (5.3)

a) Measured in water at 20°C. Values in parentheses were measured in ethanol-water (1:1 v/v) at 25°C.

$$R\text{-}C(=N\text{-}OH)\text{-}NH_3^+ \overset{Ka_1}{\rightleftharpoons} R\text{-}C(=N\text{-}OH)\text{-}NH_2 \overset{Ka_2}{\rightleftharpoons} R\text{-}C(=N\text{-}O^-)\text{-}NH_2$$

b) At 5°C.

The surface tension - concentration plots (by the Wilhelmy method) of aqueous solutions of amide oximes (C_mE3AX and C_mE4AX) are shown in Fig. 5-1. The T_{cp}, CMC, the lowering ability of surface tension (γ_{CMC}) and the adsorption area/molecule at the surface (A) of **IIg** and **IIIa-f** are summarized in Table 5-3.

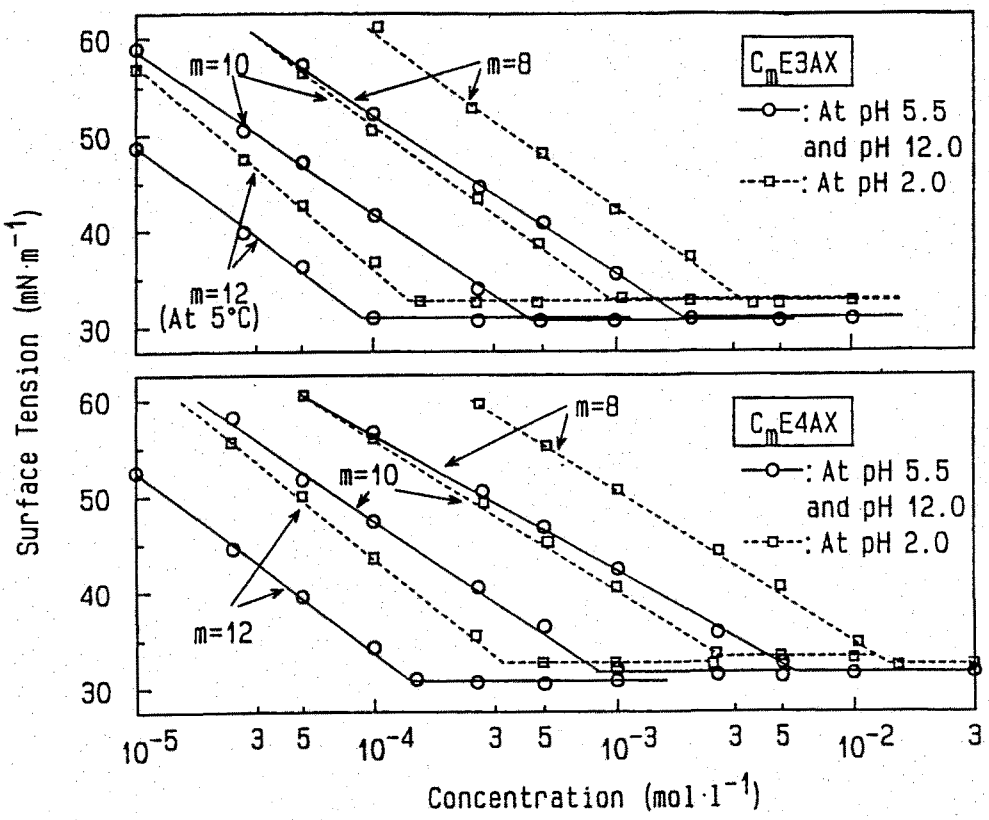


Fig. 5-1 Surface tension - concentration plots of aq amide oxime solutions under various pH conditions at 20°C.

Table 5-3 Surface active properties of nitrile (IIg) and amide oximes (IIIa-f).

Compound	T_{cp}[a] (°C)	10^4CMC[b] ($mol.l^{-1}$)	γ_{CMC}[b] ($mN.m^{-1}$)	10^2A (nm^2)
C_{10}E7CN (**IIg**)	41.0	9.6	34.0	76
C_8E3AX (**IIIa**)	43.0	18 (36)	31.0 (33.0)	58
C_8E4AX (**IIIb**)	65.0	60 (120)	32.0 (33.0)	66
C_{10}E3AX (**IIIc**)	24.5	4.4 (9.2)	31.0 (33.0)	56
C_{10}E4AX (**IIId**)	45.0	8.5 (24)	32.0 (33.5)	58
C_{12}E3AX (**IIIe**)	6.0	0.85[c] (1.6)[c]	31.0[c] (33.0)[c]	47[c]
C_{12}E4AX (**IIIf**)	22.5	1.4 (3.5)	31.0 (33.0)	50

a) At 1 wt%.

b) Amide oximes were measured under acidic (pH 2.0), neutral (pH 5.5), and basic (pH 12.0) conditions, and the same value was obtained at pH 5.5 and 12.0. Data in parentheses were values at pH 2.0.

c) At 5°C.

Nitriles (**IIa-f**) having three or four oxyethylene units were insoluble in water. Because the T_{cp} of C_{10}E7CN (**IIg**) containing seven oxyethylene units was about 20°C lower than that of decyl hexa(oxyethylene) monoether (C_{10}E6; T_{cp}= 60°C)[6] with only six oxyethylene units, the terminal cyanoethyl group seemed to behave as a hydrophobic part. On the other hand, the T_{cp} values of amide oximes (III) were similar to those of alcohol ethoxylates with one more oxyethylene unit than corresponding amide oximes (for example: C_8E5; T_{cp}= 55°C, C_{10}E5; 36°C, C_{12}E5; 25°C).[6] The terminal amide oxime group seemed to contribute to the hydrophilic

property. The satisfactory results will be attained in the practical application if compounds (III) have tetra(oxyethylene) units.

The surface tension of aqueous amide oxime (III) solutions was measured under acidic (pH 2.0), neutral (pH 5.5) and basic (pH 12.0) conditions, and two types of surface tension - concentration curves were found for each compound (III). One was obtained under neutral and basic conditions, while the other was in an acidic solution. Under acidic conditions, the hydrophilicity of the molecule might increase by the protonation of amide oxime group, so that the break in the curve (CMC) shifted to a higher concentration than that under neutral condition. On the other hand, because similar curves were found under neutral and basic conditions, III could act as nonionic surfactants as discussed above about pKa values.

The γ_{CMC} values of neutral and basic aqueous amide oxime solutions were good as nonionic surfactants. The γ_{CMC} values of III under acidic condition were higher than those under other conditions. This tendency caused by ionization of surfactants was also found in the case of hydroxamic acids and oximes, as mentioned in Chapters 3 and 4. The adsorption area/molecule (A) of III decreased with both an increase in the number of carbon atoms in the lipophilic group and a decrease in the number of oxyethylene units. This trend is generally evident in nonionic surfactants.[7)]

The foaming properties determined by the semi-micro TK method[8)] are given in Table 5-4.

Table 5-4 Foaming properties of nitrile (IIg) and amide oximes (IIIa-f).

Compound	Condition[a]	Foam Volume[b] (ml)					
		0'	30"	1'	1'30"	2'	5'
C_{10}E7CN (IIg)	N	90	15	0			
C_8E3AX (IIIa)	N,B	30	0				
"	A	60	10	0			
C_8E4AX (IIIb)	N,B	20	0				
"	A	30	0				
C_{10}E3AX (IIIc)	N,B	130	50	30	10	0	
"	A	220	180	150	100	60	0
C_{10}E4AX (IIId)	N,B	80	10	0			
"	A	100	40	20	10	0	
C_{12}E3AX (IIIe)	N,B[c]	180	120	90	70	50	0
"	A[c]	260	260	260	260	260	240[d]
C_{12}E4AX (IIIf)	N,B	140	90	60	20	0	
"	A	240	120	60	30	20	0

a) N: neutral condition (pH 5.5), B: basic condition (pH 12.0), A: acidic condition (pH 2.0).

b) By the semi-micro TK method[8] at 1 wt% and 20°C.

c) At 5°C.

d) 10', 200 ml; 30', 100 ml; 50', 10 ml; 80', 0 ml.

For amide oximes (III) the measurement was carried out under various pH conditions, and similar results were obtained at pH 5.5 and 12.0. The foaming ability and foam stability of III with the cationic character were superior to those of III with the nonionic character. Though similar oximes showed excellent antifoaming property (see in Chapter 4), these amide oximes did not have as much antifoaming character as expected. The foam stability of III

seemed medium compared with the corresponding alcohol ethoxylates.

The surface active properties mentioned above afford much information to the application of amide oximes to ion-flotation systems because the HLB and interfacial properties of surfactant collector types are very important factors for such objects.[3)]

5-4 References

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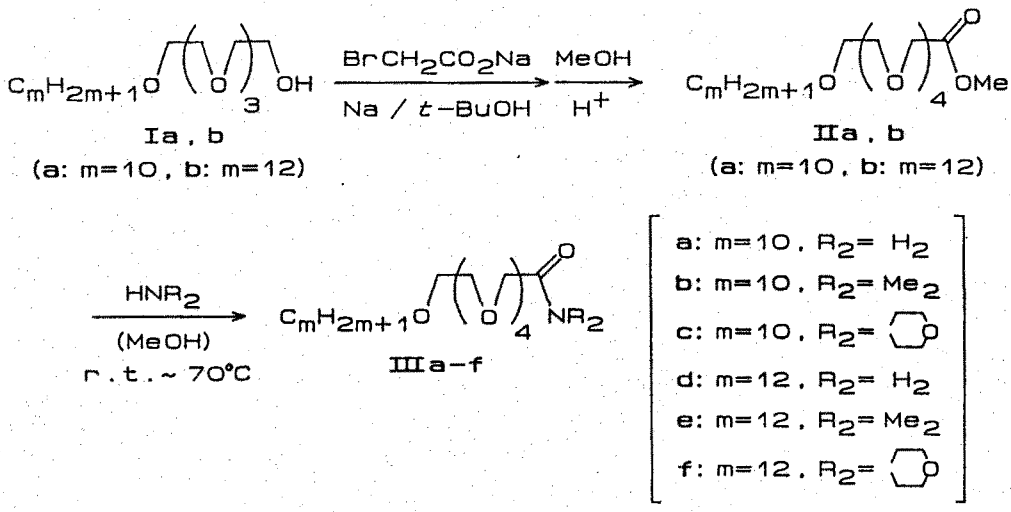
CHAPTER 6 SYNTHESIS AND PROPERTIES OF SURFACE ACTIVE AMIDES

6-1 Introduction

The investigation of surfactants with a sequestering ability for calcium and magnesium ions is still continuing to develop new types of phosphate-free detergents, builders and lime-soap dispersing agents (LSDA).[1] An amide group has attracted interest in this field because this group is known to have a strong affinity for calcium ions.[2] Linfield et al. have already reported that oxyethylated fatty amides can be applied to LSDA[3] and soil wetting agents[4] with excellent ability. They have also clarified that an oxyethylene group can make a significant contribution to the lime-soap dispersing ability.[3]

The author prepared a series of "functional" surfactants by a relatively simple modification of the terminal hydroxyl group of alcohol ethoxylates and have studied their extra functions besides their basic surface active properties. This time, the author synthesized three kinds of amide compounds (**IIIa-f**; see Scheme 6-1) with different terminal structures from the alkyl tetra(oxyethylene) monoethers (**Ia,b**; alkyl: decyl or dodecyl). There is a patent concerning detergents thickened with terminal dialkanol amide type of alcohol ethoxylates which are the familiar types of III, but their properties were not characterized at all.[5] In this chapter, the author reported the surface active properties of compounds (III) both in pure water and in hard water, and their lime-soap dispersing ability. The author also

clarified the effect of the terminal amide structure on these properties and compared these amides with other alcohol ethoxylate derivatives developed by us. The synthetic route for the amides is shown in Scheme 6-1.



Scheme 6-1 Preparation of amides (III) from alcohol ethoxylates (I).

6-2 Experimental

Materials. Methyl [α-alkyltetra(oxyethylene)-ω-yloxy]acetates (II) were prepared according to the method described in Chapter 3, Section 2. (60-80 % yield) Three kinds of [α-alkyltetra(oxyethylene)-ω-yloxy]acetamides (III) with different terminal structures were synthesized by the reaction of II with ammonia, dimethylamine or morpholine. The reaction was carried

out in methanol at room temperature except for **IIIc** and **IIIf**, which were prepared at 70°C without any solvent. Pure amides were obtained by Kugelrohr distillation or recrystallization from hexane.

[α-Alkyltetra(oxyethylene)-ω-yloxy]acetamide (III): Typical procedure. The methyl ester (**IIb**; 3.0 g, 6.9 mmol) in methanol (5 ml) was dropped into a 20 ml of aqueous ammonia (28 % solution) at ca. 20°C. After 2 hr of stirring at room temperature and subsequent evaporation of the solvent and excess ammonia, the residue was dissolved in 50 ml of water. After extraction of this solution with ether (100 ml, 3 times), crude amide (mp: 37-40°C, 3.0 g) was obtained as a residue after evaporation of the solvent. Recrystallization of the crude product from hexane gave pure 3,6,9,12,15-pentaoxaheptacosanamide (**IIIb**; mp: 39.2-39.8°C, 2.0 g, 70 % yield).

The structure of III was confirmed by gas-liquid chromatography (GLC), spectral (IR, mass and ^{1}H NMR) and elemental analyses (within $\pm$0.4 %). It was also assessed from the observed sharp break in surface tension - concentration curves. Their properties are summarized in Table 6-1.

Methods. The cloud point (T_{cp}) and other surface active properties of aqueous solutions of these amides were measured by the methods described in Chapter 3. The stability of compounds (III) for calcium and magnesium ions was determined in 0.5 % solutions by the modified Hart method.[6] The solutions contained up to 2000 ppm of total hardness as $CaCO_3$. Surface active properties were also measured in hard water with 1000 ppm of total

Table 6-1 Preparation and properties of amides (**IIIa-f**)[a].

Compound (m,R_2)	Yield[b] (%)	mp (°C) or bp (°C/Torr)[c]	^{1}H NMR[d] ($CDCl_3$) (δ)	mass (70 eV) m/e (rel.intens.)	Anal. Found(Calcd)
IIIa (10, H_2)	66	waxy product	0.83(t,3H), 1.2-1.8(m,16H), 3.42(t,2H), 3.6-3.8(m,16H), 3.6-3.8(m,16H), 3.97(s,2H), 5.6-6.2(br,2H)	391(M^+,Amp), 102(100), 89 (25), 45 (50)	C, 61.33(61.35) H, 10.32(10.55) N, 3.45 (3.58)
IIIb (10,Me_2)	78	140/0.02	0.85(t,3H), 1.2-1.8(m,16H), 2.90(s,3H), 2.97(s,3H), 3.42(t,3H), 3.6-3.8(m,16H), 4.20(s,2H)	419(M^+,Amp), 130(100), 87 (34), 45 (41)	C, 62.98(62.97) H, 10.81(10.81) N, 3.09 (3.39)
IIIc (10, ⌒O)	71	180/0.06	0.88(t,3H), 0.2-1.7(m,16H), 3.44(t,2H), 3.5-3.8(m,24H), 4.21(s,2H)	461(M^+, 18), 172(100), 128 (30), 57 (28)	C, 62.23(62.44) H, 10.38(10.26) N, 2.98 (3.03)
IIId (12, H_2)	70	39.2-39.8	0.83(t,3H), 1.2-1.8(m,20H), 3.42(t,2H), 3.6-3.8(m,16H), 3.97(s,2H), 5.6-6.2(br,2H),	419(M^+,Amp), 102 (65), 89 (71), 45(100)	C, 62.78(62.97) H, 10.83(10.81) N, 3.22 (3.39)
IIIe (12,Me_2)	72	150/0.02	0.85(t,3H), 1.2-1.8(m,20H), 2.90(s,3H), 2.98(s,3H), 3.42(t,2H), 3.6-3.8(m,24H), 4.20(s,2H)	447(M^+,Amp), 130(100), 87 (40), 45 (40)	C, 64.58(64.39) H, 11.08(11.03) N, 2.89 (3.13)
IIIf (12, ⌒O)	70	160/0.06	0.85(t,3H), 1.2-1.7(m,20H), 3.42(t,2H), 3.6-3.8(m,24H), 4.20(s,2H)	489(M^+, 2), 172(100), 128 (40), 57 (55)	C, 63.82(63.77) H, 10.52(10.50) N, 2.97 (2.86)

a) IR spectra: **IIIa,d**; 3400, 2940, 2850, 1650, 1460, 1350, 1290, 1250, 1110, and 960 cm^{-1} (neat), **IIIb,c,e,f**: 2920, 2850, 1650, 1450, 1350, 1280, 1110, and 950 cm^{-1} (neat).

b) Based on methyl ester (II).

c) Kugelrohr distillation.

d) 100 MHz.

hardness as $CaCO_3$ which was prepared by the use of $CaCl_2 \cdot 2H_2O$ and $MgCl_2 \cdot 6H_2O$ (a hardness composition of 68 % Ca^{2+}, 32 % Mg^{2+}). The lime-soap dispersing requirement (LSDR) was determined in 333 ppm of hard water by the Borghetty-Bergmann method.[7)]

6-3 Results and Discussion

The preparation of the amides was very easy and they could be isolated in good yield. All these amides (III) were readily soluble in water. It was clarified by the measurement using the modified Hart method that compounds (III) didn't precipitate and were stable in hard water above 2000 ppm of total hardness as $CaCO_3$.

The surface tension - concentration plots of III both in pure water and in hard water measured by the Wilhelmy method are shown in Fig. 6-1. The T_{cp}, CMC, the lowering ability of surface tension (γ_{CMC}) and the adsorption area/molecule at the surface (A) of III both in pure water and in hard water are summarized in Table 6-2. In the case of amides with the same alkyl group, the T_{cp} values of the dimethylamides (**IIIb,e**) or acylmorpholines (**IIIc,f**) were higher than those of the corresponding N-unsubstituted amides (**IIIa,d**) by about 15 to 25°C. This means that these N,N-disubstituted amides are more hydrophilic than the N-unsubstituted amides. It may be considered that the intramolecular hydrogen bond of a terminal amide group with a carbonyl or ether oxygens contributes to the hydrophobic character

of the N-unsubstituted amides. The T_{cp} values of all compounds in hard water are about from 1 to 9°C lower than those in pure water, probably because of the salting-out effect.[8] Because the T_{cp} of the most hydrophobic, **IIId** with a dodecyl group, is higher than room temperature, all these compounds seem to possess sufficient hydrophilicity even in hard water.

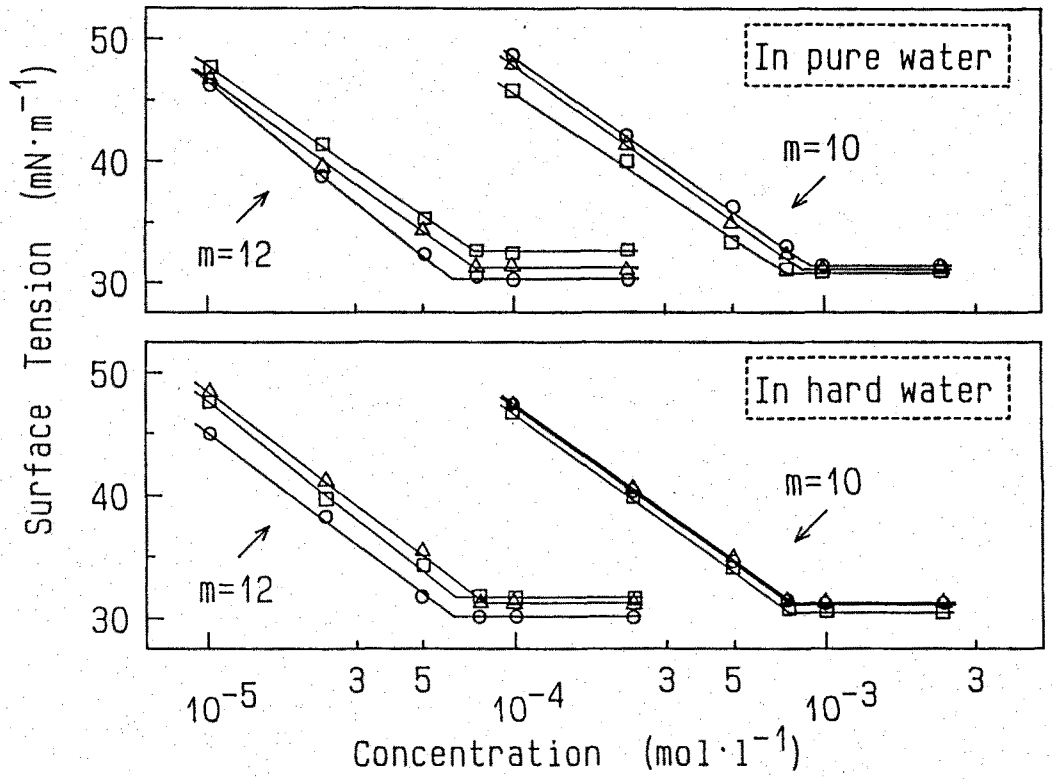


Fig. 6-1 Surface tension - concentration plots of amides (III) in pure water and in hard water with 1000 ppm of total hardness (as $CaCO_3$) at 20°C. ○, **IIIa,d** (R_2= H_2); △, **IIIb,e** (R_2= Me_2); □, **IIIc,f** [R_2= $-(C_2H_4OC_2H_4)-$].

Table 6-2 Surface active properties of amides (**IIIa-f**)[a].

Compound (m,R_2)	Condition[b]	T_{cp}[c] (°C)	10^4CMC ($mol \cdot l^{-1}$)	γ_{CMC} ($mN \cdot m^{-1}$)	10^2A (nm^2)
IIIa	P	45.9	9.1	31.2	54
(10, H_2)	H	45.7	8.0	31.2	50
IIIb	P	66.8	8.5	31.1	54
(10,Me_2)	H	57.0	8.3	31.4	54
IIIc	P	59.5	7.6	30.9	57
(10, ⌒O)	H	57.0	8.0	30.7	56
IIId	P	26.0	0.60	30.3	47
(12, H_2)	H	25.8	0.60	30.1	47
IIIe	P	50.5	0.75	31.2	52
(12,Me_2)	H	45.0	0.75	31.8	52
IIIf	P	50.8	0.75	32.7	55
(12, ⌒O)	H	49.8	0.60	32.0	52

a) CMC, γ_{CMC} and A: at 20°C.

b) P: in pure water, H: in hard water (total hardness: 1000 ppm as $CaCO_3$).

c) At 1 wt%.

The author found that the T_{cp} of a series of alcohol ethoxylate derivatives changed considerably with the structure of terminal group. (Chapters 3, 4, and 5) The T_{cp} values of dodecyl tetra(oxyethylene)oxy derivatives with various terminal groups (Z) previously developed by us are illustrated in Fig. 6-2. Acylmorpholine and dimethylamide showed the highest T_{cp} values among these alcohol ethoxylate derivatives, and N-unsubstituted amide showed a nearly similar T_{cp} value to that of alcohol ethoxylate with one more oxyethylene unit ($C_{12}E5$). Therefore, it can be concluded that the hydrophilicity of these amides (III) is very good for this series of alcohol ethoxylate derivatives.

The CMC values of each compound in pure water and in hard water were almost the same. In addition, amides with the same alkyl group showed similar CMC values regardless of the structure of the terminal group. The CMC values of amides with a dodecyl group were about one-tenth smaller than those of amides with a decyl group. As a result, it is clear that the CMC of III also depends on the type of hydrophobic groups rather than the structure of the hydrophilic group like other "functional" alcohol ethoxylates. The γ_{CMC} values of each compound in both solution systems were almost the same and were good for a series of nonionic surfactants.

The adsorption area/molecule (A) of amides with a dodecyl group (IIId-f) was smaller than A of IIIa-c with a decyl group. In each compound, the A value in hard water was almost the same or a little smaller than that in pure water. The A values of the acylmorpholines (IIIc,f) were larger than other amides probably

because of the bulkiness of the hydrophilic terminal group.

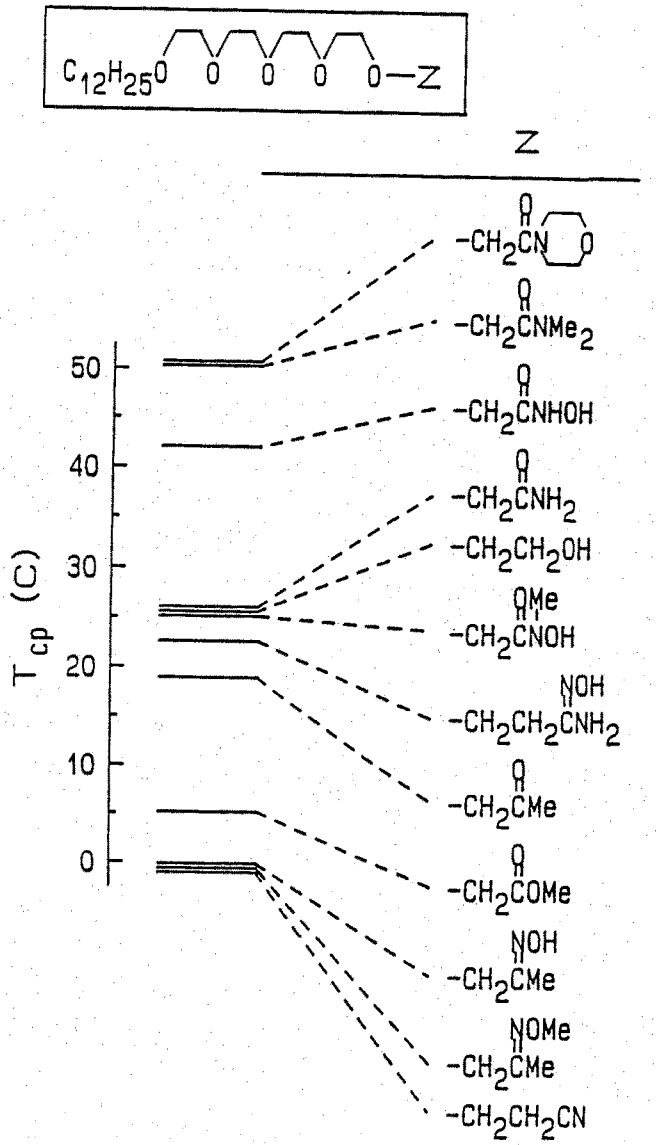


Fig. 6-2 The effect of terminal structures of alcohol ethoxylate derivatives on the T_{cp}.

The foaming properties determined by the semi-micro TK method[9] both in pure water and in hard water are given in Table 6-3.

Table 6-3 Foaming properties of amides (**IIIa-f**)[a].

Compound (m,R_2)	Condition[b]	Foam Volume (ml)					
		0'	0.5'	1'	1.5'	2'	5'
IIIa	P	90	20	0			
(10, H_2)	H	110	20	0			
IIIb	P	210	140	90	50	20	0
(10,Me_2)	H	160	70	30	20	0	
IIIc	P	180	110	30	20	0	
(10, ⬡O)	H	175	110	30	20	0	
IIId	P	240	220	200	170	130	0
(12, H_2)	H	240	200	140	120	90	0
IIIe	P	240	160	90	50	20	0
(12,Me_2)	H	260	200	100	50	20	0
IIIf	P	130	30	0			
(12, ⬡O)	H	140	40	10	0		

a) At 20°C, 1 wt% solution.

b) P: in pure water, H: in hard water (total hardness: 1000 ppm as $CaCO_3$).

The foaming ability and foam stability of III in both solution systems were almost the same. Unexpectedly, the foaming properties of acylmorpholine with a dodecyl group (IIIf) were inferior to IIIc with a decyl group. But, overall, the foaming properties of these amides are judged as medium for a series of our prepared alcohol ethoxylate derivatives.

Finally, results of the LSDR of III and some reference compounds are listed in Table 6-4.

Table 6-4 Lime-soap dispersing requirement (LSDR) of amides (**IIIa-f**) and reference compounds at 20°C.

Amide (m,R_2)	LSDR	Reference Compound	LSDR
IIIa (10, H_2)	14.0	Linear Alkylbenzene Sulfonate[a]	40
IIIb (10,Me_2)	15.2	Sodium Dodecyl Sulfate	30.0
IIIc (10, O)	13.4	$C_{10}H_{21}O(CH_2CH_2O)_6H$	26.5
IIId (12, H_2)	6.5	$RC(=O)N[(CH_2CH_2O)_7H]_2$[b]	2
IIIe (12,Me_2)	6.0		
IIIf (12, O)	6.0		

a) Ref.(10).

b) Ref.(1b); R refers to a tallow-derived alkyl group.

Since the LSDR of amides with a decyl group was about 14 and that of amides with a dodecyl group was about 6, it was found that **III** had better lime-soap dispersing ability than LAS, SDS and a normal alcohol ethoxylate. But, our results were not beyond the LSDR of an oxyethylated fatty amide with a tallow-derived alkyl group. Linfield et al. have reported that the LSDR of oxyethylated fatty amides decreased smaller with an increase in the number of oxyethylene units.[10] Therefore, there is a possibility that our types of compounds with longer alkyl and oxyethylene groups may show smaller LSDR values.

6-4 References

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CONCLUSION

This thesis mainly deals with synthesis and properties of functional compounds containing oligo(oxyethylene) groups. The results and findings obtained through this work are summarized as follows:

In Chapter 1, N-oligo(oxyethylene) monoaza crown ether derivatives and urethane types of crown ethers were synthesized, and their complexing ability with various cations was determined. Since the stability constants (log K_1') of monoaza crown ethers having an oligo(oxyethylene) sidearm with Na^+ and K^+ were larger than those of N-unsubstituted or N-long-chain alkyl monoaza crown ethers with the same ring size, it was clear that oxyethylene oxygen atoms in the sidearm made a remarkable contribution to the complexation with metal cations. From the cloud point (T_{cp}) values of monoaza crown compounds containing a long-chain alkyl group, the contribution of the oligo(oxyethylene) group in the side chain to the hydrophilicity of the molecule was evaluated. The T_{cp} values of a series of monoaza crown ethers in the presence of metal chlorides were higher than those in the absence of metal salts ($\Delta T_{cp} > 0$) with the exception of a few cases. The ΔT_{cp} values depended on both the number of oxygen atoms in the side chain and the kinds of metal cations. It became clear that by the measurement of the ΔT_{cp} values the complexing ability of monoaza crown derivatives with metal cations in water could be evaluated indirectly because the good correlation between the ΔT_{cp} and the log K_1' values was recognized. Furthermore, new urethane types of

crown ethers were easily obtained by the intramolecular cyclization of thermolysis of N-ammonioamidates having an ω-hydroxy-oligo(oxyethylene) group in an acyl moiety.

In Chapter 2, N-ammonioamidates containing a hydroxyl group in an acyl moiety were prepared from commercially available lactones or α-hydroxy carboxylates and their thermolytic reactions were carried out under various conditions. Urethane compounds obtained by thermolysis were separated into three fractions [intramolecular cyclization products, intermolecular reaction products (chloroform soluble fractions), and intermolecular reaction products (chloroform insoluble fractions)]. The fraction ratio considerably depended on both the structure of N-ammonioamidates and the concentration of the solutions. N-Ammonioamidates having a hydroxyl group, oxyalkylene units, and an alkylene chain or a phenyl group in the same molecule were synthesized as model compounds of a new type of SPU precursors, and their thermolytic reactions were investigated. The information about the structure of N-ammonioamidates which afforded urethane polymers with the highest molecular weight was obtained by characterization of the thermolytic products.

From Chapter 3 to Chapter 6, various terminal modified types of alcohol ethoxylates were synthesized, and their properties were studied.

In Chapter 3, terminal hydroxamic acid types of alcohol ethoxylates were found to act as both nonionic surfactant under acidic and neutral conditions and anionic ones under basic conditions (above pH 7). They formed a water soluble complex with

iron(III) ion at pH 2 and these complexes also showed surface active properties. It was proved that these hydroxamic acids showed better surface active properties than that the corresponding ketones, methyl esters or typical alcohol ethoxylates. Furthermore, hydroxamic acids containing a dodecyl or tetradecyl group as the hydrophobic part showed excellent micellar catalytic activity in the deacylation of hydrophobic p-nitrophenyl carboxylates in water.

In Chapter 4, surface active properties of monodispersed or dispersed alcohol ethoxylates having an acetonyl or oxime end group were measured under various pH conditions. The T_{cp} values of oximes were found to be much lower than those of the corresponding ketones and alcohol ethoxylates. Since these oximes showed much lower foaming ability and foam stability than others, they would function as a kind of end-blocked nonionics with the low foaming or antifoaming property.

In Chapter 5, amide oximes were obtained from nitriles which were prepared by the cyanoethylation of alcohol ethoxylates. It was found that they acted as cationic surfactants under acidic conditions (below pH 5) and nonionic ones with excellent properties under neutral and basic conditions.

In Chapter 6, three kinds of amide types of alcohol ethoxylates with the different terminal groups were prepared. The T_{cp} values of N,N-dimethylamides and acylmorpholines were higher than those of other corresponding alcohol ethoxylate derivatives in this thesis. They showed excellent surface active properties not only in pure water but also in hard water with 1000 ppm of

total hardness as $CaCO_3$ and they had better lime-soap dispersing ability than parent alcohol ethoxylates.

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