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Synthesis and characterization of 1,6,11-triazacyclopentadecane and its zinc(II) complex

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Abstract

A new triazamacrocycle, 1,6,11-triazacyclopentadecane (tacpd), has been synthesized and its complexation behaviors toward nickel(II), copper(II) and zinc(II) ions have been examined. tacpd formed a Zn(II) complex of the composition $Zn_3(tacpd)_2Cl_6$ but no discrete complexes with Ni(II) and Cu(II) ions. The ^1H and ^{13}C NMR spectra indicated that the zinc complex is stable in *N,N*-dimethylformamide and formulated as $[Zn(tacpd)Cl]_2[ZnCl_4]$ in which $[Zn(tacpd)Cl]^+$ assumes a tetrahedral structure formed by the chloride ion and three nitrogens of tacpd.

Introduction

The coordination chemistry of synthetic macrocycles has been the subject of many studies over the past few decades [1–4]. Koyama and Yoshino [5] first reported metal complexes of fully saturated triazamacrocycles (Fig. 1), 1,4,7-triazacyclononane ($l=m=n=2$), 1,4,7-triazacyclodecane ($l=m=2$, $n=3$), 1,4,8-triazacycloundecane ($l=2, m=n=3$) and 1,5,9-triazacyclododecane ($l=m=n=3$). Thereafter saturated triazamacrocycles of various ring sizes have been synthesized and utilized as ligands [6–9]. The previous studies have revealed that the complexation behavior of triazamacrocycles varies depending upon the ring size, i.e. the total methylene number $t(=l+m+n)$ of the three bridging chains [8] (see Fig. 1). The bis(triazamacrocycle) complexes, $[ML_2]^{n+}$ ($n=2$, 3), are generally obtained with triazamacrocycles of $t<8$. When the ring size becomes larger, bis-type complexes are no longer available and nickel complexes of the type $[NiLCl]^+$ have been obtained with macrocycles of $t\geqslant 9$. It should be noted that metal complexes with triazamacrocycles so far isolated are limited to those of macrocycles of two ethylene ($l=m=2$), two trimethylene ($l=m=3$), or one ethylene and one trimethylene ($l=2$ and $m=3$) bridging chains. Such structural features of triazamacrocycles have been believed to be a requisite to afford stable metal complexes. In fact, to the best of our knowledge, no metal complexes of large macrocycles of $l>3$, $m>3$ and $n>3$ have ever been isolated.

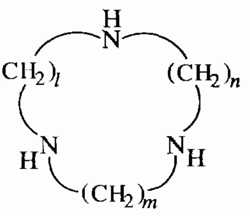

Fig. 1. Chemical structure of triazamacrocycles.

The aim of this study was to synthesize a new triazamacrocycle, 1,6,11-triazacyclopentadecane (abbreviated as tacpd hereafter), which may function as a tridentate ligand. Our interest is to examine the complexating behaviour of tacpd toward divalent transition metal ions (Ni(II), Cu(II), Zn(II)), since this triazamacrocycle is rare in its large ring size ($t=12$) and bridging chains ($l=m=n=4$) forming three seven-membered chelate rings. This paper reports the synthesis and the characterization of tacpd and its zinc(II) complex $Zn_3(tacpd)_2Cl_6$, which should be formulated as $[Zn(tacpd)Cl]_2[ZnCl_4]$.

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Experimental

Synthesis of tacpd

The synthetic scheme of tacpd is shown in Fig. 2.

N-(4-Bromobutyl)phthalimide (1)

It was obtained by the literature method [10, 11] as colorless prisms melting at 77.5 °C in 78% yield.

N,N-Di(4-phthalimidobutyl)-p-toluenesulfonamide (2)

A mixture of *p*-toluenesulfonamide (29.5 g) and sodium hydride (60% in oil suspension, 6 g) in anhydrous tetrahydrofurane (200 cm^3) was stirred at room temperature for 2 h. To this was added **1** (42.9 g) and the mixture was stirred at 90 °C for 2 h. To the cooled mixture was added sodium hydride (6 g) and the stirring at room temperature was continued for 2 h. Then, **1** (42.9 g) was added to this solution and the mixture was stirred at 90 °C for 3 h. The solvent was evaporated to dryness under reduced pressure to give an oily substance, which solidified when triturated with water (100 cm^3). It was crystallized from ethanol as almost colorless crystals melting at 153–154 °C. The yield was 75 g (85%).

Anal. Found: C, 64.80; H, 5.46; N, 7.38. Calc. for $C_{31}H_{31}N_3O_6S$: C, 64.91; H, 5.45; N, 7.32%.

N,N-Bis(4-aminobutyl)-p-toluenesulfonamide dihydrochloride (3)

To a stirred suspension of **2** (82 g) in ethanol (500 cm^3) was added dropwise hydrazine hydrate (14.4 g) and the mixture was refluxed for 2 h. Water (300 cm^3) was added to the reaction mixture and the pH of the solution was adjusted to 1 by adding hydrochloric acid (6 M). Resulted solid materials were separated and washed with two 20 cm^3 portions of water. The filtrate and the washings were combined and concentrated to dryness to give colorless hygroscopic crystals. It was washed with ethanol and dried *in vacuo*. The yield was 40.6 g (73.5%).

Anal. Found: C, 45.73; H, 7.62; N, 10.86. Calc. for $C_{15}H_{29}Cl_2N_3O_2S\cdot0.5H_2O$: C, 45.57; H. 7.65; N, 10.63%.

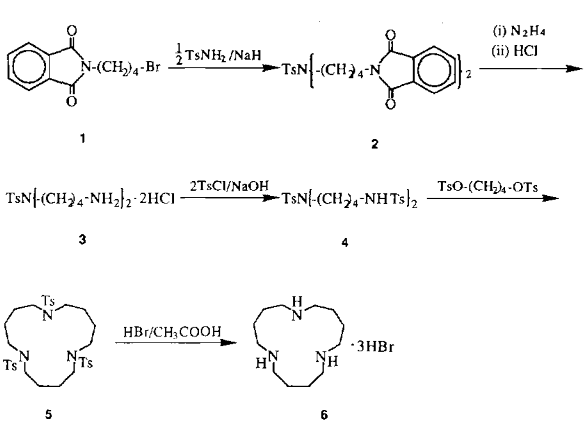

Fig. 2. Synthetic scheme of 1,6,11-triazacyclopentadecane (tacpd).

N,N′,N″-Tris(p-toluenesulfonyl)-1,6,11-triazapentadecane (4)

To an aqueous sodium hydroxide solution (NaOH 30 g in 280 cm^3 H_2O) of **3** (71.4 g) was added dropwise an ethereal solution (350 cm^3) of *p*-toluenesulfonyl chloride (71 g) with vigorous stirring. The oily substance thus formed was separated by decantation, washed with dilute hydrochloric acid (*c*. 2 M) and then with water, and dried over P_2O_5 in a vacuum desiccator. It was used for the next reaction without further purification.

N,N′,N″-Tris(p-toluenesulfonyl)-1,6,11-triazacyclopentadecane (5)

A mixture of **4** (4.70 g) and sodium hydride (60% in oil, 0.8 g) in anhydrous *N,N*-dimethylformamide (dmf) (40 cm^3) was stirred for 2 h. The reaction mixture was heated at 100 °C and a solution of 1,4-bis(*p*-toluenesulfonyloxy)butane (2.9 g) in anhydrous dmf (30 cm^3) was added dropwise with vigorous stirring. After stirring at this temperature for 2 h the reaction mixture was concentrated to dryness to give a viscous oily substance, which solidified when triturated with water. The solid mass was washed with water and crystallized from acetic acid as colorless crystals melting at 135–138 °C. The yield was 3.5 g (70%).

Anal. Found: C, 58.40; H, 6.84; N, 6.18. Calc. for $C_{33}H_{45}N_3O_6S_3$: C, 58.64; H, 6.71; N, 6.22%.

1,6,11-Triazacyclopentadecane trihydrobromide (6)

A mixture of **5** (3.5 g), hydrobromic acid (47%, 16 cm^3), and acetic acid (24 cm^3) was refluxed for 30 h and concentrated to dryness. The residue was dissolved in water (20 cm^3) and the solvent was evaporated to dryness under reduced pressure. The operation of the dissolution in water and the evaporation to dryness was repeated three times. The crude product was dissolved in a minimum amount of water and diffused with ethanol to give colorless microcrystals. The melting point was higher than 240 °C. The yield was 1.6 g (82%).

Anal. Found: C, 31.87; H, 6.58; N, 8.96. Calc. for $C_{12}H_{30}Br_3N_3$: C, 31.60; H, 6.63; N, 9.21%.

Synthesis of zinc(II) complex .

1,6,11-Triazacyclopentadecane trihydrobromide (tacpd·3HBr (**6**)) was converted into the free form by the use of Dowex IX8. To a stirred solution of tacpd (107 mg) in absolute methanol (10 cm^3) was added dropwise an absolute methanol solution of zinc(II) chloride (68 mg). Soon a pale yellow precipitate deposited, which was collected and washed with hot absolute methanol. The crude product was dissolved in hot anhydrous dmf, and the solution was diluted with absolute methanol until the solution became turbid and allowed to stand in a refrigerator to give pale yellow microcrystals. The operation for the crystallization was repeated twice. The product was washed with methanol and dried at 100 °C under reduced pressure.

Anal. Found: C, 34.23; H, 6.69; N, 10.28; Zn, 23.1. Calc. for $C_{24}H_{54}N_6Zn_3Cl_6$: C, 34.50; H, 6.51; N, 10.06; Zn, 23.47%.

Physical measurements

Elemental analyses for carbon, hydrogen and nitrogen were obtained at The Service Center of Elemental Analysis, Kyushu University. Analyses of zinc were made on a Shimadzu AA-680 atomic absorption/flame emission spectrophotometer. IR spectra were recorded on a JASCO IR 810 instrument on KBr disks. Mass spectra were recorded on a JEOL JMS-D 300 mass spectrometer. ^{1}H (400 MHz) and ^{13}C NMR spectra were recorded on a JEOL JNM-GX 400 spectrometer in d$_7$-dmf, using tetramethylsilane as the internal standard.

Results and discussion

Preparation and characterization of tacpd

The synthesis of tacpd was carried out using the modification of Richmann and Atkins [12] of the cyclization reaction first employed by Koyama and Yoshino [5]. *N,N′,N″*-Tris(*p*-toluenesulfonyl)-1,6,11-triazapentadecane (**4**) is the key precursor compound for tacpd. As the starting material for **4**, *N,N*-bis(4-phthalimidobutyl)-*p*-toluenesulfonamide (**2**) was prepared by the reaction of *N*-(4-bromobutyl)-phthalimide (**1**) and *p*-toluenesulfonamide. **2** was hydrolyzed to *N,N*-bis(4-aminobutyl)-*p*-toluenesulfonamide (**3**), which was then converted into **4** by the usual reaction with *p*-toluenesulfonylchloride. The cyclic compound **5** was obtained in a tolerable yield (70%) though any high-dilution technique was not adopted.

The identification of tacpd was made by mass spectra and ^{1}H and ^{13}C NMR spectra. The FAB mass spectra of tacpd showed a peak at $m/e = 213$ which exactly corresponds to the parent peak of the macrocycle. No dominant peak appeared in the region higher than the parent peak.

The 400 MHz ^{1}H NMR spectra of tacpd (in d$_7$-dmf) showed only two signals of comparable intensity at 2.721 and 1.660 ppm. The former appears formally as a triplet ($J = 5.75$ Hz) but further small splittings are superposed. This signal is assigned to the protons on the α-carbon atoms of the 1,4-butylene chain ($-NH^{\alpha}CH_2{}^{\beta}CH_2{}^{\beta}CH_2{}^{\alpha}CH_2NH-$). The latter signal appearing as a quintet ($J = 2.93$ Hz) is assigned to the protons on the β-carbon atoms of the chain. The amino protons are seen as a broad band near 2.62 ppm. The ^{13}C NMR spectra also showed only two signals at 47.83 and 26.51 ppm which are assigned to the α- and β-carbon atoms of the 1,4-butylene chain, respectively. The NMR spectral results indicate that tacpd assumes a D_3 symmetry but the conformational change of the butylene chain is relatively slow.

Complexation behavior of tacpd

Complexations of tacpd toward nickel(II), copper(II) and zinc(II) ions have been examined. The reactions of tacpd with nickel(II) salts (chloride, nitrate, perchlorate) resulted in the precipitation of nickel hydroxide in all cases. Such a tendency to yield $Ni(OH)_2$ was recognized previously for triazamacrocycles of $t \geq 11$ [8]. It was reported that including an anion such as NCS^- is important to obtain stable cobalt(II) and nickel(II) complexes with triazamacrocycles [8, 9]. When tacpd, nickel(II) acetate tetrahydrate, and NH_4NCS in the molar ratio of 1:1:7 were mixed in methanol, a clear bluish green solution was formed. However, we were unsuccessful in isolating any solid complex from this solution.

The reaction of tacpd with a copper(II) salt such as chloride or perchlorate in methanol afforded a blue precipitate which was hardly soluble in common inorganic and organic solvents. The product appeared to involve tacpd judging from its IR spectra, but further characterization of this compound was not made in this study.

The reaction of tacpd with zinc(II) chloride in methanol gave colorless hygroscopic microcrystals, which were formulated as $Zn_3(tacpd)_2Cl_6$ based on elemental analyses. On the other hand, the use of zinc(II) acetate dihydrate, zinc(II) sulfate hexahydrate, or zinc(II) nitrate hexahydrate as the metal source resulted in the formation of an oily substance which could not be crystallized. It appears that chloride ion plays an essential role in coordination in $Zn_3(tacpd)_2Cl_6$. Our efforts to grow single crystals suitable for X-ray structural analysis were all in vain.

Zinc(II) complexes of triazamacrocycles have been less studied compared with nickel(II) and cobalt(II) complexes. Equilibria between triazamacrocycles and zinc(II) ion were studied by means of potentiometric titrations in aqueous solution [13]. It is known that zinc(II) ion forms a 1:1 complex (ZnL^{2+}) in solution and the stability decreases as the ring size becomes larger. Very recently a zinc(II) complex of 1,5,9-triazacyclododecane (tacdd) was structurally characterized to have a tetrahedral $[Zn(tacdd)OH]^+$ core [14]. Therefore, such a tetrahedral structure seems common for zinc complexes of triazamacrocycles. However, we cannot rule out the possibility that tacpd coordinates planarly to afford a trigonal surrounding the zinc(II) ion, since tacpd has a large cavity compared with 1,5,9-triazacyclodecane. ^1H and ^{13}C NMR spectra of the zinc complex were measured to see the stability in solution and to determine the coordination mode of tacpd. The NMR spectral results are summarized in Table 1 together with those for free tacpd.

NMR spectral results demonstrate that the zinc complex is stable in dmf as discussed below. The ^1H NMR spectrum of the zinc complex (400 MHz, in d_7-dmf) shows two broad signals at 2.875 and 1.739 ppm which are assigned to the protons on the α- and β-carbons, respectively. The former is shifted by 0.15 ppm to a lower field relative to that of free tacpd. The latter is also shifted to lower field on complexation but the shift is small (0.08 ppm). A large shift on complexation was found for the amino proton signal that appeared as a broad band centered around 4.35 ppm. In the ^{13}C NMR spectrum of the complex, on the other hand, there were observed four signals for each of the α- and β-carbon atoms (see Fig. 3). This fact suggests that the zinc complex in the solution is a mixture of isomeric forms and the interconversion among the isomers is slow relative to the time-scale of ^{13}C NMR spectroscopy. When tacpd is disposed planarly about a metal ion two geometrical isomers are possible with respect to the orientation of the three NH groups, i.e. in one isomer all the three nitrogen protons being on the same side of the trigonal plane and in the other isomer one of the three nitrogen protons being on the opposite side of the trigonal plane to the remaining two (see Fig. 4). When tacpd is disposed tetrahedrally about a metal ion, four geometrical isomers are considered because of an approximate C_{3v} symmetry of the ligand (see Fig. 5). Owing to the macrocyclic effect that may retard the Zn–N bond dissociation [1], the interconversion among the geometrical isomers must be slow so as to be detected by ^{13}C NMR spectroscopy. In addition to such geometrical isomers the conformational isomers with respect to the butylene chain may be considered if the free movement of the butylene chain is sterically hindered. Based on examination of the Dreiding model, tacpd adopts an extended conformation in the trigonal disposition

TABLE 1. ^1H and ^{13}C NMR spectral results of tacpd and its zinc(II) complex

	^1H NMR			^{13}C NMR	
	α-H	β-H	N–H	α-C	β-C
tacpd	2.721 (t, 5.75)	1.660 (qi, 2.93)	2.62 (b)	47.83	27.51
Zn complex	2.875 (b)	1.739 (b)	4.35 (b)	48.85 48.67 48.53 48.38	27.79 27.56 25.57 25.21

t = triplet, qi = quintet, b = broad. The values in parentheses are the coupling constants given in Hz.

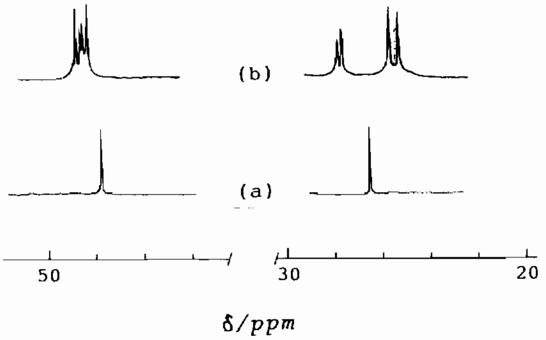

Fig. 3. ^{13}C NMR spectra of (a) tacpd and (b) its zinc(II) complex $Zn_3(tacpd)_2Cl_6$.

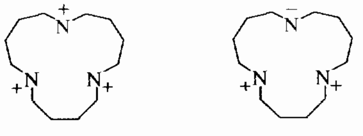

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Fig. 4. Two isomeric forms of tacpd in the planar disposition. The + and − signs indicate the H atom disposed above and below with respect to the trigonal coordination plane, respectively.

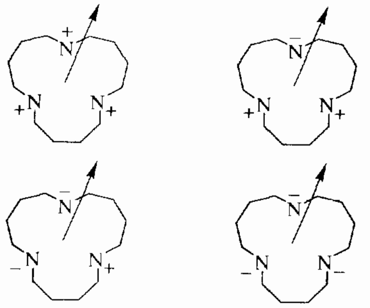

Fig. 5. Four isomeric forms of tacpd in the tetrahedral disposition. The + and − signs indicate the H atom disposed above and below the plane defined by the three nitrogen atoms, respectively, and the arrow is C_3 axis taken from the center of tacpd to the metal ion.

about the zinc(II) ion, so that free conformational change of the butylene chain may occur. The α-carbon atoms are all equivalent in isomer **I** and nearly equivalent in isomer **II**. This is also the case for the β-carbon atoms. Thus, we expect one or two signals at best for both the α- and β-carbon atoms in ^{13}C NMR spectra. In the tetrahedral disposition about zinc(II) ion, tacpd adopts a folded conformation so that the conformational change of the butylene chain seems not to be feasible. In this case the geometrical isomers of the complex each may adopt a specific butylene conformation, showing many signals for both the α- and β-carbon atoms. Such a ^{13}C NMR spectral feature has been indeed observed for the present zinc complex. Thus, we may formulate the complex as $[Zn(tacpd)Cl]_2[ZnCl_4]$ in which $[Zn(tacpd)Cl]^+$ assumes a tetrahedral configuration. Our attempts to replace the anion $[ZnCl_4]^{2-}$ with other ions such as tetraphenyl borate or hexafluorophosphate ion were unsuccessful probably because of high hygroscopicity of those salts.

The present study has revealed that tacpd of a large ring size ($t = 12$) forms a tetrahedral zinc(II) complex $[Zn(tacpd)Cl]^+$ which is stable in dmf solution.

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