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Syntheses of Aromatic Bridged Cryptophanes and their Complexing Abilities with Alkyl Ammonium Cations

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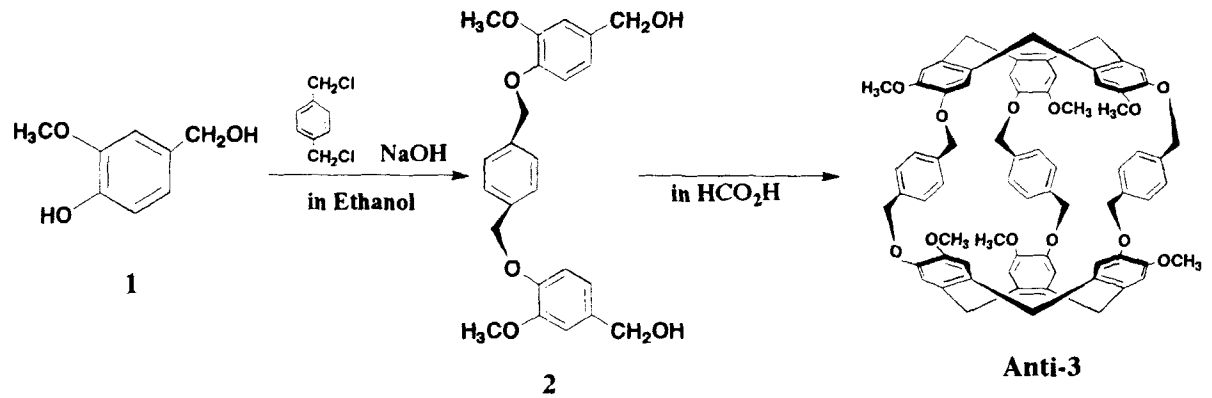
Several aromatic bridged cryptophanes were successfully synthesized. p-Xylene bridged cryptophane **Anti-3** was prepared by the direct trimerization of α,α′-bis[4-hydroxymethyl-2-methoxyphenoxy]-p-xylene. The synthesis of o-xylene bridged cryptophane **Anti-8** was carried out by the direct trimerization and/or the stepwise method from vanillyl alcohol. The o-[4,5-bis-(methoxycarbonyl)]xylene bridged cryptophanes **Anti-15a** and **Syn-15b** were also prepared by the stepwise method from vanillyl alcohol. **Anti-3** was capable of complexing with almost all the quaternary alkylammonium cations among the primary, secondary, tertiary and quaternary ammonium cations, and selectively prefered to complex with the NEt_3Me^+ cation as a guest. From the complexation of the o-xylene bridged cryptophanes **Anti-8**, and the analogs **Anti-15a** and **Syn-15b** with the NMe_4^+ cation, the cryptophanes **Anti-8** and **Syn-15b** were confirmed to complex with the guest cation, however, **Anti-15a** was not confirmed to be included.

INTRODUCTION

During the complexation of the host molecules such as cyclophanes and cryptophanes having an elliptical hole with various guest molecules, the three dimensional agreement between the cavity of the host molecule and the size and shape of the guest molecule should be important for forming a stable complex.[1,2] Actually, the spherical shape of the guest molecule, which capable of being fit for the hole of the cryptophane as the host molecule, was known to be favorable for the recognition of the incorporation.[2] The investigations for the syntheses of several kinds of cryptophanes and their complexing abilities with neutral guest molecule and alkylammonium cations have been carried out by A. Collet et al..[3] We have already reported the syntheses and the complexing abilities of the diethyleneoxy bridged cryptophanes which have oxygen atoms that can act as the electron donors in the bridged chains.[3] In order to study the effect of the increase of hydrophobility in the cavity of the cryptophane on the complexing ability and the influence of the bridge moieties on the inclusion, the p-xylene and o-xylene bridged cryptophanes were synthesized and the complexing abilities of these cyptophanes with the alkylammonium cation as guest molecules investigated.

* Corresponding author.



SCHEME 1 Synthesis of p-xylene bridged cryptophane **Anti-3**

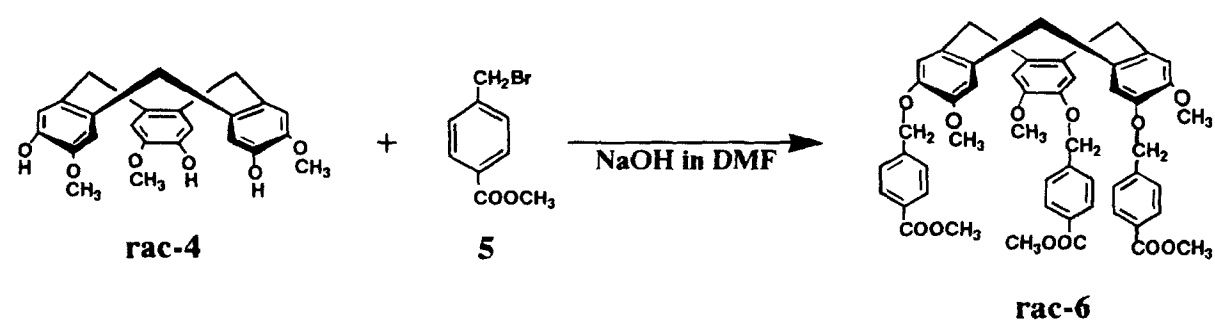
RESULTS AND DISCUSSION

Syntheses of Cryptophanes

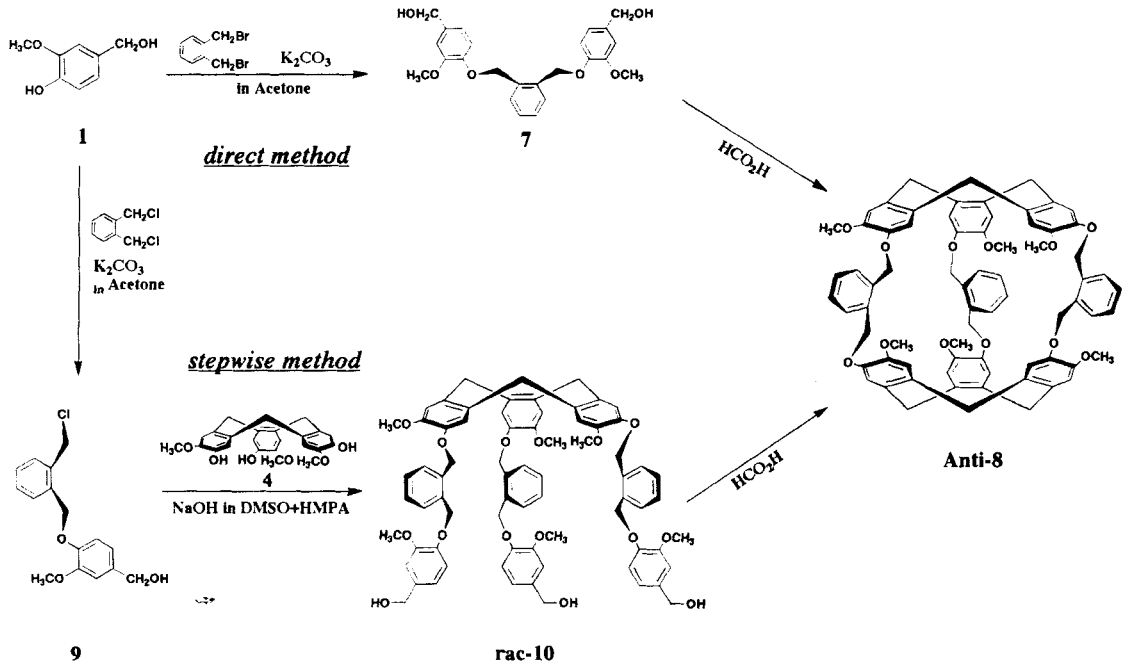
The synthesis methods of the cryptophanes were similar to those described in a previous paper.[4] The synthetic route of the p-xylene bridged cryptophane **Anti-3** is shown in Scheme 1. The reaction of vanillyl alcohol **1** with α,α′-dichloro-p-xylene afforded α,α′-bis[4-hydroxymethyl-2-methoxyphenoxy]-p-xylene **2** in 75% yield. The direct intramolecular trimerization of **2** in formic acid produced the p-xylene bridged cryptophane **Anti-3** in 3% yield.

The synthetic route of the p-xylene bridged cryptophane analog **rac-6** is shown in Scheme 2. **Rac-6** was prepared by the reaction of methyl 4-bromomethyl benzoate **5** with C_3-cyclotriguaiacylene **rac-4**, which is the basic cryptophane skeleton, in 80% yield. The synthetic routes of the o-xylene bridged cryptophane **Anti-8** are shown in Scheme 3. α,α′-Bis[4-hydroxymethyl-2-methoxyphenoxy]-o-xylene **7** was synthesized by the reaction of vanillyl alcohol **1** with α,α′-dibromo-o-xylene in 86% yield. The direct trimerization of the precursor **7** in formic acid produced o-xylene bridged cryptophane **Anti-8** in 3% yield. The host molecule **Anti-8** was also synthesized by a stepwise method from **1**. The reaction between **1** and α,α′-dichloro-o-xylene gave 4-[1-(2-chloromethylphenyl)methoxy]-3-methoxybenzenemethanol **9** in 38% yield. The cyclic precursor **rac-10** was obtained by the reaction of **9** with C_3-cyclotriguaiacylene **rac-4** in 28% yield. Finally, intramolecular cyclization of **rac-10** in formic acid gave **Anti-8** in 28% yield.

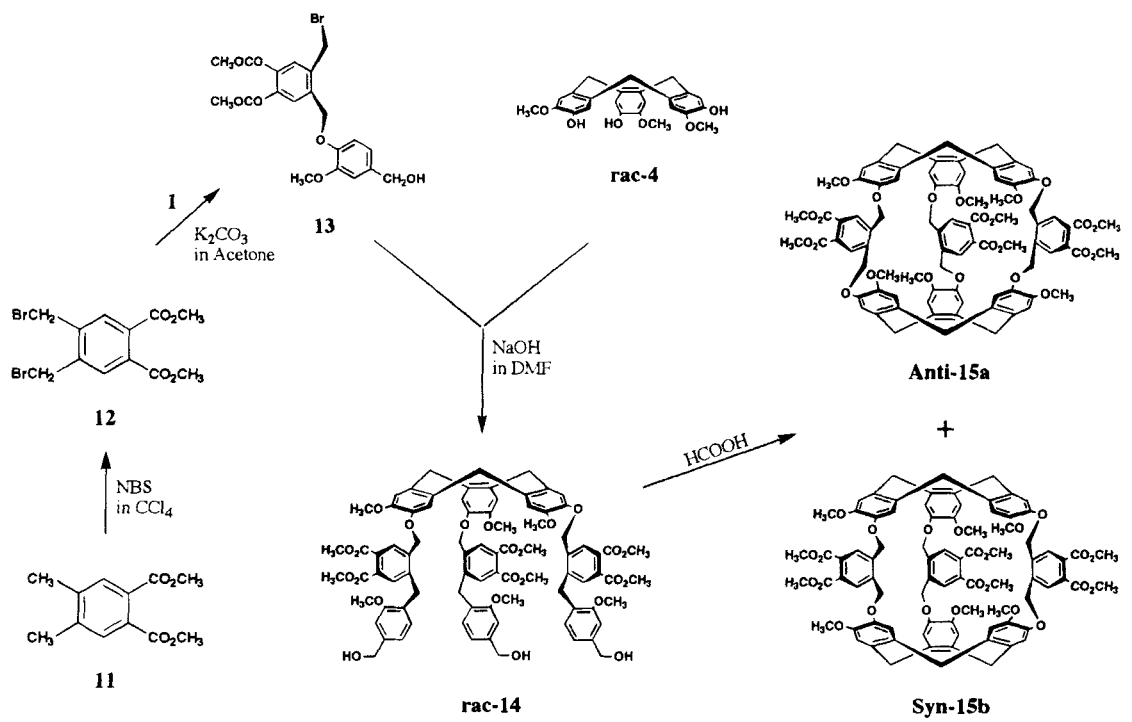
The synthetic route of **Anti-15a** and **Syn-15b** is shown in Scheme 4. Reduction of dimethyl



SCHEME 2 Synthesis of the analogue **rac-6** of p-xylene bridged cryptophane



SCHEME 3 Two synthetic routes of o-xylene bridged cryptophane **Anti-8**



SCHEME 4 Synthetic routes of o-[4,5-bis(methoxycarbonyl)]-xylene bridged cryptophanes **Anti-15a** and **Syn-15b**

4,5-dimethylphthalate **11** by NBS produced dimethyl 4,5-bis(bromomethyl)phthalate **12** in 56% yield. Compound **13** was obtained by the reaction of **12** with **1** in 57% yield. The reaction of **13** with **rac-4** afforded the precursor **rac-14** in 39% yield. The o-[4,5-bis(methoxycarbonyl)]xylene bridged cryptophanes **Anti-15a** and **Syn-15b** were prepared by the intramolecular cyclization of **rac-14** in 29% and 43% yields, respectively.

The structures and configurations of the synthesized cryptophanes have been determined by ^{1}H-NMR and Mass spectroscopy, elemental analyses and high-performance liquid chromatography (HPLC). HPLC analysis of **Anti-3** with an optically active column of chiralpak-OT(+)[5] gave two peaks (the integral ratio was 1:1), representing the two optical isomers ((+) and (−)-form), so that the racemic **Anti** structure was assigned to **3**. The **Anti** structure of **8** was also determined by X-ray analysis. **Anti-15a** and **Syn-15b** gave two peaks (1:1 in integral) and one peak, respectively. Therefore, it was determinated that **Anti-15a** was a racemic molecule and **Syn-15b** was a meso molecule.

Complexing Abilities of Cryptophane with Alkylammonium Cations

The cryptophanes possessing an elliptical cavity have been known to prefer spherical guest molecule for the inclusion.[2,6] In order to investigate the inclusion abilities of the above cryptophanes, various alkylammonium cations as guest molecules were employed. It is known that the incorporated guest molecule in the cryptophane show upfield shifted ^{1}H-NMR peaks compared with the free guest molecule.[2,7] The measurements of ^{1}H-NMR spectra were carried out to estimate the complexing abilities of these cryptophanes.

All alkylammonium cations were used as the picrate salts. As shown in Fig. 1, the ^{1}H-NMR spectra at 300 K of $NEt_3Me^+Pic^-$ (Pic=picrate anion) in the solvent (CD_2Cl_2:CD_3OD=9:1) showed the methyl and methylene protons of the ethyl group, and the methyl protons at δ (ppm) 1.35 and 3.32, and 2.96, respectively. After adding 0.5 equivalent of **Anti-3**, the peaks of the cation were completely shifted upfield and broadened, therefore, the complexing ability at 300 K was not estimated. In order to determine the inclusion ability, variable temperature ^{1}H-NMR measurements (300–210 K) were carried out. At low temperature (210 K), slow exchange on the NMR time scale was observed and new peaks due to the included NEt_3Me^+ cation appeared at δ −1.54 ($C\underline{H}_3CH_2N$), −0.84, −1.03 ($CH_3C\underline{H}_2N$) and −1.34 (CH_3N) together with the free guest cation at δ 1.27 ($C\underline{H}_3CH_2N$), 3.23 ($CH_3C\underline{H}_2N$) and 2.90 (CH_3N), respectively. The huge upfield shifts of the NEt_3Me^+ cation are in agreement with its inclusion in the cavity of **Anti-3**. The apparent equilibrium constant K for the complexation was estimated by the integral ratio between the free and complexed peak areas of the guest cation to be $K \approx 1000\ M^{-1}$, which was the apparent constant in the competition with the solvent, and the free energy change ΔG was calculated as −2.9kcal/mol at 210 K. The results of the temperature dependence ^{1}H-NMR measurements suggested that the complexing ability of **Anti-3** with the NEt_3Me^+ cation increased with decreasing temperature. Under the coexistence of the NEt_3Me^+ cation and 0.5 equivalent of **Anti-3**, furthermore, the peak of the benzyl protons of the bridged chains of the host molecule was changed from a single peak (δ 5.13) at 300 K to double-doublet peaks (δ 5.18 and 5.12, dd, J = 13.8 Hz) at 220 K according to the temperature decrease together with the upfield peaks of the complexed guest cation. The coalescence temperature, Tc for the benzyl protons of the host molecule was determinated as 233 K in Fig. 2, and the activation energy, $\Delta G^{\ddagger}$, for the rotation of the bridges in **Anti-3** was estimated as 11.9 kcal/mol at this temperature. Furthermore, the peaks of the methylene protons of the included NEt_3Me^+ cation are shown as two sets of multiplets at δ −0.84 and −1.03 ($CH_3C\underline{H}_2N$;

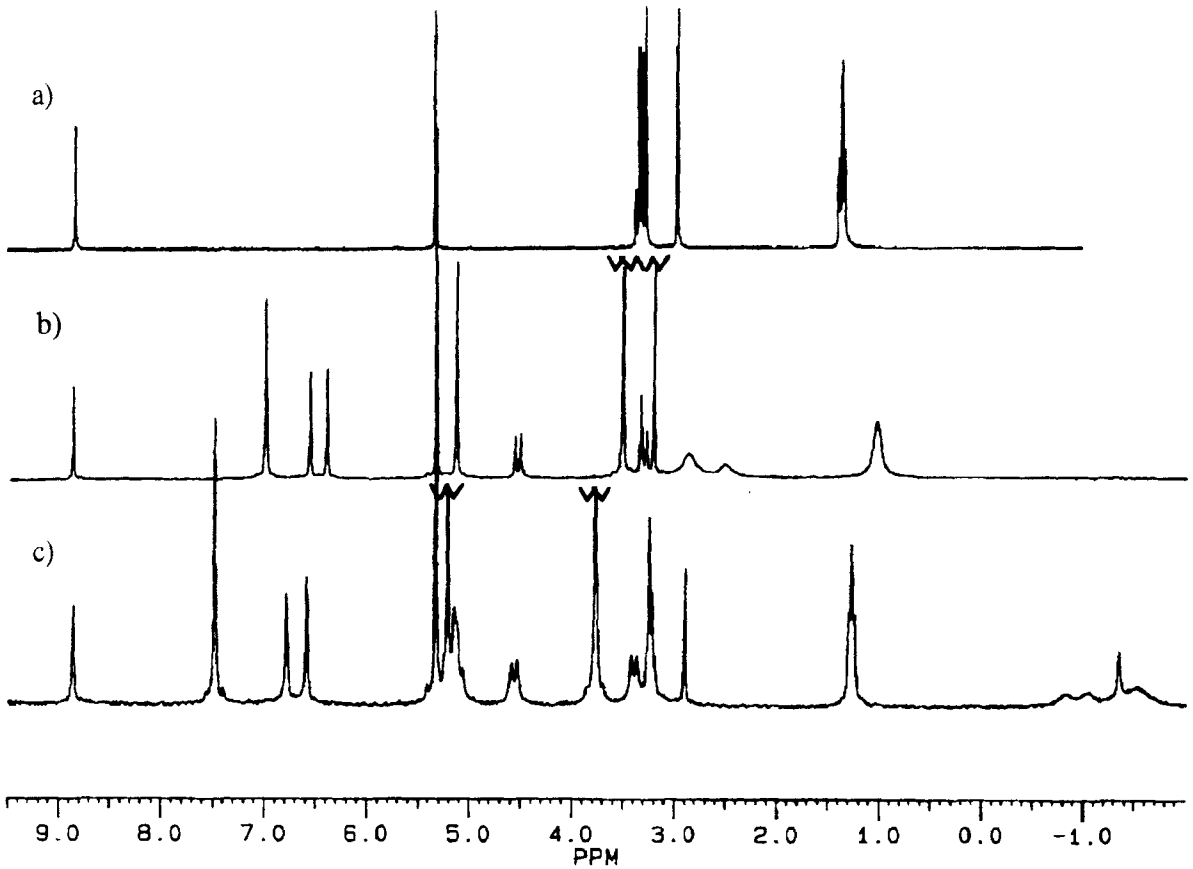


FIGURE 1 Variable temperature ^{1}H-NMR spectra of NEt_3MePic in the presence of **Anti-3** in CD_2Cl_2:CD_3OD=9:1. a) ^{1}H-NMR spectra of NEt_3MePic at 300K. b), c) ^{1}H-NMR spectra of the mixture of NEt_3MePic and **Anti-3** at 300, 210K, respectively. **Anti-3** = 5.0×10^{-3}M and NEt_3MePic = 1.0×10^{-2}M.

210 K), so that the complexed cation seemed to be tightly incorporated in the cave of **Anti-3**. The measurements of the ^{1}H-NMR spectra were extended to other alkylammonium cations. The chemical shift changes of the guest cations during the complexing of **Anti-3** at 210K are summarized in Table I together with the equilibrium constants and the free energy changes for the inclusion at 210K. The picrate anion of the guest molecule was negligibly shifted by adding the host molecule. It is considered that the picrate anion is affected by the solvation, and acts as a separated counter anion which could not enter the cavity of the host molecule.

The inclusion abilities of the diethyleneoxy bridged cryptophanes **Anti-16a** and **Syn-16b** for alkylammonium cations have already been reported.[3] The chemical shifts changes, $\Delta\delta$ (ppm), of the NEt_4^+ cation as a guest by inclusion in the cavity of **Anti-16a** were 1.41 ($C\underline{H}_3CH_2N$) and 3.16 ($CH_3C\underline{H}_2N$), however, the chemical shift change values of the NEt_4^+ cation by complexing of **Anti-3** were 2.81 ($C\underline{H}_3CH_2N$) and 4.13 ($CH_3C\underline{H}_2N$), respectively. Therefore, the upfield shifts of the guests due to the inclusion of **Anti-3** was 1 ppm larger than that of **Anti-16a** on the average. These differences seem to be caused by the additional contribution of the benzene rings

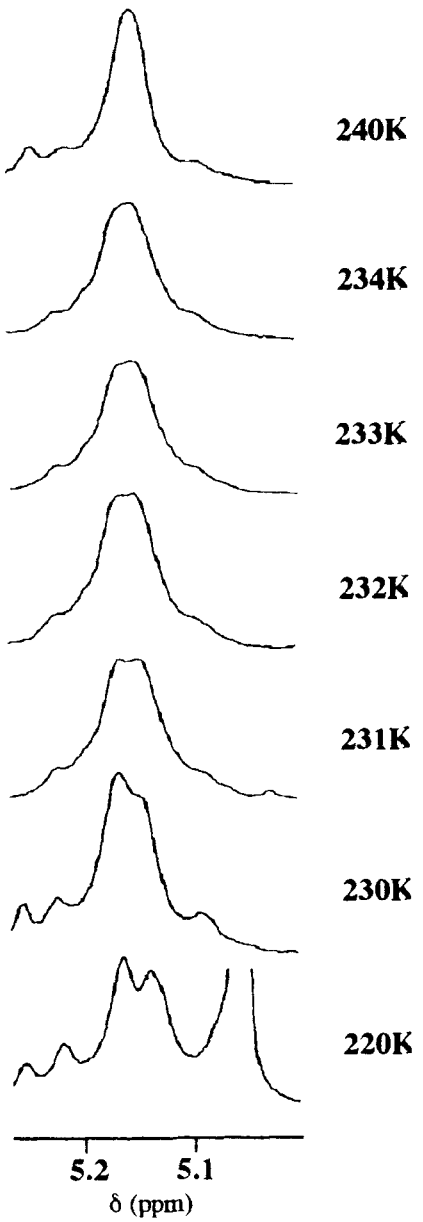


FIGURE 2 The variable tempreture ^{1}H-NMR spectra of the benzyl moieties of the bridged chains on **Anti-3** as host molecule in the presence of $Et_3MeNPic$ as guest molecular; **Anti-3** = 5.0×10^{-3}M and $Et_3MeNPic$ = 1.0×10^{-2}M in CD_2Cl_2:CD_3OD (9:1, v/v) The coalescence temperature Tc for the benzyl protons of the host was determinated as 233K by the spectra.

of the bridged moities in **Anti-3**.[6] The correlation between the inclusion abilities of **Anti-3** and the volumes of the guest cations is shown in Fig. 3. As shown in Fig. 4, the distance between the two methylene portions of p-xylene (ca. 5.8 Å) used as the bridge moieties of **Anti-3** was longer than that (ca. 4.6 Å) of the diethyleneoxy portions of **Anti-16a**, however, **Anti-3** was capable of selectively complexing the NEt_3Me^+ cation which is smaller than NEt_4^+ which is most favorable for the complexation of **Anti-16a**. The aromatic bridges of **Anti-3** are so bulky that the its windows and cavity seem to be narrow compared with **Anti-16a**. These differences in the bridges structure might lead to the selectivity difference between these hosts. The dependence of the complexing abilities on the size of the guest cation was also apparent. The complexing ability of **Anti-3** decreased when the size of guest cation was larger or smaller than NEt_3Me^+. Only most of the quaternary ammonium cations were permitted to be incorporated into the cave of **Anti-3**.[8] The tertiary ammonium cation was capable of complexing with **Anti-16a** together with the quaternary ammonium cations.[3] The oxygen atoms of the bridges can possibly interact with the hydrogen atom of the incorporated tertiary ammonium cation for stabilizing in the cavity of **Anti-16a**. In the aromatic bridged cryptophane, however, the aromatic rings of the bridges could act to increase the lipophilicity of the cavity of **Anti-3**, so that the tertiary ammonium cation should be inhibited by the hydrophilicity of the cation during the complexation of this host molecule.

When the smallest quaternary ammonium cation NMe_4^+ was added in the solution of 0.5 equivalent of **Anti-3** as a host, the benzyl protons of the bridges on the host molecule have been shown to be changed from a singlet to double-doublet peaks at 300 K and the guest cation's peak mostly vanished from the ^{1}H-NMR spectra. This means that the ammonium cation was enough small to be easily complexed in the cavity of **Anti-3** through the windows of the bridges of the host molecule and capable of hindering the motion of the benzene rings of the bridges in **Anti-3** at this temperature.

The thermodynamic parameters for the complexations of **Anti-3** with various ammonium cations were estimated from the van't Hoff plots

TABLE I The chemical shift changes (Δδ ppm) on the ^{1}H-NMR of guest molecule between free and complexed by p-xylene bridged cryptophane,[a] and equilibrium constants and the thermodynamic parameters for the complexation of p-xylene bridged cryptophane with alkylammonium cations.[b]

	NEt_4^+		NEt_3Me^+			$NEtMe_3^+$			NMe_4^+	
	$CH_3CH_2N^+$	Pic	$CH_3CH_2N^+$	CH_3N^+	Pic	$CH_3CH_2N^+$	CH_3N^+	Pic	CH_3N^+	Pic
free	1.23 3.51	-	1.27 3.23	2.90	-	1.34 3.35	3.07	-	3.16	-
complex	−1.58 −0.98	-	−1.54 −0.84 −1.03	−1.34	-	−1.46 −0.70	−0.74	-	−0.60	-
Δδ	2.81 4.13	0.00	2.81 4.07 4.26	4.24	−0.01	2.80 4.05	3.81	−0.04	3.76	0.02
K (M^{-1})	792		≈1054			484			342	
ΔG (kcal/mol)	−2.75		−2.91			−2.58			−2.43	
ΔH (kcal/mol)	−3.47 ± 0.52		−4.05 ± 1.18			−1.64 ± 0.44			−1.98 ± 0.38	
ΔS (cal/mol/K)	−3.3 ± 2.3		−5.8 ± 5.3			4.6 ± 1.9			2.2 ± 1.7	

[a] ^{1}H-NMR conditions: **Anti-3** = 5.0X10^{-3} M and guest molecule = 1.0X10^{-2}M at 210K in CD_2Cl_2:CD_3OD = 9:1. The picrate anion was negligible shifted by adding host molecule, and the above values of picrate showed the change between the only guest molecule and after adding host molecule. The positive Δδ shows the up field shift and negative is the down field shift.
[b] K values were estimated by ^{1}H-NMR spectra: ΔG values were calculated from K (ΔG = −RTlnK). ΔH and ΔS were estimated from van't Hoff plot (lnK vs 1/T). The errors of ΔH and ΔS were the estimated standard errors calculated from least-squares linear regression by the literature; N. R. Draper and H. Smith, *"Applied Regression Analysis"* John Willy & Sons, Inc., New York, (1966).

(lnK vs 1/T), and the results are listed in Table I. The changes in enthalpy, ΔH, were suggested to be comparable to the ΔG values. Furthermore, the changes in entropy, ΔS, seemed to be shown

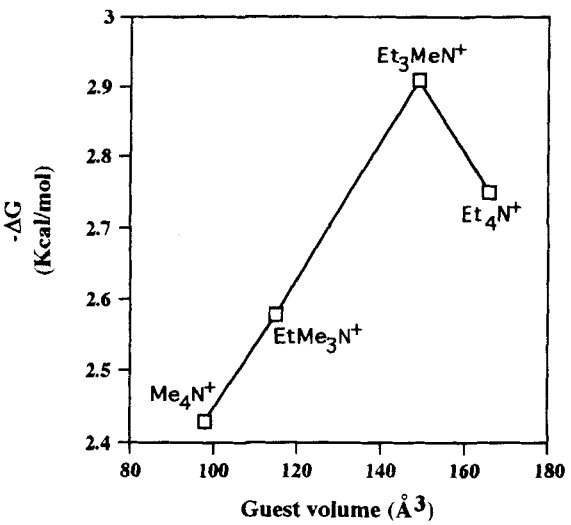


FIGURE 3 Correlation between -ΔG of the complexation of **Anti-3** with tetraalkylammonium cations and the guest alkylammonium cation's volume (Å^3). The ΔG values were calculated from equilibrium constant K estimated by ^{1}H-NMR spectra under same condition; **Anti-3** = 5.0 × 10^{-3}M and guest cation = 1.0 × 10^{-2}M at 210K in CD_2Cl_2:CD_3OD=9:1.
The van der Waals volumes of guest cations were calculated by the literature; A. Bondi, *J. Phys. Chem.*, **68**, 441 (1964).

to influence the guest volume. The complexations of **Anti-3** with NMe_4^+ and $NEtMe_3^+$ cations resulted in the positive values of ΔS as 2 and 4 cal/mol/K, respectively. These guest cations were capable of easily entering into the cave of the host molecule using the CPK model study between the guest volume and the window and hole size of the host molecule. On the other hand, the larger sized guest cations of NEt_3Me^+ and NEt_4^+, which were difficult to incorporate in the hole of this host molecule compared with the above two guest cations, have been complexed in the cavity of **Anti-3** producing the negative values of ΔS as −6 and −3 cal/mol/K, respectively. A similar result was observed for the inclusion of **Anti-16a**; the negative ΔS was shown in the complexation with the NPr_3Et^+ cation which was more much tightly incorporated into the cavity of the host molecule. These results suggested that the guest cation was tightly included into the cave of the host molecule resulting in the negative value of ΔS for the complexation and the negative ΔS means destablilizing the complex at higher temperature.

Compared with the p-xylene bridged cryptophane, the windows and the cavities of the o-

xylene bridged cryptophanes **Anti-8** and its analogs **Anti-15a** and **Syn-15b** were narrow and small, and it was expected that these cryptophanes could complex only with a small guest molecule. Thus, in order to investigate the inclusion abilities of these o-xylene bridged cryptophanes and their analogs, the smallest quaternary ammonium cation, NMe_4^+ was used as a guest. The solvent used was the same described above CD_2Cl_2:CD_3OD (9:1, v/v). The chemical shift changes of the guest cations during the complexing of **Anti-8**, and **Anti-15a** and **Syn-15b** are summarized in Table II together with the values of **Anti-3**. The equilibrium constants, K, and the free energy changes, ΔG, for the inclusion are also listed in Table II. By adding 0.5 equivalent of the host molecule **Anti-8** to the guest of NMe_4Pic solution, the upfield shifted peaks appered due to the complexed guest at δ −0.09. When **Anti-15a** and **Syn-15b** were added, only **Syn-15b** gave the complexed peaks at δ 0.36 and 0.20 at 210K and the new peak of the incorporated guest molecule did not appeare by adding **Anti-15a** as the host molecule. The equilibrium constants, K, of **Anti-8** and **Syn-15b** were determined as 10 and 40.0 M^{-1}, respectively. These values were obviously smaller than that (K = 430 M^{-1}) of **Anti-3** with NMe_4^+, apparently due to the structural difference in the windows and the cavity by varying the bridged moieties of these cryptophanes. That is confirmed no complexation of **Anti-15a** at any temperature. It seems that the bridged moieties of **Anti-15a** were apparently bulky and hindered the incorporation of the guest molecule into the cavity compared with **Anti-8**, which possesses no functional groups on the bridged aromatic rings, due to the two methoxycarbonyl groups in the each benzene rings as the bridged chains in **Anti-15a**. Similar to the p-xylene bridged cryptophane **Anti-3**, it was observed that the complexation abilities of **Anti-8** and **Syn-15b** with the NMe_4^+ cation increased with decreased temperature. Thus, it was considered that the o-xylene moieties as bridges of these hosts also have a swing motion, and act to inhibit the complexation. Small new peaks for the incorporated NMe_4^+ cation are shown at δ 0.16 together with that (δ 3.24) of the free guest cation at 300K in the presence of 0.5 equivalent **Anti-8**. Compared with **Anti-3**, the cavity of **Anti-8** should be small (Fig. 4), so that they prefer small guests, and the resulting inclusion for this cation was a reversibly slow exchange on the ^{1}H-NMR time scale at even 300K. During the complexation of **Syn-15b**, the NMe_4^+ cation showed only a new peak (δ

TABLE II The chemical shift changes (Δδ ppm) on the ^{1}H-NMR of tetramethylammonium cation between free and complexed, equilibrium constants and the thermodynamic parameters for the complexation of several aromatic bridged cryptophanes with tetramethylammonium cations.[a]

		Anti-3	Anti-8	Anti-15a[b)]	**Syn-15b**
	free	3.16	3.16	3.16	3.16
NMe_4^+	complex	−0.60	−0.09	–	0.36, 0.20
	Δδ	3.76	3.25	–	2.80, 2.96
Pic		0.02	0.03	–	0.13
K(M^{-1})		342	10.4	–	40.0
ΔG (kcal/mol)		−2.43	−0.98	–	−1.54
ΔH (kcal/mol)		−1.98 ± 0.38	−1.39 ± 0.56	–	−4.98 ± 0.64
ΔS (cal/mol/K)		2.2 ± 1.7	−1.7 ± 2.2	–	−16.2 ± 2.8

[a] ^{1}H-NMR conditions: each cryptophane = 5.0X10^{-3}M and NMe_4Pic = 1.0X10^{-2}M at 210K in CD_2Cl_2:CD_3OD=9:1. The picrate anion was negligible shifted by adding host molecule, and the above values of picrate showed the change between the only guest molecule and after adding host molecule. The positive Δδ shows the up field shift. K values were estimated by ^{1}H-NMR spectra: ΔG values were calculated from K (ΔG = -RTlnK). ΔH and ΔS were estimated from van't Hoff plot (lnK vs 1/T). The errors of ΔH and ΔS were the estimated standard errors calculated from least-squares linear regression by the literature; N. R. Draper and H. Smith, *"Applied Regression Analysis"* John Willy & Sons, Inc., New York, (1966).

b) It was not confirmed the complexation of **Anti-15a** with NMe_4^+.

0.36) as the included guest at 250K, however, the incorporated cation's peaks appeared as two peaks (δ 0.36 and 0.20) at lower temperature (230–210K). This seems to be explained similarly to above, that is, the incorporated guest cation may be tightly complexed in the hole of the host molecule. The influence of the difference between the bridged moieties of the o-xylene bridged cryptophanes **Anti-8** and the analog **Syn-15b** was observed in the chemical shift changes of the guest cation by the complexation as well as the complexing abilities. The NMe_4^+ cation was affected the upfield shift of Δδ 3.25 ppm during the complexation of **Anti-8**. This value was greater than the Δδ 2.80 and 2.96 obtained by the inclusion of **Syn-15b**. Unexpectedly, the difference in the upfield shift can be explained that the o-xylene moieties might have a shielding effect toward the incorporated guest cation. The two carbonyl groups as the electron withdrawing groups exist on the o-xylene moieties of the bridges in **Syn-15b**, so that the electron densities of the benzene rings of **Syn-15b** are lower than that of **Anti-8** due to the carbonyl groups. Therefore, **Syn-15b** probably appeared as having a weaker shielding effect compared with **Anti-8**, thus resulting in the difference in the chemical shift changes that were obtained between the two cryptophanes.

The thermodynamic parameters for the complexation of **Anti-8** and **Syn-15b** with the NMe_4^+ cation were calculated from the van't Hoff plot and are shown in Table II. From the fact that the ΔS values were negative values of −1.7 and −16.2 cal/mol/K, respectively, in the incorporation of **Anti-8** and **Syn-15b**, the NMe_4^+ cation is considered to be tightly complexed in the caves of the o-xylene bridged cryptophane and the analog.

All equilibrium constants described above were the apparent stability constants in competition with the solvent. In order to investigate the influence of the solvent on the complexing abilities of these cryptophanes, the complexation of these hosts with the undeuterated solvent (CH_2Cl_2 and CH_3OH) as a guests were measured by a similar method using the variable temperature NMR (210–300K), however, no complexing could be observed. When an excess of CH_2Cl_2 as a guest molecule was added to the solution of the cryptophanes in $CDCl_3$, no changes in the chemical shift due to guest cation were observed in the spectra. Therefore, the complexing abilities with solvents as guests were not determined because the equilibrium of the complexation with the solvent is very fast on the NMR time scale due to the mismatch between the volume of solvents as a guest molecule and the cavity size of the host molecule. Thus, the complexing abilities with the solvent (CD_2Cl_2 and CD_3OD) were neglected in the investigation of the inclusion abilities with ammonium cations.

To compare with the cryptophane having an almost constant and rigid cavity shape, the analog **rac-6** of the p-xylene bridged cryptophane, which possess three flexible aromatic chains between the two cyclotriveratrylene units and has no constant hole shape, was used as the host molecule, in order to study the complexing ability with the NMe_4^+ cation. The result indicated, however, that no complex was estimated by the ^{1}H-NMR spectra. It suggested that when the host molecule has a suitable structural cavity in which the guest can be incorporated, the complexation of the host molecule with the spherical guest molecule is possible.

CONCLUSION

The aromatic bridged cryptophanes **Anti-3**, **Anti-8**, and **Anti-15a** and **Syn-15b** were synthesized. p-Xylene bridged cryptophane **Anti-3** was capable of selectively complexing with quaternary alkylammonium cations among the investigated primary, secondary, tertiary and quaternary ammonium cations, probably due to the aromatic rings of the three bridged chains of the

host molecule. Furthermore, from the complexation with various quaternary cations, **Anti-3** showed highly selective inclusion ability for the triethylmethylammonium cation. In the o-xylene bridged cryptophanes **Anti-8** and the analogs **Anti-15a** and **Syn-15b**, **Anti-8** and **Syn-15b**, which have a larger cavity and window between the two bridges than **Anti-15a**, were estimated to be able to incorporate the tetramethylammonium cation as a guest.

EXPERIMENTAL

Melting points were determinated by Yazawa micro mp apparatus and MEL-TEMP II apparatus of Laboratory devices, and are uncorrected. ^{1}H-NMR spectra were measured by Hitachi R-1100 (60 MHz) and Bruker AC250 (250 MHz) with TMS as the internal standard. Elemental analyses were carried out using a Perkin-Elmer 2400 instrument. Mass spectra were recorded on Hitachi M-80 (electron Impact-EI) and M-2000 (field desorption-FD). The high performance liquid chromatography (HPLC) were measured by a JASCO HPLC system with a chiralpak-OT(+) column monitored with UV absorption measurements.

MATERIALS

Vanillyl alcohol **1**,[9] C_3-cyclotriguaiacylene **rac-4**,[10] methyl 4-bromomethyl benzoate **5**,[11] and dimethyl 4,5-dimethylphthalate **11**[12] were prepared according to the methods described in the literatures.

Synthesis of p-xylene Bridged Cryptophane α,α′-Bis[4-Hydroxymethy-2-Methoxyphenoxy]-P-Xylene (2)

Vanillyl alcohol **1** (23.1 g, 0.15 mol) and α,α′-dichloro-p-xylene (13.2 g, 0.075 mol) were dissolved in ethanol (120 mL) and 15 mL of aqueous sodium hydroxide (10N) was added. The solution was refluxed for 3 h under a nitrogen atmosphere. Then, the solution was poured into water, and the resulted precipitate was filtered, washed with water and dried. The residue was recrystallized from ethanol to give **2** as colorless needles. Yield 74.9%; mp 118–120°C; MS(EI) m/z 411(M^+ + 1); Anal. Calc. for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38%. Found: C, 70.24; H, 6.50%; ^{1}H-NMR(60 MHz; $CDCl_3$): δ 3.08(s, 2H, OH), 3.85(s, 6H, OCH_3), 4.51(s, 4H, $C\underline{H_2}OH$), 5.10(s, 4H, $ArOC\underline{H_2}$), 6.78–7.13(m, 6H, Ar), 7.47(s, 4H, Ar).

P-Xylene Bridged Cryptophane (Anti-3)

Compound **2** was dissolved in formic acid (2000 mL) and stirred at room temperature for 24 h. The solution was concentrated in vacuo and extracted with chloroform. The extract was washed with water to be neutral, dried and evaporated. The residue was chromatographed on alumina using chloroform as eluent. Then, the crude product was recrystallized from chloroform/methanol to give **Anti-3** as colorless plates. Yield 2.9%; mp > 240°C (dec.); MS(FD) m/z 1122(M^+-1); Anal. Calc. for $C_{72}H_{66}O_{12}\cdot CH_3OH$: C, 75.88; H, 6.05%. Found: C, 75.65; H, 6.04%; ^{1}H-NMR(250 MHz; $CDCl_3$): δ 3.29(d, J = 13.7 Hz, 6H, He), 3.48(s, 18H, OCH_3), 4.52(d, J = 13.7 Hz, 6H, Ha), 5.15(d, J = 14 Hz, 6H, OCH_2-), 5.23(d, J = 14 Hz, 6H, OCH_2-), 6.36(s, 6H, Ar), 6.56(s, 6H, Ar), 6.97(s, 12H, Ar).

Synthesis of the Analogue of p-Xylene Bridged Cryptophane (±)-2,7,12-Trimethoxy-3,8,13-Tris[4-(Methoxycarbonyl)Benzyloxy]-10,15-Dihydro-5H-Tribenzo [a,d,g]-Cyclononene; Analogue of P-Xylene Bridged Cryptophane (rac-6)

c_3-Cyclotriguaiacylene **rac-4** (2.04 g, 5.0 mmol) was dissolved in 150 mL of DMF and then 2.4 mL of 25% aqueous sodium hydroxide was

added. After stirred for 20 min. at room temperature under a nitrogen atmosphere, methyl 4-bromomethyl benzoate **5** (3.44 g, 15.0 mmol) was added and the suspension was agitated for 1 h. Furthermore, 1.2 mL of 25% aqueous sodium hydroxide and **5** (1.72 g, 7.5 mmol) was added and stirred for 1 h. The solution was poured into water, the precipitate was filtered, washed with water and dried. The crude product was recrystallized from benzene-hexane (3:1 v/v) to give **rac-6** as white powders. Yield 79.8%; mp 175–177°C; MS(FD) m/z 853(M^+); Anal. Calc. for $C_{51}H_{48}O_{12}$: C, 71.82; H, 5.67%. Found: C, 71.80; H, 5.79%. ^{1}H-NMR(60 MHz; $CDCl_3$):δ 3.47(d, J = 13.8 Hz, 3H, He), 3.72(s, 9H, OCH_3), 3.95(s, 9H, $COOCH_3$), 4.71(d, J = 13.8 Hz, 3H, Ha), 5.20(s, 6H, $OC\underline{H}_2$), 6.72(s, 3H, Ar), 6.87(s, 3H, Ar), 7.57(d, J = 8.4 Hz, 6H, Ar), 8.13(d, J = 8.4 Hz, 6H, Ar).

Synthesis of O-Xylene Bridged Cryptophane

The Direct Method

α,α′-Bis[4-Hydroxymethyl-2-Methoxyphenoxy]-O-Xylene (7)

Vanillyl alcohol **1** (6.1 g, 0.04 mol), α,α′-dibromo-o-xylene (5.2 g, 0.02 mol) and potassium carbonate (5.5 g, 0.04 mol) were added in acetone (60 mL). The mixture was refluxed for 13 h under a nitrogen atmosphere. The reaction mixture was poured into water and the precipitate was filtered, wash with water and dried. The residue was recrystallized from ethanol to give **7** as colorless needles. Yield 86%; mp 112–112.5°C; MS(EI) m/z 411(M^+ + 1); Anal. Calc. for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38%. Found: C, 69.99; H, 6.46%; ^{1}H-NMR(60 MHz; $CDCl_3$):δ 1.96(s, 2H, OH), 3.85(s, 6H, OCH_3), 4.58(s, 4H, $C\underline{H}_2OH$), 5.30(s, 4H, $ArOC\underline{H}_2$), 6.74–6.87(m, 6H, Ar), 7.20–7.63(m, 4H, Ar).

O-Xylene Bridged Cryptophane (Anti-8)

The precursor **7** (4.0 g, 9.7 mmol) was added to formic acid (2L) and the mixture was stirred at room temperature for 24 h. The solvent was evaporated under vacuo, and the residue was extracted with chloroform. The extract was washed with water, dried and concentrated under reduced pressure. The residue was chromatographed on alumina using chloroform as eluent. The crude product was recrystallized from chloroform-methanol to give **Anti-8** as colorless plates. Yield 3.3%; mp > 220°C(dec.); MS(FD) m/z 1122(M^+-1); Anal. Calc. for $C_{72}H_{66}O_{12}\cdot 0.1CHCl_3$: C, 76.28; H, 5.87%. Found: C, 76.06; H, 5.84%; ^{1}H-NMR(250 MHz; $CDCl_3$):δ 3.49(d, J = 13.75 Hz, 6H, He), 3.68(s, 18H, OCH_3), 4.72(d, J = 13.7 Hz, 6H, Ha), 4.85(d, J = 10.5 Hz, 6H, OCH_2), 5.04(d, J = 10.5 Hz, 6H, OCH_2), 6.72(s, 6H, Ar), 6.88(s, 6H, Ar), 7.34–7.37(m, 6H, Ar), 7.49–7.53(m, 6H, Ar).

The Stepwise Method

4-[1-(2-Chloromethylphenyl)Methoxy]-3-Methoxybenzenemethanol (9)

Vanillyl alcohol **1** (7.7 g, 0.05 mol) and α,α′-dichloro-o-xylene (17.5 g, 0.1 mol) and potassium carbonate (6.9 g, 0.05 mol) were added to acetone (80 mL) and refluxed for 13 h under a nitrogen atmosphere. After concentration under reduced pressure, the residue was chromatographed on silica gel using chloroform/acetone (9:1 v/v) as eluent. The crude product was recrystallized from chloroform-hexane to give **9** as white needles. Yield 38%; mp 83–84°C; MS(EI) m/z 292(M^+); Anal. Calc. for $C_{16}H_{17}O_3Cl$: C, 65.67; H, 5.81%. Found: C, 65.72; H, 5.79%; ^{1}H-NMR(60 MHz; $CDCl_3$): δ 1.68(s br, 1H, OH), 3.90(s, 3H, OCH_3), 4.60(s, 2H, $C\underline{H}_2OH$), 4.78(s, 2H, CH_2Cl), 5.25(s, 2H, $ArOC\underline{H}_2$), 6.82–7.10(m, 3H, Ar), 7.15–7.62(m, 4H, Ar).

(±)-2,7,12-Tris[2-[4-(Hydroxymethyl)-2-Methoxyphenoxymethyl]Benzyloxy]-3,8,13-Trimethoxy-10,15-Dihydro-5H-Tribenzo [a,d,g] Cyclononene (rac-10)

c_3-Cyclotriguaiacylene **rac-4** (408 mg, 1 mmol) was dissolved into 20 mL of DMSO/HMPA (1:1,

v/v) and 0.5 mL of aqueous sodium hydroxide (25 %, 3 mmol) was added. The solution was stirred at room temperature for 10 min. under a nitrogen atmosphere, then compound **9** (0.88 g, 3 mmol) was added and the reaction mixture was agitated at room temperature for 1 h. Furthermore, 0.125 mL of aqueous sodium hydroxide (25%, 0.75 mmol) and **9** (0.22 g, 0.75 mmol) were added and stirred for 1 h. The solution was poured into water and the resulted precipitate was filtered, washed with water and dried. The crude **rac-10** was chromatographed on silica gel using ethyl acetate as eluent. The main fraction was collected and recrystallized from chloroform/hexane to give **rac-10** as white powders. Yield 28%; mp 113–116°C; MS(FD) m/z 1176(M^+-1); Anal. Calc. for $C_{72}H_{72}O_{15}\cdot 0.4CHCl_3$: C, 70.98; H, 5.96%. Found: C, 71.09; H, 6.10%; ^{1}H-NMR(250 MHz; $CDCl_3$):δ 2.00(s, 3H, OH), 3.44(d, 3H, J = 13.5 Hz, He), 3.53(s. 9H, OCH_3), 3.71(s. 9H, OCH_3), 4.51(s, 6H, $C\underline{H_2}OH$), 4.68(d, 2H, J = 13.5 Hz, Ha), 5.14–5.26(m, 12H, $OC\underline{H_2}$-), 6.65–6.88(m, 15H, Ar), 7.24–7.31(m, 6H, Ar), 7.42–7.48(m, 6H, Ar).

O-Xylene Bridged Cryptophane (Anti-8)

The solution of precursor **rac-10** (0.6 g, 0.5 mmol) in dichloromethane (5 mL) was added to formic acid (1 L) and stirred at room temperature for 24 h under a nitrogen atmosphere. After concentration of the solution under vacuo, the residue was extracted with chloroform and chromatographed on alumina using chloroform as eluent. The crude product was recrystallized from chloroform/methanol to give **Anti-8** as colorless plates. Yield 28%; mp > 220°C(dec.); MS(FD) m/z 1122(M^+-1); Anal. Calc. for $C_{72}H_{66}O_{12}\cdot 0.1CHCl_3$: C, 76.28; H, 5.87%. Found: C, 76.06; H, 5.84%; ^{1}H-NMR(250 MHz; $CDCl_3$):δ 3.49(d, J = 13.75 Hz, 6H, He), 3.68(s, 18H, OCH_3), 4.72(d, J = 13.7 Hz, 6H, Ha), 4.85(d, J = 10.5 Hz, 6H, OCH_2), 5.04(d, J = 10.5 Hz, 6H, OCH_2), 6.72(s, 6H, Ar), 6.88(s, 6H, Ar), 7.34–7.37(m, 6H, Ar), 7.49–7.53(m, 6H, Ar).

Syntheses of o-[-Bis(Methoxycarbonyl)]Xylene Bridged Cryptophanes Dimethyl 4,5-Bis(Bromomethyl)Phthalate (12)

To the solution of dimethyl 4,5-dimethylphthalate **11** (20.0 g, 0.09 mol) in tetrachloromethane (200 mL), NBS (32.0 g, 0.18 mol) and benzoyl peroxide (1.0 g, 4 mmol) were added and stirred at 60°C for 22 h. After the residue was filtered off, the filtrate was evaporated and the residue was chromatographed on silica gel using benzene as eluent. The main fraction was collected and recrystallized from chloroform/methanol to give **12** as white needles. Yield 56%; mp 98–99°C; MS(EI) m/z 452(M^+); ^{1}H-NMR(60 MHz; $CDCl_3$):δ 3.97(s, 6H, OCH_3), 4.69(s, 4H, CH_2), 7.80(s, 2H, Ar).

Dimethyl 4-(4-Hydroxymethyl-2-Methoxyphenoxymethyl)-5-Bromomethylphthalate (13)

Vanillyl alcohol **1** (1.69 g, 11 mmol), **12** (8.0 g, 21 mmol) and potassium carbonate (1.53 g, 11 mmol) were added to acetone (65 mL) and refluxed for 5 h under a nitrogen atmosphere. The solution was concentrated under reduced pressure and chromatographed on silica gel using ethyl acetate/chloroform (1:3 v/v) as eluent. The crude product was recrystallized from chloroform/hexane to give **13** as white needles. Yield 57%; mp 161–163°C; MS(EI) m/z 453(M^+); ^{1}H-NMR(250 MHz; $CDCl_3$):δ 3.89(s, 9H, OCH_3), 4.64(s, 2H, $C\underline{H_2}OH$), 4.66(s, 2H, CH_2Br), 5.26(s, 2H, $ArOC\underline{H_2}$), 6.85–6.98(m, 3H, Ar), 7.76(s, 1H, Ar), 7.86(s, 1H, Ar).

(±)-2,7,12-Tris[2-[4-(Hydroxymethyl)-2-Methoxyphenoxymethyl]-4,5-Bis(Methoxycarbonyl)Benzyloxyl-3,8,13-Trimethoxy-10,15-Dihydro-5H-Tribenzo[a,d,g]Cyclononene (rac-14)

To the solution of **rac-4** (0.408 g, 1.0 mmol) in DMF (20 mL), 0.5 mL of aqueous sodium hydroxide (25 %, 3 mmol) was added and stirred at

room temperature for 10 min under a nitrogen atmosphere. Compound **13** (1.35 g., 3 mmol) was added and agitated for 1 h. Furthermore, 0.125 mL of aqueous sodium hydroxide (25 %, 0.75 mmol) and **13** (0.33 g, 0.75 mmol) was added and stirred for 1 h. The reaction mixture was poured into water, and the resulted precipitate was filtered. The residue was chromatographed on silica gel using ethyl acetate as eluent and recrystallized from chloroform/hexane to give **rac-14** as white powders. Yield 39 %; mp 161–163 °C; ^{1}H-NMR(250 MHz; $CDCl_3$):δ 2.68(s, 3H, OH), 3.46(d, J =12.7 Hz, 3H, He), 3.56(s, 9H, OCH_3), 3.69(s, 9H, OCH_3), 3.85(s, 9H, $COOCH_3$), 3.86(s, 9H, $COOCH_3$), 4.50(s, 6H, CH_2OH), 4.67(d, J = 12.7 Hz, 3H, Ha), 5.20(s, 12H, OCH_2-), 6.63–6.98(m, 15H, Ar), 7.88(s, 6H, Ar).

O-[4,5-Bis(Methoxycarbonyl)]Xylene Bridged Cryptophanes (Anti-15a and Syn-15b)

The solution of **rac-14** (0.851 g, 0.56 mmol) in dichloromethane (5 mL) was added to formic acid (1 L) and stirred at room temperature for 24 h under a nitrogen atmosphere. Water (500 mL) was added to the solution and extracted with dichloromethane. The extract was washed with water, dried and concentrated under reduced pressure. The residue was chromatographed on silica gel using dichloromethane/chloroform (1:1 v/v) as eluent. The first fraction was collected and recrystallized from chloroform/methanol to give **Anti-15a** as white powders. Yield 29 %; mp > 300°C(dec.); MS(FD) m/z 1471(M^+); Anal. Calc. for $C_{84}H_{75}O_{24}\cdot CHCl_3$: C, 64.29; H, 4.82 %. Found: C, 64.64; H, 4.97 %; ^{1}H-NMR(250 MHz; CD_2Cl_2): δ 3.50(d, J = 13.5 Hz, 6H, He), 3.70(s, 18H, OCH_3), 3.91(s, 18H, $COOCH_3$), 4.71(d, J = 13.5 Hz, 6H, Ha), 4.88(d, J = 11 Hz, 6H, $ArC\underline{H}_2$), 5.07(d, J = 11 Hz, 6H, $ArC\underline{H}_2$), 6.74(s, 6H, Ar), 6.86(s, 6H, Ar), 7.93(s, 6H, Ar).

The next fraction was collected and recrystallized from chloroform/methanol to give **Syn-15b** as colorless needles. Yield 43.4 %; mp > 300°C(dec.); MS(FD) m/z 1471(M^+); Anal. Calc. for $C_{84}H_{75}O_{24}\cdot CHCl_3$: C, 64.29; H, 4.82 %. Found: C, 63.79; H, 4.93 %; ^{1}H-NMR(250 MHz; $CDCl_3$):δ 3.49(d, J = 13.7 Hz, 6H, He), 3.67(s, 18H, OCH_3), 3.92(s, 18H, $COOCH_3$), 4.68(d, J = 13.7 Hz, 6H, Ha), 4.77(d, J = 12.7 Hz, 6H, $ArC\underline{H}_2$), 5.18(d, J = 12.7 Hz, 6H, $ArC\underline{H}_2$), 6.70(s, 6H, Ar), 6.87(s, 6H, Ar), 8.01(s, 6H, Ar).

Determination of Cryptophane Configurations

The configurations of the synthesized cryptophanes were determined by HPLC analyses using chiralpak-OT(+) column.[5] The chromatographic conditions were follows: column temperature, 5 °C; wavelength, 230 nm; flow rate, 1 mL/min.; and eluent, methanol. The solution of cryptophanes in chloroform was injected into the HPLC. **Anti-3** showed two peaks and the retention times were 23.7 and 39.4 min., respectively. The ratio of the two peaks was 1:1. Therefore, **Anti-3** was determined as a chiral of the racemic molecule. **Anti-15a** and **Syn-15b** showed two and one peaks, respectively. The retention times of **Anti-15a** and **Syn-15b** were 36.5 and 73.0 min. (ratio 1:1), and 39.6 min., respectively. Thus, **Anti-15a** was a racemic molecule, and **Syn-15b** was a meso molecule.

Complexation Studies

The inclusion abilities of these cryptophanes for the alkylammonium cation were measured by ^{1}H-NMR using a Bruker AC250 (250 MHz) spectrometer in CD_2Cl_2:CD_3OD (9:1 v/v). Alkylammonium cations were employed as the picrate salts which were prepared according to the literature.[13] The peak of the undeuterated dichloromethane of the solvent at δ 5.33 ppm was used as the internal standard. All concentrations of the host cryptophanes were ca. 5.0×10^{-3}M and all concentrations of the guest ammonium cations were ca. 1.0×10^{-2}M. The equi-

librium constant, K, and free energy change, ΔG (=-RTlnK), were estimated by the integral ratio between the approximate peak areas of the free and included guest cations. These values were the apparent stability constants in competition with the solvent. In order to study the influence of the solvent on the complexation, the undeuterated solvent (CH_2Cl_2:CH_3OH=9:1) including ca. 20% deuteration (CD_2Cl_2:CD_3OD=9:1) was employed. The incorporated peaks of CH_2Cl_2 and CH_3OH into the hole of these cryptophanes could not observed at any temperature (210–300K). Furthermore, when an excess of CH_2Cl_2 as a guest molecule was added to the solution of cryptophanes in $CDCl_3$, the peaks-due to the incorporated CH_2Cl_2 in ^{1}H-NMR spectra was not observed. Therefore, the complexation with the solvents was neglected based on the consideration of the complexations of these cryptophanes with various ammonium cations. The thermodynamic parameters for the incorporations were calculated using the van't Hoff plots (lnK vs 1/T),[14] in which the K values were from variable temperature ^{1}H-NMR (300–210K). The changes in enthalpy, ΔH, and entropy, ΔS, were determined from the slope (=-ΔH/R) and the intercept (=ΔS/R) of the plot, respectively. The errors in ΔH and ΔS were the estimated standard errors calculated from the least-squares linear regression from the literature.[15]

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References

[1] Vögtle, F. (1976). "Cyclophane Chemistry", John Willy & Sons, 1993. Kauffmann, E., Lehn, J. M., Sauvage, J. P. *Helv. Chim. Acta*, **59**, 1099.
[2] Collet, A. (1987). *Tetrahedron*, **43**, 5725.
[3] The reports of A. Collet et. al. as the pioneers of the investigation of cryptophanes were given in our previous paper: Akabori, S., Miura, M., Takeda, M., Yuzawa, S., Habata, Y., Ishii, T. (1996). *Supramol. Chem.*, **7**, 187.
[4] See ref. 3) and the references therein.
[5] Tambute, A., Canceill, J. and Collet, A. (1989). *Bull. Chem. Soc. Jpn.*, **62**, 1390.
[6] Canceill, J., Cesario, M., Collet, A., Guilhem, J., Lacombe, L., Lozach, B. and Pascard, C. (1989). *Angew. Chem. Int. Ed. Engl.*, **28**, 1246.
[7] Canceill, J., Lacombe, L. and Collet, A. (1986). *J. Am. Chem. Soc.*, **108**, 4230.
[8] The guest cations used were NH_3Et^+, $NH_2Et_2^+$, $NHMe_3^+$ and $NHEt_3^+$ as primary, secondary, and tertiary ammonium cations. It was confirmed that **Anti-3** was slightly complexed with $NH_2Et_2^+$ among the above cations. The upfield shifted peaks of the complexed $NH_2Et_2^+$ (δ 0.58–0.78 ppm) were broadened even at 210K, so that it was not only possible to estimate the equilibrium constant at K < 20.
[9] Brink, M. (1965). *Acta Univ. Lund. II*, **16**, 1.
[10] Canceill, J., Collet, A. and Gottarelli G. (1984). *J. Am. Chem. Soc.*, **106**, 5997.
[11] "Dictionary of Organic Compounds (fifth edition)" ed. by Buckingham, J. and Donaghy, S. M., Vol. 1, pp. 824, Chapman and Hall, New York, (1982).
[12] Alder, K., Muders, R., Krane, W. and Writs, P. (1959). *Ann.*, **627**, 59.
[13] Mitchell, J. Jr. and Bryant, W. M. D. (1943). *J. Am. Chem. Soc.*, **65**, 128.
[14] For examples; see ref. 6), Canceill, J., Lacombe, L. and Collet, A. (1989). *J. Am. Chem. Soc.*, **108**, 4230. Harada, T., Rudzinski, J. M. and Shinkai, S. (1992). *J. Chem. Soc., Perkin trans.* **2**, 2109.
[15] Draper, N. R. and Smith, H. (1966). "Applied Regression Analysis" John Willy & Sons, Inc., New York.