Dibridged Bis(Zn^{2+}–cyclen): A Novel Host Molecule of Malonate Dianion in Aqueous Solution

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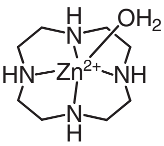
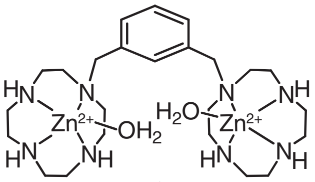
A dinuclear zinc(II) complex, *m*,*m*-bis(Zn^{2+}–cyclen) was synthesized as a novel host molecule for a malonate dianion. The dizinc(II) complex has two zinc(II)–cyclen moieties (cyclen = 1,4,7,10-tetraazacyclododecane) connected through two *m*-xylene bridges. The 1:1 association constant of $\log K$ ($K = \{[\text{malonate-bound } m,m\text{-bis}(Zn^{2+}\text{–cyclen})]/[m,m\text{-bis}(Zn^{2+}\text{–cyclen})][\text{malonate}]\}/M^{-1}$) was determined to be 3.6 by potentiometric pH titration at 25 °C with $I = 0.10$ M ($NaNO_3$) in aqueous solution. The H/D exchange reaction of methylene hydrogen atoms of malonate dianion was accelerated by *m*,*m*-bis(Zn^{2+}–cyclen) in D_2O. The half-life was determined to be 80 min for a 1:1 mixture (2 mM) of malonate and *m*,*m*-bis(Zn^{2+}–cyclen) at 25 °C and pD 7. From an aqueous solution of equimolar malonate and *m*,*m*-bis(Zn^{2+}–cyclen) however, a cyclic 2:2 malonate/*m*,*m*-bis(Zn^{2+}–cyclen) complex was isolated. The structure was confirmed by X-ray crystallography.

Recently, molecular recognition of various molecules such as carbohydrates, nucleic acids, and drugs has attracted considerable attention.[1–3] Among artificial host molecules, metal complexes with open coordination sites have found wide use in molecular recognition.[4,5] Coordination to metal ions occurs typically with large enthalpies compared to those of hydrogen bond formation or electrostatic interactions.[6–9] Thus, even a single coordinated bond may provide sufficient binding energy to result in stable host–guest complexation in aqueous solution. For example, Kimura's group reported that a mononuclear zinc(II) complex, zinc(II)–cyclen (cyclen = 1,4,7,10-tetraazacyclododecane) **1** (Chart 1) is a new host for imide anions such as thymine (pK_a 9.9) and barbital (pK_a 8.0) in aqueous solution.[4,10–17] The zinc(II) ion in the cyclen complex is acidic enough to replace the imide proton at the fifth coordination site. The resulting zinc(II)–N^- interaction is enforced by the two complementary hydrogen bonds between the imide oxygen atoms and cyclen NH groups. The anion recognition involving metal coordination provides a new class of host–guest interaction at physiological pH. Furthermore, zinc(II)–cyclen can capture various anions derived from weak acids such as thiol, carboxylic acids, and phosphoric acids.[18–22]

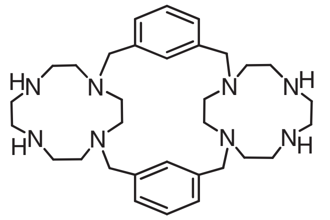
In 1996, we reported that attachment of another zinc(II)–cyclen through a *m*-xylene bridge made a stronger ditopic host, *m*-bis(Zn^{2+}–cyclen) **2** for a barbital dianion with two imide N^- donors. The 1:1 affinity is 25 times greater than that of the mononuclear zinc(II)–cyclen complex.[15] The *m*-bis(Zn^{2+}–cyclen) complex also showed stronger affinity, but not much, to a bidentate guest, 4-nitrophenyl phosphate dianion. Recently, in the course of the synthesis of the *m*-bis(Zn^{2+}–cyclen) ligand, we incidentally isolated another compound **3**. The new product is a cyclophane ligand containing two cyclen moieties



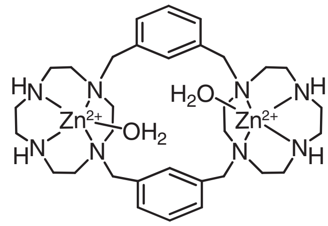
Zn^{2+}–cyclen
1



m-bis(Zn^{2+}–cyclen)
2



m,*m*-bis(cyclen)
3, L



m,*m*-bis(Zn^{2+}–cyclen)
4, Zn_2L

Chart 1.

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connected through two *m*-xylene bridges. The novel ligand **3** was termed *m*,*m*-bis(cyclen), which is more rigid than the monobridged ligand **2**. Here, we report the synthesis and characterization of **3** and its dizinc(II) complex, *m*,*m*-bis(Zn^{2+}–cyclen) **4**. Moreover, recognition behavior of *m*,*m*-bis(Zn^{2+}–cyclen) toward malonate dianion is determined.

Experimental

General Procedures. All reagents and solvents used were of analytical quality and used without further purification. All aqueous solutions were prepared using deionized and distilled water. An aqueous solution of 0.100 M NaOH for potentiometric pH titration was made by dilution of 10 M NaOH (Merck No. 6495) with decarbonated water and standardized with an aqueous solution of 0.100 M HCl. The 10 M NaOH solution is kept in a refrigerator below 5 °C for 3 days, where Na_2CO_3 in the solution is less than 0.1 M, and then taken out before raising the solution temperature. IR spectra with KBr pellets were recorded on a Horiba FT-710 infrared spectrometer at 23 °C. ^1H (500 MHz) and ^{13}C (125 MHz) NMR spectra using 99.9 atom% D_2O at 35 °C were recorded on a JEOL JMN-LA500 spectrometer. Sodium 4,4-dimethyl-4-silapentanesulfonate (in D_2O) was used as an internal reference for ^1H and ^{13}C NMR measurements. The NMR signal assignments were achieved using ^1H NOE differential 1D and 2D (COSY, HMQC, and HMBC) experiments. Elemental analysis (CHN) was performed on a Yanaco CHN CORDER MT-6. A MALDI-TOF MS spectrum (positive reflector mode) was obtained on a Voyager RP-3 BioSpectrometry Workstation (PerSeptive Biosystems) equipped with a nitrogen laser (337 nm). A matrix solution of 2,4,6-trihydroxyacetophenone in CH_3CN was used.

Synthesis of *m*,*m*-Bis(Zn^{2+}–cyclen) Complex, 4. A $CHCl_3$ solution (50 mL) of 1,3-bis(bromomethyl)benzene (1.9 g, 7.2 mmol) was mixed with a $CHCl_3$ solution (500 mL) of cyclen (2.5 g, 14.5 mmol). After Na_2CO_3 (1.8 g, 17 mmol) was added into the solution, the reaction mixture was stirred at room temperature for 24 h. After the reaction mixture was washed with distilled water (50 mL × 2), the organic solvent was evaporated. The oily residue was purified by silica gel column chromatography (Fuji Silysia silica gel 4B, eluent: $CHCl_3/MeOH/28\%\ NH_{3aq} = 25:5:1$) followed by crystallization from toluene to obtain 1,4,7,10,18,-21,24,27-octaazapentacyclo[24.8.2.2^{18,27}.1^{12,16}.1^{29,33}]-tetraconta-12,14,16(40),29,31,33,(39)-hexaene (*m*,*m*-bis(cyclen), **3**) in 10% yield based on cyclen (0.78 g): TLC (Wako silica gel 70F_{254} plate, eluent: $CHCl_3/MeOH/28\%\ NH_{3aq} = 5:4:1$) $R_f = 0.63$. IR (KBr pellet): 3420 (br), 2792, 1620 (br), 1482, 1462, 1371, 1343, 1162, 1116, 1086, 1033, 983, 755, 707 cm^{-1}. ^1H NMR (D_2O): δ 2.17–2.43 (8H, m, NCH_2), 2.43–2.56 (8H, m, NCH_2), 2.56–2.71 (8H, m, NCH_2), 2.71–2.89 (8H, m, NCH_2), 3.21 (8H, br s, $ArCH_2$), 6.97 (4H, d, $J = 7.3$ Hz, ArH), 7.12 (2H, t, $J = 7.3$ Hz, ArH), 7.74 (2H, s, ArH). ^{13}C NMR (D_2O): δ 44.5, 46.3, 50.3, 52.0, 58.5, 127.5, 129.2, 129.7, 140.0. MALDI-TOF MS: *m*/*z* 549.4 for $M + H^+$.

An aqueous solution (10 mL) containing $Zn(NO_3)_3 \cdot 6H_2O$ (0.32 g, 1.08 mmol) was added to an ethanol solution (10 mL) of *m*,*m*-bis(cyclen) (0.30 g, 0.55 mmol). The reaction mixture was allowed to stand for 20 min at 70 °C. After filtration of the solution, the filtrate was cooled to room temperature to obtain *m*,*m*-bis(Zn^{2+}–cyclen)$\cdot 4NO_3^- \cdot 1.5H_2O$ as colorless fine crystals (0.30 g) in 57% yield. Anal. Found: C, 40.3; H, 5.9; N, 17.4%. Calcd for $C_{32}H_{53}N_{12}O_{13.5}Zn_2$: C, 40.3; H, 5.6; N, 17.6%. IR (KBr pellet): 3440 (br), 3250, 2934, 2880, 1639, 1477, 1380, 1295, 1078, 1001, 971, 825, 742, 628 cm^{-1}. ^1H NMR (D_2O): δ 2.25–2.36 (4H, m, NCH_2), 2.64–2.79 (4H, m, NCH_2), 2.79–2.93 (8H, m, NCH_2), 2.99–3.39 (16H, m, NCH_2), 4.25 (4H, d, $J = 14.5$ Hz), 4.35 (4H, d, $J = 14.5$ Hz), 7.54 (4H, d, $J = 7.8$ Hz, ArH), 7.61 (2H, t, $J = 7.8$ Hz, ArH), 7.72 (2H, s, ArH). ^{13}C NMR (D_2O): δ 52.1, 54.2, 56.3, 61.0, 66.5, 139.6, 140.8, 141.8, 145.4.

Syntheses of the Malonate-Bound *m*,*m*-Bis(Zn^{2+}–cyclen) Complex, 9. An aqueous solution (200 mL) containing $Zn(NO_3)_3 \cdot 6H_2O$ (0.32 g, 1.08 mmol) and malonic acid (0.11 g, 1.08 mmol) was added to an ethanol solution (10 mL) of *m*,*m*-bis(cyclen) (0.30 g, 0.55 mmol). The solution pH was adjusted to pH 7 with 1.0 M NaOH. The reaction mixture was heated to 70 °C for 20 min and then cooled to room temperature. After the solvent was evaporated, the residue was crystallized from water to obtain colorless crystals, one of which was subject to X-ray crystallography. The crystals were dried under 5 mmHg at 25 °C for 5 h to obtain white fine powder of **9**$\cdot 4NO_3^- \cdot 4H_2O$ (0.20 g) in 39% yield. Anal. Found: C, 44.8; H, 6.1; N, 14.9%. Calcd for $C_{35}H_{58}N_{10}O_{12}Zn_2$: C, 44.6; H, 6.2; N, 14.9%. IR (KBr pellet): 3430 (br), 2938, 2879, 1598 (CO), 1476, 1442, 1384, 1249, 1107, 999, 970, 740, 719 cm^{-1}. ^1H NMR (D_2O): δ 1.97–2.12 (4H, m, NCH_2), 2.18–2.32 (4H, m, NCH_2), 2.64–2.93 (24H, m, NCH_2), 3.52 (2H, br s, $COCH_2CO$), 3.90 (4H, d, $J = 14.8$ Hz), 3.99 (4H, d, $J = 14.8$ Hz), 7.16 (4H, d, $J = 7.4$ Hz, ArH), 7.27 (2H, t, $J = 7.4$ Hz, ArH), 7.44 (2H, s, ArH). ^{13}C NMR (D_2O): δ 42.1, 44.2, 45.5 (CH_2 of malonate), 46.1, 50.7, 55.9, 128.8, 129.7, 132.0, 135.5, 174.5 (CO of malonate).

Potentiometric pH Titrations. The electrode system consists of a Horiba pH/Ion meter F-53, a Horiba combination pH electrode 9611, and Hiranuma auto buret UCB-900. The pH calibration method is as follows: An aqueous solution (50.0 mL) containing 4.00 mM HCl and 96 mM $NaNO_3$ ($I = 0.10$ M) was prepared under nitrogen atmosphere (>99.999% purity) at 25.0 ± 0.1 °C and then the first pH value (pH_1) was read. After 0.100 M NaOH (4.00 mL) was added to the acidic solution, the second pH value (pH_2) was read. The theoretical pH values corresponding to pH_1 and pH_2 are calculated to be $pH_1' = 2.481$ and $pH_2' = 11.447$, respectively, using $\log K_W$ ($K_W = a_{H^+} \cdot a_{OH^-}/M^2$) $= -14.00$, $\log K'_W$ ($K'_W = [H^+][OH^-]/M^2$) $= -13.79$, and f_{H^+} ($= a_{H^+}/H^+$) $= 0.825$). The correct pH values ($pH = -\log a_{H^+}$) can be obtained using the following equations: $a = (pH_2' - pH_1')/(pH_2 - pH_1)$; $b = pH_2' - a \times pH_2$; $pH = a \times$ (pH-meter reading) $+ b$. The potentiometric pH titrations of 1.00 mM Zn_2L were carried out in the absence and presence of 1.00, 2.00, and 5.00 mM malonate at 25.0 ± 0.1 °C with $I = 0.10$ M ($NaNO_3$), where two independent titrations were performed. The two deprotonation constants (K_1 and K_2) and the malonate association constant (K) were determined by means of the pH-titration program BEST.[23] The pH fit values (σ) defined in the program are smaller than 0.02 for K_1 and K_2, and 0.05 for K. Relative species concentrations (%) at various pH values ($pH = -\log\{a_{H^+}/M\} = -\log\{[H^+]/M\} + 0.084$) were calculated using the program SPE.[23]

X-ray Crystallography. X-ray data of the 2:2 complex **9** were collected on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Cu Kα radiation ($\lambda = 1.54187$ Å) at −180 ± 1 °C. The structure was solved by the direct method (SHELX97 developed by G. M. Sheldrick) and expanded using Fourier techniques (DIRDIF99).[24] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. All calculations were performed using the Crystal-Structure[25] crystallographic software package except for refinement using SHELX97. The sequential numbers for each element

Table 1. Crystallographic Data for **9**

Crystal color, Habit	Colorless, needle
Formula	$C_{70}H_{138}N_{20}O_{35}Zn_4$
Formula weight	2081.49
Crystal dimensions/mm^3	0.20 × 0.06 × 0.03
Crystal system	Orthorhombic
Space group	$Pca2_1$ (#21)
a/Å	66.1658(11)
b/Å	16.1102(2)
c/Å	17.4020(3)
V/Å^3	18549.6(5)
Z	8
D_{calcd}/Mg m^{-3}	1.491
$F(000)$	8784
μ/cm^{-1}	19.701
No. of observations	30848
No. of variables	2324
$R1 = \Sigma \lvert\lvert F_o\rvert - \lvert F_c\rvert\rvert/\Sigma \lvert F_o\rvert$, $(I > 2\sigma(I))$	0.0951
$wR2 = [\Sigma (w(F_o^2 - F_c^2)^2)/\Sigma w(F_o^2)^2]^{0.5}$ (All reflections)	0.2906

were adopted for the X-ray crystal structure: Zn(1–8), C(1–140), N(1–40), and O(1–70). Crystallographic data and refinement parameters are listed in Table 1. The crystal data have been deposited at the Cambridge Crystallographic Data Center; the deposition number is CCDC 744746. Copies of this information may be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing: data_request@ccdc.cam.ac.uk, or contacting CCDC, 12, Union Road, Cambridge, CB2 1EZ, U.K. [Fax: +44 1223 336033].

Results and Discussion

Syntheses of *m,m*-Bis(cyclen) and Its Zinc(II) Complexes. A macrocyclic tetraamine, 1,4,7,10-tetraazacyclododecane (cyclen) was allowed to react with equimolar amounts of 1,3-bis(bromomethyl)benzene in $CHCl_3$ at room temperature. Two main products, 1,4,7,10,18,21,24,27-octaazapentacyclo-[24.8.2.2^{18,27}.1^{12,16}.1^{29,33}]-tetraconta-12,14,16(40),29,31,33,(39)-hexaene (**3**) (*m,m*-bis(cyclen), L) and 1,3-bis[(1,4,7,10-tetra-azacyclododecan-1-yl)methyl]benzene (**5**) (*m*-bis(cyclen)) were obtained in 10% and 15% yields, respectively (Figure 1). The dizinc(II) complex, *m,m*-bis(Zn^{2+}–cyclen) **4** (Zn_2L) was crystallized as nitrate salts from an aqueous EtOH solution containing equimolar amounts of **3** and $Zn(NO_3)_2 \cdot 6H_2O$. The 2:2 cyclen/*m*-xylene composition of *m,m*-bis(cyclen) was determined by 1D and 2D NMR, elemental analysis (C, H, N), MALDI-TOF MS, and potentiometric pH titration. The obtained evidence is as follows: i) The ^{1}H NMR signals of **3** are assigned to a symmetric 1,3-substituted benzene derivative. ii) The ^{13}C NMR of **3** showed nine signals, which is consistent with a structure containing a 1,4-substituted cyclen moiety. iii) The nuclear overhauser effects, NOEs of the benzyl protons of **3** were observed with two kinds of Bz–NCH_2 protons (e.g., C1, C2, C3, and C8), but not with $HNCH_2$ protons (e.g., C4, C5, C6, and C7): the carbon atom numbers are shown in the X-ray crystallography section. iv) The MS signal of **3** ($M + H^+$) was observed at m/z 549.4. v) The dizinc(II) complex **4** has two pK_a values assigned to two zinc(II)-bound water molecules (see below).

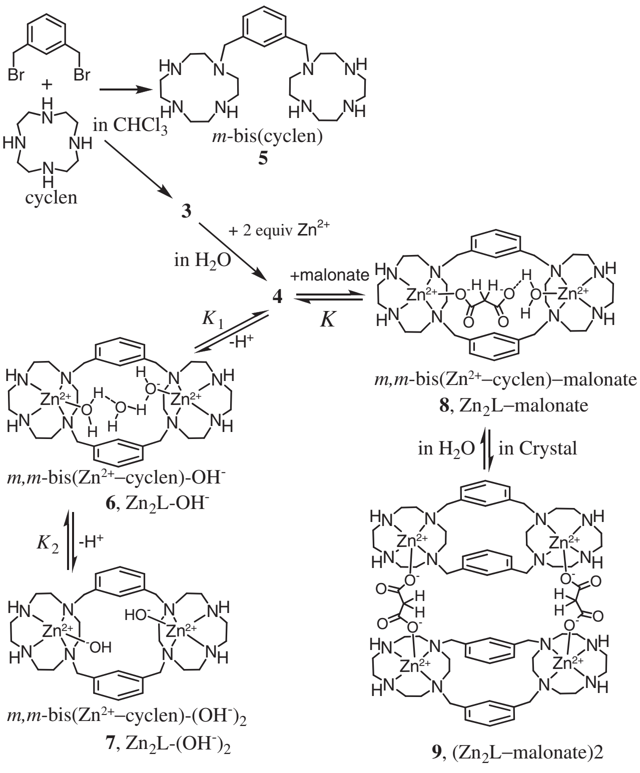

Figure 1. Synthesis and equilibria of *m,m*-bis-(Zn^{2+}–cyclen) **4**.

Equilibria in Aqueous Solution. The potentiometric pH titrations were performed with an aqueous solution of 1.00 mM **4** (Zn_2L) at 25 °C with $I = 0.10$ M ($NaNO_3$). A typical pH titration curve for Zn_2L is shown in Figure 2a. The titration data were analyzed for two deprotonation equilibria (1) and (2). The deprotonation constants (pK_1 and pK_2) of 6.39 ± 0.03 and 8.15 ± 0.03 are assigned according to Figure 1. The first deprotonation occurs at lower pH and the second one at higher pH compared with the zinc(II)-bound water of zinc(II)–cyclen **1** (p$K_a = 7.9$).[18] The nonequivalent pK_a values of zinc(II)-bound waters indicate that the zinc(II)-bound OH^- and H_2O molecule in **6** stay in a distance for electrostatic interaction such as $Zn–OH^- \cdots H_2O \cdots H_2O–Zn$ (Figure 1). Further deprotonation or precipitation of $Zn(OH)_2$ was not observed below pH 11. NMR spectra of **4** (pD 5), **6** (pD 7), and **7** (pD 11) disclosed a symmetric structure for the two zinc(II)–cyclen moieties in D_2O solution, so that the proton exchange reaction between the $Zn^{2+}–OH_2$ and $Zn^{2+}–OH^-$ in **6** is sufficiently fast in aqueous solution.

$$Zn_2L\ (\mathbf{4}) = Zn_2L–OH^-\ (\mathbf{6}) + H^+;$$

$$K_1 = ([Zn_2L–OH^-]a_{H^+}/[Zn_2L])/M \tag{1}$$

$$Zn_2L–OH^-\ (\mathbf{7}) = Zn_2L–(OH^-)_2\ (\mathbf{7}) + H^+;$$

$$K_2 = ([Zn_2L–(OH^-)_2]a_{H^+}/[Zn_2L–OH^-])/M \tag{2}$$

The association constant of the 1:1 malonate-bound di-zinc(II) complex (1.0 mM) was determined by the potentiometric pH titrations in the presence of 1.0, 2.0, and 5.0 mM malonate dianion at 25 °C with $I = 0.10$ M ($NaNO_3$). A typical titration curve with 2.0 mM disodium malonate salt is presented

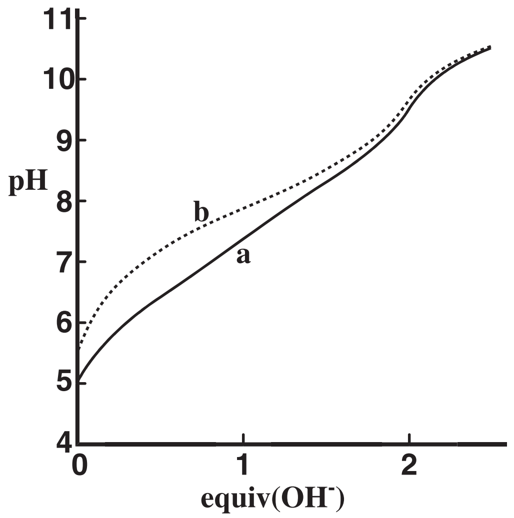

Figure 2. Typical pH titration curves for 1 mM **4** (Zn_2L) at 25 °C with $I = 0.10$ M ($NaNO_3$) in aqueous solution: (a) in the absence of malonate and (b) in the presence of 2 mM malonate. equiv(OH^-) is the number of equivalents of base added.

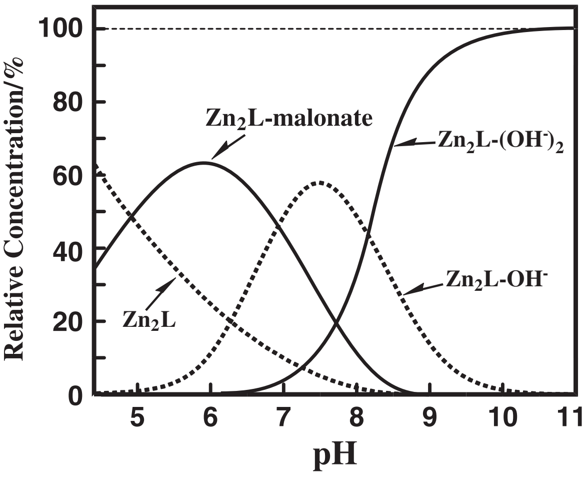

Figure 3. Distribution diagram for 2 mM **4** (Zn_2L) in the presence of 2 mM malonate as a function of pH ($-\log a_{H^+}$) at 25 °C with $I = 0.10$ M ($NaNO_3$). The data for malonate monoanion ($pK_a = 5.28$) and malonate dianion are omitted for clarity.

in Figure 2b. From the comparison of the titration curves in the presence and absence of malonate, we concluded that a malonate-bound complex **8** (Zn_2L–malonate) is formed in the titration pH range from 5 to 8, but the OH^--bound complexes **6** and **7** coexist at alkaline pH. Elaborate calculations using the titration data are consistent with the equilibrium (3) and the 1:1 association constant, $\log K$ value of 3.6 ± 0.1. Even at 5 equivalents of malonate (5 mM), 2:1 and 2:2 malonate/*m*,*m*-bis(Zn^{2+}–cyclen) complexes were not confirmed from the pH titration data. We proposed a structure of 1:1 malonate-bound complex containing a zinc(II)-bound water, **8** in Figure 1 from the following facts: i) The distance between two anionic oxygen atoms of malonate ($O^-\cdots O^-$ distance less than 5 Å) is too short to bridge the intramolecular two zinc(II) ions of *m*,*m*-bis(Zn^{2+}–cyclen) (the Zn···Zn distance more than 7 Å), as shown by its CPK molecular model and the X-ray crystal of 2:2 malonate/*m*,*m*-bis(Zn^{2+}–cyclen) complex (see next section). ii) The pH difference of the titration region at $0 <$ equiv(OH^-) < 1 between the absence and presence of 2 mM malonate is much larger than that at $1 <$ equiv(OH^-) < 2 (Figure 2). This fact indicates that the malonate coordination would be stabilized by an intramolecular hydrogen bond with the zinc(II)-bound water (Zn–malonate···H_2O–Zn). In addition, the following deprotonation of the zinc(II)-bound water of **8** (i.e., OH^- binding) would destabilize the 1:1 malonate complex by electrostatic repulsion between the Zn-unbound carboxylate anion and Zn–OH^-). iii) The ^1H NMR signals of **8** (2 mM) in D_2O solution at 35 °C are almost the same as shown those for the symmetric *m*,*m*-bis(Zn^{2+}–cyclen), so that the ligand exchange reaction between malonate dianion and water molecule in **8** is sufficiently fast in aqueous solution.

$$Zn_2L\ (\mathbf{4}) + \text{malonate} = Zn_2L\text{–malonate}\ (\mathbf{8});$$
$$K = ([Zn_2L\text{–malonate}]/[Zn_2L][\text{malonate}])/M^{-1} \qquad (3)$$

A typical diagram for species distribution as a function of pH at [total dizinc(II) complex] = [total malonate] = 2 mM is displayed in Figure 3, which shows an appropriate pH for the anion complexation is around pH 6. In the ^1H NMR analysis of **8**, we found that the methylene hydrogen atoms (δ 3.2 at 2 mM **8**) of the zinc(II)-bound malonate dianion were readily exchanged for deuterium in D_2O. The half-life for the H/D exchange was determined to be 80 min for 1:1 mixture (2.0 mM) of malonate and *m*,*m*-bis(Zn^{2+}–cyclen) at 25 °C and pD 7.0. Under the experimental conditions, the pseudo-first-order rate constant is $1.4 \times 10^{-4}\,s^{-1}$. After the end of the reaction, the solution pD was not changed and the other C-bound proton and carbon signals remained the same as those of freshly prepared sample, indicating that no side reaction (e.g., decarboxylation) occurred. In the absence of **4**, no H/D exchange of the methylene group was observed after leaving for 24 h. Since the reported pseudo-first-order rate constant for the H/D exchange of malonate dianion is $1.2 \times 10^{-6}\,s^{-1}$ at 25 °C at pD 7,[26] the acceleration factor of 2 mM *m*,*m*-bis(Zn^{2+}–cyclen) is about 10^2. Furthermore, we determined similar H/D exchange reactions using 2-methyl malonate and succinate diaions. Under the same conditions used for malonate, the half-life of 500 min for deuteration of the methine hydrogen of 2-methyl malonate was estimated to be a greater value than that for malonate, which is possibly due to an electron donor of the methyl group. On the other hand, the hydrogen atoms of a 2-methyl group showed no H/D exchange even after 1 day. As for succinate dianon, no H/D exchange reaction of the methylene groups was observed under the experimental conditions.

Synthesis and X-ray Crystal Structure of 2:2 Malonate/*m*,*m*-Bis(Zn^{2+}–cyclen) Complex 9. The malonate/*m*,*m*-bis(Zn^{2+}–cyclen) complex was crystallized as its nitrate salt from an aqueous solution (pH 7) containing *m*,*m*-bis(cyclen), two equivalent of zinc(II) nitrate, and two equivalents of disodium malonate. After drying under a pressure of 5 mmHg at 25 °C, the colorless crystals changed to white powder, which indicated that some lattice water molecules in the crystal are easily removed. The elemental analysis (C, H, N) and its NMR

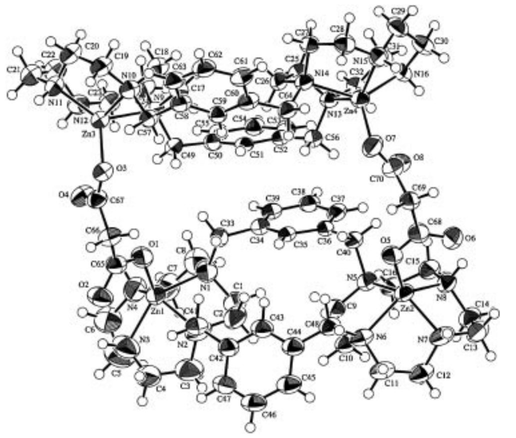

Figure 4. One of the crystallographically independent molecules of **9**. Atoms are drawn with 50% probability ellipsoids. Four nitrate ions, hydrogen atoms, and 15 water molecules are omitted for clarity.

data of the obtained powder suggested the formula $(Zn_2L–malonate\cdot(NO_3)_2\cdot 2H_2O)_n$. The crystal of the malonate/*m*,*m*-bis(Zn^{2+}–cyclen) complex was subjected to X-ray structure analysis at −180 °C. The crystal structure provided unequivocal evidence for the 2:2 malonate/*m*,*m*-bis(Zn^{2+}–cyclen) complex **9**, which is shown in Figure 4. We failed to isolate the originally intended 1:1 complex **8** with various other counter anions such as Cl^-, ClO_4^-, or SO_4^{2-}. The complex **9** has a cyclic structure constructed with two malonate dianions and two *m*,*m*-bis(Zn^{2+}–cyclen) complexes. The malonate dianion bridges the two Zn_2L units through the Zn^{2+}–O^- bonds. Each zinc(II) ion is surrounded in a distorted tetragonal pyramidal environment by the four nitrogen atoms of each cyclen and an anionic malonate oxygen. Selected bond lenghs and angles around zinc(II) ions are listed in Table 2. The average Zn^{2+}–O^- bond length of 1.96 Å is shorter than of the Zn^{2+}–N bond length of 2.16 Å. As we estimated, the intramolecular distances between two zinc(II) ions (ca. 9.3 Å) are much longer than those between two oxygen anions of malonate moieties (ca. 4.1 Å) in **9**. The cyclic structure of **9** is similar to that of the previous *m*-bis(Zn^{2+}–cyclen) complex with barbital dianion.[16]

Conclusion

A new bis(Zn^{2+}–cyclen) complex **4**, which consists of two zinc(II)–cyclen moieties and two *m*-xylene bridges, has been synthesized for the recognition of malonate dianion. In aqueous solution, the dizinc(II) complex **4** firmly captures an equimolar malonate dianion to form the 1:1 complex **8** at pH ca. 6. In the presence of **4**, H/D exchange reaction of the methylene protons of the malonate dianion was accelerated in D_2O at 35 °C. It is worthwhile to consider the use of the dizinc(II) complex **4** as a novel Lewis acid catalyst to form a malonate carbanion ($HC^-(COO^-)_2$) in solution. Furthermore, the malonate-bound complex was isolated as colorless crystals of 2:2 malonate/*m*,*m*-bis(Zn^{2+}–cyclen) complex **9**. The cyclic structure was confirmed by X-ray crystal analysis. The present findings will be useful in the further design of host molecules for various anions based upon zinc(II)–cyclen complexes.

Table 2. Selected Bond Lengths/Å and Angles/° around Zinc(II) Ions of **9**

Zn1–O1	1.944(6)	Zn1–N1	2.199(5)
Zn1–N2	2.195(5)	Zn1–N3	2.119(6)
Zn1–N4	2.135(6)	Zn2–O5	1.947(6)
Zn2–N5	2.185(5)	Zn2–N6	2.198(5)
Zn2–N7	2.118(5)	Zn2–N8	2.135(5)
Zn3–O3	1.954(6)	Zn3–N9	2.192(5)
Zn3–N10	2.195(5)	Zn3–N11	2.118(5)
Zn3–N12	2.137(5)	Zn4–O7	1.976(6)
Zn4–N13	2.188(4)	Zn4–N14	2.197(4)
Zn4–N15	2.123(5)	Zn4–N16	2.142(5)
O1–Zn1–N1	103.1(2)	O1–Zn1–N2	105.3(2)
O1–Zn1–N3	121.1(2)	O1–Zn1–N4	119.3(2)
N1–Zn1–N2	80.8(2)	N1–Zn1–N3	135.4(2)
N1–Zn1–N4	81.5(2)	N2–Zn1–N3	82.3(2)
N2–Zn1–N4	134.7(2)	N3–Zn1–N4	81.8(2)
O5–Zn2–N5	106.7(2)	O5–Zn2–N6	104.2(2)
O5–Zn2–N7	116.5(2)	O5–Zn2–N8	120.9(2)
N5–Zn2–N6	81.16(19)	N5–Zn2–N7	136.3(2)
N5–Zn2–N8	81.8(2)	N6–Zn2–N7	82.2(2)
N6–Zn2–N8	134.6(2)	N7–Zn2–N8	81.8(2)
O3–Zn3–N9	104.4(2)	O3–Zn3–N10	101.7(2)
O3–Zn3–N11	118.6(2)	O3–Zn3–N12	123.2(2)
N9–Zn3–N10	81.07(19)	N9–Zn3–N11	136.2(2)
N9–Zn3–N12	81.8(2)	N10–Zn3–N11	82.4(2)
N10–Zn3–N12	134.6(2)	N11–Zn3–N12	81.6(2)
O7–Zn4–N13	120.9(2)	O7–Zn4–N14	105.8(2)
O7–Zn4–N15	102.7(2)	O7–Zn4–N16	119.3(2)
N13–Zn4–N14	81.11(18)	N13–Zn4–N15	136.0(2)
N13–Zn4–N16	81.80(19)	N14–Zn4–N15	82.15(18)
N14–Zn4–N16	134.3(2)	N15–Zn4–N16	81.5(2)

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