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valve. (3) The more hydrophobic polymers are more effective in controlling the permeation of small NaCl. For relatively large permeants, a graft polymer having a suitably hydrophobic nature can largely change the permeability by ambient pH.

The valve of the graft polymer can also be opened or shut reversibly by temperature changes[17] or redox reactions[1] in addition to ambient pH changes, when poly(*N*-alkylacrylamide) or viologen-containing polymers are grafted on the capsule membrane, respectively. The capsule membrane having a signal-receptive permeation valve should be useful for new drug release devices. Since graft polymers are covalently bonded onto the capsule membrane, the capsule can be used repeatedly without damaging the permeation valve.

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Registry No. ACl, 814-68-6; A-C_5-COOH, 20766-85-2; A-C_{11}-COOH, 45235-77-6; A-C_4-COOH, 73029-81-9; A-C_{10}-NMe_2, 105430-98-6; M-C_{10}-NMe_2, 105430-93-1; NQ_1, 99646-33-0; NQ_2, 97732-71-3; MACl, 920-46-7; NaCl, 7647-14-5; $NH_2(CH_2)_5CO_2H$, 60-32-2; $NH_2(CH_2)_{10}CO_2H$, 693-57-2; $Me_2NC(Me_2)CH_2OH$, 7005-47-2; $Me_2N(CH_2)_{10}OH$, 27397-09-7; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot AA$ copolymer, 91310-37-1; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot MA$ copolymer, 91310-36-0; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot VP$ copolymer, 91310-35-9; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot A$-$C_5$-COOH copolymer, 105430-94-2; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot A$-$C_{11}$-COOH copolymer, 105430-95-3; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot M$-$C_{11}$-COOH copolymer, 105430-96-4; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot A$-$C_4$-$NMe_2$ copolymer, 105430-97-5; $NH_2(CH_2)_2NH_2\cdot ClCO(CH_2)_{10}COCl\cdot A$-$C_{10}$-$NMe_2$ copolymer, 105430-99-7; nylon 2,12 (SRU), 41724-60-1; nylon 2,12 (copolymer), 41510-72-9.

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"Complete" Thermocontrol of Ion Permeation through Ternary Composite Membranes Composed of Polymer/Liquid Crystal/Amphiphilic Crown Ethers[1]

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ABSTRACT: Composite membranes composed of polymer (polycarbonate (PC))/liquid crystal (*N*-(4-ethoxybenzylidene)-4′-butylaniline (EBBA))/amphiphilic crown ethers (**1a**, **2a**, and **2b**) have been prepared. The DSC study established that **1a** (single-chain amphiphile) is dispersed homogeneously in the PC/EBBA composite membrane, whereas **2a** and **2b** (double-chain amphiphiles) exist as phase-separated aggregates in the membrane. Also prepared were ternary composite membranes containing natural ionophores such as X-537A (lasalocid) or monensin, which were dispersed homogeneously in the PC/EBBA composite membrane. Above T_{KN} (crystal–nematic liquid crystal phase transition temperature of EBBA), ion permeation through these composite membranes was very fast (19–34-fold compared with the conventional membranes). This is due to the high fluidity of EBBA forming a continuous phase in the composite membrane. Permeation of K^+ ion through PC/EBBA/**1a** and PC/EBBA/natural ionophore was observed below and above T_{KN}, and the Arrhenius plots consisted of two straight lines intersecting at T_{KN}. This indicates that carrier-mediated K^+ permeation is directly affected by the molecular motion of the liquid crystal phase. Surprisingly, K^+ permeation through PC/EBBA/**2a** and PC/EBBA/**2b** was "completely" suppressed below T_{KN} and increased with increasing transport temperature above T_{KN}. Furthermore, Cs^+, which forms sandwich-type complexes with 18-crown-6 and its analogues, could permeate through PC/EBBA/**2a** but not at all through PC/EBBA/**1a** above T_{KN}. The difference in the permeation mechanism between PC/EBBA/**1a** and PC/EBBA/**2a** is discussed in relation to the dispersion state of the crown ethers. The Arrhenius thermodynamic parameters show a good enthalpy–entropy compensation relationship expressed by $E_a = 5.42 \log A + 50.4$, but the permeability coefficient for K^+ (P_{K^+}) was affected more significantly by the log A term. Finally, the PC/EBBA/**2a** membrane, which exhibits an all-or-nothing change in the ion permeability, was applied to the reversible thermocontrol of K^+ permeation and to the temperature-dependent "catch-and-release" of K^+ ion. This is the first example for "complete" thermocontrol of ion permeation through the polymer composite membrane.

Biological membranes are composed of various kinds of phospholipids, cholesterols, and proteins, and the fundamental functions such as permeation and selectivity are closely associated with the gel–liquid crystal phase transition. Therefore, the phase transition would be one of the most essential functions provided by phospholipid bio-

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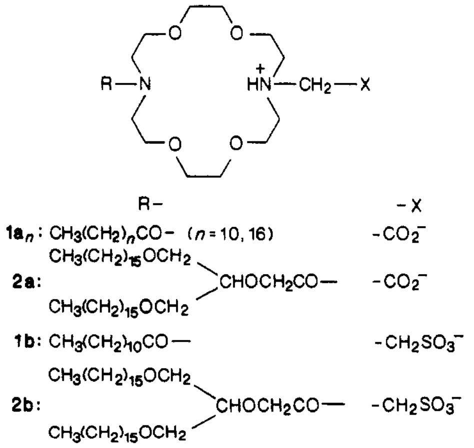
membranes. Recently, totally synthetic amphiphiles that contain a molecule with both a hydrophobic group of two alkyl chains and an appropriate hydrophilic group[4,5] have been shown to also form oriented aggregates in water with a phase diagram very similar to that of natural phospholipids.[6] They may be regarded as a new class of biomembrane models. To apply these new materials to practical systems, one has to "stabilize" them against heat, pH change, organic solvent, etc. without their losing membrane mimetic functions. Two elegant stabilization methods have been developed so far: one method is the polymerization of synthetic amphiphiles[4,5,7-17] and the other is the composition with polymers.[18-20] More recently, Kajiyama and co-workers[21-23] demonstrated that composite membranes in which the liquid crystalline material (instead of synthetic amphiphiles) is embedded in a polymer matrix are applicable to membrane mimetic permeation control, because a distinct change in thermal molecular motion occurs at the crystal–liquid crystal phase transition temperature, as in the case of membrane-forming surfactants, that causes a jump of water or gas permeability coefficients (*P*). Therefore, one may consider that polymer/liquid crystal composite membranes still possess the membrane mimetic properties with respect to the phase transition phenomena.

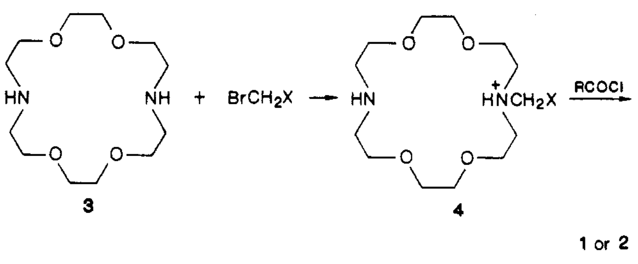
We report here on the thermocontrol of ion (K^+ and Cs^+) permeation through ternary composite membranes composed of polymer (polycarbonate (PC)), liquid crystal (*N*-(4-ethoxybenzylidene)-4′-butylaniline (EBBA)), and amphiphilic crown ethers (**1a**$_{10}$, **1a**$_{16}$, **2a**, and **2b**). We have found that the rate of ion permeation is governed by the dispersion state of the amphiphilic crown ether in the composite membrane and that when EBBA and the amphiphilic crown ether form discrete aggregates in the polymer matrix; ion permeation can be suppressed "completely" below T_{KN} (crystal–nematic liquid crystal phase transition temperature of EBBA) while it increases with the transport temperature above T_{KN}. This is the first example for the complete thermocontrol of ion permeation through the polymer composite membrane.



	R–	–X
1a$_n$:	$CH_3(CH_2)_nCO-$ (*n* = 10, 16)	$-CO_2^-$
2a:	$(CH_3(CH_2)_{15}OCH_2)_2CHOCH_2CO-$	$-CO_2^-$
1b:	$CH_3(CH_2)_{10}CO-$	$-CH_2SO_3^-$
2b:	$(CH_3(CH_2)_{15}OCH_2)_2CHOCH_2CO-$	$-CH_2SO_3^-$

Experimental Section

Materials. The general scheme to synthesize the amphiphilic crown ethers is shown below.



Preparation of 1-dodecanoyl-10-(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxa-18-crown-6 (**1a**$_{10}$) was described previously.[24]

1-Octadecanoyl-10-(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxa-18-crown-6 (1a$_{16}$). Octadecanoyl chloride (3.05 g, 10.1 mmol) was added dropwise to 40 mL of a dimethylformamide (DMF) solution containing 1-(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxa-18-crown-6 (**4**, 3.70 g, 10.8 mmol)[24] and triethylamine (4 mL) at room temperature. The reaction mixture was diluted with water and extracted with chloroform, and the chloroform solvent was evaporated to dryness. The residual solid was dissolved in chloroform and washed with an aqueous solution adjusted to pH 6.5 (with 0.1 M phosphate). The chloroform layer was separated, dried over Na_2SO_4, and concentrated in vacuo. The product (**1a**$_{16}$) was isolated by a preparative TLC method (silica gel, chloroform:ethanol = 4:1 v/v): mp 65–67 °C; yield 20%; IR (KBr) $\nu_{C=O}$ 1621 and 1720 cm^{-1}, ν_{C-O-C} 1115 cm^{-1}. Anal. ($C_{32}H_{62}N_2O_7$) C, H, N.

1-[*O*-(1′,3′-Bis(hexadecyloxy)prop-2′-yl)glycolyl]-10-(carboxymethyl)-1,10-diaza-4,7,13,16-tetraoxa-18-crown-6 (2a). *O*-(1,3-Bis(hexadecyloxy)prop-2-yl)glycolic acid was prepared from epichlorohydrin and hexadecanol in a manner similar to the synthesis of *O*-(1,3-bis(octadecyloxy)prop-2-yl)glycolic acid:[25] mp 60–62 °C; yield 73%; IR (KBr) $\nu_{C=O}$ 1745 cm^{-1}, ν_{C-O-C} 1155 cm^{-1}. Anal. ($C_{37}H_{74}O_5$) C, H. *O*-(1,3-Bis(hexadecyloxy)prop-2-yl)glycolic acid was converted to its acid chloride by reaction with thionyl chloride. The acid chloride was treated with **4** in DMF in the presence of excess triethylamine. The method is similar to that described above for the synthesis of **1a**$_{16}$. The final chloroform solution was subjected to separation by a preparative TLC method (silica gel, chloroform:ethanol = 4:1 v/v): mp 44–46 °C; yield 27%; IR (KBr) $\nu_{C=O}$ 1620 and 1680 cm^{-1}, ν_{C-O-C} 1120 cm^{-1}; NMR ($CDCl_3$) δ 0.84 (6 H, t, CH_3), 1.23 (56 H, m, $(CH_2)_{14}$), 2.90 and 3.80 (8 H, m, CH_2N in the ring), 3.29 (2 H, s, NCH_2CO), 3.4–3.8 (24 H, m, CH_2O both in the proton and in the chain), 3.80 (2 H, s, OCH_2CO), 4.23 (1 H, p, CHO). Anal. ($C_{51}H_{100}N_2O_4$) C, H, N.

2-(1′-Dodecanoyl-1′,10′-diaza-4′,7′,13′,16′-tetraoxacyclooctadec-10′-yl)ethanesulfonate (1b). An aqueous solution (50 mL) of **3** (2.00 g, 7.62 mmol) and sodium ethanesulfonate (2.04 g, 8.41 mmol) was heated at the reflux temperature for 5 days. The progress of the reaction was followed by a paper chromatographic method. The solution was adjusted to pH 12 with 0.1 N NaOH and extracted with chloroform to remove unreacted **3**. The aqueous phase was evaporated to dryness, the solid residue being extracted with ethanol. From this ethanol solution we could obtain 2-(1′,10′-diaza-4′,7′,13′,16′-tetraoxacyclooctadec-10′-yl)-ethanesulfonate in 85% yield: IR (KBr) ν_{SO_3} 1175 cm^{-1}, ν_{C-O-C} 1137 and 1105 cm^{-1}; NMR (D_2O) δ 3.04 (2 H, t, CH_2S), 3.26 (10 H, m, CH_2N), 3.71 (16 H, m, CH_2O). Anal. ($C_{14}H_{30}N_2O_7S\cdot1.5H_2O\cdot1.0NaBr$) C, H, N. 2-(1′,10′-Diaza-4′,7′,13′,16′-tetraoxacyclooctadec-10′-yl)ethanesulfonate was treated with dodecanoyl chloride in a manner similar to that described for the synthesis of **2a**. The product (**1b**) was isolated by a preparative TLC method (silica gel, chloroform:ethanol = 4:1 v/v): mp 50–52 °C; yield 27%; IR (KBr) $\nu_{C=O}$ 1630 cm^{-1}, ν_{SO_3} 1210 cm^{-1}, ν_{C-O-C} 1090 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (3 H, t, CH_3), 1.26 (18 H, m, $(CH_2)_9$), 2.28 (2 H, t, CH_2CO), 2.68 and 3.85 (8 H, t, CH_2N in the ring), 2.92 (2 H, t, CH_2N), 3.04 (2 H, t, CH_2S), 3.68 (16 H, m, CH_2O). Anal. ($C_{26}H_{52}N_2O_8S$) C, H, N.

2-[1′-[*O*-(1″,3″-Bis(hexadecyloxy)prop-2″-yl)glycolyl]-1′,10′-diaza-4′,7′,13′,16′-tetraoxacyclooctadec-10′-yl]ethanesulfonate (2b). **2b** was synthesized from 2-(1′,10′-diaza-4′,7′,13′,16′-tetraoxacyclooctadec-10′-yl)ethanesulfonate and *O*-(1,3-bis(hexadecyloxy)prop-2-yl)glycolyl chloride in a similar manner. The product (**2b**) was isolated by a preparative TLC method (silica gel, methanol): mp 36–37 °C; yield 14%; IR (KBr) $\nu_{C=O}$ 1640 cm^{-1}, ν_{SO_3} 1185 and 1040 cm^{-1}, ν_{C-O-C} 1100 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (6 H, t, CH_3), 1.26 (56 H, m, $(CH_2)_{14}$), 2.26 and 3.80 (8 H, m, CH_2N in the ring), 3.04 (2 H, t, CH_2N), 3.42 (8 H, m, CH_2O), 3.54 (2 H, t, CH_2S), 3.64 (16 H, m, CH_2O in the ring), 3.80 (2 H, s, OCH_2CO), 4.30 (1 H, p, CHO). Anal. ($C_{51}H_{102}N_2O_{11}S$) C, H, N.

Preparation and Characterization of Composite Membranes. The composite membranes were prepared by casting a 6 wt % (total) 1,2-dichloroethane solution of PC (supplied from Idemitsu Kosan Co.), EBBA, and crown on a glass plate at room temperature: PC/EBBA = 40:60 wt/wt; ionophore (**1**, **2**, lasalocid,

Table I
DSC Data of Amphiphilic Crown Ethers

amphiphilic crown	mp, K	peak temperature of crowns in PC/EBBA	peak temperature of crowns in PC/DBP	peak temperature of crowns in Pelprene	ΔH, kJ mol^{-1} solid sample	ΔH, kJ mol^{-1} in PC/EBBA	ΔH, kJ mol^{-1} in PC/DBP	ΔH, kJ mol^{-1} in Pelprene
1a$_{10}$	oil	none	none					
1a$_{16}$	338–340	none	none					
2a	317–319	317	317	317	94	85	90	68
1b	323–325							
2b	309–310	309	307	313	95	78	90	135

and monensin) 2.9 mol % of EBBA (i.e., 6.1×10^{-5} mol/g of (PC + EBBA)). PC was used as the matrix substance for the composite membranes because it exhibits no thermal transition in the temperature range studied here.[21] After 1 day, the membranes were dried at 0.1 mmHg for 4 h and then kept under reduced pressure for 3 days. The thickness of the membranes thus obtained was 60 ± 0.2 μm. In the ion-transport experiments, the membrane surface in contact with the glass plate was directed toward the IN (source) aqueous phase.

We also prepared two conventional polymeric membranes according to a similar casting method; these were used as reference membranes in a DSC (differential scanning calorimetry) study. The PC/dibutyl phthalate (DBP)/crown (90:10:15 wt/wt/wt) membranes were prepared by casting a 5 wt % (total) 1,2-dichloroethane solution. Pelprene (supplied from Toyobo Co.; for the structure see Results and Discussion) is a very "soft" polymer and can form an elastic polymeric membrane without a plasticizer such as DBP.[25] The Pelprene/crown (crown 2.7×10^{-4} mol/g of Pelprene) membranes were prepared by casting a 3 wt % (total) chloroform solution. The thickness of the membranes was 20 ± 1 μm.

The aggregate formation of the amphiphilic crown ethers in these membranes was investigated by DSC (Daini Seikosha SSC-560). The membranes containing EBBA gave two endothermic peaks around 304 K (crystal–nematic liquid crystal phase transition temperature: T_{KN}) and around 355 K (nematic liquid crystal–isotropic phase transition temperature: T_{NI}). When the amphiphilic crown ether forms discrete aggregates in the PC/EBBA composite membrane, it gives a new DSC peak in addition to those of EBBA.

Ion Transport. Thermocontrol of ion permeation was estimated in a U tube immersed in a thermostated water bath. The membrane area was 3.46 cm^2, and IN (source) and OUT (receiving) aqueous phases (30 mL each) were stirred at a constant speed (ca. 250 rpm). Further details of the transport system are recorded in footnotes to Table II. The rates of ion transport were estimated by measuring the concentration of alkali-metal cations in the OUT aqueous phase by atomic absorption spectroscopy (Shimadzu AA-640). After an induction period (3–8 h), the metal ion concentration in the OUT aqueous phase increased linearly with the transport time. One transport experiment was continued for 20 h, and the ion flux (J, mol s^{-1} cm^{-2}) was determined from the slope of the [M$^+$] vs. time plot. The permeability coefficients (P_{M^+}, s^{-1} cm^2) were calculated from eq 1, where l is the membrane thickness and C_{IN} and C_{OUT} are the concentrations of M$^+$ in the IN and the OUT aqueous phase, respectively.

$$P_{M^+} = Jl/(C_{IN} - C_{OUT}) \tag{1}$$

Results and Discussion

Dispersion State of Amphiphilic Crown Ethers in the Composite Membrane. The composite membrane is a multicomponent film prepared by casting a 1,2-dichloroethane solution of PC and EBBA. The aggregation state of EBBA in composite membranes has been investigated in detail by DSC, wide-angle X-ray diffraction, and electron microscopy.[21-23,26] The DSC study established that EBBA molecules (40–60 wt %) can form aggregate domains in the polymer matrix.[21] An important fact obtained from electron microscopy is that in these composite membranes the EBBA domain is present as a continuous phase which is surrounded by the polymer fibrillar network.[26] Therefore, the composite membranes are analogous to "immobilized" liquid membranes above the phase transition temperature.

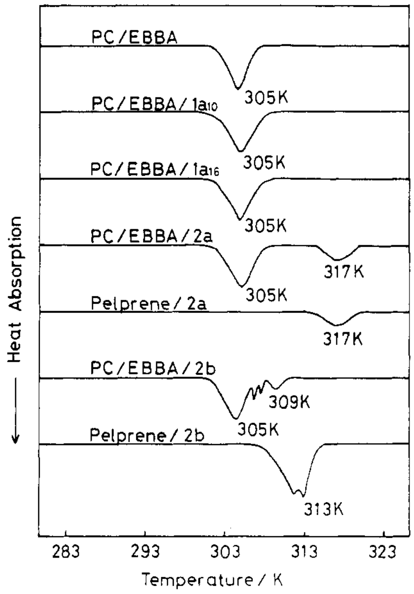
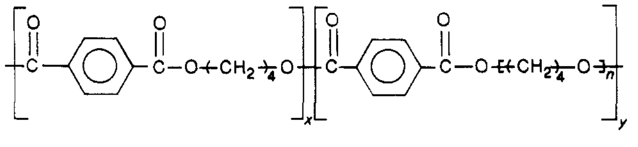


Figure 1. DSC curves for PC/EBBA, PC/EBBA/crown, and Pelprene/crown membranes. Two small peaks between 305 and 309 K in PC/EBBA/**2b** are ascribed to EBBA because they frequently appear in the PC/EBBA binary membrane.

The object of this investigation has been to elucidate any potential relationship between the ion transport ability and the dispersion state of crown ethers in the composite membrane. To change the solubility of crown ethers in the composite membrane we synthesized crown ethers **1** and **2** bearing both a lipophobic anionic group and one or two lipophilic alkyl chains. It is generally observed that anion-capped crown ethers can carry metal cations very efficiently,[24,27-32] so that the anionic groups in **1** and **2** would serve not only to change the dispersion state but also to enhance the ion flux across the composite membrane.

In order to determine whether the amphiphilic crown ethers might leak out of the membranes into the IN aqueous phase, chipped pieces of the composite membrane in an aqueous solution adjusted to pH 10.0 with 0.015 M K_2CO_3 were stirred at 30 °C for 1 day. HPLC analysis of the aqueous solution indicated that **1a**$_{10}$, **1a**$_{16}$, and **2a** do not leak at all, **2b** leaks slightly (less than 3%), and a significant amount of **1b** leaks into the aqueous phase (30–33 mol%). We therefore did not use the **1b**-containing membranes in the ion-transport experiments.[33]

The aggregate formation of the amphiphilic crown ethers in the PC/EBBA/crown ternary composite membranes was studied by DSC and compared with the formations of the conventional polymeric membranes such as PC/DBP/crown and Pelprene/crown. Typical examples are illustrated in Figure 1, and the results are summarized in Table I.



Pelprene

The PC/EBBA (40:60 wt/wt) binary composite membrane gave a characteristic DSC peak at 305 K, which corresponds to the crystal–nematic liquid crystal phase transition temperature of EBBA (304 K).[21-23] The peak was not affected by the addition of $\mathbf{1a}_{10}$, $\mathbf{1a}_{16}$, lasalocid, and monensin (2.9 mol % of EBBA) into the membrane. The melting point of $\mathbf{1a}_{16}$ is 338–340 K, but the endothermic peak was not found at this temperature region in the PC/EBBA/$\mathbf{1a}_{16}$ ternary composite membrane. This finding supports the conclusion that these ionophores are homogeneously dispersed in the composite membrane. In contrast, the addition of **2a** and **2b** (2.9 mol % of EBBA) gave new peaks at 317 and 309 K, respectively, in addition to that of EBBA (Figure 1). Similar endothermic peaks for **2a** and **2b** were observed in PC/DBP and Pelprene. These peak temperatures are very close to their melting points, and the ΔH values are also close to each other (Table I). One can conclude on the basis of these data that **2a** and **2b** exist as phase-separated aggregates not only in the PC/EBBA composite membrane but also in the conventional polymeric membranes such as PC/DBP and Pelprene.[33]

Temperature Dependence of Ion Permeation Rates. In membrane transport two different types of membranes have been used, that is, a liquid membrane system and a polymeric membrane system. Both systems have merits and demerits. The liquid membrane can provide a large ion flux but is not convenient for practical applications. On the other hand, the polymeric membrane is very practical, but the ion flux is frequently too small. The polymer/liquid crystal composite membrane can compensate for these demerits: that is, it is apparently a polymeric solid membrane but can provide a relatively large ion flux owing to the high fluidity of the continuous liquid crystal phase.[21-23] Therefore, one may call it "a liquid membrane in polymer clothing".

First, we compared the permeability coefficients for K^+ (P_{K^+}) between PC/EBBA/crown and the conventional polymeric membrane at 313 K (above T_{KN}). As the PC/crown membrane was too brittle to use for the transport experiment, we used the Pelprene/crown membrane as a reference of the polymeric membrane. As shown in Table II, the P_{K^+} values for PC/EBBA/crown are greater, 5.6-fold ($\mathbf{1a}_{10}$), 4.3-fold ($\mathbf{1a}_{16}$), and 7.6-fold (**2a**), for Pelprene/crown. The crown concentration in Pelprene is higher by a factor of 4.4 than that in PC/EBBA (see Experimental Section). Provided that the P_{K^+} is correlated with the first power of the crown concentration, the rate difference corresponds to 25-fold ($\mathbf{1a}_{10}$), 19-fold ($\mathbf{1a}_{16}$), and 34-fold (**2a**), respectively. These results support the conclusion that PC/EBBA/crown composite membranes have P_{K^+} values much greater than those of the conventional polymeric membranes.

Lasalocid and monensin are the polyether antibiotics that represent the class of monobasic carrier-type ionophores.[27,34] The transport mechanism by which the ions are carried rapidly across biomembranes has been studied in detail; that is, they feature a structural change between the cyclic and the noncyclic form in response to the pH of the aqueous phase.[27,34-37] A similar structural change is expected to occur in the PC/EBBA membrane phase above T_{KN} because the IN and OUT aqueous phases were adjusted to pH 7.8 and 3.5, respectively. We measured the permeation rate from the neutral IN to the acidic OUT aqueous phase, which is the optimum transport condition of these natural ionophores.[34,35] At 313 K, the P_{K^+} values for lasalocid and monensin were smaller by 2.2- and 12.8-fold, respectively, than that for PC/EBBA/$\mathbf{1a}_{10}$. This suggests that the amphiphilic crown ethers can act as ion carriers comparable with or superior to natural antibiotics. Similar superiority of lipophilic crown ethers over natural antibiotics has been demonstrated in a liquid membrane system.[27]

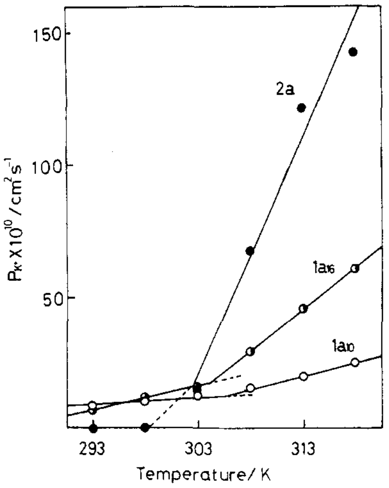


Figure 2. Temperature dependence of P_{K^+} for PC/EBBA/$\mathbf{1a}_{10}$ (○), PC/EBBA/$\mathbf{1a}_{16}$ (◑), and PC/EBBA/**2a** (●).

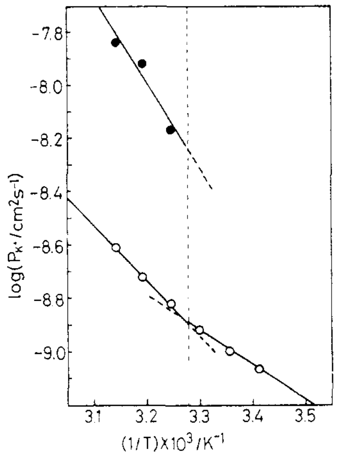


Figure 3. Typical Arrhenius plots: PC/EBBA/$\mathbf{1a}_{10}$ (○); PC/EBBA/**2a** (●).

Now we discuss the temperature dependence of ion (M^+ = K^+ and Cs^+) permeability. The pK_a's for $\mathbf{1a}_{10}$ and **2b** were determined previously:[24,33] $\mathbf{1a}_{10}$, pK_{a1} = 3.45 for $>NH^+CH_2COOH \rightleftharpoons >NH^+CH_2COO^-$ and pK_{a2} = 6.99 for $>NH^+CH_2COO^- \rightleftharpoons >NCH_2COO^-$; **2b**, p$K_a$ = 7.10 for $>NH^+CH_2CH_2SO_3^- \rightleftharpoons >NCH_2CH_2SO_3^-$. **2a** gave a slightly turbid dispersion in water, so that the pK_a values could not be determined precisely. The previous transport study with $\mathbf{1a}_{10}$ in a liquid membrane system established that $>NCH_2COO^-$ effectively extracts K^+ into the membrane phase with the aid of the anionic carboxylate cap, while $>NH^+CH_2COO^-$ rapidly releases K^+ into the aqueous phase because of protonation of the ring nitrogen.[24] Thus, the pH's of the IN (containing 0.30 M MSCN) and OUT aqueous phases were adjusted to 10.0 and 7.0 with K_2CO_3 (0.015 M)–HCl and Me_4NOH–H_3PO_4 (0.010 M), respectively. Figure 2 shows plots of P_{K^+} vs. transport temperature for $\mathbf{1a}_{10}$, $\mathbf{1a}_{16}$, and **2a**. Permeation of K^+ ion through

Table II
Permeability Coefficients (P_{M^+}) and Arrhenius Thermodynamic Parameters (E_a and log A)

membrane	ionophore	M$^+$	$10^9P_{M^+}$, cm^2 s^{-1} at 293 K	$10^9P_{M^+}$, cm^2 s^{-1} at 313 K	E_a, kJ mol^{-1} below T_{KN}	E_a, kJ mol^{-1} above T_{KN}	log A below T_{KN}	log A above T_{KN}
PC/EBBA[a]	**1a**$_{10}$	K$^+$	0.84	1.92	25.9	37.2	−4.54	−2.14
PC/EBBA[a]	**1a**$_{10}$	Cs$^+$	0	0				
PC/EBBA[a]	**1a**$_{16}$	K$^+$	0.77	4.51	49.4	61.1	−0.29	1.84
PC/EBBA[a]	**2a**	K$^+$	0	12.1		64.0		2.39
PC/EBBA[a]	**2a**	Cs$^+$	0	14.3				
PC/EBBA[a]	**2b**	K$^+$	0	43.6		99.2		9.11
PC/EBBA[b]	lasalocid	K$^+$	0.60	0.87	11.9	16.9	−7.96	−6.24
PC/EBBA[b]	monensin	K$^+$	0.08	0.15	20.9	32.6	−6.52	−4.70
Pelprene[a]	**1a**$_{10}$	K$^+$		0.34				
Pelprene[a]	**1a**$_{16}$	K$^+$		1.05				
Pelprene[a]	**2a**	K$^+$		1.60				

[a] IN aqueous phase, 0.30 M MSCN, pH 10.0 with 0.015 M M_2CO_3–HCl; OUT aqueous phase, pH 7.0 with Me_4NOH–0.010 M H_3PO_4. [b] IN aqueous phase, 0.30 M MSCN, pH 7.8 with Me_4NOH–0.050 M H_3PO_4; OUT aqueous phase, pH 3.5 with Me_4NOH–0.005 M DL-tartaric acid.

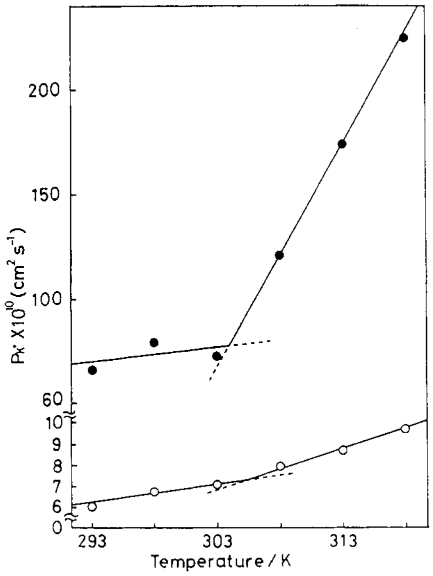


Figure 4. Temperature dependence of P_{K^+} for PC/EBBA/lasalocid (●) and PC/EBBA/monensin (○).

PC/EBBA/**1a**$_{10}$ and PC/EBBA/**1a**$_{16}$ was observed below and above T_{KN}, and the plots had break points around T_{KN}. In fact, the Arrhenius plots consisted of two straight lines intersecting at T_{KN} (Figure 3). The ternary composite membranes containing lasalocid or monensin provided a similar temperature dependence which featured break points at T_{KN} (Figure 4). Carrier-mediated K$^+$ permeation through the PC/EBBA composite membrane must thus be directly affected by the molecular motion of the liquid crystal phase. From the Arrhenius plots we determined the thermodynamic parameters (E_a and log A) and summarized them in Table II.

In contrast to the permeation behavior of these membranes, K$^+$ permeation through PC/EBBA/**2a** and PC/EBBA/**2b** was completely suppressed below T_{KN} and increased with increasing transport temperature above T_{KN} (Figures 2 and 5). This indicates that ion permeation below T_{KN} is largely governed by the dispersion state of the carriers and that the ion flux can be completely stopped by separating the carriers in aggregate domains. We estimated the thermodynamic parameters from the Arrhenius plots above T_{KN} (Table II).

A more exciting difference between the "homogeneously dispersed" membranes and the "phase-separated" membranes was found for Cs$^+$ transport (Table II). Cs$^+$ could not permeate through the PC/EBBA/**1a**$_{10}$ composite membrane below and above T_{KN} (283–323 K). Cs$^+$ permeation through the PC/EBBA/**2a** composite membrane was also suppressed below T_{KN}, but it did occur above T_{KN}, the P_{Cs^+} at 313 K (1.43 × 10^{-8} cm^2 s^{-1}) being ever greater than P_{K^+} (1.21 × 10^{-8} cm^2 s^{-1}). It is known that Cs$^+$ forms 1:2 metal/crown sandwich complexes with 18-crown-6 and its analogues because the ionic radius is too large to fit the inner cavity of the crown ethers. Therefore, Cs$^+$ permeation through PC/EBBA/**2a** above T_{KN} would be rationalized in terms of the formation of 1:2 metal/crown sandwich complexes between Cs$^+$ and aggregated **2a**.

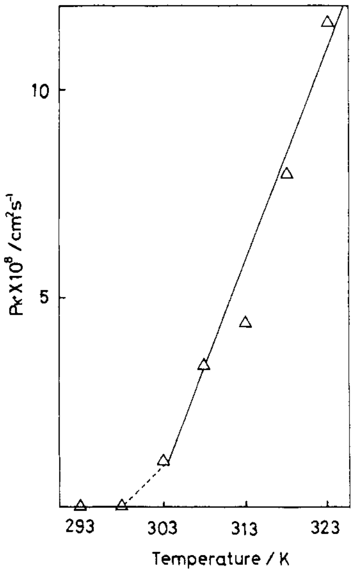


Figure 5. Temperature dependence of P_{K^+} for PC/EBBA/**2b**.

Comments on the Transport Mechanism. The polymer/liquid crystal composite membrane can provide two different transport systems below and above T_{KN}: it serves as an analogue of liquid membranes above T_{KN}, while it is a crystalline membrane below T_{KN}. Above T_{KN}, alkali-metal cations would permeate through the membrane according to the carrier-mediated ion-transport mechanism as in the liquid membrane system. Examination of the thermodynamic parameters above T_{KN} (Table II) reveals that (1) the membranes containing natural ionophores (lasalocid and monensin) give small values of E_a and negatively large values of log A, (2) E_a and log A for the phase-separated **2a**- and **2b**-containing membranes are significantly greater than those for the homogeneous **1a**-containing membranes, and (3) P_{K^+} is correlated with the increase in log A and almost inversely with the decrease in E_a. Fact 3 suggests that K$^+$ permeation is governed by the entropy term rather than by the enthalpy term. For example, the P_{K^+} for PC/EBBA/**2b** is greater by 22.7-fold than that for PC/

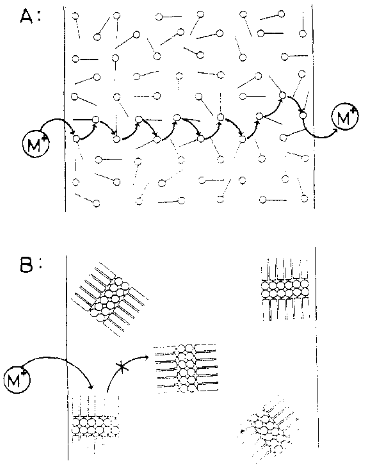


Figure 6. Schematic representation of ion transport below T_{KN}: (A) a site-to-site jump mechanism in homogeneously dispersed membranes; (B) an energetically unfavorable aggregate-to-aggregate (interaggregate) jump mechanism in phase-separated membranes.

EBBA/**1a**$_{10}$. As for the thermodynamic parameters, log A for PC/EBBA/**2b** is greater by 11.25, but E_a is also greater by 62.0 kJ mol^{-1}. Conceivably, the permeation rates are significantly associated with the diffusion of the crown–metal complexes in the membrane phase, and the enthalpy term reflecting the association–dissociation phenomena of the complexes would be less important. The E_a values for the PC/EBBA/crown membranes (37.3–99.2 kJ mol^{-1}) are comparable with those for the related crown-containing polymeric membranes (50 kJ mol^{-1})[39] and the carrier-mediated liposomal membranes (90–120 kJ mol^{-1}).[40] These data support again the conclusion that the high permeability of the present composite membranes is due to the large values of the log A term (−2.14 to 9.11 compared to −8 to −10 in the crown-containing polymeric membranes[40]). In other words, the metal complexes can diffuse easily in the fluid liquid crystal membrane phase of the composite membrane. Fact 1 implies that the diffusion of the natural ionophores is rather disadvantageous. The molecular structure of the polyether antibiotics is relatively "rigid". It is likely, therefore, that they cannot diffuse in the nematic liquid crystal phase so easily as the "flexible" crown ethers do. As for (2), it is not clear yet why the phase-separated membranes give the large E_a and log A values. One possible explanation would be that the phase-separated aggregates might disorder the liquid crystal structure more efficiently, leading to the fast diffusion in the membrane phase. This problem should be studied further in the related systems.

Below T_{KN}, the thermal molecular motion of EBBA is frozen. The diffusion of the crown–metal complexes across such crystalline membranes would be almost disregarded. As expected, the log A values below T_{KN} are significantly smaller than those above T_{KN}, the difference being 2.13–2.40 for PC/EBBA/**1a** and 1.72–1.82 for PC/EBBA/natural ionophores. On the contrary, the E_a values below T_{KN} are smaller than those above T_{KN}: 11.4–11.7 kJ mol^{-1} for PC/EBBA/**1a** and 5.0–11.7 kJ mol^{-1} for PC/EBBA/natural ionophores. Anyway, P_{K^+} is correlated with log A but not with E_a, so that the P_{K^+} values below T_{KN} are very suppressed. The extreme case is the phase-separated membranes such as PC/EBBA/**2a** and PC/EBBA/**2b**.

It is interesting to discuss why ion permeation is completely suppressed below T_{KN} in these membranes. Above T_{KN}, ions are carried by the crown ethers because they can diffuse in the fluid liquid crystal phase. Below T_{KN}, on the other hand, such a carrier mechanism is no longer operative because the crown ethers are fixed in the crystal lattice of EBBA. In such a case, ions are transported according to a site-to-site jump mechanism (Figure 6A) which is generally proposed for crown-containing polymeric membranes.[39] When the carrier sites are dispersed homogeneously (e.g., PC/EBBA/**1a**), this jump mechanism would possibly be operative because the metal cation nesting in the crown could find the next crown in the vicinity. This is probably why ion permeation still takes place below T_{KN}. However, when the carriers form the phase-separated aggregates (e.g., PC/EBBA/**2a**), an aggregate-to-aggregate (interaggregate) jump of ions would be almost impossible (Figure 6B). This may cause the complete suppression of ion permeation below T_{KN}. Recently, we prepared a new polymer/liquid crystal composite membrane containing a crown with a fluorocarbon chain.[41] This crown compound also formed phase-separated aggregates in the composite membrane owing to the lipophobic nature of the fluorocarbon chain. As expected, ion permeation could be stopped completely below T_{KN}. Thus, the dispersion state of the carriers should be associated generally with the ion permeability.

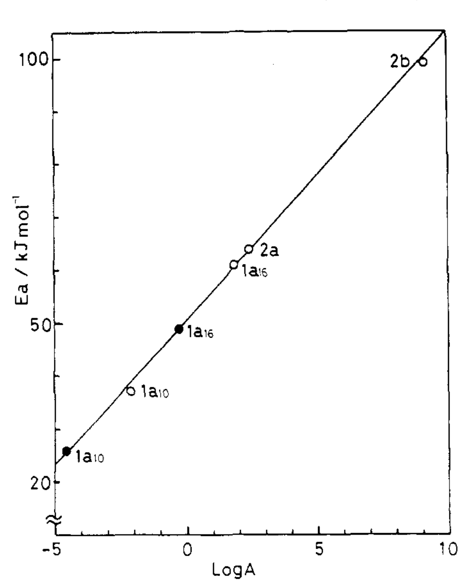


Figure 7. E_a–log A compensation relationship: (○) above T_{KN}; (●) below T_{KN}.

Figure 7 shows a plot of log A vs. E_a for the PC/EBBA/crown membranes. Four points for $T > T_{KN}$ give an excellent linear relationship (r = 0.999) expressed by eq 2.

$$E_a = 5.46 \log A + 50.2 \tag{2}$$

This indicates that the change in the entropy term is compensated for in part by the change in the enthalpy term, although P_{K^+} is actually governed by the entropy term (i.e., log A). A similar compensation relationship has been found by Pownall et al.[42] for transport of pyrenyl alkanes across single bilayer vesicles. We expected that two points obtained below T_{KN} might deviate from eq 2 because the transport mechanism is quite different from that above T_{KN}. In fact, however, the two points (filled circles in Figure 7) were also included in the linear line given by eq 2. Equation 3 (r = 0.999) computed by the

$$E_a = 5.42 \log A + 50.4 \tag{3}$$

least-squares procedure for six points is essentially identical with eq 2. Therefore, the thermodynamic parameters for

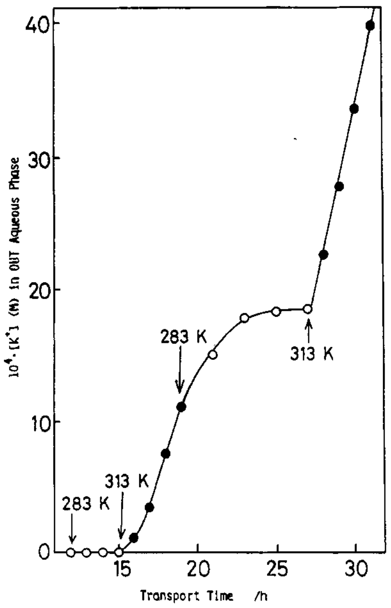


Figure 8. Thermocontrol of K^+ permeation through the PC/EBBA/**2a** composite membrane.

the present membrane transport system can be summarized by a single enthalpy–entropy compensation relationship.

New Applications as Switch-Functionalized Membranes. The fact that PC/EBBA/**2a** and PC/EBBA/**2b** exhibit an all-or-nothing change in the ion permeability suggests that these membranes are applicable to the reversible thermocontrol of ion permeation and to the temperature-dependent "catch-and-release" of ions. Figure 8 shows the reversible thermocontrol of K^+ permeation through the PC/EBBA/**2a** composite membrane. In response to a temperature change in the water bath (283 → 313 → 283 → 313 K), the rate of K^+ permeation showed an all-or-nothing change. The response (i.e., K^+ concentration in the OUT aqueous phase) for the change from 283 to 313 K is fast, whereas that for the change from 313 to 283 K is relatively slow, taking about 4 h to stop K^+ permeation completely. This slow response is attributed either to a leakage of K^+ dissolved in the membrane phase during the 313 K period or to an induction period for reorganization of the gel phase. As described below, we tested the K^+ release from the composite membrane below and above T_{KN}. As a result, we confirmed that the K^+ leakage does not occur from the K^+-containing membrane below T_{KN}. One may conclude, therefore, that the transient leakage for the change from 313 to 283 K stems from slow reorganization of the liquid crystal phase to the gel phase in the polymer matrix.

The temperature-dependent release of ions and organic molecules (especially drugs) has been widely investigated.[43] We tested an application of the PC/EBBA/**2a** composite membrane to the catch-and-release of alkali-metal cations ($M^+ = K^+$ and Cs^+). The PC/EBBA/**2a** membrane (0.138 g of **2a**, 8.00×10^{-6} mol) was stirred in an aqueous solution (50 mL, pH 10.0 with 0.015 M M_2CO_3–HCl) containing 0.39 M of MSCN at 318 K for 10 h. During this period M^+ should permeate into the membrane. The solution was kept at 288 K for 4 h, and then the membrane was washed with cold water (ca. 5 °C). This membrane was put into an aqueous solution (50 mL, pH 7.0 with 0.010 M phosphate–Me_4NOH). The solution was stirred at a constant speed (ca. 150 rpm), and the increase in the M^+ concentration was followed by atomic absorption spectroscopy. As shown in Figure 9, the metal ions are scarcely released from the membrane at 288 K. The metal concentrations begin to increase immediately after the temperature change to 318 K and reach an equilibrium value after about 30 min. This equilibrium value corresponds to 70 mol % of **2a**. Since the crown ring of **2a** possibly forms a 1:1 metal/crown complex with K^+, this value is quite resonable in the K^+ uptake. However, it becomes unreasonable in the Cs^+ uptake if the crown ring forms a 1:2 metal/crown sandwich complex with Cs^+; that is, the equilibrium value should not exceed 50 mol %. This dilemma would be accommodated in terms of the formation of an *n*:*n* + 1 metal/crown "poly-sandwich" complex. Crown ethers can form not only 1:2 metal/crown sandwich complexes but also 2:3 metal/crown club-sandwich complexes with large alkali-metal cations.[44] Therefore, an *n*:*n* + 1 metal/crown poly-sandwich complex could be formed when crown ethers are properly aligned. Provided that **2a** forms the bilayer-like aggregates in the membrane phase, stacks of the crown ethers would be composed on the surface of the aggregates. The stacks would possibly form the *n*:*n* + 1 metal/crown poly-sandwich complex with Cs^+. In any case, the temperature dependence in Figure 9 indicates that the PC/EBBA/**2a** membrane exhibits a complete catch-and-release function.

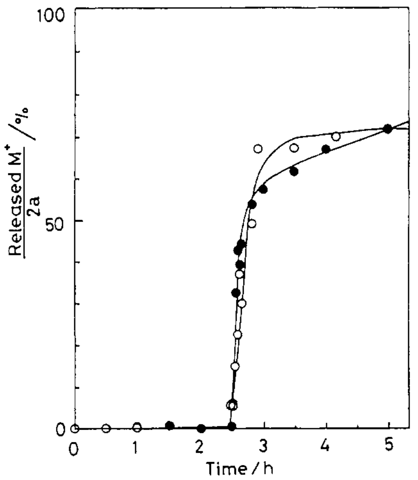


Figure 9. Catch-and-release to and from the PC/EBBA/**2a** composite membrane: (○) K^+; (●) Cs^+. The aqueous solution (pH 7.0 with 0.010 phosphate–Me_4NOH) was kept at 288 K for 0–2.5 h, and then the temperature was raised to 318 K.

Conclusion

This study demonstrated that ion permeation through the polymer/liquid crystal/crown ternary composite membranes is directly affected by the molecular motion of the liquid crystal phase. Further important is the finding that when the amphiphilic crown ethers form phase-separated aggregates, the ion flux can be stopped completely. This novel phenomenon is readily applicable to the reversible thermocontrol of ion permeation and to the temperature-dependent catch-and-release. We expect that further elaborations of this concept might lead to a more generalized method to control the ion permeability by an *on–off temperature switch.*

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Registry No. **1a**$_{10}$, 82353-43-3; **1a**$_{16}$, 105064-39-9; **1b**, 101373-57-3; **1b** (R = H), 105064-38-8; **2a**, 96259-20-0; **2b**, 105064-40-2; **3**, 23978-55-4; **4**, 82353-42-2; EBBA, 29743-08-6;

$H_3C(CH_2)_{16}COCl$, 112-76-5; $(CH_3(CH_2)_{15}OCH_2)_2CHOCH_2CO_2H$, 105064-37-7; $H_3CCH_2SO_3Na$, 5324-47-0; K^+, 24203-36-9; Cs^+, 18459-37-5; $H_3C(CH_2)_{10}COCl$, 112-16-3; laslocid, 25999-31-9; monensin, 17090-79-8.

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