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SYNTHESIS AND COMPLEXING PROPERTIES OF CROWNOPHANES POSSESSING CARBOXYL GROUP

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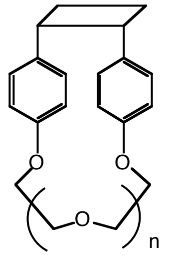
Abstract- A new series of crown compounds bearing two carboxyl groups (**2a**-**c**; crownophanedicarboxylic acids) were prepared *via* intramolecular [2 + 2] photocycloaddition of bis-styrene derivatives. In the liquid-liquid extraction, crownophanedicarboxylic acids (**2a**-**c**) showed a low affinity toward alkali metal cations, though both **2b** and **2c** showed an extraordinary high affinity toward zinc cation among heavy metal cations examined.

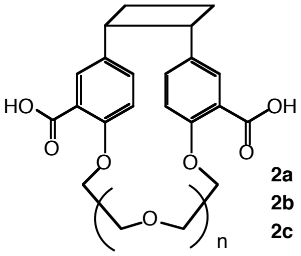
INTRODUCTION

A large number of crown compounds having proton-ionizable groups such as triazole, hydroxypyridine, pyridone, sulfonamide, dialkylhydrogenphosphonate, thiopyridone, and phenol have been prepared and named proton-ionizable crown ethers by Bradshaw *et al.*[1-13] Bartsch and co-workers have also prepared a variety of acyclic and cyclic polyethers with carboxylic and hydroxamic groups used as carriers for alkali, alkaline earth, and lanthanide metal ions.[14-35] A very significant advantage of these ionizable compounds is that they act as both ion exchangers and chelators.[36-38]

Recently, we have prepared a number of crown compounds fused with cyclophane skeleton by intramolecular [2 + 2] photocycloaddition of styrene derivatives in excellent yields and have named them crownophanes.[39] Their specific complexing ability was disclosed by solid-liquid and liquid-liquid extractions. Among the prototypical crownophanes (**1a-c**), (**1b**) with five ethereal oxygen atoms exhibited a greater complexing ability toward Li^+ than the conventional lithiophilic 12-crown-4 and dibenzo-14-crown-4 by solid-liquid extraction[40] and liquid membrane transport.[41] Introduction of carboxyl groups into **1** provides new proton-ionizable crown compounds (**2a-c**). In this paper we describe the photosynthesis of crownophanes possessing two carboxyl groups (**2a-c**) and their complexing properties.



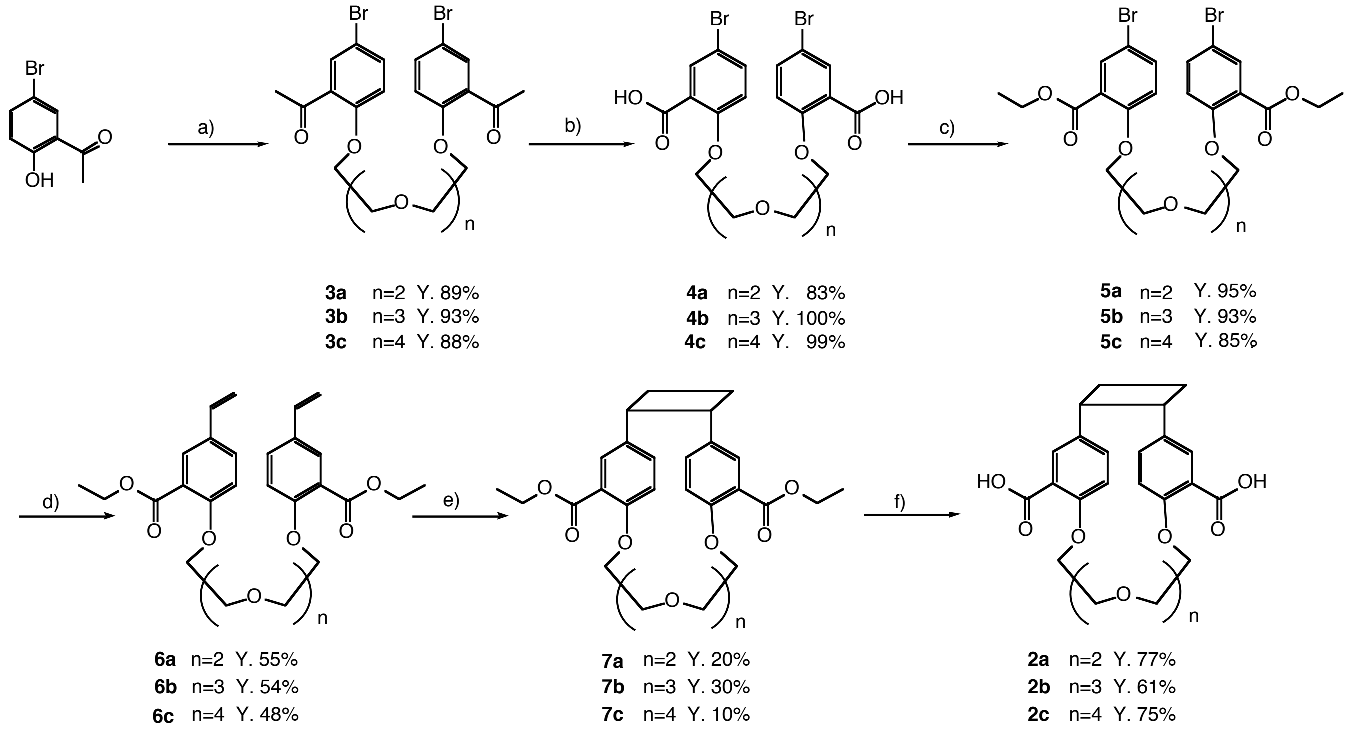
1a n=2
1b n=3
1c n=4



2a n=2
2b n=3
2c n=4

RESULTS AND DISCUSSION

Synthesis of crownophanedicarboxylic acids



a) $Ts(C_2H_4O)_{n+1}Ts$, K_2CO_3/DMF. b) NaOH, Br_2/1,4-dioxane, H_2O. c) EtOH/H_2SO_4. d) CH_2=CHSn(n-Bu)$_3$, Pd(PPh$_3$)$_4$, 2,6-di-*tert*-butyl-*4*-methylphenol/toluene.
e) hν(>280 nm)/MeCN. f) 1. NaOH/EtOH. 2. HCl/MeOH.

Scheme 1

α,ω-Bis(2-acetyl-4-bromophenyl)oligo(oxyethylene)s (**3a-c**) were easily prepared by a conventional method and converted to the corresponding dicarboxylic acids (**4a-c**) by haloform reaction in high yield. The carboxylic acids were esterified and then converted to styrene derivatives (**6a-c**) by Stille reaction.[42] Intramolecular photocycloaddition of these olefins was carried out by using a 400-W high-pressure mercury lamp through Pyrex filter in MeCN. The yields of crownophanedicarboxylic acid diethyl esters (**7a-c**) were 10-30% after chromatographic purification. The hydrolysis of diesters afforded target crownophanedicarboxylic acids (**2a-c**). All crownophanedicarboxylic acids were of *cis*-configuration which was proved by characteristic methine proton signals at δ=3.98-4.04.[43]

Complexing ability of crownophanedicarboxylic acids toward alkali metal cations

Table 1. Extraction of alkali metal cations with ligands.

ligand	Extractability (%)[a]				
	Li^+	Na^+	K^+	Rb^+	Cs^+
1a	0(7.1)	0(7.1)	0(7.1)	0(7.0)	0(7.0)
1b	0(7.1)	0(7.1)	0(7.2)	0(7.0)	0(7.0)
1c	0(7.2)	0(7.1)	0(7.1)	0(7.0)	0(7.0)
2a	5(7.0)	7(6.9)	6(6.9)	4(7.0)	0(6.9)
2b	5(7.1)	8(6.9)	7(6.9)	4(6.9)	0(7.0)
2c	5(7.0)	8(6.9)	6(6.9)	5(6.9)	0(6.9)
7a	0(7.1)	0(7.1)	0(7.1)	0(7.0)	0(7.0)
7b	0(7.1)	0(7.0)	0(7.1)	0(7.0)	0(7.0)
7c	0(7.1)	0(7.1)	0(7.2)	0(7.0)	0(7.0)

[a] Extraction conditions: Aq. phase (5 mL), [metal nitrate]= 1.0 x 10^{-1} mol dm^{-3}; Org. phase, CH_2Cl_2 (5 mL), [ligand]= 1.0 x 10^{-4} mol dm^{-3}; *ca.* 20 °C, shaken for 2 h. The values were based on the concentration of the crown compounds. Values in parenthesis were pH of the aqueous phase after extraction which were regulated by 1 M Me_4NOH.

Crownophanedicarboxylic acids and reference compounds (**1a-c**) were used as extractants for alkali metal nitrates in a liquid-liquid system. The extraction was carried out in H_2O-CH_2Cl_2 systems. As shown in Table 1, both crownophanes (**1a-c**) without carboxyl group and crownophanedicarboxylic acid diethyl esters (**7a-c**) did not extract any cation under neutral conditions, while **2a**-**c** showed low extractability toward all alkali metal cations except for Cs^+, indicating an active function of the carboxyl groups even in the neutral conditions. In other words, the carboxyl groups are thought to dissociate into protons and carboxylate anions to catch a cation in cooperation with crown ether moiety, however, their function was very low due to high hydration ability of alkali metal cations.

ESIMS spectroscopy is one of the most simple and useful method to clarify the complexing behavior of host compounds with cations in a homogeneous system.[44] Thus, we investigated the interaction between the crownophanedicarboxylic acids and alkali metal cations in MeCN-H_2O by using ESIMS spectroscopic method. As shown in Figure 1, only the 1:1 complexes between **2b** and all alkali metal cations is observed. Note that every case show no peak due to free host molecule. To simplify the data the relative intensity vs. cations complexed with **2a**, **2b**, and **2c** were illustrated by graph in Figure 2. Although **2a** efficiently interacted with Li^+, Na^+, and K^+, both **2b** and **2c** showed high Na^+-selectivity in this method. The results with regard to relative intensity of these complexes were not always in good accord with the extent determined by the extraction experiment in the CH_2Cl_2-H_2O system.

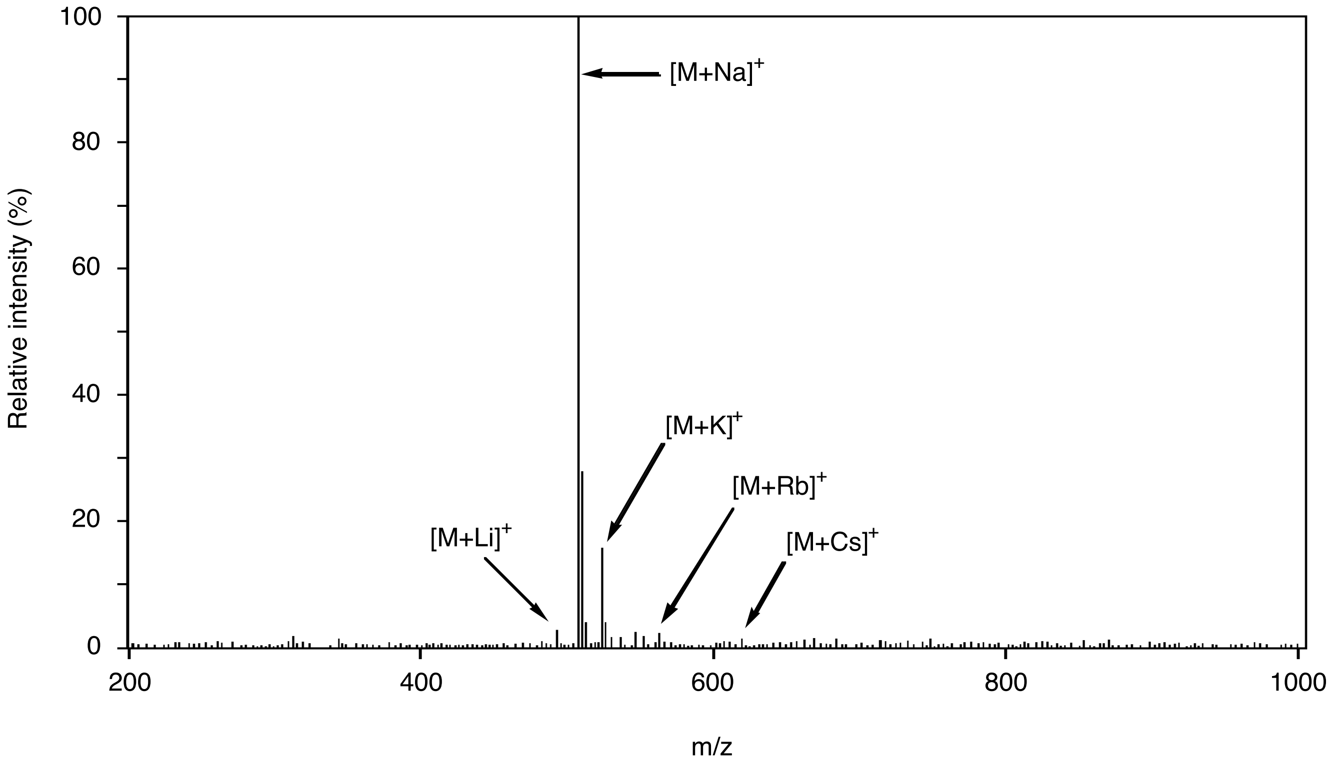


Figure 1. ESIMS spectrum of **2b** in 4:1 (v/v) MeCN-H_2O containing equimolar mixture of $LiClO_4$, $NaClO_4$, $KClO_4$, $RbClO_4$, and $CsClO_4$.

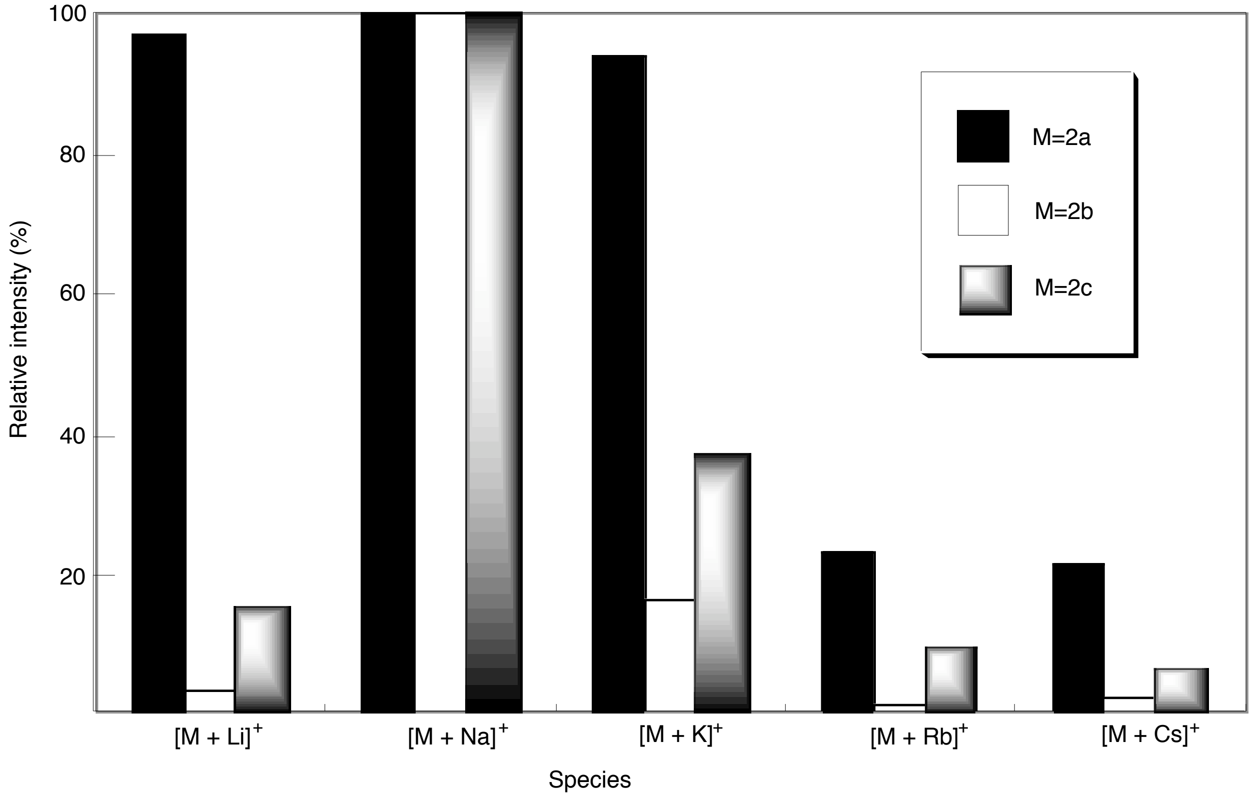


Figure 2. Relative intensity of alkali metal cations complexed with **2a-c** in ESIMS spectral analysis.

Complexing ability of crownophanedicarboxylic acids toward heavy metal cations

Table 2. Extraction of heavy metal cations with ligands.

Ligand	Extractability (%)[a]							
	Ag^+	Pb^{2+}	Cu^{2+}	Mn^{2+}	Zn^{2+}	Ni^{2+}	Co^{2+}	Fe^{3+}
1a	0(4.5)	5(4.2)	1(4.4)	0(5.0)	0(5.6)	0(6.1)	3(6.3)	9(1.4)
1b	0(4.7)	5(4.3)	1(4.5)	0(5.5)	0(5.8)	0(6.5)	3(6.4)	9(1.5)
1c	0(4.6)	5(4.2)	1(4.4)	0(5.7)	0(5.7)	0(6.1)	3(6.5)	9(1.4)
2a	0(4.3)	5(4.2)	1(4.4)	0(5.0)	0(5.5)	0(6.0)	3(6.3)	9(1.4)
2b	2(4.8)	25(4.2)	1(4.4)	0(6.0)	100(5.7)	0(6.3)	2(6.5)	10(1.5)
2c	2(4.9)	26(4.4)	2(4.4)	0(6.1)	52(5.8)	4(6.5)	3(6.4)	9(1.5)

[a] Extraction conditions: Aq. phase (5 mL), [metal nitrate]= 1.0 x 10^{-1} mol dm^{-3}; Org. phase, CH_2Cl_2 (5 mL), [ligand]= 1.0 x 10^{-4} mol dm^{-3}; *ca.* 20 ºC, shaken for 2 h. The values were based on the concentration of the crown compounds. Values in parentheses were equilibrium pH of aqueous phase.

Crownophanedicarboxylic acids and reference compounds (**1a-c**) were also used as extractants for heavy metal nitrates in a liquid-liquid system. The results are summarized in Table 2.

Crownophanedicarboxylic acid (**2a**) showed a low extractability toward these heavy metal cations. Ligand (**2b**) quantitatively extracted Zn^{2+}, and **2c** moderately did it. Since the diameter of Zn^{2+} (1.48 Å),[46] which is nearly the same size to Li^+ (1.52 Å),[46] is just fitted to the cavity of **2b**, Zn^{2+} is thought to be incorporated in the cavity of **2b** in a similar fashion to that reported for Li^+-**1b** complexation in which Li^+ is located at the one corner of oxyethylene ring units farthest from the aromatic nuclei,[41] and the positive charge of Zn^{2+} is neutralized with two negative charge of the host molecule at the same time. The complex structure is also supported by the space-filling model examination. The cavity of **2c** is slightly larger to the cation, and it of **2a** is too small to accommodate the cation. In addition to this, other stereochemical factors besides the size can be responsible for the strength of the complexing ability.[48] It was clarified that the function of carboxylic groups on the aromatic nuclei of the crownophane is important to incorporate the cation from the fact that reference compounds (**1a-c**) without carboxylic group did not extract any cation under the conditions. Additionally, both **2b** and **2c** extracted Pb^{2+} to some extent.

It is clearly revealed that **2b** and **2c** are useful ligands for recovering heavy metal cations, especially Zn^{2+} and Pb^{2+}, from waste stream and for detecting the metal cations in biological systems which generally contain a plenty of alkali metal cations, because **2** did not interact any alkali metal cations efficiently.

Electrospray ionization mass spectroscopic method was again used in order to disclose the complexing behavior of **2** with Zn^{2+} and Pb^{2+} in CH_3CN-H_2O. Phane (**2b**) formed the 1:1 complexes with both Zn^{2+} and Pb^{2+}, thought a slight amount of the free host molecule was observed. The relative intensity illustrated by graph in Figure 3 is in good agreement with the extent determined by the extraction experiment in the CH_2Cl_2-H_2O system.

Separation of Zn^{2+} and Cd^{2+} is important from environmental and industrial point of view.[48,49] Recently, competitive flotation of Cd(II) and Zn(II) from aqueous solution by dibenzo-16-crown-5 derivative of lariat ether phosphonic acid as a collector was reported. The lariat ether showed high selectivity toward Cd(II) and the selectivity was dependent on the structure of the collector, concentration of the collector, and pH value of the aqueous solution with the both cations.[36]

ESIMS spectroscopic method was again used in order to clarify the complexing behavior of **2b** with Zn^{2+} and Cd^{2+} in MeCN-H_2O. As shown in Figure 4, it was found that **2b** forms the 1:1 complexes with both

Zn^{2+} and Cd^{2+}. Although a slight amount of the free host with proton was observed in the spectrum, almost all **2b** employed was found to form 1:1 complexes with both Zn^{2+} and Cd^{2+}. It was also clear that **2b** shows selectivity toward zinc over cadmium from the relative intensity between [**2b**-H + Zn]$^+$ and [**2b**-H + Cd]$^+$ in the spctrum.

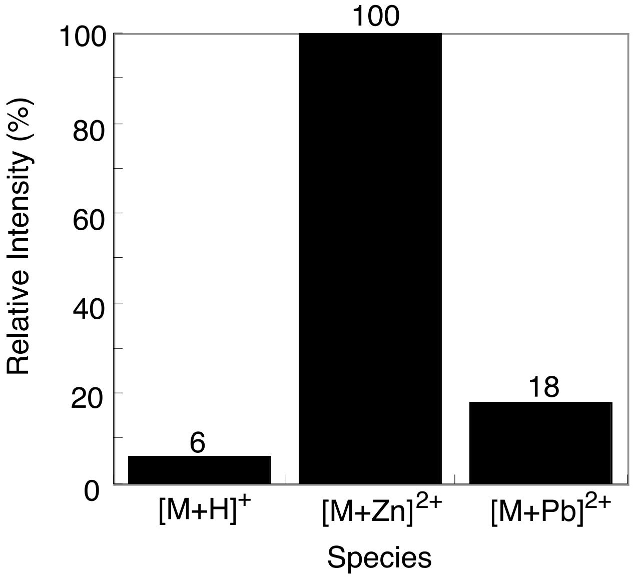


Figure 3. Relative intensity of zinc and lead cation complexed with **2b** in ESIMS analysis. The sample solution was 4:1 (v/v) MeCN-H_2O containing an equimolar mixture of $Zn(NO_3)_2$ and $Pb(NO_3)_2$.

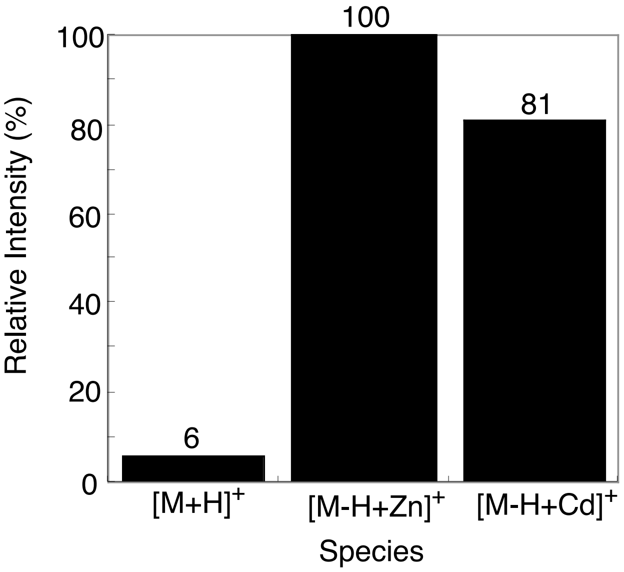


Figure 4. Relative intensity of zinc and cadmium cation complexed with **2b** in ESIMS analysis. The sample solution was 4:1 (v/v) MeCN-H_2O containing an equimolar mixture of $Zn(ClO_4)_2$ and $Cd(ClO_4)_2$.

CONCLUSION

The crownophanedicarboxylic acids were synthesized by convenient method including intramolecular [2 + 2] photocycloaddition of styrene derivatives. The host molecules showed specific metal cation-selectivity in liquid-liquid extraction due to the function of carboxyl groups in cooperation with polyether moiety even at neutral conditions.

EXPERIMENTAL

Apparatus. Elemental analysis was carried out in Technical Research Center for Instrumental Analysis, Gunma University. ^{1}H- and ^{13}C NMR spectra were recorded on a JEOL α-500 FT NMR spectrometer. HPLC analysis was performed with a Shimadzu LC-6A pump, an LC-6A UV detector, and an RC-4A data processor. UV-VIS spectra were recorded by a Hitachi U-3210 spectrophotometer. ESIMS spectra were obtained on a Perkin Elmer Sciex API-100 electrospray ionization mass spectrometer under the following conditions: A sample solution was sprayed at a flow rate of 2 μL min^{-1} at the tip of a needle biased by a voltage of 4.5 kV higher than that of a counter electrode. HRMS spectra were determined by a JEOL JSM-BU25.

Reagents. Paracrownophanes (**1a-c**) were prepared by the method reported previously.[41] Guaranteed reagent grade DMF was used without purification. Ethanol was distilled after Na was added to remove water. Guaranteed reagent grade $CH_2Cl_2$was distilled before use.

Commercially available highest-grade alkali and heavy metal nitrates were used. All aqueous solutions were prepared with distilled, deionized water.

Preparation of α,ω-bis(2-acetyl-4-bromophenyl)oligo(oxyethylene)s (**3a-c**)**.** To a suspension of K_2CO_3 (25.71 g, 0.186 mol) in 200 mL DMF a mixture of 5'-bromo-2'-hydroxyacetophenone (20.00 g, 0.093 mol) and corresponding oligoethyleneglycol ditosylate (0.023 mol) in DMF (250 mL) was added at room temperature for 1 h under a nitrogen atmosphere. The mixture was stirred at 55 °C for 3 days. The reaction mixture was poured into water (800 mL), extracted with CH_2Cl_2, and the extract was washed with water (500 mL x 3), and dried over $MgSO_4$. After filtration of the organic layer, the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography using a gradient mixed solution of toluene and ethyl acetate to obtain the desired compounds. **3a**: Yield 11.14 g (89%); mp 120-121 °C (acetone-hexane). ^{1}H NMR ($CDCl_3$) δ; 7.83 (2H, d, *J*=2.7 Hz), 7.51 (2H, dd, *J*=8.8 and 2.7 Hz), 6.83 (2H, d, *J*=8.8 Hz), 4.18 (4H, t, *J*=4.6 Hz), 3.86 (4H, t, *J*=4.6 Hz), 3.70 (4H, s), 2.63 (6H, s). Anal. Calcd for $C_{22}H_{24}O_6Br_2$: C, 48.55; H, 4.44. Found: C, 48.78; H, 4.44. **3b**: Yield 12.58 g (93%); mp 122-123 °C (acetone-hexane). ^{1}H NMR ($CDCl_3$) δ; 7.84 (2H, d, *J*=2.8 Hz), 7.51 (2H, dd, *J*=2.8 and 8.8 Hz), 6.83 (2H, d, *J*=8.8 Hz), 4.18 (4H, t, *J*=4.6 Hz), 3.87 (4H, t, *J*=4.6 Hz), 3.68-

3.63 (8H, m), 2.63 (6H, s). Anal. Calcd for $C_{24}H_{28}O_7Br_2$: C, 49.00; H, 4.80. Found: C, 48.91; H, 4.83. HRMS(EI) calcd for $C_{24}H_{28}O_7Br_2$ (M^+): 586.0202. Found, 586.0203. **3c**: Yield 12.79 g (88%); mp 51-52 °C (acetone-hexane). ^1H NMR ($CDCl_3$) δ; 7.85 (2H, d, *J*=2.5 Hz), 7.52 (2H, dd, *J*=2.5 and 8.6 Hz), 6.85 (2H, d, *J*=8.6 Hz), 4.19 (4H, t, *J*=4.6 Hz), 3.87 (4H, t, *J*=4.6 Hz), 3.69-3.62 (12H, m), 2.63 (6H, s). Anal. Calcd for $C_{26}H_{32}O_8Br_2$: C, 49.39; H, 5.10. Found: C, 49.46; H, 5.16.

Preparation of α,ω-bis(2-carboxy-4-bromophenyl)oligo(oxyethylene)s (4a-c). Bromine (12.33 g, 77.1 mmol) was added dropwise to a stirred aqueous solution of NaOH (12.50 g, 0.313 mol) at 0-10 °C. To this mixed solution, a solution of **3** (9.19 mmol) in dioxane (20 mL) was added at 10-20 °C during 1 h. After the reaction mixture was stirred for 1 day, $NaHSO_3$ was added to the mixture and then it was extracted with $CHCl_3$ (300 mL x 3) to remove the tedious materials. The aqueous layer was acidified with conc. HCl, extracted with $CHCl_3$ (300 mL x 3). After evaporation of the organic layer, the residue was purified by recrystallization from a mixed solvent of toluene and ethyl acetate to obtain the desired compounds. **4a**: Yield 4.18 g (83%); mp 132-133 °C (acetone-hexane). ^1H NMR ($CDCl_3$) δ; 8.17 (2H, d, *J*=1.4 Hz), 7.60 (2H, dd, *J*=1.4 and 8.9 Hz), 6.91 (2H, d, *J*=8.9 Hz), 4.33 (4H, t, *J*=4.6 Hz), 3.91-3.89 (4H, m), 3.74 (4H, s). Anal. Calcd for $C_{20}H_{20}O_8Br_2$: C, 43.82; H, 3.68. Found: C, 43.79; H, 3.61. **4b**: Yield 5.44 g (100%); viscous liquid. ^1H NMR ($CDCl_3$) δ; 8.19 (2H, d, *J*=2.6 Hz), 7.60 (2H, dd, *J*=2.6 and 8.9 Hz), 6.93 (2H, d, *J*=8.9 Hz), 4.34 (4H, t, *J*=4.3 Hz), 3.92 (4H, t, *J*=4.3 Hz), 3.74-3.67 (8H, m). Anal. Calcd for $C_{22}H_{24}O_9Br_2$: C, 44.62; H, 4.08. Found: C, 44.13; H, 4.07. **4c**: Yield 5.79 g (99%); mp 92-93 °C (acetone-hexane). ^1H NMR ($CDCl_3$) δ; 8.21 (2H, d, *J*=2.5 Hz), 7.61 (2H, dd, *J*=2.5 and 8.8 Hz), 6.93 (2H, d, *J*= 8.8 Hz), 4.34 (4H, t, *J*=4.3 Hz), 3.91 (4H, t, *J*=4.3 Hz), 3.74-3.63 (12H, m). Anal. Calcd for $C_{24}H_{28}O_{10}Br_2$: C, 45.30; H, 4.44. Found: C, 45.21; H, 4.42.

Preparation of α,ω-bis(2-ethoxycarboxy-4-bromophenyl)oligo(oxyethylene)s (5a-c). A mixed solution of **4** (3.98 mmol), ethanol (18.29 g, 0.870 mol), and H_2SO_4 (0.78 g, 17.4 mmol) was reflux for 8 h. The mixture was cooled to ambient temperature and then poured into water (150 mL). After extraction of the aqueous layer with CH_2Cl_2 (200 mL x 3), the organic layer was washed with water (500 mL) and 1% aqueous K_2CO_3 (400 mL), and again with water (150 mL x 3). The organic layer dried over $MgSO_4$ was filtrated and concentrated in vacuo. The residue was purified by silica gel column chromatography using a gradient mixed solution of toluene and ethyl acetate to obtain the desired compounds. **5a**: Yield 2.28 g (95%); mp 82-83 °C (acetone-hexane). ^{1}H NMR ($CDCl_3$) δ; 7.87 (2H, d, *J*=2.7 Hz), 7.50 (2H, dd, *J*=2.7 and 9.0 Hz), 6.87 (2H, d, *J*=9.0 Hz), 4.33 (4H, q, *J*=7.0 Hz), 4.15 (4H, t, *J*=4.9 and 5.2 Hz), 3.88 (4H, t, *J*=4.9 and 5.2 Hz), 3.74 (4H, s), 1.37 (6H, t, *J*=7.0 Hz). Anal. Calcd for $C_{24}H_{28}O_8Br_2$: C, 47.70; H, 4.67. Found: C, 47.60; H, 4.65. **5b**: Yield 2.40 g (93%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.87 (2H, d, *J*=2.5 Hz), 7.51 (2H, dd, *J*=2.5 and 8.9 Hz), 6.87 (2H, d, *J*=8.9 Hz), 4.33 (4H, q, *J*=7.0 Hz), 4.16 (4H, t, *J*=4.9 and 5.0 Hz), 3.87 (4H, t, 4.9 and 5.0 Hz), 3.74-3.72 (4H, m), 3.66-3.64 (4H, m), 1.37 (6H, t, *J*=7.0 Hz). **5c**: Yield 2.34 g (85%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.88 (2H, d, *J*=2.4 Hz), 7.52 (2H, dd, *J*=2.4 and 8.5 Hz), 6.88 (2H, d, *J*=8.5 Hz), 4.34 (4H, q, *J*=7.0 Hz), 4.17 (4H, t, *J*=4.3 Hz), 3.88 (4H, t, *J*=4.3 Hz), 3.75-3.63 (12H, m), 1.37 (6H, t, *J*=7.0 Hz).

Preparation of α,ω-bis(2-ethoxycarboxy-4-vinylphenyl)oligo(oxyethylene)s (6a-c). A solution of the **5** (3.23 mmol), tributylvinylstanane (2.46 g, 7.76 mmol), $Pd(PPh_3)_4$ (0.25 g, 0.216 mmol), and 2,6-di-*tert*-butyl-4-methylphenol (15 mg) in toluene (100 mL) was heated to reflux for 5 h. After the mixture was cooled to ambient temperature, large excess of 1.2 M aqueous KF solution was added, and the resulting mixture was stirred for 2 h at the same temperature. The organic layer was separated from sludgy and aqueous layer and then dried on magnesium sulfate. The concentrated crude material was purified by silica gel column chromatography using a gradient mixed solution of toluene and ethyl acetate to afford the divinyl derivatives. **6a**: Yield 0.88 g (55%); mp 48-49 °C (acetone-hexane). ^{1}H NMR ($CDCl_3$) δ; 7.80 (2H, d, *J*=2.4 Hz), 7.46 (2H, dd, *J*=2.4 and 8.5 Hz), 6.93 (2H, d, *J*=8.5 Hz), 6.65 (2H, dd, *J*=11.0 and 17.7 Hz), 5.65 (2H, d, *J*=17.7 Hz), 5.19 (2H, d, *J*=11.0 Hz), 4.34 (4H, q, *J*=7.0 Hz), 4.19 (4H, t, *J*=5.2 and 4.8 Hz) 3.89 (4H, t, *J*=5.2 and 4.8 Hz), 3.76 (4H, s), 1.37 (6H, t, *J*=7.0 Hz). HRMS(EI) calcd for $C_{28}H_{34}O_8$ (M^+): 498.2254. Found, 498.2263. **6b**: Yield 0.95 g (54%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.80 (2H, d, *J*=2.5 Hz), 7.47 (2H, dd, *J*=2.5 and 8.5 Hz), 6.93 (2H, d, *J*=8.5 Hz), 6.65 (2H, dd, *J*=11.0 and 17.7 Hz), 5.66 (2H, d, *J*=17.7 Hz), 5.19 (2H, d, *J*=11.0 Hz), 4.35 (4H, q, *J*=7.3 Hz), 4.18 (4H, t, *J*=5.5 and 4.8 Hz), 3.88 (4H, t, *J*=5.5 and 4.8 Hz), 3.75-3.73 (4H, m), 3.67-3.66 (4H, m), 1.38 (6H, t, *J*=7.3 Hz). HRMS(EI) calcd for $C_{30}H_{38}O_9$ (M^+): 542.2516. Found, 542.2508. **6c**: Yield 0.91 g (48%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.80 (2H, d, *J*=2.1 Hz), 7.47 (2H, dd, *J*=2.1 and 8.6 Hz), 6.93 (2H, d, *J*=8.6 Hz), 6.65 (2H, dd, *J*=10.7 and 17.9 Hz), 5.65 (2H, d, *J*=17.9 Hz), 5.19 (2H, d, *J*=10.7 Hz), 4.36 (4H, q, *J*=7.0 Hz), 4.20 (4H, t, *J*=5.2 and 4.9 Hz), 3.89 (4H, t, *J*=5.2 and 4.9 Hz), 3.74-3.72 (4H, m), 3.66-3.64 (8H, m), 1.38 (6H, t, *J*=7.0 Hz). HRMS(EI) calcd for $C_{32}H_{42}O_{10}$ (M^+): 586.2778. Found, 586.2778.

Preparation of crownophanedicarboxylic acid diethyl esters (7a-c). Into a 1 L Pyrex flask with a magnetic stirrer and N_2 inlet was placed 2 mmol of **6** dissolved in toluene (800 mL) and nitrogen was bubbled for 15 min. The solution was irradiated by a 400-W high-pressure mercury lamp. The progress of the reaction was monitored by HPLC. After irradiation for 2 h, the reaction mixture was evaporated. The crude reaction product was purified by silica gel column chromatography with a gradient solution of toluene and ethyl acetate to afford the crownophanedicarboxylic acid diethyl esters. **7a**: Yield 0.20 g (20%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.32 (2H, d, *J*=2.3 Hz), 6.80 (2H, dd, *J*=2.3 and 8.5 Hz), 6.71 (2H, d, *J*=8.5 Hz), 4.30 (4H, q, *J*=7.0 Hz), 4.20-4.18 (4H, m), 3.97 (2H, m), 3.71-3.69 (4H, m), 3.59 (4H, s), 2.45 (4H, m), 1.36 (6H, t, 7.0 Hz). HRMS(EI) calcd for $C_{28}H_{34}O_8$ (M^+): 498.2254. Found, 498.2260. **7b**: Yield 0.32 g (30%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.39 (2H, s), 6.80 (2H, d, *J*=8.6 Hz), 6.71 (2H, d, *J*=8.6 Hz), 4.31 (4H, q, *J*=7.0 Hz), 4.12 (4H, m), 3.96 (2H,m), 3.79 (4H, m), 3.65-3.60 (8H,m), 2.44 (4H, m), 1.36 (6H, t, *J*=7.0 Hz). HRMS(EI) calcd for $C_{30}H_{38}O_9$ (M^+): 542.2516. Found, 542.2514. **7c:** Yield 0.12 g (10%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.43 (2H, s), 6.79 (2H, d, *J*=8.4 Hz), 6.68 (2H, d, *J*=8.4 Hz), 4.31 (4H, q, *J*=7.0 Hz), 4.09 (4H, m), 3.95 (2H, m), 3.81 (4H, m), 3.67-3.64 (12H, m), 2.44-2.41 (4H, m), 1.37 (6H, t, *J*=7.0 Hz). HRMS(EI) calcd for $C_{32}H_{42}O_{10}$ (M^+): 586.2778. Found, 586.2783.

Preparation of crownophanedicarboxylic acids (2a-c). A mixture of **7** (0.202 mmol), NaOH (0.32 g, 8.00 mmol), and ethanol (9.02 g, 0.196 mol) was reflux for 3 h. The mixture was evaporated under reduced pressure after acidification with conc. HCl-methyl alcohol, and then extracted with CH_2Cl_2. The organic layer was filtrated and concentrated in vacuo. The residue was purified by GPC. **2a**: Yield 0.069 g (77%); mp 135-136 ˚C (acetone-hexane). ^{1}H NMR ($CDCl_3$) δ; 7.30 (2H, dd, *J*=2.4 and 8.2 Hz), 7.04 (2H, d, *J*=2.4 Hz), 6.84 (2H, d, *J*=8.2 Hz), 4.27-4.35 (4H, m), 4.04 (2H, m), 3.78-3.77 (4H, m), 3.69 (4H, s), 2.49 (4H, m). ^{13}C NMR ($CDCl_3$); 165.7, 155.7, 135.4, 133.3, 132.7, 118.0, 114.2, 69.9, 69.5, 67.6, 44.8, 21.3. HRMS(EI) calcd for $C_{24}H_{26}O_8$ (M^+): 442.1628. Found, 444.1629. **2b**: Yield 0.060 g (61%); mp 86-87 ˚C (acetone-hexane). ^{1}H NMR ($CDCl_3$) δ; 7.31 (2H, dd, *J*=2.4 and 8.5 Hz), 7.11 (2H, d, *J*=2.4 Hz), 6.87 (2H, d, *J*=8.5 Hz), 4.30 (4H, m), 3.98 (2H, m), 3.80 (4H, m), 3.66 (8H, m), 2.47-2.46 (4H, m). ^{13}C NMR ($CDCl_3$); 166.6, 154.5, 134.4, 132.7, 132.1, 118.9, 112.1, 70.4, 70.0, 68.4, 68.3, 44.4, 22.0. HRMS(EI) calcd for $C_{26}H_{30}O_9$ (M^+): 486.1890. Found, 486.1888. **2c**: Yield 0.080 g (75%); viscous liquid. ^{1}H NMR ($CDCl_3$) δ; 7.33 (2H, d, *J*=2.1 Hz), 7.24 (2H, dd, *J*=2.1 and 8.5 Hz), 6.87 (2H, d, *J*=8.5 Hz), 4.29 (4H, m), 3.99 (2H, m), 3.82 (4H, m), 3.68-3.66 (12H, m), 2.46-2.45 (4H, m). ^{13}C NMR ($CDCl_3$); 165.8, 155.1, 134.9, 133.9, 132.7, 117.9, 113.3, 70.7, 70.7, 70.4, 69.2, 68.4, 44.5, 23.0. HRMS(EI) calcd for $C_{28}H_{34}O_{10}$ (M^+): 530.2152. Found, 530.2150.

Liquid-liquid extraction of alkali metal cations. Crownophanes were used as an extractants for alkali metal nitrates in a liquid-liquid system together with reference compounds. A CH_2Cl_2 solution of the host compound (1×10^{-4} mol dm^{-3}, 5 mL) and an aqueous metal nitrate solution (0.1 mol dm^{-3}, 5 mL) containing prescribed concentration of tetramethyl ammonium hydroxide as pH regulator were shaken in a 20-mL test tube equipped with a ground glass stopper at room temperature (20-22 °C) for 2 h. Two liquid phases were separated, and the equilibrium pH of the aqueous phase was measured. An aliquot (2 mL) of the organic phase was evaporated under reduced pressure, and then 0.1 mol dm^{-3} HNO_3 aqueous solution (2 mL) was added to the residue, and finally the extracted cation was analyzed by atomic absorption analysis.

Liquid-liquid extraction of heavy metal cations. A CH_2Cl_2 solution of crownophanedicarboxylic acid (1×10^{-4} mol dm^{-3}, 5.0 mL) and an aqueous metal nitrate solution (0.1 mol dm^{-3}, 5.0 mL), whose pH value was adjusted as high as possible without precipitation of the hydroxides, were shaken in a 20-mL test tube with a ground-glass stopper at ambient temperature (20-22 °C) for 2 h. Two liquid phases were separated, and the equilibrium pH of the aqueous phase was measured. Then the cation extracted into the organic phase was measured by the same manner as described in the experiment of liquid-liquid extraction of alkali metal cations.

ESI-MS measurement of crownophanedicarboxylic acids in the presence of metal salt. The sample solution was 4:1 (v/v) MeCN-H_2O containing a crownophane (0.1 mM) and metal salt (0.1 mM).

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