¹³C and ⁵¹V Nuclear Magnetic Resonance Studies of Vanadium(V)-α-Hydroxycarboxylate Complexes

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The interaction of vanadium(V) with various α-hydroxycarboxylate ligands in aqueous solution at pH 3.2 have been studied by ⁵¹V and ¹³C NMR spectroscopies. From the results it is supposed that vanadates mainly form the octahedral complexes with lactate, 2-hydroxybutyrate, glycerate, and malate. While, vanadates form the trigonal-bipyramidal complexes with glycolate, tartarate, and 2-hydroxy-3-methylbutyrate, and tetrahedral complexes with pyruvate(diol), 2-hydroxyisobutyrate, and 2-hydroxy-3-methylbutyrate. The bipyramidal products are formed as monomeric compounds. The octahedral products are formed as dimeric compounds with no evidence for a significant proportion of the monomeric derivatives. The complexes are mainly formed through the coordination at the carboxylate and the 2-hydroxyl groups of the ligands.

Introduction

The chemistry of vanadium(V) in aqueous solution is very complex because of oxidation of ligand by vanadium(V) and oligomerization of vanadium(V) species. But the aqueous chemistry of vanadium(V) is of particular interest since there is considerable evidence which suggests that vanadium is an essential element. It is well-known that vanadium in moderate levels has a significant impact on the function of enzymes and of biological systems.[1,2] It has been suggested that vanadate plays a role similar to phosphate by acting as a phosphate analogue. Vanadate spontaneously esterifies hydroxyl groups, which are then accepted as enzyme substrates in lieu of the normally phosphorylated substrate. It has recently been shown that glucose 6-vanadate is accepted in place of glucose 6-phosphate by glucose 6-phosphate dehydrogenase for the oxidation of glucose to gluconic acid.[3] Thus most of the research about vanadium(V) complexes have mainly been focused on the various hydroxyl group bearing compounds.

The formation of vanadate esters in aqueous solution has been studied for ethanol,[4] phenol,[5] ethyleneglycol,[6] 1,2-cyclohexanediol,[7] and 1,2-aromatic diols[8] by ⁵¹V NMR spectroscopy. When in combination with ethanol, vanadate forms acyclic mono- and di-esters in which the geometries about vanadium are tetrahedral. While, vanadate forms cyclic trigonal bipyramidal complex with ethyleneglycol in addition to acyclic esters. Vanadate reacts with *cis*- and *trans*-1,2-cyclohehanediol to give acyclic esters and cyclic complexes analogous to those observed with ethyleneglycol. The occurrence of similar products has also been reported for the interaction of vanadate with lactate and glycerate.[9] The spontaneous formation of trigonal bipyramidal products, requiring either vicinal hydroxyls, α-hydroxycarbonyls or α-hydroxycarboxylates, must be partially governed by conformational and steric requirements of the ligand. Such properties have, to a small extent, been investigated in acyclic ligand systems.

Oxalic acid, 1,2-dicarboxylic acid, is known to form an octahedral bis(oxalato) complex with vanadate, its structure having been assigned on the basis of X-ray diffraction[10,11] and

NMR studies.[9,12-14] Bis(oxalato)dioxovanadate(V) complex has a *cis*-VO₂ core. No bipyramidal complex is observed with oxalic acid. Oxalic acid is a strongly electron withdrawing ligand. We have studied vanadium(V) complexes of aminoplycarboxylic acids to obtain information about the structures of the complexes in aqueous solution.[15-17]

Since there have been rare studies on the vanadium(V) complexes of α-substituted carboxylic acids, we are planning to investigate more about them. In this paper we report the studies on the structures of vanadium(V) complexes of various α-hydroxycarboxylic acids in aqueous solution by ¹³C and ⁵¹V NMR spectroscopies. Of the α-substituted carboxylates amino groups do not seem to be involved in the complexation with vanadate while hydroxyl groups form complexes. We expect that ⁵¹V NMR spectroscopy will provide information about the geometry around vanadium in the complexes and ¹³C NMR spectroscopy will provide further information concerning the arrangement of the ligands in the complexes.

Experimental

Materials. All chemicals were of reagent grade (Aldrich Chemical Co. *et al.*) and used without further purification. Pyruvate and 2-hydroxybutyrate were used as Na salts, glycerate as Ca salt, and other α-hydroxycarboxylate liands were used as free acids.

Preparation of Sample Solutions. Sample solutions for NMR measurements were prepared by dissolving weighed amounts of NH_4VO_3 and ligand in D_2O-H_2O (20 : 80) to provide 2 : 1, 1 : 1, and 1 : 2 mole ratios and adjusting pH of the solution to 3.2 or 6.2 with concentrated NaOH or H_2SO_4. The concentration of vanadium in solution was maintained at 0.25 M. The correction of pH in the solution from D_2O was not made.

NMR Spectroscopy. ¹³C and ⁵¹V NMR Spectra of sample solutions were recorded at 62.90 and 65.79 MHz, respectively, on a Bruker AM-250 NMR spectrometer operating at 288 K. To reduce the oxidation of ligand by vanadium(V) in solution, the spectra were obtained immediately after preparing sample solutions. For obtaining ¹³C spectra samples
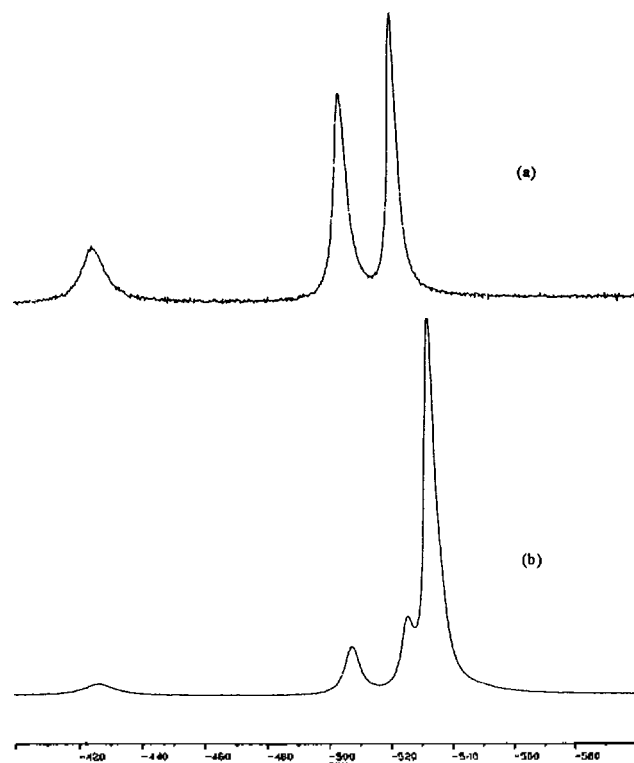
Figure 1. ^{51}V NMR spectra of (a) vanadate and (b) vanadium (V)-lactate (1 : 1) solutions at pH 3.2 (external reference: VOCl$_3$).

Table 1. ^{51}V Chemical Shift Data of Vanadium(V) Complexes

Complex	δ (ppm)[a]	Line-width (Hz)
V-glycolate	−523.9	170
V-lactate	−533.9	190
V-2-hydroxybutyrate	−535.5	360
V-glycerate	−533.1	370
V-malate	−533.9	530
	−547.6[b]	250
V-tartarate	−523.4	200
V-2-hydroxyisobutyrate	−548.9	310
V-2-hydroxy-2-methyl-butyrate	−551.3	440
V-2-hydroxy-3-methyl-butyrate	−527.5	380
V-pyruvate(diol)	−550.6	340

[a]Relative to VOCl$_3$(positive is downfield). [b]Minor product.

were run in 10 mm tubes with broadband proton noise decoupling. Pulse width of 4 μs, spectral width of 18 kHz, acqusition time of 0.92 s, and accumulation of ca. 2000 were used throughout. ^{13}C chemical shifts were measured relative to internal dioxane and referenced to sodium 2,2-dimethyl-2-silapentane-5-sulfonate(DSS) using the relationship δ$_{DSS}$= δ$_{dioxane}$+69.14 ppm. For obtaining ^{51}V spectra pulse width of 15 μs, spectral width of 63 kHz, acquisition time of 0.06 s, and accumulation of 500 were used. ^{51}V chemical shifts were measured to external VOCl$_3$ (δ=0 ppm). Samples were also run in 10 mm tubes.

Results and Discussion

Most of sample solutions had pale yellow color and turned green within a few hours at 298 K, indicating reduction of vanadium(V) by the ligand to produce a paramagnetic blue VO^{2+} species. This oxidation-reduction reaction was acid-catalyzed and, thus, the color change of the solutions was more pronounced at pH 3.2 than at pH 6.2. In general the ligand bearing hydroxyl group easily shows this phenomenon. Most of the ligands formed more stable complexes with vanadate at pH 3.2 than at pH 6.2, and types of the species formed are frequently affected by pH of the solution.

Vanadate solution has been known to give complex ^{51}V NMR spectra which are dependent on both concentration and pH of the solution.[12,18-22] Dioxovanadium ion, VO$_2^+$, readily hydrolyzes to HVO$_5^{4-}$ and VO$_3^-$ and also polymerizes to decavanadate ion in moderately acidic solution. ^{51}V NMR spectra of vanadate and vanadium(V)-lactate solutions at pH 3.2 are shown in Figure 1. Three peaks at −425.1, −504.5 and −521.5 ppm with relative intensities of 1 : 2 : 2 are assi-

gned to the decavanadate ion, [V$_{10}$O$_{28}$].[6-] The chemical shifts agree well to the reported values (−425, −504 and −519 ppm) of decavanadate ion which exist in the range of pH 6.5-2.[12,22] It is supposed that, thus, the major species of vanadium at pH 3.2 is decavanadate ion. The new vanadium peak appeared at −533.9 ppm in addition to the peaks of decavanadate ion when complexation of lactate occurred. ^{51}V chemical shifts of the vanadium complexes are give in Table 1. The signals occurring near −523 ppm has been assigned to pentacoordinate, possibly trigonal-bipyramidal, products similar to those formed with ethyleneglycol[6] and cyclohexanadiol.[7] Vanadate, in the presence of uridine, also give a ^{51}V peak near −520 ppm, indicating the formation of a vanadate-uridine-ribonuclease complex.[23,24] A crystalline product, which presumably is the same enzyme derivative found in solution, show trigonal-bipyramidal geometry about vanadium.[24] The formation of trigonal-bipyramidal complexes occurs readily in aqueous solution when vanadate is in the presence of 1,2-diol functionalities such as ethyleneglycol, cyclohexanaediol, etc. Those signals near −534 ppm are attributed to octahedral complexes. Bix (oxalato)dioxovanadate which is known as octahedral complex shows ^{51}V peaks at −536 ppm.[9] The peaks at higher field (near −550 ppm) are from tetrahedral complex, analogous to ethylvanadate(V) which shows peak at −555 ppm.[4,6] The broad peak reflects an increased rotational reorientation correlation time and an increased electric field gradient at the vanadate nucleus. Octahedral species give rise to significantly broader peaks than pentacoordinate species.

The complex formation would be easily detected by the appearance of sets of new ^{13}C NMR peaks which were distinct from those of free ligand. And the bounding sites of ligand in the complex are easily determined from the comparision of ^{13}C shifts between the complex and the free ligand. As example ^{13}C NMR spectra of lactate and vanadium(V)-lactate solutions are shown in Figure 2. The free ligand, lactate, showed ^{13}C peaks at 22.09, 69.30, and 181.60 ppm which are assigned to carbons of CH$_3$, CH, and COO groups, respectively. A set of new peaks at 21.17, 85.87, and 186.60 ppm appeared when complexation occurred. Usually the large downfield shift of ^{13}C occurred when complexation formed.

NMR Studies of Vanadium(V)-α-Hydroxycarboxylates

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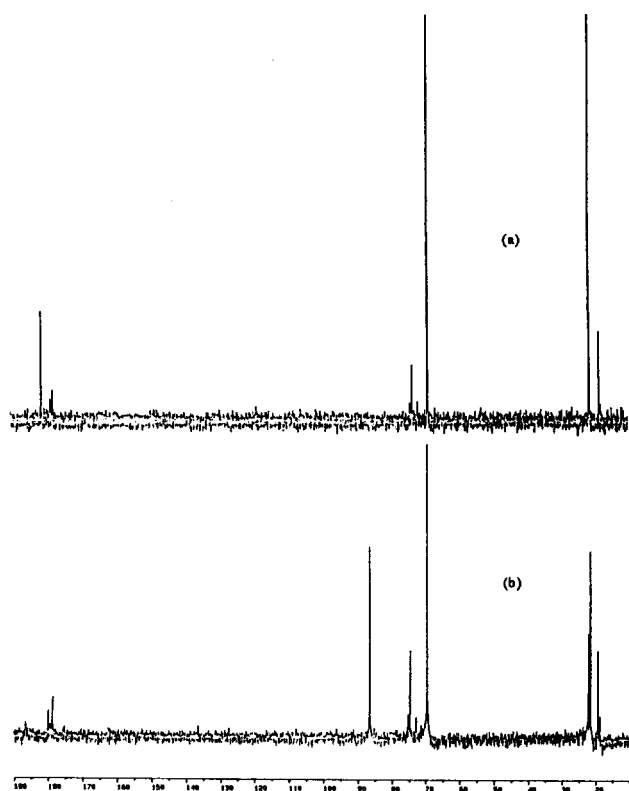
Figure 2. ¹³C-NMR spectra of (a) lactate and (b) vanadium (V)-lactate (1 : 1) solutions at pH 3.2 (the peak at 69.14 ppm is assigned to dioxane as internal reference).

The minor peaks in lactate are attributed to polymeric species in aqueous solution. ^{13}C chemical shifts of free ligands and their vanadium complexes are shown in Table 2. Upon complexation the ligands generally showed downfield shifts. No coupling between vanadium and carbons of ligand was observed in all complexes studied. The ^{13}C peaks were generally sharp and therefore consistent with the slow exchange of ligand between free and complexed states on NMR time scale.
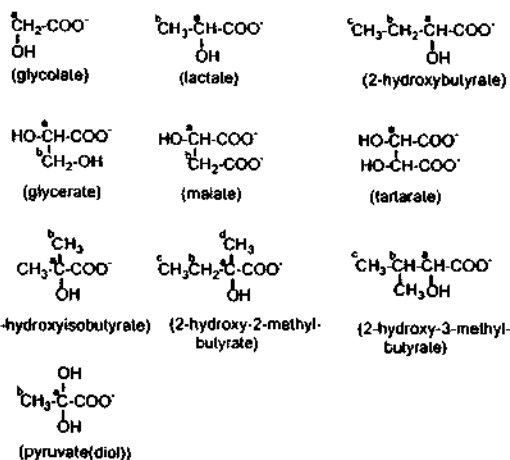
Lactate, 2-Hydroxybutyrate, Glycerate, and Malate. It is supposed that vanadates formed binuclear octahedral complexs with these ligands at pH 3.2 as shown in (I). These complexes showed ^{51}V peaks near −534 ppm, indicating octahedral structure. The products were formed as anhydrides, binuclear in vanadium, with no evidence for the formation of monomeric products. It has been reported from ^{51}V NMR

(I)
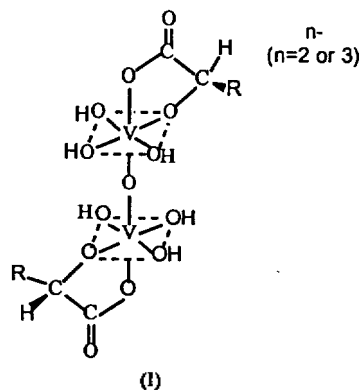
Table 2. ¹³C Chemical Shift Data(in ppm) of Free Ligands and Complexed Ligands(in parantheses)

| Compound[a]	a	b	c	d	COO	
glycolate	63.63					
	(79.54)				181.19	
					(184.06)	
lactate	69.30	22.02				
	(85.87)	(21.17)			181.60	
					(186.60)	
2-hydroxybutyrate	74.52	29.36	11.08		185.45	
	(89.97)	(28.04)	(8.99)		(185.45)	
	(88.67)[b]	(27.60)[b]	(8.75)[b]		(185.45)[b]	
glycerate	75.85	66.25			179.67	
	(90.08)	(64.25)			(183.30)	
malate	70.18	42.53			180.40,	178.02
	(84.97)	(39.42)			(184.43)	(176.25)
	(83.55)[b]	(39.42)[b]			(178.02)[b]	(176.25)[b]
tartarate	75.80				179.59	
	(91.77)				(185.77)	
2-hydroxyiso-butyrate	75.36	28.86			183.53	
	(88.19)	(27.37)			(187.89)	
2-hydroxy-2-methyl-butyrate	78.46	35.14			183.01	
	(91.76)	(33.60)			(187.19)	
2-hydroxy-3-methyl-butyate	78.56	34.17	10.02	27.46	181.12	
	(95.48)	(36.00)	(10.36)	(27.01)	(185.24)	
pyruvate(diol)	95.97	27.83	18.35	(20.80)	179.52	
	(103.98)	(26.11)	(18.85)	(19.94)	(182.70)	
		(26.39)				

[a]Structural assignment:

[b]Minor compound.

study that the vanadate forms small amounts of binuclear octahedral complexes with lactate and glycerate and the major products are trigonal-bipyramidal at pH 7.5.[9] But at pH 3.2 lactate and 2-hydroxybutyrate coordinated to vanadium *via* carboxylate and hydroxyl groups to form the binuclear octahedral complexes. Formation of the octahedral complex is accompanied by protonation, and thus its formation is favored at lower pH.[9] From the pK_a of the vanadium(V)-lactate complex which is 8.4,[9] it is assumed that the octahedral complexes are still protonated at pH 3.2. At pH 3.2 trigonal-bipyramidal products were not observed from ^{51}V spectra. The formation of trigonal-bipyramidal complex might not favored

relative to the octahedral complex as the pH is decreased. The interactions of glycerate and malate with vanadates are more complicated than those of lactate and 2-hydroxybutyrate. With glycerate there are two possibilities of complex formation that involve the vicinal 2,3-hydroxyl groups or the carboxylate and the 2-hydroxyl groups. The first case is similar to the reaction of vanadate with ethyleneglycol while the second case is similar to the reaction with lactate. It is supposed that the glycerate complex is formed *via* the carboxylate and 2-hydroxyl groups rather than two hydroxyl groups as for ethyleneglycol from ^{13}C chemical shift data, indicating the large shift of CH group from 75.85 to 90.08 ppm when complexation occurred. Malate have a hydroxyl and two carboxylate groups, of which a hydroxyl and a 1-carboxylate groups coordinate to vanadium. Also malate formed the tetrahedral product in small quantity which was more pronounced at pH 6.2. The octahedral complexes are dimeric, not monomeric as in the case of oxalate complexes.[13]

Glycolate, Tartarate, and 2-Hydroxy-3-methylbutyrate. The vanadate mainly formed trigonal-bipyramidal complexes with these ligands at pH 3.2 as shown in (II). The


(II)
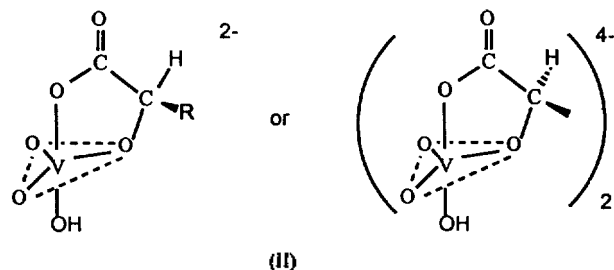
complexes of glycolate and 2-hydroxybutyrate are assumed to 1 : 1 monomeric compounds, but tartarate formed 2 : 1 binuclear complex. Glycolate is bound to vanadium *via* both the carboxylate and the hydroxyl groups in the complex. Tartarate(consists of two glycolate units) have two hydroxyl and two carboxylate groups which can complete to coordinate to vanadium, but 2 : 1 product was formed. It seems likely that bridging through the glycol unit occurs to give the symmertric complex. Also it was found that the acyclic ester of tartarate was formed in small quantity as in the case of ethyleneglycol complex.[6]

Pyruvate(diol), 2-Hydroxyisobutyrate, and 2-Hydroxy-2-methylbutyrate. It is assumed that vanadate formed the tetrahedral complex with these ligands at pH 3.2 as shown in (III). The complexes showed ^{51}V NMR peaks near −550 ppm, indicating the tetrahedral structure.

(III)
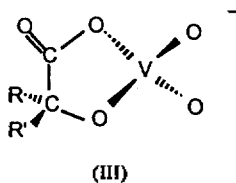
Of the α-hydroxycarboxylates studied these ligands are bulkier 2,2-disubstituted α-hydroxycarboxylate, which could not make octahedral or trigonal-bipyramidal product. The steric hindrance in the complex might play an important role to determine the structure. These ligands bound to vanadium via the carboxylate and hydroxyl groups. Pyruvate

is known to exist as keto and diol forms in aqueous solution, and 14% of the total pyruvate is in diol form.[25,26] Pyruvate also dimerizes in aqueous solution although the rate is slow for pH≤5 and in the absence of metal ions.[26] Of the two

keto-form   diol-form

(Species present in pyruvate solution)
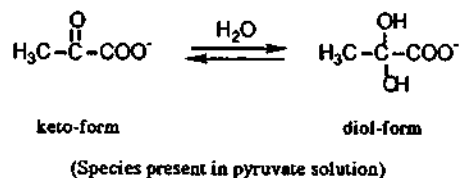
forms in pyruvate solution only diol-form formed complex *via* the carboxylate and the 2-hydroxyl groups.

In conclusion ^{51}V and ^{13}C NMR spectroscopies proved to be a powerful tool in the characterization of vanadium(V) complexes with various α-hydroxycarboxylates in aqueous solution. ^{51}V NMR spectroscopy provided the geometry around the vanadium and ^{13}C NMR spectroscopy provided the information concerning the arrangement of the ligands in the complexes.

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Formation of Cadmium(II) Nitrate Complexes with Macrocycles

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The twelve macrocycle (L) complexes of cadmium(II) nitrate have been synthesized: $CdL(NO_3)_2$. All the complexes have been indetified by elemental analysis, electric conductivity measurements, IR and NMR spectroscopic techniques. The molar electric conductivities of the complexes in water and acetonitrile solvent were in the range of 236.8-296.1 $cm^2 \cdot mol^{-1} \cdot ohm^{-1}$ at 25°C. The characteristic peaks of macrocycles affected from Cd(II) were shifted to lower frequencies as compared with uncomplexed macrocycles. A complex with 1,4,8,11-tetrakis (methylacetato)-1,4,8,11-tetraazacyclodecane (L_4) exhibited two characteristic bands such as strong stretching (1646 cm^{-1}), and weaker symmetric stretching band (1384 cm^{-1}). NMR studies indicated that all nitrogen donor atoms of macrocycles have greater affinity to cadmium (II) metal ion than do the oxygen atoms. The ^{13}C-resonance lines of methylene groups neighboring the donor atom such as N and S were shifted to a direction of high magnetic field and the order of chemical shifts were $L_1 < L_2 < L_3 < L_6 < L_4$. Also the chemical shifts values were larger than those of methylene groups bridgeheaded in side-armed groups. This result seems due to not only the strong interaction of Cd(II) with nitrogen donors according to the HSAB theory, but weak interaction of Cd(II) and COO^- ions or sulfur which is enhanced by the flexible methylene spacing group in side-armed groups. Thus, each additional gem-methyl pairs of L_3, L_4 and L_6 macrocycles relative to L_1, L_2, and L_5 leads to an large enhancement in Cd(II) affinity. ^{13}C-NMR spectrum of the complex with L_{12} (1,5,9,13-tetracyclothiacyclohexadecane-3,11 diol) reveals the presence of two sets of three resonance lines, and intensities of the each resonance line have the ratio of 1 : 2 : 2. This molecular conformation is predicted as structure of tetragonal complex to be formed by coordinating two sulfur atoms and the other two sulfur atoms which is affected by OH-groups.

Introduction

The 14-membered macrocycle, 1,4,8,11-tetraazacyclotetradecane[1,2] (cyclam), has been the subject of numerous investigations. Cyclams are large enough to encircle a range of metal ions. X-ray diffraction studies confirm that *trans*-planar coordination occurs for this ligand in complexes of Ni(II), Ni(III), Co(II), Cu(II) and Tc(V). N-tetramethylated cyclam[3] tends to promote the formation of five coordinate metal complexes. Thus, X-ray diffraction studies of [NiLCl₃] and [ZnLCl]⁺,[5] indicate square pyramidal structures for these complexes with the monodentate ligands occupying axial positions.

The S_4 systems[6-10] are the derivatives of a series of related S_4-macrocycles having ring sizes between 12 and 16 members. As for the cooresponding N_4-analogues, this ligand series has been used to investigate the effect of ring size on the coordination behavior of this ligand type[11]. Similarly, the mixed donor species[11-13] is a number of a related N_2S_2-

series of macrocycles. These ligands have also been used to study the effect of ring and donor atom position on the complexation behavior of such ligands. Typically, double-armed crown ethers form encapsulated complexes with several metal cations and provide characteristic chemical function[14,15]. Since high mobility of ligating pendant arms promises kinetically albile complexation, these armed macrocycles are recently recognized as the most suitable candidates for synthetic ionophores of metal cations.

The interaction between macrocycles and cadmium(II) compounds have not mostly been studied as compared with macrocyclic complexes with the other metals. This is unfortunate if one considers the importance of cadmium(II) as a polluting agent and its toxicologic aspects for living creatures. The design of synthetic receptors which could scanvenge this element from industrial wastes or even from biological fluids need for a broader study of this field. The calculations reported by izatt[16] for association constants of