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Calixarene·Tetracyanoethylene Complexes. On the Selective Complexation with Calix[4]arene Conformers

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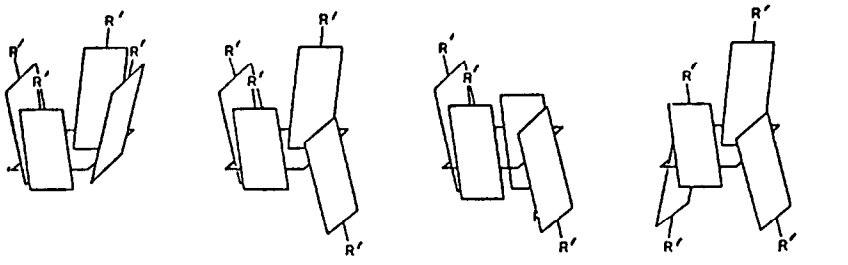
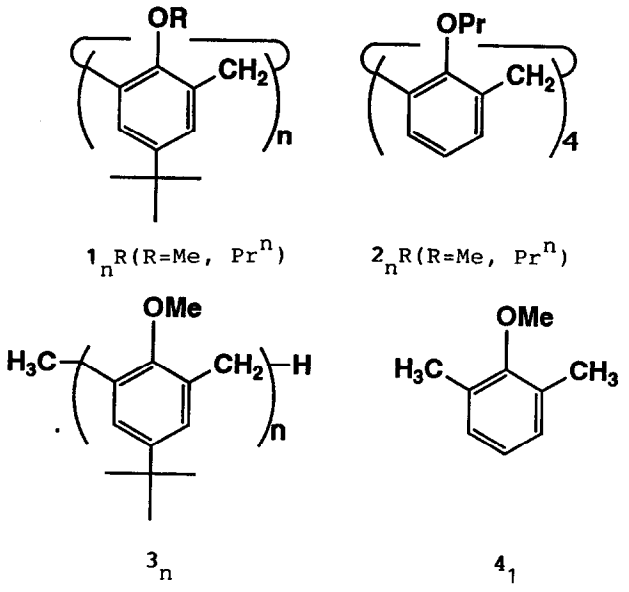
Abstract: The complexation behaviors of O-alkylated p-t-butylcalix[n]arenes ($\mathbf{1}_n$R), calix[n]arenes ($\mathbf{2}_n$R), and their noncyclic analogs were investigated in dichloromethane. All compounds formed a 1:1 complex with TCNE, indicating that complexation with the first TCNE suppresses further complexation with the second TCNE. The λ_{max} values for the CT complexes with $\mathbf{1}_6$R and $\mathbf{1}_8$R (496-498 nm) were comparable with those for the noncyclic analogs, whereas the λ_{max} values for the CT complexes with $\mathbf{1}_4$R shifted to longer wavelengths (525-567 nm): the order (from longer to shorter wavelength) for $\mathbf{1}_4$Pr^n is 1,3-alternate > partial cone > 1,2-alternate > cone. The association constants (K) for $\mathbf{1}_4$R were small in comparion to the λ_{max}. It was shown on the basis of ^{1}H NMR measurements that "out" - $\mathbf{1}_4$R (four alkyl groups are turned outward) is sterically-stable but cannot accept TCNE because of steric crowding on the benzene ring whereas "in" - $\mathbf{1}_4$R (one alkyl group is turned inward) is sterically-unstable but can provide a room to accept TCNE. In $\mathbf{1}_4$R, therefore, the complex formation occurs in conjugation with "out"-to-"in" displacement. This is the first example for the selective CT complexation with calix[4]arene conformers.

Introduction

Calix[n]arenes are cyclic oligomers made from phenol and formaldehyde which belong to the class of [1$_n$]metacyclophanes. Because of the cylindrical architecture it has been expected that they would form host-guest-type solution complexes.[1-4] In the first stage, evidence for solution complexes was sought in organic solvents because conventional calix[n]arenes are soluble to some extent in certain organic solvents. However, the successful studies have been very limited in organic solvents.[5] When host-guest complexes are formed in organic solvents,

inclusion of the guest molecule into the host cavity must overcome solvation of the guest molecule by solvent molecules. This is why the formation of solution complexes is difficult in organic solvents. On the other hand, several lines of unequivocal evidence for the formation of host-guest-type complexes have been obtained in aqueous systems[6-11] where the guest molecule is scarcely solvated by water molecules and thus the complex is stabilized by the hydrophobic force. Then, is it difficult to find evidence for solution complexes in organic solvents ? The foregoing considerations suggest that one should use some secondary force which effectively operates even in organic solvents. It is well-known that cyclophanes form charge-transfer complexes with tetracyanoethylene (TCNE) in organic solvents, the stability of which is basically related to the π-basicity of aromatic rings.[12-15] In small cyclophane systems, the TCNE complexes are specially stabilized by intraannular π-π interactions.[12-15] In unmodified calix[4]arenes and tetramethoxycalix[4]arenes the oxygen-through-the-annulus rotation is allowed, so that the conformation is still mobile.[1-4,16-20] In contrast, introduction of bulky substituents into the OH groups can inhibit the rotation: we found that the Pr^n group is large enough to suppress the rotation.[17,19,21] Thus, four conformational isomers result: they are cone, partial cone, 1,2-alternate, and 1,3-alternate. We were interested in how these conformational isomers act as π-donors for TCNE and if there is some special π-π interaction in the small calix[4]arene ring.





1_nR(R=Me, Pr^n) 2_nR(R=Me, Pr^n)

3_n 4_1

Calix[n]arenes and their noncyclic analogs: "n" denotes the number of benzene units.

Results and Discussion

It is known that the absorption maximum (λ_{max}) and the association constant (K) for TCNE complexes are basically associated with the π-basicity of the aromatic ring.[12-15,22] Thus, electron-donating substituents shift the λ_{max} to longer wavelength and enhance the K: in dichloromethane at 25 °C, for example, λ_{max} and K are 384 nm and 2.00 M^{-1} for benzene, 406 nm and 3.70 M^{-1} for toluene, and 545 nm and 263 M^{-1} for hexamethylbenzene.[22] In the present study, 2,6-dimethyl-4-t-butylanisole (3_1) and 2,6-dimethylanisole (4_1) afforded a new CT band at 489 and 456 nm, respectively, on the addition of TCNE (dichloromethane, 25 °C). From a plot of OD_{489} versus [3_1 (or 4_1)] we could estimate that these compounds form a 1:1 complex with TCNE: K = 270 and 240 M^{-1}, respectively (Table 1). The results indicate that the methoxy group, which shows the electron-donating nature stronger than the methyl group, effectively induces the red shift of the λ_{max} and enhances the K. The pentamer 3_5 showed the similar λ_{max} and K (Table 1). Interestingly, the stoichiometry was 1:1, indicating that complexation of the first TCNE with one anisole unit in 3_5 suppresses complexation of the second TCNE with residual anisole units (negative allostericity). This suggests that five benzene rings in 3_5 are not independent but are influenced by each other.

Unmodified calix[4]arenes favorably adopt a cone conformation.[1-5,23] This is due to the stabilization arising from intramolecular hydrogen-bonding interactions.[1-5,23] In 1_nMe, on the other hand, such effects no longer exist and

Table. 1. Absorption maxima (λ_{max}) and association constants (K) in dichloromethane at 25 °C

	TCNE		I_2
	λ_{max}(nm)	K(M^{-1})	λ_{max}(nm)
$\mathbf{1}_4$Me	566	310	360
$\mathbf{1}_6$Me	498	270	320
$\mathbf{1}_8$Me	496	260	305
Cone-$\mathbf{1}_4$Prn	525	30	363
Partial-cone-$\mathbf{1}_4$Prn	553	180	363
1,2-Alternate-$\mathbf{1}_4$Prn	546	140	361
1,3-Alternate-$\mathbf{1}_4$Prn	567	280	362
Cone-$\mathbf{2}_4$Prn	522	230	360
1,3-Alternate-$\mathbf{2}_4$Prn	534	280	359
$\mathbf{3}_1$	489	270	305
$\mathbf{3}_5$	498	240	352
$\mathbf{4}_1$	456	240	305

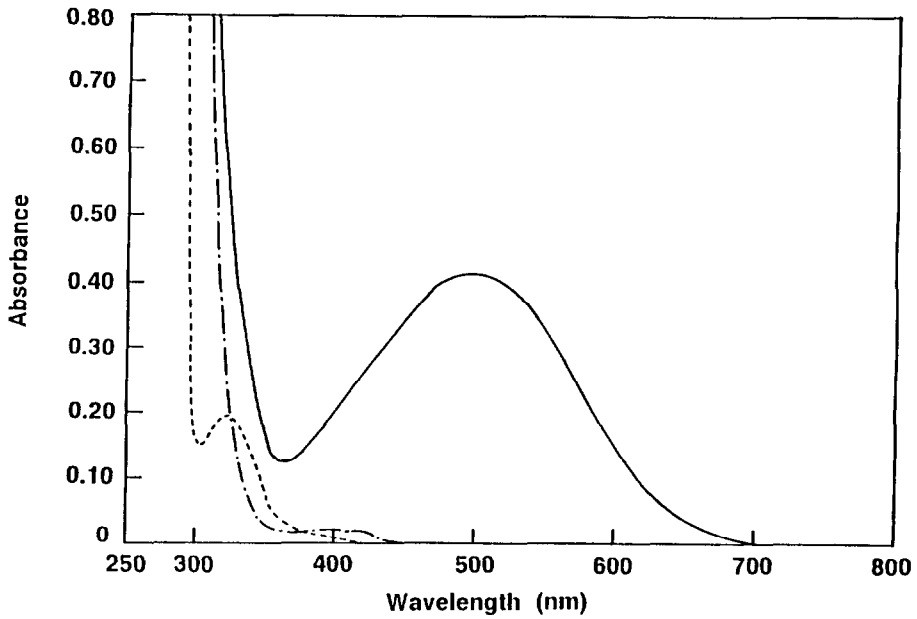


Figure 1. Absorption spectra of $\mathbf{1}_6$Me, TCNE, and CT complex in dichloromethane at 25 °C: - - - $\mathbf{1}_6$Me (1.5 x 10 mM), — · — TCNE (1.5 x 10 mM), —— CT complex ([$\mathbf{1}_6$Me] = [TCNE] = 1.5 x 10 mM)

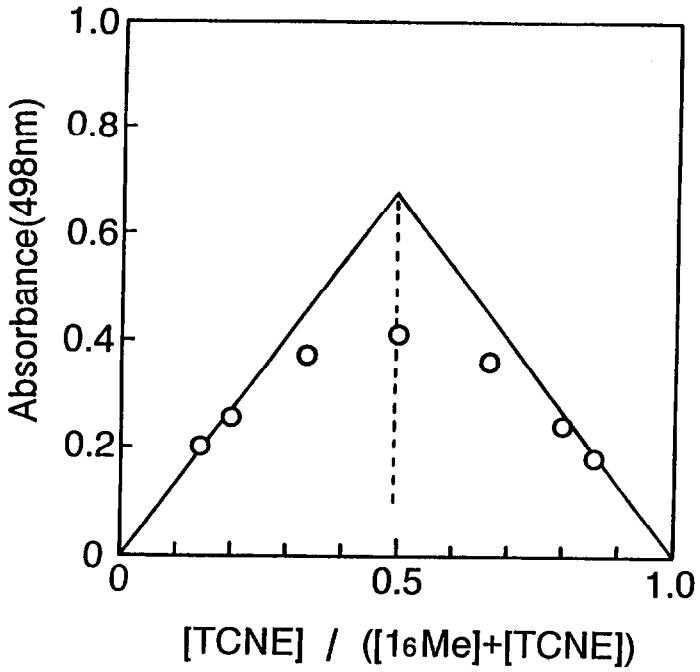


Figure 2. Continuous variation plot for $\mathbf{1}_6$Me + TCNE ([$\mathbf{1}_6$Me] + [TCNE] = 3.0 x 10 mM (constant))

therefore they are conformationally mobile.[16-20] Since the solubility of $\mathbf{1}_n$Me is inferior to that of $\mathbf{3}_n$, we employed a continuous variation method for determining the stoichiometry and association constants.[24] The typical absorption spectra and plots are illustrated in Figures 1 and 2, respectively. The results are summarized in Table 1.

The stoichiometry for $\mathbf{1}_n$Me was all 1:1. The result indicates that complexation of TCNE and $\mathbf{1}_n$Me is also subjected to the negative allostericity. The K values (260-310 M^{-1}) are comparable with or slightly greater than that for $\mathbf{3}_1$ (270 M^{-1}). We noticed, however, that the CT band for $\mathbf{1}_4$Me appears at unusually longer wavelength region (566 nm, 60-70 nm red shift from λ_{max} for $\mathbf{1}_6$Me and $\mathbf{1}_8$Me). We thus considered that this phenomenon would merit further investigation.

Although $\mathbf{1}_4$Me is conformationally mobile, the rate of interconversion between conformational isomers is slow enough to discretely observe four isomers by ^{1}H NMR spectroscopy.[17-20] The ^{1}H NMR study of $\mathbf{1}_4$Me in CD_2Cl_2 at -25 °C established that the conformer distribution consists of 18.8% cone, 74.0% partial cone, 7.2% 1,2-alternate, and no 1,3-alternate. A continuous variation plot for $\mathbf{1}_4$Me

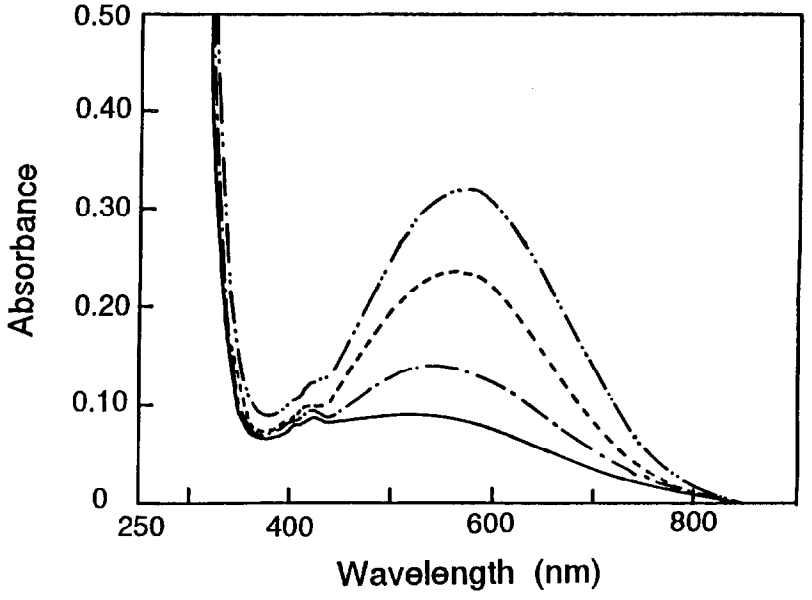
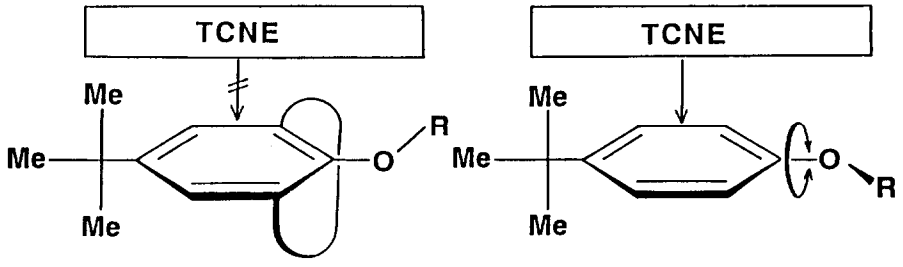


Figure 3. Absorption spectra of conformational isomers of 1_4Pr (dichloromethane, 25 °C): [1_4Pr^n] = [TCNE] = 3.0 x 10 mM, —— cone, - - - partial cone, – – –1,2-alternate, –·· –1,3-alternate



Steric hindrance in cone-1_4R·TCNE complex

3_1·TCNE complex

showed the 1:1 stoichiometry. This "apparent" stoichiometry probably reflects the complexation with major species, partial-cone-1_4Me. We previously found that in contrast to conformationally-mobile 1_4Me, 1_4Pr^n is conformationally immobile.[17-19] This implies that the n-propyl group is bulky enough to inhibit the oxygen-through-the-annulus rotation. To specify the complexation properties of each conformational isomer we synthesized four isomers of 1_4Pr^n according to the

literature[21] and estimated the stoichiometry and K. We also synthesized cone-$\mathbf{2}_4$Prⁿ and 1,3-alternate-$\mathbf{2}_4$Prⁿ in order to estimate the effect of the p-t-butyl group. The typical absorption spectra are shown in Figure 3. The four isomers of $\mathbf{1}_4$Prⁿ and the two isomers of $\mathbf{2}_4$Prⁿ all showed the 1:1 stoichiometry. However, they showed several unique properties which probably stem from the small cyclic calix[4]arene structure: that is, (i) as observed for $\mathbf{1}_4$Me (λ_{max} 566 nm), the CT bands appeared at longer wavelength (522-567 nm), the λ_{max} for $\mathbf{1}_4$Prⁿ being in the order (from longer to shorter wavelength) of 1,3-alternate > partial cone > 1,2-alternate > cone, (ii) the K value for $\mathbf{1}_4$Prⁿ is in the order (from large to small K) of 1,3-alternate > partial cone > 1,2-alternate > cone, which is in line with the order of λ_{max}, and (iii) the K value for cone-$\mathbf{1}_4$Prⁿ is exceptionally small (about one-ninth of 1,3-alternate-$\mathbf{1}_4$Prⁿ) and the CT band is extremely weak, whereas the K value for cone-$\mathbf{2}_4$Prⁿ is comparable with that for 1,3-alternate-$\mathbf{2}_4$Prⁿ and the strength of the CT band is normal.

Facts (i) and (ii) can be explained on the same basis: that is, the aromatic ring with the high π-basicity possesses the high association ability. This implies that calix[4]arenes possess the π-basicity higher than calix[6]arenes and calix[8]arenes. We confirmed this through CT complexation with I_2 which is scarcely affected by steric hindrance.[15] As shown in Table 1, the λ_{max} values for $\mathbf{1}_4$Me, $\mathbf{1}_4$Prⁿ, and $\mathbf{2}_4$Prⁿ appear at longer wavelenth region. We now consider that as observed for small cyclophanes,[12-14] the π-electrons in calix[4]arenes repulse each other, enhancing the π-donation ability to electron-deficient guest molecules.

Fact (iii) clearly supports the view that the p-t-butyl groups in $\mathbf{1}_4$Prⁿ provide serious steric hindrance on the formation of the CT complex. Then, how can we explain the fact that $\mathbf{3}_1$, which also has both a methoxy and a p-t-butyl group, is not subjected to such steric hindrance ? We previously found on the basis of a computational study that cone-$\mathbf{1}_4$R having the R group turned "outward" is more stable than that having the R group turned "inward".[18,25] In cone-$\mathbf{1}_4$Me, for example, the steric energy for "out"-$\mathbf{1}_4$Me (four methyl groups are turned outward) is lower by 4.59 kcal mol^{-1} than that for "in"-$\mathbf{1}_4$Me (one methyl group is turned inward). This implies that the R groups in cone-$\mathbf{1}_4$R are mostly placed at the exo-annulus position. As a result, not only the p-t-butyl group but also the R group interferes with the approach of TCNE. On the other hand, the Me group in $\mathbf{3}_1$ can rotate and therefore does not interfere with the approach of TCNE.

Here, a question remains as to the serious discrepancy between λ_{max} and K. Why does cone-$\mathbf{1}_4$Prⁿ result in the red-shifted λ_{max} in spite of the small K ? This question is extended to other $\mathbf{1}_4$Prⁿ's because K values are still small in comparison to their red-shifted λ_{max} although the discrepancy is not so obvious as in cone-$\mathbf{1}_4$Prⁿ. To answer this question we measured ^{1}H NMR spectra of $\mathbf{1}_4$R in the absence and the presence of TCNE. In Figure 4 the change in the chemical shift (δ) induced by the

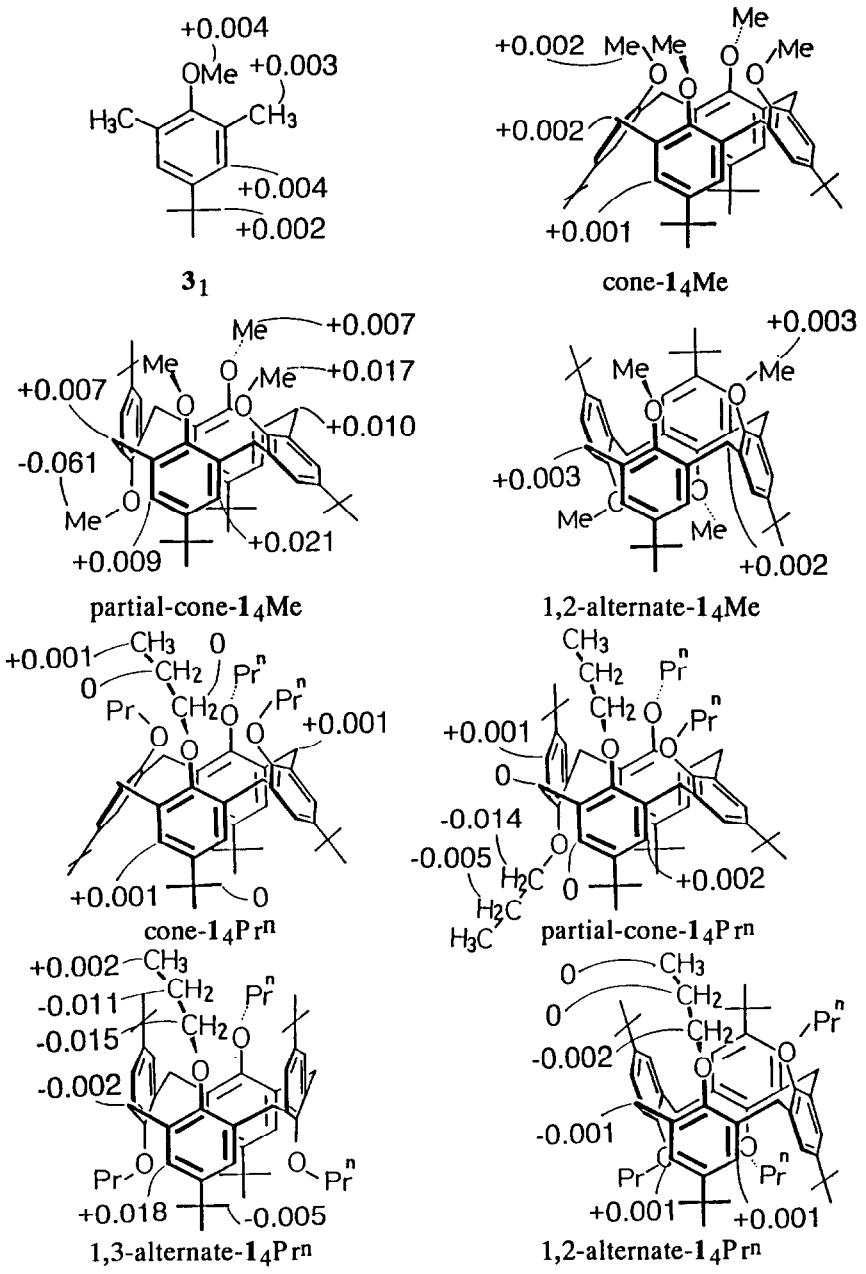


Figure 4. Change in the chemical shift induced by the addition of TCNE (CD_2Cl_2, 400MHz, [$\mathbf{3}_1$], [$\mathbf{1}_4$Pr^n] = 25 °C, [$\mathbf{1}_4$Me] = -35 °C, [$\mathbf{3}_1$] = 5.0 mM, [$\mathbf{1}_4$Me] = [$\mathbf{1}_4$Pr^n] = 5.0 mM, [TCNE] = 5.0 x 10 mM)

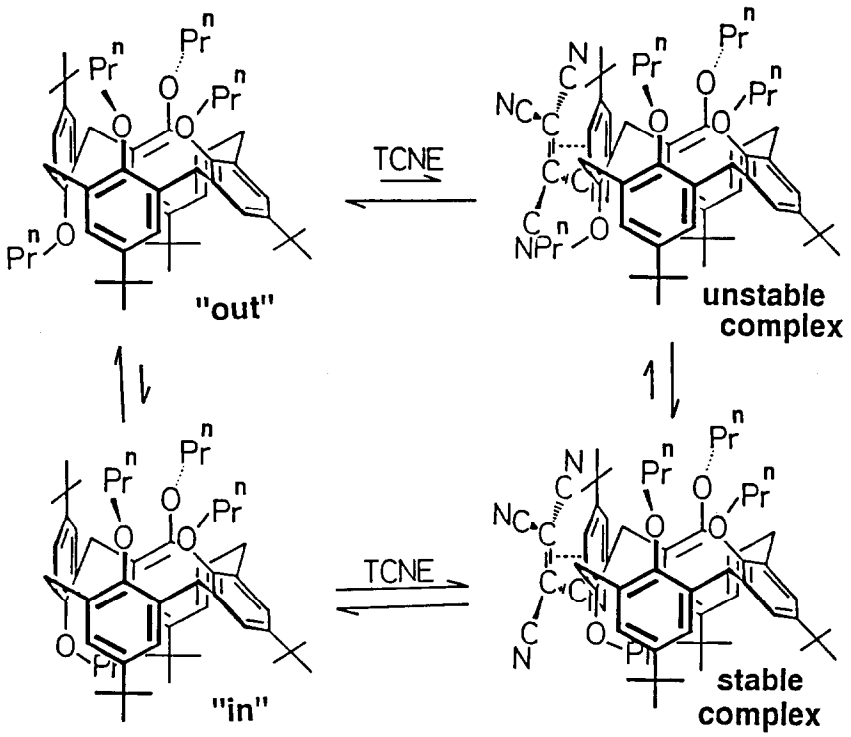


Figure 5. "Out"-"in" equilibrium and TCNE complexation equilibrium

addition of TCNE is recorded (+ denoted the downfield shift whereas - denotes the upfield shift). On the addition of TCNE the δ in $\mathbf{3}_1$ moved slightly to lower magnetic field. This reflects the electron-deficiency of the benzene ring induced by complexation with TCNE. The significant change in δ was not observed for cone-$\mathbf{1}_4$Pr^n. In partial cone-$\mathbf{1}_4$Pr^n and 1,3-alternate-$\mathbf{1}_4$Pr^n, in contrast, the δ for certain n-propyl protons moved to *"higher magnetic field"*. The unusual upfield shift is rationalized in terms of "out"-to-"in" displacement of the Pr^n group: in "in"-$\mathbf{1}_4$Pr^n the n-propyl protons strongly undergo the anisotropic effect of the benzene ring current. The finding substantiates the following complexation manner (Figure 5). TCNE cannot associate, because of steric hindrance, with sterically-stable "out"-$\mathbf{1}_4$Pr^n. "In"-$\mathbf{1}_4$Pr^n is sterically-unstable but provides a room for the CT complex formation. Thus, CT complexation occurs when the energy loss (mainly ΔS loss) caused by "out"-to-"in" displacement is fully compensated by the energy gain (mainly ΔH gain) caused by the association with TCNE. The similar trend is observed for cone-$\mathbf{1}_4$Me and partial-cone-$\mathbf{1}_4$Me which exist under an equilibrium in solution but can be discriminated by ^{1}H NMR spectroscopy.[16-20] The δ values for cone-$\mathbf{1}_4$Me were scarcely affected by the addition of TCNE whereas the methyl protons in an inversed phenyl unit of partial-cone-$\mathbf{1}_4$Me shifted to higher magnetic field.

We can now elucidate the discrepancy between λ_{max} and K in $\mathbf{1}_4$R. The aromatic rings in $\mathbf{1}_4$R have the high π-basicity but are hard to associate with TCNE because of steric hindrance. Thus, the K values, which are estimated on the basis of the total concentration of $\mathbf{1}_4$R, are apparently small. Once "out"-to-"in" displacement takes place, the strong CT complex is formed, resulting in red-shifted λ_{max}. Presumably, "out"-to-"in" displacement is most difficult in cone-$\mathbf{1}_4$R because in the cone conformation four RO groups are sterically crowded on the narrow lower rim of calix[4]arenes.

In conclusion, the present study shows that (i) the π-basicity of $\mathbf{1}_4$R is higher than that in $\mathbf{1}_6$R, $\mathbf{1}_8$R, and noncyclic analogs, (ii) the magnitude of the association constants reflects the conformational difference in $\mathbf{1}_4$R, and (iii) the λ_{max}-K correlation is not observed because of a concomitant "out"-"in" equilibrium. We are currently investigating these problems on the basis of a computational method.

Experimental

Materials

Compounds $\mathbf{1}_n$Me were synthesized according to the literatures.[26,27] The syntheses of four conformational isomers of $\mathbf{1}_4$Pr^n were reported previously.[19,21]

25,26,27,28-Tetrapropoxycalix[4]arene ($\mathbf{2}_4$Pr^n). Cone-$\mathbf{2}_4$Pr^n was synthesized from calix[4]arene-25,26,27,28-tetrol and propyl bromide via an O-tri-substituted intermediate. The operation method was described previously[28]: mp 197-199 °C, yield 61%; ^{1}H NMR ($CDCl_3$) δ 0.92 (CH_3, t (J=7.5 Hz), 3H), 1.85 ($CH_2(CH_3)$, m, 2H), 3.06 and 4.37 ($ArCH_2Ar$, d each (J=13 Hz), 1H each), 3.77 (OCH_2, t (J=7.5 Hz), 2H), 6.49-5.56 (ArH, m, 3H). Anal. Calcd for $(C_{10}H_{12}O)_4$: C, 81.04; H, 8.16%. Found: C, 81.14; H, 8.18%. 1,3-Alternate-$\mathbf{2}_4$Pr^n was synthesized from calix[4]arene-25,26,27,28-tetrol and propyl bromide in the presence of Cs_2CO_3. The operation method is similar to that described for the synthesis of 1,3-alternate-$\mathbf{1}_4$Pr^n[19,21]: mp 251-252 °C, yield 33%; ^{1}H NMR ($CDCl_3$) δ 0.84 (CH_3, t (J=7.5 Hz), 3H), 1.58 ($CH_2(CH_3)$, m, 2H), 3.45 (OCH_2, t (J=7.5 Hz), 2H), 3.52 ($ArCH_2Ar$, s, 2H), 6.56 and 6.91 (ArH, t and d (J=7.6 Hz), 1H and 2H). Anal. Calcd for $(C_{10}H_{12}O)_4$: C, 81.04; H, 8.16%. Found: C, 80.76; H, 8.15%.

2,6-Bis{[2-methoxy-3-(2-methoxy-3-methyl-5-t-butylphenyl)methyl-5-t-butylphenyl]methyl}-4-t-butylanisole ($\mathbf{3}_5$). This compound was synthesized from 2,6-bis{[2-hydroxy-3-(2-hydroxy-3-methyl-5-t-butylphenyl)methyl-5-t-butylphenyl]methyl}-4-t-butylphenol[29] and MeI in the presence of K_2CO_3 and recrystallized from chloroform-methanol. The method is similar to that described for methylation of calixarenes[19,21,26,27]: mp 121-123 °C, yield 85%; ^{1}H NMR ($CDCl_3$) δ 0.88-1.40 (CH_3 in Bu^t, m, 45H), 2.29 ($ArCH_3$, s, 6H),

3.40-3.75 (OCH_3, m, 15H), 3.92-4.28 ($ArCH_2Ar$, m, 8H), 7.12-7.73 (ArH, m, 10H). Anal. Calcd for $C_{61}H_{84}O_5$: C, 81.65; H, 9.44%. Found: C, 81.63; H, 9.63%.

Spectroscopic Measurements

The apparatus used for the measurement of ^1H NMR spectra was a JEOL GX-400 (400 MHz).

The continuous variation method was employed to estimate the stoichiometry and K in dichloromethane at 25 °C. The concentration of [$\mathbf{1}_n$R, $\mathbf{2}_n$R, $\mathbf{3}_n$, or $\mathbf{4}_1$] + [TCNE] was maintained constant (3.0 x 10 mM): only for $\mathbf{1}_8$Me, the concentration was reduced to 1.5 x 10 mM because of the high absorbancy arising from eight benzene units. The K values for a 1:1 complex were determined by the equation,

$$K = \frac{A / A_{ext}}{[1-(A / A_{ext})]^2 C}$$

where A and A_{ext} denote the observed absorbance and the absorbance for a complex (e.g., in Figure 2 the absorbance of a point of intersection at [TCNE]/([$\mathbf{1}_6$Me] + [TCNE]) = 0.5).[30]

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