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The unique properties observed for the unsymmetrical macrocyclic compounds with the highly distorted structure

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Abstract—A new class of aza-macrocycles with the highly distorted structure was found to exhibit unique properties. These macrocycles react with various lithium salts to form lithium complexes and their lithium complexation reactions depend on a substituent on the macrocyclic ring; slower rates and larger equilibrium constants were observed for the macrocycle with a bulkier substituent. The irradiation of these macrocycles by UV light was found to lead to the isomerization, and the photoisomerization rate of macrocycle with the bulky substituent was much faster. The highly distorted structure of these macrocycles makes it much easier to change the conformation of macrocyclic skeleton and these macrocycles have a variety of conformations. The factors to govern this conformational change were therefore explored. The solvent effect was examined by ^{1}H NMR spectroscopy, because these macrocycles have a strong intramolecular hydrogen bond in the ring. As a result, the solvent was found to have a big effect on the ^{1}H NMR spectra of macrocycles that could be explained in terms of the conformational change of macrocycle. This finding suggests the solvent to be an important way of controlling the conformation.

1. Introduction

The macrocyclic compounds including pyridines have become a widely used complexing agents for various metal ions. Furthermore, a variety of attractive abilities of these macrocycles have been found in the process of exploring their chemical and physical nature. For example, a pronounced feature is that some macrocycles are capable of exhibiting high selectivity for binding to specific alkali metal ion.[1,2]

We recently reported the syntheses and properties of new macrocycles bearing two bipyridine moieties and their metal complexes.[3–5] The evolution of this new family of macrocycles involves the color switching property of macrocycle **1**–Zn complex to provide the possibility that a new switching system for display may be developed.[6–8] This color switching is that the color of macrocycle **1**–Zn complex solution is controlled easily by the solvent or the acid–base system.[3] This property of macrocycle **1**–Zn complex has been turned to further investigation to explore the essential nature of metal free macrocycle **1** itself, because the detailed properties of metal free macrocycle **1** have not been elucidated yet.

The most remarkable structural feature of metal free macrocycle **1** is the hybrid structure consisting of planar and nonplanar moieties. Owing to the strained macrocyclic ring, macrocycle **1** is expected to exhibit a diversity of properties with the variation of chemical and physical environment. Thus, our approach to elucidate the properties of metal free macrocycle **1** is to explore more detailed behavior under various conditions. Another approach of carrying out this research is to synthesize the structurally similar derivatives of macrocycle **1** and to compare their properties. We therefore synthesized new macrocycle **2** with benzyl group by using a new synthetic method, while macrocycle **1** has dodecyl group. Since these groups interact with the macrocyclic skeleton from the upper side of the plane of macrocycle, the specific ability of macrocycles can be explored by comparing the two macrocycles **1** and **2**.

As previously reported, we had found the conformational changes of the macrocyclic skeleton with the temperature by the variable-temperature ^{1}H NMR spectral experiments.[3] Further investigation of this finding is needed, because there is a possibility of providing the clue to know more detailed properties of new macrocycles. Specifically, it is extremely important to determine some factors to govern the conformational change of macrocyclic skeleton. Our approach of finding these factors is to study the ^{1}H NMR spectral changes under the wide range of conditions, although the exact

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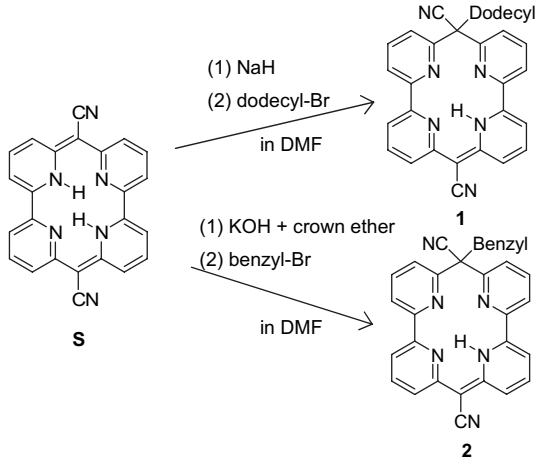
structure of macrocycle is, of course, not directly measurable. One of the typical ideas to change the ^{1}H NMR spectrum is believed to be the solvent effect, because macrocycle **1** has the strong intramolecular hydrogen bond and this hydrogen bond may be affected by the property of solvent.[9] Attempts were therefore made, and as a result, the solvent was found to have a big effect on the spectrum, indicating that the solvent is one of the some factors to induce the conformational changes.

Herein, we report the lithium complexation reactions of macrocycles **1** and **2**, their photochemistry, and the results obtained from the ^{1}H NMR and UV–visible spectral measurements of macrocycles **1** and **2** in various solvents. Additionally, the possibility of systematically controlling the conformation of macrocycle **1** has also been discussed.

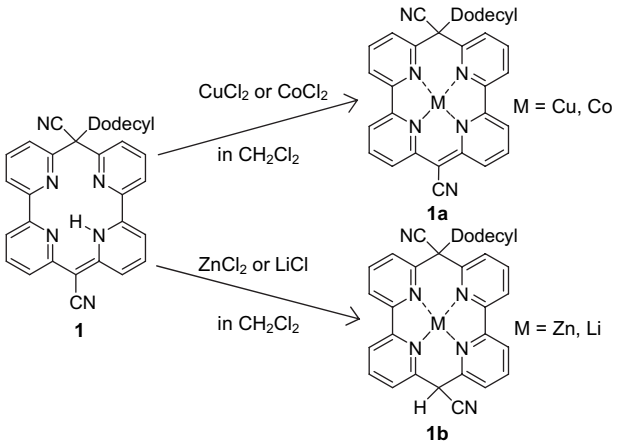
2. Results and discussion

One approach of elucidating more detailed properties of macrocycle **1** with a dodecyl group on the macrocyclic ring is to synthesize a structurally similar compound with the electronic and stereochemical differences. We decided to replace dodecyl group by benzyl group as a substituent on the macrocyclic ring, because the benzyl group is bulkier and has the π electrons capable of conjugating to adjacent groups. We reported the synthetic method of macrocycle **1** with one dodecyl group by using NaH,[3] but macrocycle **2** with one benzyl group was unable to be synthesized by the same method. We therefore tried to develop a new synthetic method. Finally, macrocycle **2** was able to be synthesized by using crown ether and KOH as phase transfer catalysts. These synthetic methods are shown in Scheme 1.



Scheme 1.

As previously reported, the reactions of macrocycle **1** with metal salts are extremely specific;[3] as shown in Scheme 2, the reactions of macrocycle **1** with $CuCl_2$, $CoCl_2$, $FeCl_2$, $EuCl_3$, and $SnCl_2$ in dichloromethane form the macrocycle–metal complexes **1a** with alkyl-di(2-pyridyl)acetonitrile and 2-pyridyl-2-(1*H*)-pyridylideneacetonitrile moieties. In contrast, the reaction of macrocycle **1** with zinc or lithium salt in dichloromethane afforded complex **1b** with two di(2-pyridyl)acetonitrile moieties.



Scheme 2.

The formation of complex **1b** is permitted under limited reaction conditions, and then this reaction is extremely unique. Accordingly, we selected this unique reaction to elucidate the properties of these macrocycles (**1** and **2**) and studied this reaction in detail. Furthermore, the studies on the photochemistry about macrocycles **1** and **2** were carried out, because similar hydrogen transfers were found to occur under irradiation by the light.

2.1. The reactions of macrocycles 1 and 2 with lithium salts in acetonitrile

The formation reaction of complex **1b** with the hydrogen atom on the ring was found to proceed not only in dichloromethane, but also in acetonitrile. Additionally, the solubility of lithium salt in acetonitrile is much higher. The studies on the complexation reactions of macrocycles **1** and **2** with lithium salts were therefore carried out in acetonitrile. The lithium salts used in this experiment are LiBr, LiI, and $LiClO_4$. The reaction rates in this homogeneous system were measured by using the decrease of absorption at 355 nm of macrocycles with time. The initial reaction rate and equilibrium constants obtained in this experiment are summarized in Table 1. The noticeable fact is that all of the rates of macrocycle **2** with benzyl group are slower than those of macrocycle **1** with dodecyl group, but all of the equilibrium constants of macrocycle **2** are much larger than those of macrocycle **1**. One possible explanation for these results is as follows. The benzyl group is bulkier compared with the dodecyl group, and the distortion of macrocyclic skeleton

Table 1. The initial reaction rate constants of macrocycles with lithium salts and their equilibrium constants in acetonitrile

	LiBr	LiI	$LiClO_4$
Initial rate constant k ($l\,s^{-1}\,M^{-1}$)[a]			
Macrocycle **1**	23	43	33
Macrocycle **2**	20	30	9
Equilibrium constants K[b] (M^{-1})			
Macrocycle **1**	120	63	17
Macrocycle **2**	990	300	81

[a] The reaction rate during initial 10 s in the following reactions. Macrocycle + LiX $\xrightarrow{k}$ [macrocycle Li^+]X^-, $X^- = Br^-$, I^-, ClO_4^-.
[b] The equation of equilibrium constant is as follows: K = [macrocycle Li^+X^-]/[macrocycle][LiX].

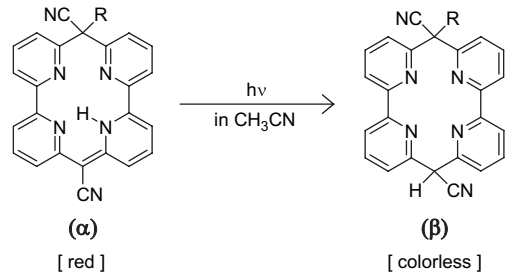
of macrocycle **2** is larger than that of macrocycle **1**. At the initial step of lithium complexation reaction, the high steric hindrance makes the complexation reaction of macrocycle **2** more difficult. As a result, the initial reaction rates of macrocycle **2** with bulkier group become slower compared with those of macrocycle **1**. However, once the complexation reactions of macrocycle **2** with lithium salts are completed, macrocycle **2**–lithium complexes (**2b**) are stabilized greatly, because the distortion of macrocyclic ring is released by the conversion from the planar structure of the 2-pyridyl-2-(1*H*)-pyridylideneacetonitrile moiety of metal free macrocycle **2** into the nonplanar structure of the di-(2-pyridyl)acetonitrile moiety formed by lithium complexation. The bulkier substituent in complexes **2b** would also prevent reverse conversion from nonplanar structure to planar structure. Eventually, the bulkier group makes the lithium complexation slower due to the steric effect, and the equilibrium constants of complexes **2b** with bulkier group are much larger due to the relaxation of strain induced by conformational change of macrocyclic skeleton and the prevention from nonplanar structure to planar structure with higher tension.

This result obtained by lithium complexation reactions suggests an important fact that the distortion created by planar and nonplanar moieties of macrocyclic skeleton would lead to the unique reaction observed for a new class of macrocycles.

2.2. Photoisomerization of macrocycles 1 and 2 induced by the UV light

Further investigation to obtain the profound knowledge about unique characteristic is needed. One of the methods that could disturb this strained structure is to excite the macrocycles by the light. The studies on the photochemistry of these macrocycles were therefore carried out. When the acetonitrile solution of macrocycle **2** was exposed to the UV light, the color of this solution changed from red to colorless. This colorless solution did not return red even under dark. The ^{1}H NMR and UV–visible spectra of this solution were measured to explore the reason why the color of solution changes upon photoirradiation. The ^{1}H NMR spectrum of macrocycle **2** in CD_3CN showed a peak at 15.71 ppm, which is assigned to the hydrogen atom in the core of macrocyclic ring. After photoirradiation, this peak disappeared and a new peak appeared at 4.38 ppm. Two absorptions at 275 and 350 nm in the UV–visible spectrum disappeared with time under photoirradiation. By infrared spectral measurements, the peak intensity at 2180 cm^{-1} assigning to the 2-pyridyl-2-(1*H*)-pyridylideneacetonitrile moiety was found to decrease with exposure to the UV light. As described in previous paper, these spectroscopic results indicate the hydrogen atom in the core of macrocyclic ring to move to the ring. That is, the photoisomerization from α to β occurs as shown in Scheme 3 when macrocycle **2** is exposed to the UV light.

The fact that the light excitation induces the isomerization of macrocycle **2** would be due to the difference in conformational energy between α and β states. The α state is considered to be an energetically disfavored conformation, because the macrocycle of α state has the highly distorted structure owing to both planar moiety [B] and nonplanar moiety [A] in the macrocyclic ring. The light excitation would induce the isomerization of macrocycle **2** from α state with higher conformational energy to β state with lower conformational energy.



Scheme 3.

This photoisomerization was also observed for the macrocycle **1** with dodecyl group. Thus, the initial rate constants of photoisomerization were measured by using the acetonitrile solutions (5.2×10^{-5} M) of macrocycles **1** and **2**. The rate constants for macrocycles **1** and **2** were 0.6 and 2.5 h^{-1}, respectively, and the rate of macrocycle **2** with benzyl group was faster. This would be due to the fact that the conformational energy of macrocycle **2** with a bulkier group becomes higher than macrocycle **1** owing to the interaction between the distorted macrocyclic skeleton and the bulky benzyl group. This finding also suggests the unique behavior observed for macrocycles **1** and **2** to be due to the highly distorted structure.

2.3. Macrocycles 1 and 2 as a switching molecule

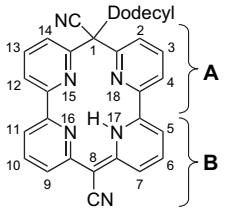
As reported previously, macrocycle **1**–Zn complex seems to be a nice example of an area known as color switching molecules.[6–8] In particular, our strategy for this synthesis was new in that the switchable property of macrocycle is caused by a labile hydrogen atom of the macrocycle.[3] Since metal free macrocycles **1** and **2** themselves have a labile hydrogen atom, we have been intrigued with the possibility of exhibiting the property as a switching molecule. As described in the above section, the α state shows red color, while the β state shows colorless. If there are some methods of inducing the interchange between α state and β state, we are able to make a new system of switching. Though we tried to develop the convenient method, we were unable to find this, because of higher stability of β state. Thus, we turned our attention to other direction and decided to examine more detailed property of macrocycle **1** of α state.

Macrocycle **1** has unsymmetrical and distorted structure, which makes it much easier to produce conformational changes of macrocycle by various factors. The conjugation system of macrocycle can be varied by the conformational change and the color of this system can be changed by the variation of the conjugation system. Thus, the conformation control of this macrocycle **1** is believed to play a central role in controlling the spectroscopic properties of macrocycle **1** of α state. That is, the key to exhibit the switching performance is to control the conformation of macrocycle and this system would enable us to construct a new switching system. Thus, the search for factors capable of controlling

the conformation of macrocycle **1** itself is of great importance.

2.4. The effect of solvent on ^{1}H NMR spectrum of macrocycle 1

As is stated above, macrocycle **1** consists of alkyl-di(2-pyridyl)acetonitrile moiety (A part) and 2-pyridyl-2-(1*H*)-pyridylideneacetonitrile moiety (B part), which are shown in Scheme 4.



Scheme 4.

The latter B has a hydrogen atom between two nitrogen atoms of two pyridine moieties. The ^{1}H NMR value of this hydrogen atom (H_{17}) of macrocycle **1** in $CDCl_3$ is 15.65 ppm, and this peak position is extremely low. As described in our earlier publication,[3] this value means that this peak corresponds to the proton signal due to the strong intramolecular hydrogen bond, indicating strong interaction among N–H–N. This hydrogen atom (H_{17}) is labile and may be very sensitive to the chemical environment. As described in the above section, the isomerization (tautomerism) between α and β states does not occur under usual conditions, because the β state is greatly stable rather than the α state; the isomer of β state is unable to return to that of α state. Thus, there is a possibility that the geometry of B part of α state is controlled by this bridging hydrogen atom. If the interaction between the hydrogen atom and two nitrogen atoms is varied by some factors, the overall geometry of macrocycle **1** itself would be changed. There are a lot of ideas about how to change this interaction. One of the typical ideas would be the solvent, because the hydrogen bond is generally believed to be affected strongly by the solvent, and the hydrogen atom itself is very sensitive to the solvent.[9] We therefore decided to focus on the solvent effect and this effect was examined by ^{1}H NMR spectroscopy.

The ^{1}H NMR spectra of macrocycle **1** were measured in various solvents and their spectra are presented in Figure 1. The proton resonances for the macrocyclic ring in $CDCl_3$ (dielectric constant, ε=4.81) exhibited the signals having two distinct parts (Fig. 1(1)[10]); the signals at lower field (7.68–7.93 ppm) were assigned to the protons of two pyridine moieties of the A part in Scheme 4, and the proton signals of the B part appeared at higher field (7.15–7.61 ppm).

Now, this Figure 1 shows that the solvent has a big effect on the ^{1}H NMR spectrum. This solvent effect produces the shifts and the changes of spectral pattern over the previously reported macrocyclic compounds. Data in $CDCl_3$, that is presented in Figure 1(1), show that these types of signals show an AMX pattern for the protons of the A part and an ABX pattern for the protons of the B part. Changing the solvent to CD_2Cl_2 (ε=8.93) caused an unexpectedly large shift in the peaks of ^{1}H NMR spectrum; the proton signals of H_5 (H_{11}) and H_6 (H_{10}) were separated (Fig. 1(2)) and the type of proton signals of the B part then changed from ABX pattern to AMX pattern. Both A and B parts of macrocycle **1** in CD_2Cl_2 showed the signal type of the AMX pattern. In addition, when the solvent was changed to CD_3CN and CD_3OD, we were able to get something very different than what we expected, that is, the proton signals of H_3 (H_{13}) and H_4 (H_{12}) appeared at similar positions. This means that the type of proton signals of the A part in CD_3CN or in CD_3OD (Fig. 1(3) and (4)) changes from AMX pattern to AB_2 or ABX pattern. This is the reverse case of change for the B part from $CDCl_3$ to CD_2Cl_2.

The signal of H_{17} proton, which is located between two nitrogen atoms of two pyridine moieties of the B part, was shifted to higher field as the polarity of solvent increased. This suggests that the smaller the polarity of solvent is, the stronger the intramolecular hydrogen bonding N–H–N is. This fact would indicate the B part of macrocycle **1** to have higher rigidity and planarity as the polarity of solvent decreases.

A relationship between the polarity of solvents and the ^{1}H NMR data for the protons of macrocycle **1** in various solvents

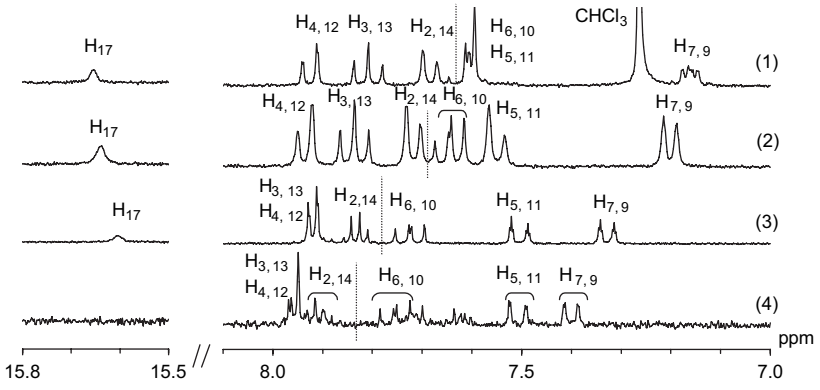


Figure 1. The change of ^{1}H NMR spectrum of macrocycle **1** with the variation of solvent: (1) $CDCl_3$, (2) CD_2Cl_2, (3) CD_3CN, and (4) CD_3OD. The ^{1}H NMR spectral measurements (270 MHz) of macrocycle **1** in the above solvents were carried out at 296 K. The dotted vertical lines represent the boundary of signals of A and B parts of macrocycle **1** shown in Scheme 4.

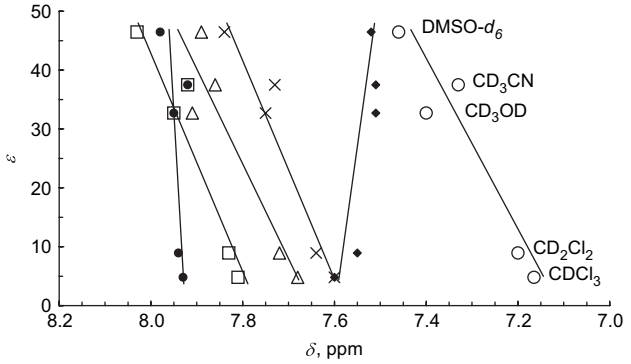


Figure 2. A relationship between the shift of proton of macrocycle **1** and the polarity of solvent: $H_{2,14}$ (△), $H_{3,13}$ (□), $H_{4,12}$ (●), $H_{5,11}$ (◆), $H_{6,10}$ (X), and $H_{7,9}$ (○). Numbering scheme of macrocycle **1** is shown in Scheme 4.

is shown in Figure 2. It has been reported in the ^{1}H NMR measurements of various pyridine derivatives that the peak positions for the protons at both *meta* and *para* positions of pyridine derivatives are trending toward lower field with increasing the polarity of solvents.[11] As shown in Figure 2, the peak appearance for H_2 (H_{14}), H_3 (H_{13}), H_6 (H_{10}), and H_7 (H_9) protons of macrocycle **1** is in good agreement with the trend reported for pyridine derivatives and a considerable amount of lower field shift was observed. The order of the shift to lower field is the same as that with increasing the polarity of the solvent. It is noticed that the lines for the proton shift almost run parallel with each other as shown in Figure 2.

The most noticeable feature observed in this figure is an unusual phenomenon of shifting toward the higher field of H_5 (H_{11}) and little or no shift for the signals of H_4 (H_{12}) with increasing the polarity of solvent. This is quite different from the case of other protons H_2 (H_{14}), H_3 (H_{13}), H_6 (H_{10}), and H_7 (H_9). Originally, the signals of H_4 (H_{12}) and H_5 (H_{11}) protons appear at much lower field than those of H_2 (H_{14}) and H_7 (H_9) protons in low polar solvents, because of the ring current effect of the neighboring pyridine ring. However, the higher the solvent polarity becomes, the closer the distance between the signal positions of H_4 (H_{12}) protons and those of H_2 (H_{14}) protons is. In the case of H_5 (H_{11}) and H_7 (H_9) protons, the similar trend is also observed. This unusual result would come from the decrease of the ring current effect for H_4 (H_{12}) and H_5 (H_{11}) protons and the reported trend of lower field shift for H_2 (H_{14}) and H_7 (H_9) protons with increasing the polarity of solvent. That is to say, the signal positions of H_2 (H_{14}) and H_7 (H_9) protons are shifted to the lower field in accord to the shift trend reported for pyridine derivatives in the polar solvents.[11] In contrast, the decrease of ring current effect with the decrease of planarity at higher polarity causes the peak positions of H_5 (H_{11}) and H_4 (H_{12}) protons to shift to the higher field. As the compensating result for down field and up field trends, the signals of H_5 (H_{11}) proton appear at higher field and those of H_4 (H_{12}) proton stay almost at the same positions.

2.5. The decrease of ring current effect with increasing the polarity of solvent

The point in explaining the shift of peak position is to provide a validation of why the decrease of the ring current effect occurs. A key element explaining this is the structure of macrocycle **1** itself. A trial to elucidate the structure of macrocycle **1** by X-ray structural determination was carried out by us, and this experiment affords the evidence that the A part has nonplanar structure and the B part has almost planar structure.[12] We also find it easy to take this structure as the preferred conformation in a solid state, because the carbon atom 1 of the A part shown in Scheme 4 is sp^3 hybridized and the carbon atom 8 of the B part is sp^2 hybridized. In our view, the intramolecular hydrogen bond is extremely responsible for this conformation.

This structure with planar moiety makes the ring current effect more strong. However, as stated above, the intramolecular hydrogen bond by labile hydrogen atom (H_{17}) is weakened as the polarity of solvent increases. The change of this interaction would lead to the conformational change of macrocycle **1**. As shown in the data (Fig. 3)[13] of X-ray structural determination in our earlier publication,[4a] *trans*-dibutyl analog **3** of this tetraaza macrocycle has the nonplanar structure of macrocyclic skeleton, showing up–down–up–down pattern for the direction of each nitrogen atoms of four pyridine moieties. Thus, this means that the structure with the larger torsion of the bipyridine moiety (e.g., the larger dihedral angle between a pyridine ring having H_{2-4} protons and a pyridine ring having H_{5-7} protons) is the most stable conformation for the macrocyclic system of macrocycle **3**. Our theoretical calculations also support such conformation; the optimized energy minimum structure by the RHF/3-21G calculations showed that the two pyridine rings in the bipyridine moiety twist and each lone pair electrons on two nitrogen atoms points in opposite directions in accord with the twisted conformation.[5b,c,16] Since the cavity of *trans*-dibutyl dicyano tetraaza macrocycle **3** is extremely small and this ring is tense, such twisted structure as a most stable conformation would be taken in order to release the strain of macrocyclic ring and this explanation includes, of course, steric repulsion between H_4 (H_{12}) and H_5 (H_{11}) protons as playing a possibly important role in the preference for this.[15]

On the other hand, macrocycle **1** with the same size of ring has the planar structure of B part, and this planarity comes

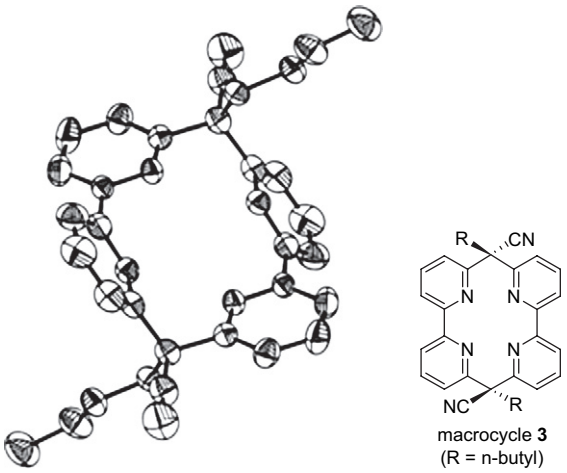


Figure 3. The structure of *trans*-dibutyl dicyano tetraaza macrocycle **3** by X-ray structural determination.[4a]

from a strong intramolecular hydrogen bond in the ring and the conjugated double bonds on the ring described in our earlier publication.[3] That is, these strong intramolecular hydrogen bond and double bonds would force macrocycle **1** into the planar structure of the B part. In other words, this forces macrocycle **1** into an energetically disfavored conformation. However, when the intramolecular hydrogen bond of H_{17} hydrogen atom becomes weaker with increasing the polarity of solvent, the energy balance between the bonds (the conjugated double bonds and the hydrogen bond) in the B part and the ring strain of the whole ring is broken and the effect by the ring strain becomes much stronger. This allows each pyridine moieties of macrocycle **1** to rotate, thus making a twist in bipyridine moieties of macrocycle **1**. Accordingly, this indicates the degree of planarity of macrocycle **1** to become lower.[14] This nonplanar structure as the preferred conformation suggests that the ring current effect decreases compared with the previous planar structure.

Eventually, macrocycle **1** takes the conformation with larger dihedral angle of bipyridine moiety with increasing the polarity of solvent, thereby decreasing the ring current effect.

2.6. The solvent control of the conformation of macrocycle 1

From the changes of ^{1}H NMR spectra of macrocycle **1** with the variation of solvent as described in the above section, the conformation of macrocycle **1** is concluded to be heavily influenced by the polarity of solvent. Thus, it would be possible, in principle, to control the conformation by the solvent system having appropriate polarity. Thus, this method has the capability of controlling the conformation of macrocycle and this control might readily be fine-tuned by employing various substituents of macrocycle **1**.

The signal positions seen for H_2 (H_{14}), H_3 (H_{13}), H_6 (H_{10}), and H_7 (H_9) protons can be used as the method of determining the degree of planarity, because the signal positions of these protons appear at higher field with increasing the planarity of macrocycle and are well proportioned to the polarity of solvent as shown in figure in such a way that a line is parallel to other lines (Fig. 2). The use of this method, which is one measure used in evaluating the planarity, is an exciting step toward exploring new factors to control the conformation. By using this method, we can evaluate the conformational change of macrocycle **1** in various solvents. For example, since there is a large difference in dielectric constant between dichloromethane (ε=8.93) and acetonitrile (ε=37.5),[14] the large difference in spectra, that depends on the conformation, is expected to be observed. In fact, ^{1}H NMR spectral pattern and signal positions of macrocycle **1** in CD_2Cl_2 are quite different from those in CD_3CN as shown in Figure 1(2) and (3).

Additionally, the spectrum of macrocycle **1** in CD_3OD is similar to that in CD_3CN. Since the polarity of these solvents is close to each other, this experimental result seems to be reasonable. However, the unexpected complication in the estimation of conformation by the polarity of solvent was found in these results. That is to say, though the polarity (ε=32.7) of methanol is slightly smaller rather than that (ε=37.5) of acetonitrile, the signal positions of its ^{1}H NMR spectrum in methanol-d_4 are lower than those in acetonitrile-d_4. This is not consistent with the above rule. We do not have a definite explanation for this exception. One of the plausible explanations is that the intramolecular hydrogen bond of macrocycle **1** is affected by intermolecular interaction due to the hydrogen atom of methanol as solvent, because the intermolecular hydrogen bond is generally believed to occur with methanol. This explanation would be supported by the fact that the ^{1}H NMR signal of the intramolecular hydrogen bond is obscure in methanol as shown in Figure 1(4). This result indicates what we have to consider to be the controlling factor, that is, the hydrogen bond is a feasible way not only to control the conformation of the macrocycle by intramolecular interaction such as N–H–N, but also to produce a new way that it can be used as an intermolecular controller such as the interaction between macrocycle and solvent.

Eventually, the solvent is one of the major factors to control the conformation of macrocycle **1**, and its conformation is fine-tuned by the polarity of the solvent and the hydrogen bond.

2.7. Another evidence for the solvent control of conformation of macrocycle 1 revealed by UV–visible spectroscopy

Further trials using simple UV–visible spectroscopic instrumentation strengthened the evidence that the geometry of macrocycle **1** is closely related with the solvent. The UV–visible spectra of macrocycle **1** in $CHCl_3$, CH_2Cl_2, CH_3CN, and CH_3OH are presented in Figure 4. These spectra are shifted from long wavelength to short wavelength side with variation of solvent in the order of $CHCl_3$, CH_2Cl_2, CH_3CN, and CH_3OH. This experimental result establishes that the degree of planarity of macrocycle **1** becomes lower in this order,[14] because the decrease of planarity of 2-pyridyl-2(1*H*)-pyridylideneacetonitrile moiety induces the decrease of conjugation system, and as a result, its peak shows the blue-shift.

The geometry of macrocyclic skeleton can be also elucidated by the peak intensity of UV–visible spectrum of macrocycle **1**. Our molecular orbital calculations about this macrocyclic system indicated a correlation between the oscillator strength and the dihedral angle of two pyridines of bipyridine moiety, that is, when the bipyridine moiety becomes more coplanar, its oscillator strength gets much larger.[5b,c,17] As described in earlier publication,[3] the UV–visible spectrum of macrocycle

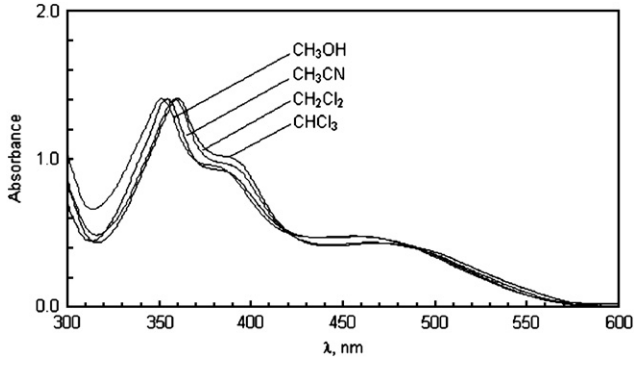


Figure 4. UV–visible spectra of macrocycle **1** measured in various solvents.

Table 2. The changes of extinction coefficient of macrocycle **1** with the variation of solvent

Solvent	Extinction coefficient[a] ($\times 10^{-4}$)	λ_{max}[b] (nm)	Chemical shift of H_{17} (δ/ppm)
CH_2Cl_2	1.49	359	15.64[c]
CH_3CN	1.42	355	15.61[d]
CH_3OH	1.34	351	

[a] Ref. 3.
[b] λ_{max} shown in Figure 4.
[c] The peak shown in CD_2Cl_2.
[d] The peak shown in CD_3CN.

1 in CH_2Cl_2 shows the strong absorption at 281 nm. This peak would be assigned to the bipyridine moiety, though bipyridine moiety is conjugated with 2-pyridyl-2(1*H*)-pyridylideneacetonitrile moiety. This assignment is due to the UV–visible spectrum observed for dibutyl dicyano tetraaza macrocycle **3**, which exhibits a large absorption at 281 nm.[4a] This result suggests that the extinction coefficient at 281 nm is closely related to the geometry of macrocyclic skeleton. Accordingly, this extinction coefficient is expected to depend on the solvent, which controls the geometry of macrocyclic skeleton. The extinction coefficients of macrocycle **1** in various solvents are summarized in Table 2. This table shows that the extinction coefficient changes with the variation of solvent, and the order of the decrease of extinction coefficient accords with that of shifting toward the blue end of the UV–visible spectrum, meaning the decrease of the planarity. That is, the geometry of the B part revealed by the peak shift of UV–visible spectrum with the change of solvent is supported by the data of peak intensity.

Eventually, the data of the peak shift and intensity of UV–visible spectrum observed for macrocycle **1** have established a definite correlation between the solvent and the conformation of macrocycle **1**.

2.8. The conformational changes of macrocycle 2 with the temperature revealed by the variable-temperature ^{1}H NMR spectroscopy

The variable-temperature ^{1}H NMR spectral experiments showed that in macrocycle **1** the conformational changes of the macrocyclic skeleton occur with the temperature.[3] The variable-temperature ^{1}H NMR spectra of macrocycle **2** were measured to examine this behavior, and the temperature dependence of these spectra was also found. This spectral pattern changes considerably compared with macrocycle **1**, because the electronic and steric effect by benzyl group differs from that by dodecyl group. However, the essential variation of spectrum of macrocycle **2** with temperature is analogous to that of macrocycle **1**. Accordingly, macrocycle **2** is considered to exhibit conformational change with the temperature. This fact indicates the temperature to be another important factor to control the conformation of new macrocycles **1** and **2**.

2.9. The solvent effect of macrocycle 2

The ^{1}H NMR spectra of macrocycle **2** were measured in various solvents to compare with those of macrocycle **1** and facilitate proper interpretation. These ^{1}H NMR spectra are highly responsive to the environment of solvent molecules around macrocycle **2** as well as the case of macrocycle **1**. The comparison between the spectra of macrocycles **1** and **2** indicates the essential feature induced by the solvent to be similar. These studies on the temperature and solvent dependence of macrocycle **2** thus tell us the important information of how the conformation of macrocycle is affected by its structural feature.

One of the structural features of macrocycles **1** and **2** is that the macrocyclic ring is unsymmetrical. Since this unsymmetry can be detected definitely by ^{1}H NMR spectroscopy, we can discuss the relationship between the conformational change and the solvent. That is, we can conduct this research work by using the unique multi-peaks observed in ^{1}H NMR spectrum that these macrocycles exhibit, though most of the bipyridine macrocycles yield diffuse spectrum, which makes it difficult to assign each peaks.

3. Conclusion

A new type of macrocycles having the hybrid property of planar and nonplanar macrocycles showed unique properties. That is, the lithium complexation rates of macrocycles **1** and **2** depend on a substituent on the macrocyclic ring; the reaction rate of macrocycle **2** with a benzyl group being bulkier group is slower than macrocycle **1** with a dodecyl group. The photoisomerization of macrocyclic skeleton by the UV light was also observed, and the isomerization rate of macrocycle **2** with a bulkier group was faster than macrocycle **1**. These findings raise the possibility that the highly distorted cyclic structure caused by planar and nonplanar moieties of macrocyclic skeleton may be a key to lead to the unique properties.

Since this distorted structure makes it much easier to change the conformation, these macrocycles have various conformations, which is closely related to their spectroscopic properties. Thus, another focus of this research is to understand how the conformation of macrocycle can be controlled, and we have engaged in a new approach to control the conformation of macrocycles **1** and **2**. Our approach is based on the use of hydrogen bond in the macrocyclic ring that is the pronounced feature of these macrocycles. Since it is widely accepted that the hydrogen bond is affected by the solvent, we tried to explore the effect of solvent on the conformation of these macrocycles by means of ^{1}H NMR spectroscopy. As a result, we found that the solvent has a big effect on ^{1}H NMR spectrum of macrocycles, and this comes from the conformational changes. Accordingly, the solvent is one of the factors that control the conformation. This finding suggests that when the solvent systems that precisely match the conformation are used systematically, we can control the conformation of macrocycles **1** and **2** that may lead to the creation of new switching system.

4. Experimental section

4.1. Instruments

^{1}H NMR spectra were measured on a JEOL JNM GX-270 spectrometer (270 MHz) and recorded at 298 K with

$SiMe_4$ as an internal reference, and chemical shifts of peaks are reported with parts per million units. UV–visible spectra were obtained on a Shimadzu UV-2200 spectrometer at room temperature in 1 cm quartz cell. The mass spectra were measured on a JEOL JMS-700 spectrometer. The solvents used in these measurements were purified and dried by the published methods. The deuterio-solvents were used as received.

4.2. Syntheses

Macrocycle S was prepared by a literature procedure.[4a] *cis*-Dicyclohexano-18-crown-6 (mixture of *syn*–cis and *anti*-cis isomers) was purchased from Acros Organics Co. and was used as received. The other reagents used in this study were purchased from Wako Chemical Co. and Kanto Chemical Co. Diethyl ether and toluene were dried by distillation from sodium under a dry nitrogen atmosphere.

4.3. Macrocycle 1 (monododecyl dicyano tetraaza macrocycle)[3]

Since alkylation of macrocycle S in *N*,*N*-dimethylformamide (DMF) is proceeded by using sodium hydride, dry DMF is required for this synthesis. Thus, the moisture in DMF was removed completely by drying over 3 Å molecular sieves and subsequent distillation under vacuum, and dry DMF obtained was kept under an argon atmosphere. The detailed synthetic procedures of macrocycle **1** were reported in our earlier publications.[3] Since the yield of cyclization between 2,9-dibromo-bipyridine and $NCCH_2CONH_2$ was not high as reported in our previous paper,[3] a trial to obtain higher yield was carried out by using supercritical liquid of carbon dioxide as the solvent. However, positive results about yields were not obtained. Since alkylation of the macrocycle by using 1-bromododecane and sodium hydride affords both monoalkylated and dialkylated macrocycles, the reaction to obtain monoalkylated macrocycle should proceed exactly under the reaction condition described in our previous paper.[3] Since pure macrocycle **1** was required for this study, crude products were purified by column chromatography. For column chromatography, Wakogel (silica gel) C-300 (particle size 45–75 μm) was packed into glass tube (100 cm) and chloroform was used as eluants. The mass spectrum of purified compound showed the parent peak at 554 (*m*/*z*). A crystal for X-ray structural determination of macrocycle **1** was obtained by recrystallization from methanol.[12]

4.4. Macrocycle 2 (monobenzyl dicyano tetraaza macrocycle)

cis-Dicyclohexano-18-crown-6 (0.093 g, 1.0×10^{-4} mol), powdered KOH (0.056 g, 1×10^{-3} mol), and macrocycle S (0.04 g, 1.0×10^{-4} mol) shown in Scheme 1 were added to DMF (10 mL) under a nitrogen atmosphere. This mixture was heated to 80 °C and then benzyl chloride (0.1 mL, 8×10^{-1} mol) was added to this solution. This reaction mixture was stirred for 5 h at 80 °C. After this reaction, the reaction mixture was filtered and the solvent was removed by rotary evaporator. This crude product was purified by silica gel column chromatography using chloroform as eluant. The second fraction was the product, which showed red color. ^{1}H NMR ($CDCl_3$, 298 K) δ 15.71 (H_{17}), 7.80 (d, $H_{4,12}$), 7.76 (t, $H_{3,13}$), 7.71 (d, $H_{2,14}$), 7.64 (d, $H_{6,10}$), 7.63 ($H_{5,11}$), 7.22 ($H_{7,4}$), 6.94 (Ph), 5.47 (CH_2); *m*/*z* 476.

4.5. Macrocycle 3 (dibutyl dicyano tetraaza macrocycle)

The synthetic method for macrocycle **3** was published by us.[4a]

4.6. Measurements

The initial reaction rate constants of macrocycles (**1** and **2**) with lithium salts (LiBr, LiI, and Li ClO_4) and their equilibrium constants were measured in acetonitrile. Since the peak at 355 nm in the UV–visible spectra of macrocycles decreased with Li-complexation, these constants were determined by using the decrease of this peak intensity with time. The acetonitrile solutions (0.02 M) of lithium salts were added to the acetonitrile solutions (5.2×10^{-5} M) of macrocycles and the changes of peak intensity with time were measured. The initial rate constants of photoisomerization were also measured by using the acetonitrile solutions (5.2×10^{-5} M) of macrocycles. The changes of peak intensities (275 and 350 nm) of macrocycles were measured under UV light.

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10. This spectrum was published in our paper of Ref. 3.
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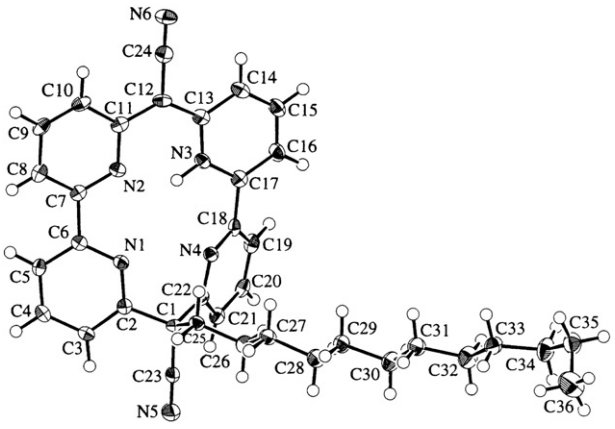
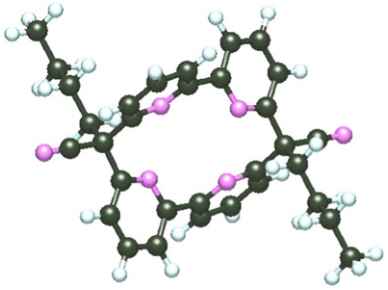
12. Uchida, T.; Tsuchiya, S.; Ogawa, S. The ORTEP drawing is shown below and the details of which will be reported elsewhere.



13. The result about X-ray structural determination published in our paper is given in Ref. 4a.
14. The stability effect by dipole–dipole interaction supports this conclusion. Since the distorted molecule has higher dipole moment, this system could be stabilized in the solvent with the higher polarity that has higher dipole moment.
15. This would be one of the reasons why the tautomerism between α and β states does not occur as described above.
16. The energy minimum structure of macrocycle **3** obtained by geometry optimizer at ab initio RHF/3-21G.[5c]



17. When the dihedral angle ϕ(NCCN) of $N_{15}CCN_{16}$ (or $N_{18}CCN_{17}$) in the bipyridine moiety for the macrocycle changes from 78° to 5°, the oscillator strength becomes two times larger (from 0.35 to 0.7) as shown in Ref. 5c.