Coordination Chemistry Reviews, 28 (1979) 205—229

CHROMATOGRAPHIC RESOLUTION OF METAL COMPLEXES ON SEPHADEX ION EXCHANGERS

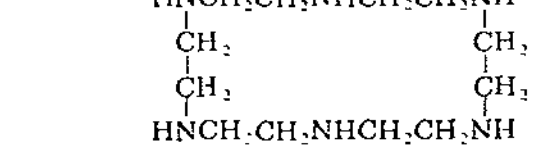
YUZO YOSHIKAWA* and KAZUO YAMASAKI

Department of Chemistry, Faculty of Science, Nagoya University, Chikusa, Nagoya, 464 (Japan)

(Received 14 November 1978)

CONTENTS

LIGAND ABBREVIATIONS

acac	acetylacetonate, $CH_3COCHCOCH_3^-$
ala	alaninate, $H_2NCH(CH_3)COO^-$
β-ala	β-alaninate, $H_2NCH_2CH_2COO^-$
amb	4-aminobutanoate, $H_2NCH_2CH_2CH_2COO^-$
bn	1,3-butanediamine, $H_2NCH(CH_3)CH_2CH_2NH_2$
bpy	2,2′-bipyridine
chxn	1,2-cyclohexanediamine
cptn	1,2-cyclopentanediamine
dabp	2,2′-diaminobiphenyl
daes	di(2-aminoethyl)sulfide, $H_2NCH_2CH_2SCH_2CH_2NH_2$
deb	*cis*-2-butene-1,4-diamine, $H_2NCH_2CH{=}CHCH_2NH_2$
dema	N-methylbis(2-aminoethyl)amine, $H_2NCH_2CH_2N(CH_3)CH_2CH_2NH_2$
dien	diethylenetriamine, $H_2NCH_2CH_2NHCH_2CH_2NH_2$
dmbpy	3,3′-dimethyl-2,2′-bipyridine
dmgH	dimethylglyoximate, $HONC(CH_3)C(CH_3)NO^-$
don	1,12-dodecanediamine, $H_2N(CH_2)_{12}NH_2$
dppn	1,3-diphenyl-1,3-propanediamine, $H_2NCH(C_6H_5)CH_2CH(C_6H_5)NH_2$
en	ethylenediamine, $H_2NCH_2CH_2NH_2$
etaH	2-aminoethanol, $H_2NCH_2CH_2OH$
gly	glycinate, $H_2NCH_2COO^-$
hexaen	1,4,7,10,13,16-hexaazacyclooctadecane, 
ibn	2-methyl-1,2-propanediamine, $H_2NC(CH_3)_2CH_2NH_2$
ida	iminodiacetate, $^-OOCCH_2NHCH_2COO^-$
ileu	isoleucinate, $H_2NCH[CH(CH_3)(CH_2CH_3)]COO^-$
isopraH	1-amino-2-propanol, $H_2NCH_2CH(CH_3)OH$
linpen	1,14-diamino-3,6,9,12-tetraazatetradecane, $H_2NCH_2CH_2NHCH_2CH_2NHCH_2CH_2NHCH_2CH_2NHCH_2CH_2NH_2$
mal	malonate, $^-OOCCH_2COO^-$
malato	malate, $^-OOCCH(OH)CH_2COO^-$
mbn	*meso*-2,3-butanediamine, $H_2NCH(CH_3)CH(CH_3)NH_2$
meen	N-methylethylenediamine, $H_2NCH_2CH_2NH(CH_3)$
mepenten	N,N,N′,N′-tetrakis(2′-aminoethyl)-1,2-propanediamine, $(H_2NCH_2CH_2)_2NCH(CH_3)CH_2N(CH_2CH_2NH_2)_2$
ox	oxalate, $^-OOCCOO^-$
pea	1-(2′-pyridyl)ethylamine
penten	N,N,N′,N′-tetrakis(2-aminoethyl)ethylenediamine, $(H_2NCH_2CH_2)_2NCH_2CH_2N(CH_2CH_2NH_2)_2$

phen	1,10-phenanthroline
pn	1,2-propanediamine, $H_2NCH(CH_3)CH_2NH_2$
praH	2-amino-1-propanol, $H_2NCH(CH_3)CH_2OH$
ptn	2,4-pentanediamine, $H_2NCH(CH_3)CH_2CH(CH_3)NH_2$
py	pyridine
sar	sarcosinate, $HN(CH_3)CH_2COO^-$
stien	1,2-diphenyl-1,2-ethanediamine, $H_2NCH(C_6H_5)CH(C_6H_5)NH_2$
tame	1,1,1-tris(aminomethyl)ethane, $(H_2NCH_2)_3CCH_3$
tart	tartrate, $^-OOCCH(OH)CH(OH)COO^-$
tmd	1,4-butanediamine, $H_2NCH_2CH_2CH_2CH_2NH_2$
tn	1,3-propanediamine, $H_2NCH_2CH_2CH_2NH_2$
tren	2,2′,2″-triaminotriethylamine, $(H_2NCH_2CH_2)_3N$
trien	triethylenetetramine, $H_2NCH_2CH_2NHCH_2CH_2NHCH_2CH_2NH_2$
val	valinate, $H_2NCH[CH(CH_3)_2]COO^-$

A. INTRODUCTION

It is well known that Werner, the founder of coordination chemistry, established the octahedral configuration of cobalt(III) complexes by proving experimentally the presence of geometrical isomers and, further, by resolving optical isomers [1]. Since then the classical fractional crystallization of diastereoisomers initiated by Pasteur has been widely used. This method, however is tedious; numerous attempts have been made to find other ways of resolving optical isomers, and various methods have been proposed [2—5].

In this review the results of the chromatographic resolution of optical isomers and the separation of geometrical isomers of mostly cobalt(III) complexes using methods which we have developed will be presented [6a—c].

B. CHROMATOGRAPHIC RESOLUTION OF METAL COMPLEXES

In 1935 Tsuchida and co-workers, in trying to find out whether the neutral complex $[CoCl(dmgH)_2(NH_3)]$ has a resolvable structure, devised a method called preferential adsorption [7]. They put powders of dextro- and laevorotatory quartz into an aqueous solution of the above neutral complex, and observed a small angle of rotation for the supernatant liquid. For example, when 1.03 g of dextrorotatory quartz powder was put into 10 ml of a 0.054 M aqueous solution of $[CoCl(dmgH)_2NH_3]$, the supernatant solution showed an angle of rotation of $-0.03°$ for the Fraunhofer C line. Similarly, when laevorotatory quartz (1.42 g) was used, an angle of $+0.02°$ was observed for the same wavelength. The method invented by Tsuchida was followed by many similar methods using optically active substances, such as quartz [8,9], starch [10—14], cellulose [13,14], acetylcellulose [15], sodium chlorate [16], lactose [17,18], alumina treated with (+)-tartaric acid [19], and ion exchange resins saturated with optically active ions [20], etc. Ion exchange cellulose was also

used to resolve cobalt(III) complexes [21,22] chromatographically, and total resolution of a polynuclear cobalt chelate was observed for the first part of its effluent [21], although complete separation of the adsorbed band was not found. Further, paper [23], gas [24], paper electrophoretic [25], thin layer [26,27], and centrifuged column [28] chromatographic methods have been developed.

In the course of our studies of optically active complexes, we tried to improve the method of Tsuchida, using an ion exchange cellulose, P-cellulose, as the adsorbent instead of quartz powder [6a,c]. As the complex ion, $[Co(en)_3]^{3+}$ was used and loaded on a column of P-cellulose. When eluted by 0.1 M HCl, resolution of only 7% was observed for the first effluent fraction. The resolution percentage, however, was greatly enhanced to 80% by the use of optically active eluting agents like sodium (+)-tartrate. After several attempts to increase resolution percentage, ion exchange Sephadex was finally adopted as the adsorbent, and total resolution of $[Co(en)_3]^{3+}$ was achieved. This was the first example of column chromatographic preparation of both optical antipodes in pure states. This method is not only effective for the complete resolution and preparative separation of optical isomers, but is also effective for the separation of geometrical isomers, which is difficult by other chromatographic methods. Other adsorbents may also be used [6a,c,29] to test resolvability, but the numerous examples listed in Table 2 clearly indicate the usefulness of this method for preparative purposes.

C. SEPHADEX ION EXCHANGERS

Sephadex is composed of a three dimensional network in which dextran is bridged by epichlorohydrin [30,31]. Dextran is a polysaccharide composed of D-glucose units which are joined mainly by means of α-1,6-glycosidic bonds, and partially by α-1,3- and/or α-1,4-bonds [32]. Sephadex is stable to alkali and weak acids [33,34] and can be heated without any change in properties to 110°C in the swollen state and to 120°C in the dry state.

The hydroxyl groups of the dextran gels are reactive; therefore, ion-exchanging groups can be introduced into them by etherification or esterification. For cation-exchanging SE-, SP-, and CM-Sephadex, sulfoethyl, sulfopropyl, and carboxymethyl groups respectively are chemically bound (Fig. 1). For anion-exchanging DEAE- and QAE-Sephadex, diethylaminoethyl and diethyl-2-hydroxypropylammonium groups are bound, respectively. There have been very few examples of chromatographic applications to anionic metal complexes (see p. 223), and in this review mostly cationic complexes will be dealt with.

As the commercially available Sephadex ion exchangers are produced as colorless beads, they are suitable for dealing with colored complexes. The problem is that Sephadex is rather expensive, although it can be used repeatedly after appropriate conditioning.

As will be shown in the examples to be given later, chromatography on

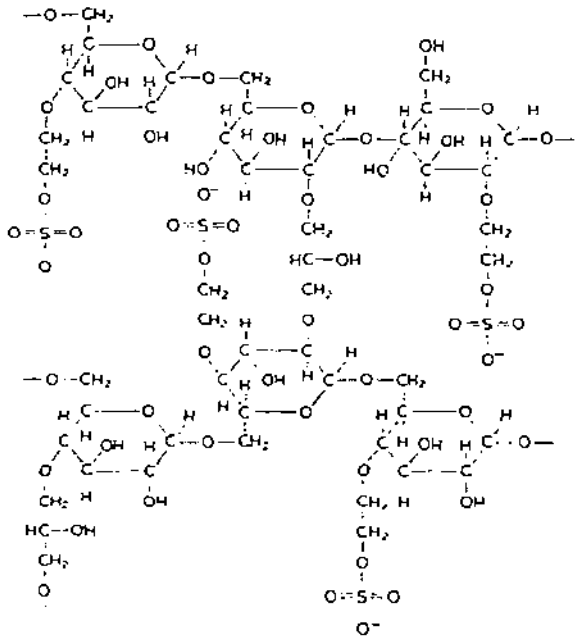


Fig. 1. Structure showing the essential features of SE-Sephadex.

Sephadex ion exchangers is very effective in separating multivalent cations which cannot be separated by other techniques such as chromatography using ion exchange resins. This is one of the characteristics of Sephadex ion exchangers. They swell in water much more than resins, and their ion exchange groups become well separated from each other in the three-dimensional network structures. This may be one of the reasons why multivalent cations which are strongly bound on ion exchange resins are adsorbed moderately on Sephadex ion exchangers and eluted rather easily.

D. EXPERIMENTAL TECHNIQUES

Since the experimental technique is basically similar to those of column chromatography on ion exchange resins, only the salient features involved in practice will be described here, and the solvent used is limited to water.

(i) General precautions

Usually a glass tube is employed for a column 50 cm long or shorter, and the outlet of the tube is kept open. Air does not permeate into such a column, while for a longer column the outlet of the tube must be closed in order to prevent air from permeating into the column. Small air bubbles trapped in a column during packing may be left intact, because they do not affect the elution of adsorbed bands, and in most cases they disappear during elution.

(ii) Adsorption of complex ions

First, water is poured into the column; then, after the top surface is settled *, the same ion exchanger adsorbed in advance with the complex is sprinkled into water. The other technique is first to pipette out water on the top of the column and then add the loaded Sephadex suspended in water uniformly on the top of the column.

(iii) Start of elution

The gravity-feed method is satisfactorily used for regulation of the flow rate. The excess water on the top of the column is pipetted off, and then an eluting agent solution is poured slowly and uniformly onto the column after opening the outlet. When the upper end of the adsorption band has sunk about 1 cm, further addition of the eluent can be done easily without disturbing the adsorption band.

The following technique requires less skill and is suitable for a beginner. The unloaded Sephadex ion exchanger is added in a layer 1—2 cm thick, into the water on the top of the loaded layer. Thus, the added eluting agent does not disturb the loaded layer, and the elution of the adsorbed band can be carried out smoothly.

(iv) Collection of effluents

The effluents of each elution band are collected and diluted with water about ten times for a tervalent complex, and more for bivalent or univalent complex ions. Each diluted solution is passed through a short column of the same ion exchanger and adsorbed on it. If the complex is stable in acids, we can elute the complex ions with 0.5—1.0 M HCl after washing the adsorbed column with a large amount of 0.01—0.02 M HCl. In this case, the Sephadex ion exchanger must previously be conditioned with the eluent, i.e., 0.5—1.0 M HCl. By evaporating the eluted solution containing HCl, a pure complex can be obtained. Sephadex is not hydrolyzed in 0.5—1.0 M HCl in a short time.

(v) Special techniques

(a) When a large amount of the sample is to be treated, or when a minor component in a mixture is to be isolated in substantial quantity by using a long column, the following technique is useful. Before the first sample is completely eluted out of the column, the next one is chromatographed in the same column. More samples can be chromatographed consecutively at such intervals as the fastest moving band of the succeeding sample does not overlap with the slowest moving band of the preceding sample. One of the advantages of this technique is economy of eluting agent.

(b) In column chromatography, the flow rates decrease gradually with

* The top surface of the column can be effectively brought to a horizontal level by rapidly rotating the tube.

time because the column bed shrinks and/or the passage of eluents is clogged by the degradation of ion exchangers or the growth of mold during prolonged use of the column. It is thus advisable to add an antimold agent such as toluene to any eluting agent. Occasionally an upward-flow method is effective in getting a satisfactory stability of the flow rate.

(c) As eluting agents, NaCl, Na_2SO_4, Na_3PO_4, sodium (+)-tartrate, sodium or potassium (+)-tartratoantimonate(III) are usually used. Sodium (+)-tartratoarsenate(III) is also effective, but dibutyltartrate and diacetyltartrate ions are less effective than the tartrate ion itself [35]. Among these agents, tartrate and tartratoantimonate ions are used for the separation of optical isomers as well as geometrical isomers. If the isomers to be separated are stable only in acids, eluents must be acidified with HCl, H_2SO_4, etc.; tartratoantimonate is suitable because of its intrinsic acidity. In some cases monobasic (+)-tartrates, various phosphates, and salts of other organic acids may be effectively used. As occasion demands, a mixture of eluting agents or the technique of gradient elution may also be used effectively.

(d) A very long column is often used in chromatography of isomers which are difficult to separate, but recycling chromatography is more practical for such isomers.

E. RESOLUTION OF THE TRIS(ETHYLENEDIAMINE)COBALT(III) ION

The SE-Sephadex(C-25) *, Na-form, swollen in water for one hour, was packed into a glass tube with a sintered glass plate at the lower end, and a column of ϕ 1.1 × 120 cm was prepared. About 8 mg of $[Co(en)_3]Cl_3 \cdot 3\,H_2O$ dissolved in a few ml of water was poured into the column and then eluted by a 0.4 M sodium chloride, 0.2 M sodium sulfate, 0.15 or 0.2 M sodium (+)-tartrate solution at the elution rate of 0.3—0.5 ml per minute. The absorbance of effluent at 465 nm (cell thickness, 1 cm) was plotted against the volume of the effluent (Fig. 2). After the complex had been eluted, the column shrank to a length of ca. 90—100 cm **. As is clear from Fig. 2b, the complex was completely separated into two portions when eluted by a 0.15 M sodium (+)-tartrate solution. The first portion showed $\Delta\epsilon_{490} = +1.89$, and the second portion, −1.85. These values are in good agreement with the value obtained by the conventional fractional crystallization technique, $\Delta\epsilon_{490} = +1.89$ for the $(+)_{589}$ (or Λ)-$[Co(en)_3]^{3+}$ ion, indicating complete resolution. Figure 2a shows the elution curves with three kinds of eluents containing an equal amount of sodium ions. The elution by a 0.2 M sodium (+)-tatrate solution caused less separation than a 0.15 M solution. The two optical isomers were

* SE-Sephadex is now replaced by SP-Sephadex because of its better reproducibility. According to the manufacturer, the two are almost the same in their physical and chemical properties; our experiences confirmed this so far as metal complexes are concerned.
** The column height may remain constant if the same eluting agent is used for conditioning the column.

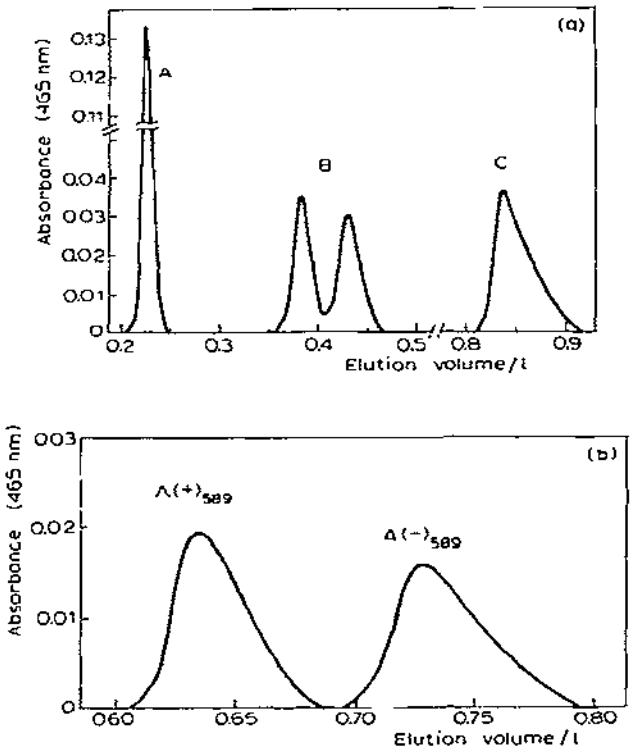


Fig. 2. Elution curves of $[Co(en)_3]^{3+}$ on an SE-Sephadex column. (a) Eluent: A, 0.2 M sodium sulfate; B, 0.2 M sodium (+)-tartrate; C, 0.4 M sodium chloride. (b) Eluent: 0.15 M sodium (+)-tartrate.

not separated by 0.4 M sodium chloride nor by 0.2 M sodium sulfate, only a few % and zero resolutions being found, respectively. The fast-moving isomer eluted by NaCl was $(-)_{589}$-$[Co(en)_3]^{3+}$, in contrast to the $(+)_{589}$-isomer eluted by sodium (+)-tartrate, and the elution order agrees with that in P-cellulose chromatography with 0.2 M HCl as the eluent [6a].

The association constants between anions in the eluting agents and $[Co(en)_3]^{3+}$ ions are known to decrease in the following order: sulfate > (+)-tartrate > chloride; furthermore, the (+)-tartrate ion has a larger ion-pair formation constant with Λ-$[Co(en)_3]^{3+}$ than with Δ-$[Co(en)_3]^{3+}$ [36—40]. Thus, it is reasonable that an anion with a larger association constant for the complex gives a larger elution rate.

The resolution was more effectively achieved by 0.15 M sodium (+)-tartratoantimonate(III) * [41], and the elution bands were completely separated on

* Sodium (+)-tartratoantimonate(III) was prepared by the following method. To a solution of sodium hydrogentartrate monohydrate ($NaC_4H_7O_6 \cdot H_2O$) (600 g) in 1.2 l of

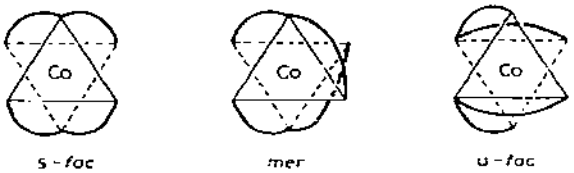


Fig. 3. Three geometrical isomers of the $[Co(dien)_2]^{3+}$ ion: s-*fac* (*trans-fac*), *mer*, and u-*fac*-(*cis-fac*) isomers.

a column 50 cm long. The elution order was the same as that by a sodium (+)-tartrate. Recently, sodium (+)-hydrogentartrate has been found to be effective for the complete resolution of the same complex [42].

F. OTHER EXAMPLES OF THE SEPARATION AND RESOLUTION OF CATIONIC COMPLEXES

(i) The bis(diethylenetriamine)cobalt(III) ion, $[Co(dien)_2]^{3+}$ (refs. 43, 44)

(a) Separation of geometrical isomers. Diethylenetriamine is a terdentate ligand; the complex ion, $[Co(dien)_2]^{3+}$, exists in three geometrical isomers (Fig. 3), and the u-*fac* and *mer* isomers have configurationally and conforma-

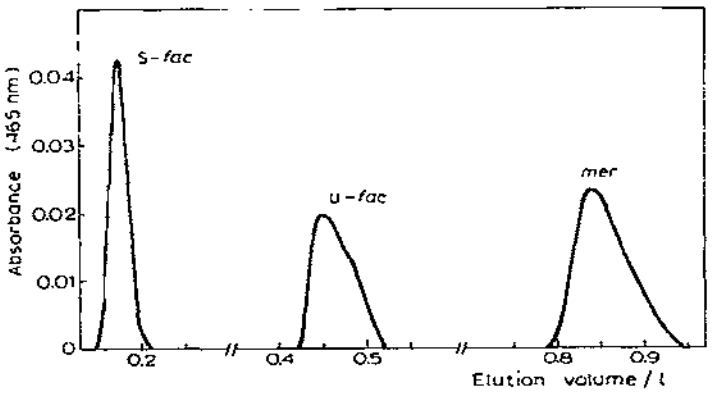


Fig. 4. Elution curves of equimolar (0.02 mmol) mixture of three isomers of $[Co(dien)_2]^{3+}$ on an SE-Sephadex column. Eluent: 0.15 M sodium (+)-tartrate.

---

water, 462 g of diantimony trioxide was slowly added with constant stirring. The mixture was stirred for 2 h at 80—90°C. After cooling, the residue was filtered off, and the filtrate was used as the eluting agent after suitable dilution with water. If necessary, the crystals were precipitated by the addition of a large amount of ethanol to the filtrate; these crystals were filtered and air-dried, and found to be $Na_2Sb_2(C_4H_2O_6)_2 \cdot 5\ H_2O$. This salt readily dissolves in water and the solution is acidic (pH 2.4 for the 0.15 M solution).

tionally resolvable structures respectively. Though the formation ratio of these three isomers depends on the preparative methods used, an equimolecular mixture (0.02 mM) was used here for illustration (Fig. 4). The mixture was poured into a column (ϕ 1.2 × 120 cm) of SE-Sephadex (C-25) and was eluted with a 0.15 M sodium (+)-tartrate solution at the rate of 1.2—1.4 ml min^{-1}. The s-*fac*, u-*fac* and *mer* isomers were eluted in this order.

(b) Resolution of the u-fac and mer isomers. The same chromatographic method was applied with success to the complete resolution of the u-*fac* and *mer* isomers. When eluted by a sodium (+)-tartrate solution, the u-*fac* isomer was not clearly separated into two bands, but the initial and last fractions eluted indicated an almost complete resolution. The use of a 0.15 M sodium (+)-tartratoantimonate(III) solution completely separated two bands corresponding to $\{+\}_{502}$ and $\{-\}_{502}$ catoptromers * in the column (ϕ 2.7 × 120 cm). The fast-moving band corresponds to the $\{+\}_{502}$ catoptromer chloride with $\Delta\epsilon_{502}$ = +0.98.

The resolution of the *mer* isomer was first carried out by the conventional fractional crystallization of the diastereoisomers [43] and later by the same chromatographic method as was used for the u-*fac* isomer [44]. When the *mer* isomer adsorbed on a column (ϕ 2.7 × 140 cm) of SE-Sephadex was eluted by a 0.15 M sodium (+)-tartratoantimonate(III) solution, first the $\{+\}_{513}$ catoptromer ($\Delta\epsilon$ = +0.096 for the chloride) and then the $\{-\}_{513}$ catoptromer were eluted, with complete separation. These catoptromers of the *mer* isomer racemize quickly in neutral and alkaline solutions; all the operations have to be performed in an aqueous solution acidified with 0.01 M HCl until the crystals are isolated.

(ii) Resolution of the N,N,N',N'-tetrakis(2-aminoethyl)ethylenediaminecobalt(III) ion, [Co(penten)]$^{3+}$ (ref. 45)

N,N,N',N'-Tetrakis(2-aminoethyl)ethylenediamine is a sexadentate ligand of the same type as EDTA, and the complex ion $[Co(penten)]^{3+}$ is resolvable. Both catoptromers were completely separated on a column of SE-Sephadex (ϕ 2.7 × 140 cm) by the use of a 0.15 M sodium (+)-tartratoantimonate(III) solution as eluent. First, the $\{-\}_{510}$ isomer and then the $\{+\}_{510}$ isomer were eluted. The CD value for the $\{+\}_{510}$ chloride was $\Delta\epsilon$ = +3.64.

The complex ion $[Co(mepenten)]^{3+}$ (mepenten being N,N,N',N'-tetrakis-(2'-aminoethyl)-1,2-propanediamine) was resolved in the same manner as $[Co(penten)]^{3+}$ [45].

(iii) The (linear pentaethylenehexamine)cobalt(III) ion, [Co(linpen)]$^{3+}$ (ref. 46)

Linear pentaethylenehexamine is able to function as a sexadentate ligand

* The symbols {+} and {−} represent the sign of the CD spectrum at a certain wavelength which usually corresponds to the maximum CD intensity of the appropriate band. For example, $\{+\}_{502}$ corresponds to $(-)_{550}$ in the u-*fac* isomer.

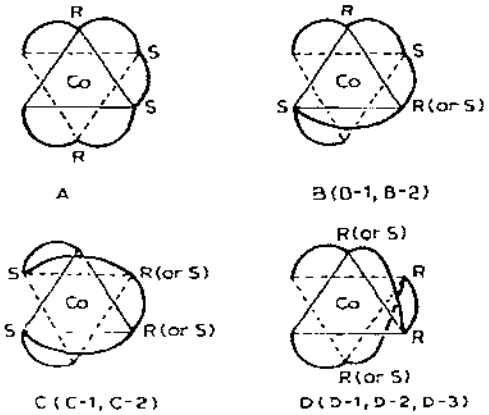


Fig. 5. Four geometrical isomers of the $[Co(linpen)]^{3+}$ ion. The absolute configuration (R and S) of secondary amine-N atoms is shown.

of stereochemical importance. In the $[Co(linpen)]^{3+}$ complex ion, four different configurational isomers can be expected (Fig. 5). If the absolute configurations around the secondary amine-N atoms are taken into account, each of the B, C, and D structures can exist in two or three isomers, which are designated in parentheses (Fig. 5).

The chromatographic separation of all the isomers was very difficult; the procedure finally evolved is illustrated in Fig. 6. A column (ϕ 2.7 × 140 cm)

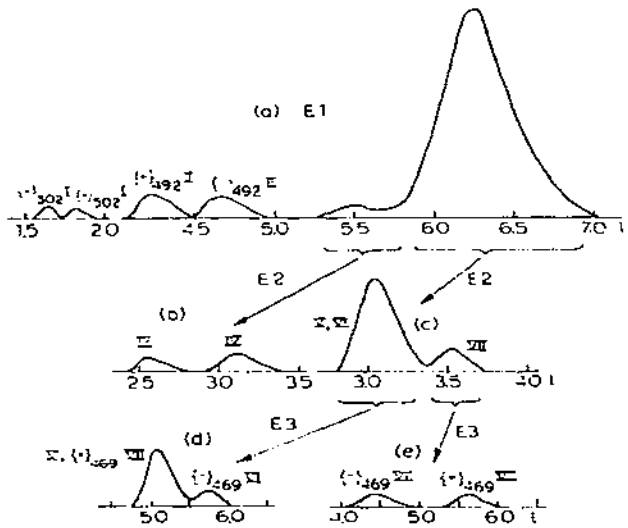


Fig. 6. Elution curves of the isomers of $[Co(linpen)]^{3+}$ on an SP-Sephadex column. Three kinds of eluents (E1, E2, and E3) were used, and five stages of separation (a—e) are shown.

TABLE 1

The assigned structures and absolute configurations of the isomers of $[Co(linpen)]^{3+}$ ion

Isomer	Structure (cf. Fig. 5)	Absolute configuration
{+}-I	A	ΔΛΛΛ
{+}-II	Mixture of conformational isomers, B-1 and B-2	ΔΛΛΛΛ
{+}-III	C-1 or C-2	ΔΔΛΛΛ
{+}-IV	C-2 or C-1	ΔΔΛΛΛ
{−}-V	D-1(SS)	ΔΔΔΔΛΛ
{−}-VI	D-2(RS)	ΔΔΔΔΛΛ
{−}-VII	D-3(RR)	ΔΔΔΔΛΛ

of SP-Sephadex(C-25) was used. As the eluting agents, 0.18 M sodium (+)-tartrate (E1), a mixture of a 0.18 M sodium sulfate and 0.01 M HCl (E2), and 0.3 M sodium (+)-tartratoantimonate (E3) were used. The absorbance of the effluents at 470 nm was plotted against effluent volume. As is shown in Fig. 6 isomers I, II, VI, and VII were chromatographically separated and resolved by using eluting agents E1, E2 and E3. The resolution of isomers III and IV, however, was difficult by chromatography alone, and optically pure isomers of III and IV were obtained by isomerizing isomers $\{+\}_{492}$- and $\{-\}_{492}$-II at pH 12. The latter gave a mixture of $\{+\}_{485}$-III and $\{+\}_{453}$-IV, which were then separated by elution with E2. Similarly isomer $\{-\}_{469}$-VI which was isolated by (d) in Fig. 6, isomerized readily in neutral and alkaline solutions to give a mixture of $\{-\}_{475}$-V, $\{-\}_{469}$-VI, and a small amount of $\{-\}_{469}$-VII. These isomers were then separated by repeating procedures (c) and (d) (Fig. 6). As isomers III—VII are labile, they should be treated in acid solution.

The structures of thus isolated isomers I—VII were assigned on the basis of the electronic absorption, CD, and PMR spectra (Table 1). These results were supported by conformational analysis [47a] and X-ray structure determination [47b].

(iv) The tris(isobutylenediamine)cobalt(III) ion, $[Co(ibn)_3]^{3+}$ (ref. 48)

As isobutylenediamine(2-methyl-1,2-propanediamine) is an unsymmetrical bidentate ligand, geometrical isomers can be expected in addition to optical isomers for the tris(ibn)cobalt complex. A mixture of $[Co(ibn)_3]^{3+}$ isomers prepared by the reaction of the ligand and $[CoBr(NH_3)_5]^{2+}$ was subjected to column chromatography (ϕ 2.7 × 130 cm) on SP-Sephadex with 0.15 M sodium (+)-tartrate as the eluent. First, the $\{+\}_{495}$-*mer*(Λ) isomer was eluted, with the $\{+\}_{495}$-*fac*(Λ) isomer following. The third band which seemed to be a mixture was again chromatographed on SP-Sephadex; the $\{-\}_{495}$-*mer*(Δ) and $\{-\}_{495}$-*fac*(Δ) isomers were subsequently eluted by a 0.15 M sodium (+)-tartratoantimonate(III) solution. If sodium tartratoantimonate was used first as the eluent, Δ-*mer* and Λ-*mer* were separated; then followed a mixture of

Δ-*fac* and Λ-*fac* isomers, which was then separated by sodium tartrate. Thus, sodium tartratoantimonate is effective in separating geometrical isomers, whereas sodium tartrate is effective in separating optical isomers.

(v) The Λ(ob_3)-tris(R-1,2-propanediamine)cobalt ion, Λ(ob_3)-[Co(R-pn)$_3$]$^{3+}$ (ref. 49)

There are four possible isomers for the [Co(R-pn)$_3$]$^{3+}$ ion, Δ(*lel*)(*fac*), Δ(*lel*)(*mer*), Δ(*ob*)(*fac*), and Λ(*ob*)(*mer*). Among them, the Δ(*lel*)(*fac*) isomer has been well studied for various properties, including the absolute configuration. In 1968 MacDermott separated the Δ(*lel*)(*mer*) isomer from the Δ(*lel*)(*fac*) isomer by fractional crystallization, but the former was isolated only as amorphous glasses, and it was not possible to determine its crystal structure [50]. The two *ob* isomers were isolated for the first time by chromatography on SP-Sephadex. When a reaction mixture of R-propylenediamine and [CoBr(NH$_3$)$_5$]Br$_2$ was subjected to chromatography on SP-Sephadex (column size: ϕ 2.7 × 135 cm) with a 0.18 M sodium sulfate solution as the eluent, first the lel_3 and then ob_3 isomers were eluted with complete separation. The fractions of the ob_3 isomers were again chromatographed on an SP-Sephadex column with a 0.15 M sodium (+)-tartrate solution, and the *mer* and *fac* isomers were eluted as fast-moving and slow-moving fractions respectively with complete separation. The CD values were $\Delta\epsilon_{475}$ = +2.48 for the *mer*-Λ(ob_3) chloride, and $\Delta\epsilon_{475}$ = +2.45 for the *fac*-Λ(ob_3) chloride. The formation ratio was lel_3: *mer*(ob_3) : *fac*(ob_3) = 30—45 : 3 : 1.

By chromatography on SP-Sephadex with a 0.18 M sodium tartrate solution, the lel_3 isomers can be separated into fast-moving *mer* and slow-moving *fac* isomers, but the separation is not complete.

(vi) The tris[(±)-1,2-propanediamine]cobalt(III) ion, [Co{(±)pn}$_3$]$^{3+}$ (ref. 51)

The complex ion [Co{(±)pn}$_3$]$^{3+}$ can exist in 24 isomers, including those described in the preceding section (v). The mixture of these isomers was first separated into 4 fractions: lel_3, lel_2ob, $lel(ob)_2$, and ob_3 with a column of SP-Sephadex, using a 0.1 M sodium phosphate solution as the eluent. Then each isomer fraction was separated into equal amounts of catoptric forms (Δ and Λ) on SP-Sephadex with 0.15 M sodium (+)-tartrate as the eluent, the Λ forms being eluted first. By a combination of paper and column chromatography some of the methyl group isomers have been partly separated.

(vii) The tris(meso-2,3-butanediamine)cobalt(III) ion, [Co(mbn)$_3$]$^{3+}$ (ref. 52)

Meso-2,3-butanediamine is a symmetrical bidentate ligand, but for the tris-(diamine) complex geometrical isomers, *mer* and *fac*, are formed by the alignment of two asymmetric carbons, R and S, for each of the absolute configurations, Δ and Λ. Theoretically, eight (lel_3, $3lel_2ob$, $3lel(ob)_2$ and ob_3) and four (lel_3, lel_2ob, $lel(ob)_2$ and ob_3) energetically unique conformational isomers can be expected for the *mer* and *fac* isomers respectively, but a rapid inversion of the chelate rings in solution will make only four isomers detectable: *mer*-Δ, *mer*-Λ, *fac*-Δ and *fac*-Λ. These four isomers were separated by column

chromatography on SP-Sephadex, with sodium (+)-tartratoantimonate(III) and (+)-tartrate as eluting agents. The former was effective in separating geometrical isomers and the latter, in separating optical isomers. The CD values found were $\Delta\epsilon_{493} = +2.92$ for the $\{+\}_{493}$-*mer*(Λ) and $\Delta\epsilon_{493} = +3.28$ for the $\{+\}_{493}$-*fac*(Λ) chloride.

(viii) The bis(ethylenediamine)(tetramethylenediamine)cobalt(III) ion, $[Co(en)_2(tmd)]^{3+}$ (ref. 53)

Tetramethylenediamine coordinated to the cobalt(III) ion as a bidentate ligand forms a seven-membered chelate ring. The complex ion $[Co(en)_2(tmd)]^{3+}$ gives the first example of a complex with a higher-membered chelate ring than six. The two catoptromers (Δ and Λ isomers) were obtained by column chromatography (ϕ 3 × 100 cm) on SP-Sephadex, with a 0.5 M sodium (+)-tartratoantimonate(III) solution as the eluent. The two isomers were completely separated on the column, the fast-moving band corresponding to the $\{+\}_{505}$ isomer with $\Delta\epsilon_{505} = +0.96$.

The same technique was also successfully applied to the complete resolution of a complex with a much higher-membered chelate ring, $[Co(en)_2(don)]^{3+}$, don being dodecamethylenediamine, $NH_2(CH_2)_{12}NH_2$.

(ix) The unsymmetrical facial diethylenetriamine(iminodiacetato)cobalt(III) ion, u-fac-[Co(ida)(dien)]$^+$ (ref. 54)

The complex ion $[Co(ida)(dien)]^+$ can exist in three geometrical isomers, just as $[Co(dien)_2]^{3+}$ (Fig. 3) can, and only the u-*fac* isomer has a configurationally resolvable structure. The resolution, however, has not been reported by Legg and Cooke, who first isolated these three geometrical isomers by chromatography on ion exchange resin [55a]. The chromatographic resolution of the u-*fac* isomer was carried out with a column (ϕ 1.3 × 130 cm) of SE-Sephadex, using a 0.015 M sodium (+)-tartratoantimonate(III) solution as the eluent. First, the $\{-\}_{541}$ isomer was eluted, and then the $\{+\}_{541}$ isomer. The effluents were diluted 20 times or more, and complex ions were adsorbed on a short column of the same Sephadex and then eluted again. The procedure was repeated until the intensity ratio of the CD spectrum at 541 nm to the absorption spectrum at 513 nm became constant. The CD value of the $\{-\}_{541}$ isomer is $\Delta\epsilon_{541} = -1.53$, and its absolute configuration was identified as Λ Δ Λ on the basis of the electronic absorption, circular dichroism data, etc. [54].

Okamoto et al. [55b] obtained the $(+)_{589}$-u-*fac*-[Co(ida)(dien)]$^+$ isomer by the conventional fractional crystallization technique, and their results agreed well with ours [54].

G. FURTHER EXAMPLES OF THE RESOLUTION OF OPTICAL ISOMERS AND THE SEPARATION OF DIASTEREOISOMERS

Further examples of the chromatographic resolution and separation of metal complexes on Sephadex ion exchangers (mainly SP-Sephadex) are summarized in Table 2.

TABLE 2

Resolution and separation of optical isomers and diastereoisomers

Complex [a]	Eluent	Fast-moving isomer, degree of separation	Ref.
$[Co(tmd)_3]^{3+}$	0.15 M K_2tartan [b]	$\{+\}_{485}$, incomplete	56
$[Co(sar)(en)_2]^{2+}$	0.11 M Na_2tartan	Δ-$[Co(R\text{-}sar)(en)_2]^{2+}$, complete	57
$[Co\{(+)\text{-tart}\}(phen)_2]^+$	0.15 M Na_2tartan	$\{-\}_{530}$, complete	58, 59
$[Co\{(-)\text{-tart}\}(phen)_2]^+$	0.15 M Na_2tartan	$\{+\}_{525}$, complete (Similar results were obtained for the corresponding bpy complexes.)	58, 59
$[Co\{(-)\text{-cptn}\}_3]^{3+}$	0.15 M Na_2HPO_4	*lel*$_3$, complete	60 [d]
$[Co(cis\text{-cptn})_3]^{3+}$ (geometrical isomers)	0.15 M Na_2HPO_4	— [c], complete	60 [d]
$[Co(cis\text{-cptn})_3]^{3+}$ (optical isomers)	0.2 M NaK(+)-tart	— [c], complete	60 [d]
α-$[Co(dabp)(trien)]^{3+}$	0.15 M Na_2(+)-tart	$(-)_{589}$, complete	61
$[Co(bpy)_2(dabp)]^{3+}$	0.125 M Na_2tartan	$\{-\}_{444}$, unseparated	61
$[Co(S\text{-}praH)(en)_2]^{3+}$	0.07 M Na_2(+)-tart	$\{+\}_{520}$, — [c]	62
$[Co(tn)_3]^{3+}$	0.14 M Na_2tartan	$\{-\}_{535}$, unseparated	41 [d]
$[Co(bpy)_3]^{3+}$	0.14 M Na_2tartan	$\{-\}_{449}$, unseparated	41 [d]
$[Co(bpy)(en)_2]^{3+}$	0.1 M Na_2tartan	$\{+\}_{480}$, unseparated	41
$[Co(bpy)_2(en)]^{3+}$	0.1 M Na_2tartan	$\{+\}_{481}$, unseparated	41
$[Co(phen)(en)_2]^{3+}$	0.1 M Na_2tartan	$\{+\}_{481}$, complete	41
cis-$[Co(NH_3)_2(en)_2]^{3+}$	0.15 M Na_2tartan	$\{+\}_{492}$, complete	41
$[Co(meen)(en)_2]^{3+}$	0.15 M Na_2tartan	Λ, complete	63
$[Co(meen)_2(en)]^{3+}$	0.15 M Na_2tartan	Λ, complete	63
$[Co(S\text{-}pea)_3]^{3+}$	0.1 M Na_2SO_4	1. $\{+\}_{472}$ *fac*-Λ(*lel*$_3$), — [c] 2. $\{-\}_{464}$ *fac*-Δ(*ob*$_3$) 3. $\{+\}_{473}$ *mer*-Λ(*lel*$_3$)	61
$[Co(NH_3)_4(R,S\text{-}isopraH)]^{3+}$	0.1 M K_2tartan	$\{-\}_{535}$, complete	65
$[Co(R,S\text{-}isopraH)(en)_2]^{3+}$	0.1 M K_2tartan	1. Λ-R, incomplete 2. Λ-S 3. Δ-S 4. Δ-R	65
$[Co(etaH)(R,R\text{-}chxn)_2]^{3+}$	0.15 M Na_2(+)-tart +0.09 M HCl	— [c], incomplete	65
$[Co(CN)_2(R,R\text{-}chxn)_2]^+$	0.05 M NaCl	1. *trans*, complete 2. *cis*-Λ 3. *cis*-Δ	66
$[Co(L\text{-}ala)(en)_2]^{2+}$	0.1 M Na_2tartan	$\{+\}_{502}$, complete	41
$[Co(ox)(en)_2]^+$	0.03 M Na_2tartan	$\{-\}_{520}$, unseparated	41
$[Co(mal)(en)_2]^+$	0.03 M Na_2tartan	$\{-\}_{525}$, unseparated	41
cis-$[Co(CN)_2(en)_2]^+$	0.03 M Na_2tartan	$\{-\}_{465}$, incomplete	41
$[Co(L\text{-}ala)(NH_3)(tame)]^{2+}$	0.075 M Na_2tartan	$\{-\}_{465}$, complete	67
$[Co(L\text{-}val)(NH_3)(tame)]^{2+}$	0.075 M Na_2tartan	$\{-\}_{465}$, complete	67
$[Co(L\text{-}ileu)(NH_3)(tame)]^{2+}$	0.075 M Na_2tartan	$\{-\}_{465}$, complete	67
cis-$[CoCl(py)(en)_2]^{2+}$	0.2 M Na_2(+)-tart	$\{+\}_{465}$, unseparated	68 [d]

TABLE 2 (continued)

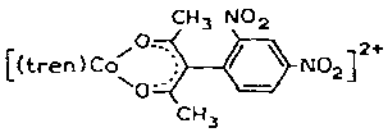
Complex [a]	Eluent	Fast-moving isomer, degree of separation	Ref.
$[Co(rac\text{-pea})_3]^{3+}$	0.2 M NaH_2PO_4 +0.02 M Na_2HPO_4	1. *fac-lel*$_3$ complete 2. *fac-lel*$_2$*ob* complete 3. *fac-ob*$_2$*lel* complete 4. *fac-ob*$_3$ complete 5. *mer*(mixture)	69
fac-lel$_3$-$[Co(rac\text{-pea})_3]^{3+}$	0.09 M Na_2(+)-tart + 0.04 M NaH(+)-tart	Λ, incomplete	69
fac-lel$_2$*ob*-$[Co(rac\text{-pea})_3]^{3+}$	0.09 M Na_2(+)-tart +0.04 M NaH(+)-tart	Λ, complete	69
fac-ob$_2$*lel*-$[Co(rac\text{-pea})_3]^{3+}$	0.09 M Na_2(+)-tart +0.04 M NaH(+)-tart	Λ, complete	69
fac-ob$_3$-$[Co(rac\text{-pea})_3]^{3+}$	0.09 M Na_2(+)-tart +0.04 M NaH(+)-tart	Λ, complete	69
cis-$[Co(N_3)_2(en)_2]^+$	0.075 M K_2tartan	$(+)_{589}$, incomplete	70
$[Co(gly)(en)_2]^{2+}$	0.1 M K_2tartan	$(+)_{589}$, complete	70
$[Co(gly)(tn)_2]^{2+}$	0.075 M K_2tartan	$(-)_{589}$, complete	70
cis(O)*cis*(N)-$[Co(gly)_2(en)]^+$	0.025 M K_2tartan	$(+)_{589}$, complete	70
cis(O)*cis*(N)*cis*(NH_3)-$[Co(gly)_2(NH_3)_2]^+$	— [c]	— [c], complete	70
$[Co(chxn)_3]^{3+}$	0.2 M Na_3PO_4	(The four racemic pairs (*lel*$_3$, *lel*$_2$*ob*, *ob*$_2$*lel*, and *ob*$_3$) were obtained.)	71 [d]
$[Co(chxn)_3]^{3+}$ (each racemic pair)	0.1 M $(NH_4)_2$(+)-tart	Λ, — [c]	71 [d]
$[Co(meso\text{-ptn})_3]^{3+}$ (geometrical isomers)	0.16 M Na_2tartan	*mer*, complete	72
$[Co(meso\text{-ptn})_3]^{3+}$ (each racemic pair)	0.16 M Na_2tartan	Δ, incomplete	72
$[Co(acac)(bpy)_2]^{2+}$	0.04 M Na_2(+)-tartan	$\{+\}_{495}$, unseparated	73
$[Co(acac)(phen)_2]^{2+}$	0.04 M Na_2(+)-tart	$\{-\}_{543}$, unseparated	73
$[Co(acac)_2(bpy)]^+$	0.01 M Na_2(+)-tart	$\{-\}_{505}$, unseparated	73
	0.1 M K_2tartan	$(-)_{589}$, complete	74
u-*fac*-$[Co(daes)_2]^{3+}$	0.3 M Na_2tartan	$\{-\}_{512}$, unseparated	75
$[Co(rac\text{-dppn})(en)_2]^{3+}$	2 M $NaClO_4$	1. Λ-SS + Δ-RR 2. Δ-SS + Λ-RR complete	76
$[Co(rac\text{-dppn})(en)_2]^{3+}$ (racemic pair 1)	0.3 M Na_2tartan	Λ-SS, complete	76

TABLE 2 (continued)

Complex [a]	Eluent	Fast-moving isomer, degree of separation	Ref.
$[Co(rac\text{-dppn})(en)_2]^{3+}$ (racemic pair 2)	0.3 M Na_2tartan	Λ-RR, complete	76
$[Co(rac\text{-dppn})(NH_3)_4]^{3+}$	0.15 M Na_2tartan	$(-)_{589}$, — [c]	76
$[Co(1\text{-stien})(en)_2]^{3+}$	— [c]	$\{+\}_{494}$, — [c]	76
$[Co(R,R\text{-ptn})(en)_2]^{3+}$	— [c]	$\{+\}_{490}$, — [c]	76
α-$[Co(en)(trien)]^{3+}$	0.18 M Na_2(+)-tart	$\{+\}_{490}$, complete	77
β-$[Co(en)(trien)]^{3+}$	0.18 M Na_2tartan	$\{+\}_{490}$, complete (for each conformational isomer) (Similar results were obtained for α- and β-$[Co(NH_3)_2(trien)]^{3+}$.)	77
$[Co(gly)(en)_2]^{2+}$	0.1 M Na_2(+)-tart or 0.08 M Na_2tartan	$(+)_{589}$, complete	78
$[Co(\beta\text{-ala})(en)_2]^{2+}$	0.1 M Na_2(+)-tart or 0.08 M Na_2tartan	$(+)_{589}$, complete	78
$[Co(amb)(en)_2]^{2+}$	0.1 M Na_2(+)-tart or 0.08 M Na_2-tartan	$(+)_{589}$, complete	78
$[Co(NH_3)_2(S,S\text{-dppn})_2]^{3+}$ (geometrical isomers)	0.15 M Na_2tartan in H_2O: DMSO (4 : 1)	*trans*, complete	79
cis-$[Co(NH_3)_2(S,S\text{-dppn})_2]^{3+}$	0.7 M $NaClO_4$ in H_2O : MeOH (2 : 1)	*cis*-Λ, complete	79
$[Co(NH_3)_2(S,S\text{-stien})_2]^{3+}$ (geometrical isomers)	0.15 M Na_2tartan in H_2O : DMSO (4 : 1) followed by 0.7 M $NaClO_4$ in H_2O : MeOH (2 : 1)	*trans*, complete	79
cis-$[Co(NH_3)_2(S,S\text{-stien})_2]^{3+}$	0.7 M $NaClO_4$ in H_2O : MeOH (2 : 1) followed by 0.5 M NaCl	*cis*-Λ, complete	79
$[Co(en)(tn)(tmd)]^{3+}$	0.18 M Na_2tartan	$(-)_{589}$, complete	80
$[Co(tn)_2(tmd)]^{3+}$	0.18 M Na_2tartan	$(+)_{589}$, incomplete	80
$[Co(en)(tmd)_2]^{3+}$	0.15 M Na_2tartan	$(-)_{589}$, incomplete	80
$[Co(tn)(tmd)_2]^{3+}$	0.18 M Na_2tartan	$(+)_{589}$, incomplete	80
$[Co(en)_2(tn)]^{3+}$	0.18 M Na_2tartan	$(+)_{589}$, complete	80
$[Co(en)(tn)_2]^{3+}$	0.18 M Na_2tartan	$(+)_{589}$, incomplete	80
$[Cr\{(+)\text{-tart}\}(phen)_2]^{+}$	0.2 M Na_2tartan	$(-)_{589}$, complete	81
$[Cr\{(+)\text{-tart}\}(bpy)_2]^{+}$	0.2 M Na_2tartan	$(-)_{589}$, complete	81

TABLE 2 (continued)

Complex [a]	Eluent	Fast-moving isomer, degree of separation	Ref.
$[Cr(cis\text{-chxn})_3]^{3+}$ (geometrical isomers)	0.15 M Na_2tartan	*fac*, — [c]	82
fac- or *mer*-$[Cr(cis\text{-chxn})_3]^{3+}$	0.2 M Na_2(+)-tart	Λ, — [c]	82
$[Co(R,R\text{-ptn})_3]^{3+}$	0.2 M Na_2SO_4	Δ(*lel*$_3$), complete	83
$[Co(NH_3)_2(R,R\text{-ptn})_2]^{3+}$	0.18 M Na_2tartan	1. *cis*-$(-)_{470}$ + *trans* 2. *cis*-$(+)_{470}$ complete	83
$[Co(NH_3)_2(R,R\text{-ptn})_2]^{3+}$ (geometrical isomers)	0.2 M Na_2SO_4	*trans*, complete	83
$[Co(tren)(dmbpy)]^{3+}$	0.1 M K_2tartan	$\{-\}_{505}$, unseparated	84
$[Co(en)_2(dmbpy)]^{3+}$	0.15 M K_2tartan	$\{+\}_{483}$, incomplete	84
cis-α-$[Co(trien)(dmbpy)]^{3+}$	0.15 M K_2tartan	$\{+\}_{482}$, complete	84
$[Co(S\text{-bn})_3]^{3+}$ (geometrical isomers and diastereoisomers)	0.2 M Na_2 tartan	1. *mer*-Δ, 2. *fac*-Δ, complete 3. *mer*-Λ + *fac*-Λ	85
$[Co(S\text{-bn})_3]^{3+}$ (geometrical isomers, *mer*-Λ and *fac*-Λ)	0.2 M Na_2SO_4	*fac*-Λ, complete	85
$[Co\{(OH)_2Co(en)_2\}_3]^{6+}$ (geometrical and optical isomers)	0.3 M Na_2(+)-tart	(The four pairs of catoptromers completely separated. First the $\{+\}_{600}$ isomer was eluted of each pair.)	86
u-*fac*-$[Co(dien)(dema)]^{3+}$	0.15 M Na_2tartan	$\{+\}_{504}$, complete	87
mer-$[Co(dien)(dema)]^{3+}$	0.15 M Na_2tartan	$\{+\}_{523}$, complete	87
$[Co(hexaen)]^{3+}$	0.18 M Na_2(+)-tart	$\{+\}_{480}$, unseparated	88
$[Cr\{(-)chxn\}_3]^{3+}$	0.1 M Na_3PO_4	*lel*$_3$, — [c]	89
$[Cr\{(\pm)chxn\}_3]^{3+}$	0.1 M Na_3PO_4	(The three racemic pairs (*lel*$_3$, *lel*$_2$*ob* and *ob*$_2$*lel*) were obtained.)	89
$[Cr\{(\pm)chxn\}_3]^{3+}$ (each racemic pair)	0.3 M Na_2(+)-tart	— [c], — [c]	89
$[Co(meso\text{-tart})(phen)_2]^{+}$ (linkage isomers)	0.15 M Na_2tartan	1. Λ-DL + Δ-DL 2. Λ-LD + Δ-LD complete	90
$[Co(meso\text{-tart})(phen)_2]^{+}$ (diastereoisomers 1)	0.2 M Na_2tartan	Λ-DL, complete	90 [e]
$[Co(meso\text{-tart})(phen)_2]^{+}$ (diastereoisomers 2)	0.2 M Na_2tartan	Δ-LD, complete	90 [e]
$[Co(D\text{-malate})(phen)_2]^{+}$	0.125 M Na_2tartan	Λ-D, complete	90 [e]
$[Co(dcb)(en)_2]^{3+}$	0.15 M K_2tartan	— [c], — [c]	91
$[Rh(en)_3]^{3+}$	0.15 M Na_2(+)-tart	$\{+\}_{319}$, complete	92

[a] See commencement of article for ligand abbreviations.
[b] The notation, tartan, represents $[Sb_2\{(+)\text{-}C_4H_2O_6\}_2]^{2-}$, (+)-tartratoantimonate(III) ion.
[c] This was not described in the report.
[d] An SE-Sephadex column was used.
[e] A CM-Sephadex column was used.

H. RESOLUTION OF NEUTRAL COMPLEXES, *fac*-[Co(β-ala)$_3$] (REF. 93)

The complex of β-alanine, *fac*-[Co(β-ala)$_3$] is a neutral complex which cannot be resolved by the formation of diastereoisomers. The resolution of this complex was attempted on a column (ϕ 3 × 113 cm) of CM-Sephadex, with 30% aqueous ethanol as the solvent. The column was charged with 70 mg of the complex dissolved in 10 ml water, and then eluted with a 0.1 M sodium (+)-tartrate in a 30% aqueous ethanol solution. First, the {—}$_{514}$ isomer, and then the {+}$_{514}$ isomer, were eluted with complete separation. A further improvement in technique is, however, desirable to make it applicable to other neutral complexes.

I. RESOLUTION OF ANIONIC COMPLEXES

The chromatographic resolution of anionic complexes, such as [Co(edta)]$^-$, and u-*fac*-[Co(ida)$_2$]$^-$, was attempted on a column of DEAE-Sephadex with optically active eluents like (—)-α-methylbenzylamine, sodium (+)-tartrate, and sodium (+)-tartratoantimonate [94]. No total resolution with a complete separation of adsorbed bands has yet been achieved, although rather high CD values were observed for the first fraction of the effluents. Further improvement in the kinds of ion exchangers and eluting agents will be made in the future.

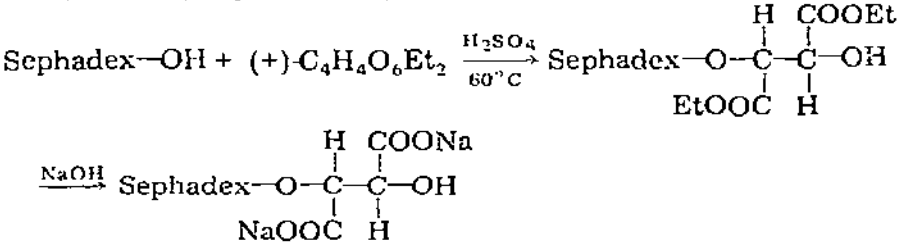
J. SEPHADEX ION EXCHANGERS WITH OPTICALLY ACTIVE ION EXCHANGE GROUPS AND THEIR CHROMATOGRAPHIC APPLICATIONS

Sephadex consists of D-glucosidic units, but they seem to contribute little to the resolution of complex ions; as was shown in the preceding examples, some optically active eluting agents, such as sodium (+)-tartrate or (+)-tartratoantimonate are needed for resolution. If ion exchangers possess optically active groups, resolution may be achieved even with inactive eluting agents. Furthermore, the use of optically active eluting agents will cause a more effective separation of optical isomers. From this point of view, preparation of some optically active Sephadex ion exchangers has been attempted.

(i) Preparation of TA-Sephadex

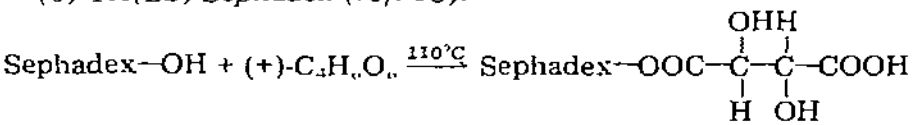
Sephadex which has a (+)-tartrate residue as the ion-exchanging group has been prepared and named as TA-Sephadex. As Sephadex has many hydroxyl groups capable of reacting as secondary alcohols, tartaric acid was made to react with Sephadex and to form an ester- or ether-form compound. The two types of TA-Sephadex thus prepared were named TA(ES)- and TA(ET)-Sephadex.

(a) TA(ET)-Sephadex (ref. 95).



The TA(ET)-Sephadex obtained after three etherification reactions was slightly yellowish in color, and its exchange capacity was 0.24 mmol $[Co(en)_3]^{3+}$ per g (dry).

(b) TA(ES)-Sephadex (ref. 95).



The H-form of TA(ES)-Sephadex was converted to the Na-form with 0.1 M NaOH, because the H-form scarcely adsorbed any $[Co(en)_3]^{3+}$ ions. The ester linkages in the TA(ES)-Sephadex may be hydrolyzed in an alkaline solution. Therefore, the pH of the solution should not be raised higher than 7 during conversion to the Na-form. The ion exchange capacity measured was 0.31 mmol $[Co(en)_3]^{3+}$ per g (dry), and the product was white in color.

(c) D-TA(ES)-Sephadex with D- or $(-)_{589}$-tartrate exchange groups (ref. 96). D-TA(ES)-Sephadex was prepared in a way similar to that described in Section J(i)(b). The resulting D-TA(ES)-Sephadex is yellowish-white in color, and the ion exchange capacity was found to be 0.17 mmol $[Co(en)_3]^{3+}$ per g (dry).

(ii) Chromatographic resolution of $[Co(en)_3]^{3+}$ on TA-Sephadex

The elution curve of $[Co(en)_3]^{3+}$ by TA-Sephadex with (+)-tartrate groups showed that the Δ-form was eluted faster than the Λ-form for both TA(ES)- and TA(ET)-Sephadex. This elution order was to be expected from the previous finding that (+)-tartrate ions interact with the Λ-form of the complex more strongly than with the Δ-form (Fig. 7) [36,37,97].

On the other hand, as is shown in Fig. 8, the Λ-form was eluted faster than the Δ-form on the D-TA(ES)-Sephadex, with (+)-tartrate as the eluent. The very effective separation of the complex into the catoptromers in spite of the low ion exchange capacity is ascribed to the double stereoselective effects of (−)- and (+)-tartrates on $[Co(en)_3]^{3+}$. The (+)-tartrate ion in the eluent interacts more strongly with the Λ-form than with the Δ-form, making D-TA(ES)-Sephadex hold the Δ-form more firmly. Thus, the Λ-form is eluted much faster.

(iii) Chromatographic resolution of $[Co(tn)_3]^{3+}$ on D-TA(ES)-Sephadex (ref. 98)

A ϕ 1.5 × 96 cm column of D-TA(ES)-Sephadex was prepared, and the [Co-

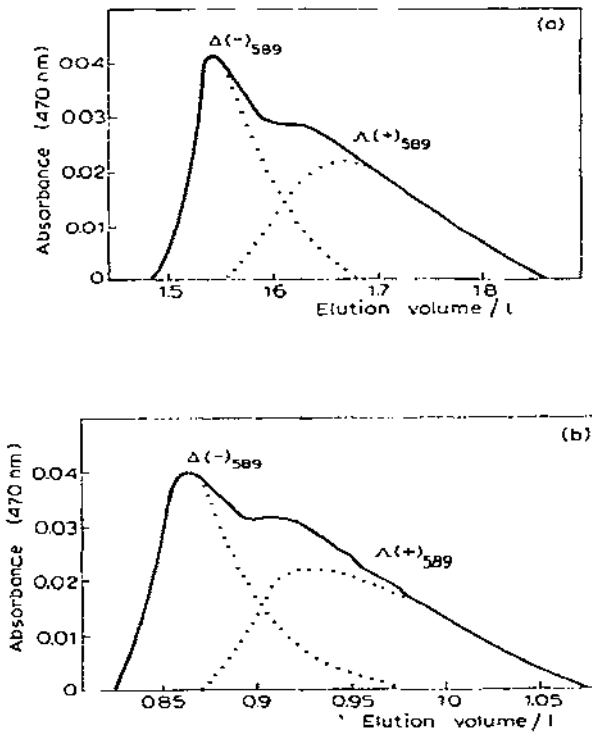


Fig. 7. Elution curves of $[Co(en)_3]^{3+}$. (a) TA(ET)-Sephadex, with 0.5 M sodium bromide as an eluent. (b) TA(ES)-Sephadex, with 0.37 M sodium bromide as an eluent.

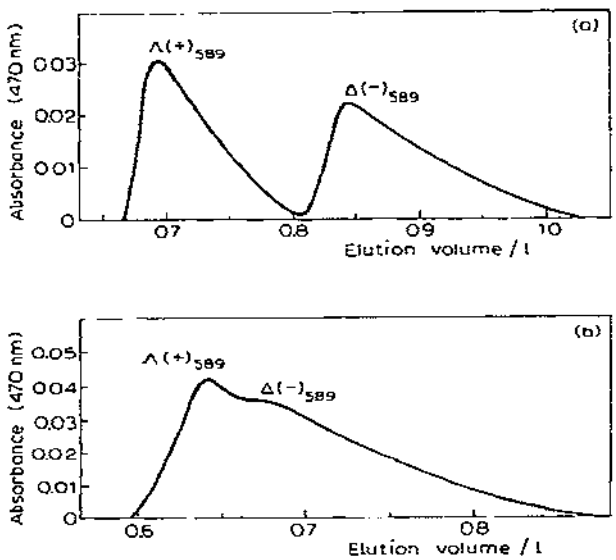


Fig. 8. Elution curves of $[Co(en)_3]^{3+}$ on a D-TA(ES)-Sephadex column. Eluent: (a) 0.06 M sodium (+)-tartrate. (b) 0.04 M sodium sulfate.

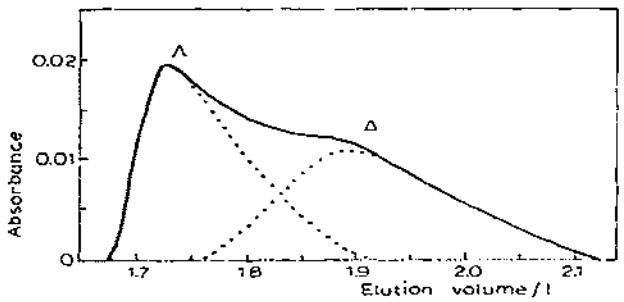


Fig. 9. Elution curves of $[Co(tn)_3]^{3+}$ on a D-TA(ES)-Sephadex column. Eluent: 0.1 M sodium (+)-tartrate.

$(tn)_3]^{3+}$ adsorbed was eluted with a 0.15 M sodium (+)-tartrate solution as the eluent (Fig. 9). Λ $[Co(tn)_3]^{3+}$ was eluted faster than the Δ-form, like $[Co(en)_3]^{3+}$ (cf. Section J(ii)). The separation was not complete, but both pure isomers were obtained from the initial and last fractions of the effluent. This complex was difficult to resolve on a column of SE-Sephadex, with sodium (+)-tartrate or (+)-tartratoantimonate as the eluent (Table 2). Therefore, the double stereoselective effect of the ion exchanger and the eluent seems to be the cause of the resolution.

The further application of this chromatographic method using the double stereoselective effect seems promising for complexes which are difficult to resolve.

ACKNOWLEDGEMENTS

We express our deep appreciation to our coworkers whose names are cited in the references for their important contribution. One of the authors (Y.Y.) would like to express his especial thanks to Professors Hideo Yamatera and Junnosuke Fujita, Nagoya University, for their encouragement and helpful discussion. Grants-in-Aid for Scientific Research from the Ministry of Education are gratefully acknowledged.

REFERENCES

1 A. Werner, Ber., 44 (1911) 1887.
2 S. Kirschner, in W.L. Jolly (Ed.), Preparative Inorganic Reactions, Vol. 1, Interscience, New York, 1964, p. 29.
3 A.M. Sargeson, in F.P. Dwyer and D.P. Mellor (Eds.), Chelating Agents and Metal Chelates, Academic Press, New York, 1974, p. 183.
4 F. Woldbye, in H.B. Jonassen and A. Weissberger (Eds.), Technique of Inorganic Chemistry, Vol. 4, Interscience, New York, 1965, p. 249.
5 R.D. Gillard, in F.A. Cotton (Ed.), Progress in Inorganic Chemistry, Vol. 7, Interscience, New York, 1966, p. 215.

6 (a) Y. Yoshikawa and K. Yamasaki, Inorg. Nucl. Chem. Lett., 4 (1968) 697.
(b) Y. Yoshikawa and K. Yamasaki, Inorg. Nucl. Chem. Lett., 6 (1970) 523.
(c) K. Yamasaki and Y. Yoshikawa, Rev. Roumaine Chim., 22 (1977) 801.
7 R. Tsuchida, M. Kobayashi and A. Nakamura, J. Chem. Soc. Jpn., 56 (1935) 1339; Bull. Chem. Soc. Jpn., 11 (1936) 38.
8 G. Karagounis and G. Coumoulos, Nature (London), 142 (1938) 162.
9 J.R. Keubler and J.C. Bailar, J. Am. Chem. Soc., 74 (1953) 3535.
10 H. Krebs and R. Rasche, Z. Anorg. Allg. Chem., 276 (1954) 236.
11 B.E. Douglas and S. Yamada, Inorg. Chem., 4 (1965) 1561.
12 J.H. Dunlop and D. Gillard, J. Chem. Soc., (1965) 6531.
13 H. Krebs, J. Diewald, H. Arlitt and J.A. Wagner, J. Chem. Soc., 287 (1956) 98.
14 L.T. Taylor and D.H. Busch, J. Am. Chem. Soc., 89 (1967) 5372.
15 H. Falk and K. Schlögl, Tetrahedron, 22 (1966) 3047.
16 E. Ferroni and R. Cini, J. Am. Chem. Soc., 82 (1960) 2427.
17 T. Moeller and E. Gulyas, J. Inorg. Nucl. Chem., 5 (1958) 245.
18 J.P. Collman, R.P. Blair, R.L. Marshall and S. Slade, Inorg. Chem., 2 (1963) 576.
19 T.S. Piper, J. Am. Chem. Soc., 83 (1961) 3908.
20 Y. Yoshino, H. Sugiyama, S. Nogaito and H. Kinoshita, Sci. Pap. Coll. Gen. Educ. Univ. Tokyo, 16 (1966) 57.
21 G.R. Brubaker, J.I. Legg and B.E. Douglas, J. Am. Chem. Soc., 88 (1966) 3446.
22 J.I. Legg and B.E. Douglas, Inorg. Chem., 7 (1968) 1452.
23 F.P. Dwyer, T.E. MacDermott and A.M. Sargeson, J. Am. Chem. Soc., 85 (1963) 2913.
24 R. Sievers, R.W. Moshier and M.L. Morris, Inorg. Chem., 1 (1962) 966.
25 H. Yoneda and T. Miura, Bull. Chem. Soc. Jpn., 43 (1970) 574; 45 (1972) 2126.
26 H. Yoneda and T. Baba, J. Chromatogr., 53 (1970) 610.
27 D.T. Haworth and Y.-W. Hung, J. Chromatogr., 75 (1973) 314.
28 D.T. Haworth, A.U. Paeglis and S.L. Wenzel, J. Chromatogr., 94 (1974) 279.
29 R.D. Gillard and P.R. Mitchell, Trans. Met. Chem., 1 (1976) 223.
30 P. Flodin, Dextran Gels and their Applications in Gel Filtration, Pharmacia, Uppsala, Sweden, 1962, p. 27.
31 H. Determann, Gel Chromatography, Springer-Verlag, New York, 1968, p. 15.
32 A. Jeanes, W.C. Haynes, C.A. Wilham, J.C. Rankin, E.H. Melvin, M.J. Austin, J.E. Cluskey, B.E. Fisher, H.M. Tsuchiya and C.E. Rist, J. Am. Chem. Soc., 76 (1954) 5041.
33 H.J. Cruft, Biochim. Biophys. Acta, 54 (1961) 611.
34 L. Fischer, in T.S. Work and E. Work (Eds.), Laboratory Techniques in Biochemistry and Molecular Biology, Vol. 1, North-Holland, Amsterdam, 1969, p. 181.
35 K. Yamasaki and Y. Yoshikawa, unpublished data.
36 K. Ogino and U. Saito, Bull. Chem. Soc. Jpn., 40 (1967) 826.
37 H. Yoneda and T. Taura, Chem. Lett., (1977) 63.
38 H. Yoneda, K. Miyoshi, S. Suzuki and T. Taura, Bull. Chem. Soc. Jpn., 47 (1974) 1661.
39 B. Norden, Acta Chem. Scand., 26 (1972) 111.
40 M. Fujita and H. Yamatera, Bull. Chem. Soc. Jpn., 49 (1976) 1301.
41 Y. Yoshikawa, unpublished work.
42 M. Fujita, Y. Yoshikawa and H. Yamatera, Bull. Chem. Soc. Jpn., 50 (1977) 3209; M. Fujita, Doctoral Thesis, Nagoya University, 1977.
43 F.R. Keene, G.H. Searle, Y. Yoshikawa, A. Imai and K. Yamasaki, Chem. Commun., (1970) 784; F.R. Keene and G.H. Searle, Inorg. Chem., 11 (1972) 148.
44 Y. Yoshikawa and K. Yamasaki, Bull. Chem. Soc. Jpn., 45 (1972) 179.
45 Y. Yoshikawa, E. Fujii and K. Yamasaki, Bull. Chem. Soc. Jpn., 45 (1972) 3451.
46 Y. Yoshikawa and K. Yamasaki, Bull. Chem. Soc. Jpn., 46 (1973) 3448.
47 (a) Y. Yoshikawa, Bull. Chem. Soc. Jpn., 49 (1976) 159.
(b) S. Sato and Y. Saito, Acta Crystallogr., Sect. B, 31 (1975) 2456.
48 M. Kojima, Y. Yoshikawa and K. Yamasaki, Bull. Chem. Soc. Jpn., 46 (1973) 1687.
49 M. Kojima, Y. Yoshikawa and K. Yamasaki, Inorg. Nucl. Chem. Lett., 9 (1973) 689.

50 T.E. MacDermott, Inorg. Chim. Acta, 2 (1968) 81.
51 S.E. Harnung, S. Kallesøe, A.M. Sargeson and C.E. Schäffer, Acta Chem. Scand., Part A, 28 (1974) 385.
52 M. Kojima, Y. Yoshikawa and K. Yamasaki, Bull. Chem. Soc., Jpn., 48 (1975) 2801.
53 H. Ogino and J. Fujita, Chem. Lett., (1973) 517.
54 Y. Yoshikawa, A. Kondo and K. Yamasaki, Inorg. Nucl. Chem. Lett., 12 (1976) 351; presented at the Symposium on Coordination Chemistry of the Chemical Society of Japan, 1973.
55 (a) J.I. Legg and D.W. Cooke, Inorg. Chem., 5 (1966) 594.
(b) K. Okamoto, J. Hidaka and Y. Shimura, Bull. Chem. Soc. Jpn., 48 (1975) 2456.
56 J. Fujita and H. Ogino, Chem. Lett., (1974) 57.
57 M. Fujita, Y. Yoshikawa and H. Yamatera, Chem. Lett., (1976) 959; Bull. Chem. Soc. Jpn., 50 (1977) 3209.
58 A. Tatehata, Chem. Lett., (1972) 561.
59 A. Tatehata, Inorg. Chem., 15 (1976) 2087.
60 H. Taftlunt and E. Pedersen, Acta Chem. Scand., 26 (1972) 4019.
61 T. Tanimura, H. Ito, J. Fujita, K. Saito, S. Hirai and K. Yamasaki, J. Coord. Chem., 3 (1973) 161.
62 K. Ogino, T. Nishide, J. Fujita and K. Saito, Chem. Lett., (1973) 679.
63 M. Kojima, Y. Yoshikawa and K. Yamasaki, Proc. 23rd Symposium on Coordination Chemistry, Fukuoka, Japan, October, 1973, p. 115.
64 K. Michelsen, Acta Chem. Scand., Part A, 28 (1974) 428.
65 T. Nishide, K. Ogino, J. Fujita and K. Saito, Bull. Chem. Soc. Jpn., 47 (1974) 3057.
66 K. Kashiwabara, T. Yamanaka, K. Saito, N. Komatsu, N. Hamada, H. Nishikawa and M. Shibata, Bull. Chem. Soc. Jpn., 48 (1975) 3631.
67 K. Yamanari, J. Hidaka and Y. Shimura, Bull. Chem. Soc. Jpn., 48 (1975) 1653.
68 I.J. Kindred and D.A. House, Inorg. Chim. Acta, 14 (1975) 185.
69 K. Michelsen, Acta Chem. Scand., Part A, 29 (1975) 301.
70 H. Yoneda, S. Yamazaki and K. Murayama, Proc. 26th Symposium on Coordination Chemistry, Sapporo, Japan, August, 1976, p. 234.
71 S.E. Harnung, B.S. Sørensen, I. Creser, H. Maegaard, U. Pfening and C.E. Schäffer, Inorg. Chem., 15 (1976) 2123.
72 M. Kojima and J. Fujita, Chem. Lett., (1976) 429.
73 K. Kashiwabara, K. Igi and B.E. Douglas, Bull. Chem. Soc. Jpn., 49 (1976) 1573.
74 Y. Nakano and H. Seki, Chem. Lett., (1976) 611.
75 G.H. Searle and E. Larsen, Acta Chem. Scand., Part A, 30 (1976) 143.
76 S. Arakawa, K. Kashiwabara, J. Fujita and K. Saito, Chem. Lett., (1976) 105.
77 K. Sakakibara, Y. Yoshikawa and H. Yamatera, to be published.
78 M. Kojima, H. Takayanagi and J. Fujita, Bull. Chem. Soc. Jpn., 50 (1977) 1891.
79 S. Arakawa, K. Kashiwabara, J. Fujita and K. Saito, Bull. Chem. Soc. Jpn., 50 (1977) 2331.
80 M. Kojima, H. Yamada, H. Ogino and J. Fujita, Bull. Chem. Soc. Jpn., 50 (1977) 2325.
81 A. Tatehata, Inorg. Chem., 16 (1977) 1247.
82 H. Taftlund and T. Laier, Acta Chem. Scand., Part A, 31 (1977) 651.
83 M. Kojima, M. Fujita and J. Fujita, Bull. Chem. Soc. Jpn., 50 (1977) 898.
84 T. Suzuki and T. Kimura, Bull. Chem. Soc. Jpn., 50 (1977) 391.
85 M. Kojima and J. Fujita, Bull. Chem. Soc. Jpn., 50 (1977) 3237.
86 T. Kudo and Y. Shimura, Proc. 27th Symposium on Coordination Chemistry, Matsumoto, Japan, September, 1977, p. 305.
87 M. Kojima, M. Iwagaki, Y. Yoshikawa and J. Fujita, Bull. Chem. Soc. Jpn., 50 (1977) 3216.
88 Y. Yoshikawa, Chem. Lett., (1978) 109.
89 S. Harnung and T. Laier, Acta Chem. Scand., Part A, 32 (1978) 41.
90 A. Tatehata, Inorg. Chem., 17 (1978) 725.

91 Y. Soma and F. Mizukami, Bull. Chem. Soc. Jpn., 51 (1978) 641.
92 K. Yamasaki and Y. Yoshikawa, unpublished results.
93 H. Yoneda and T. Yoshizawa, Chem. Lett., (1976) 707.
94 K. Yamasaki, S. Hirai and Y. Yoshikawa, unpublished results.
95 M. Fujita, Y. Yoshikawa and H. Yamatera, Chem. Lett., (1974) 1515.
96 M. Fujita, Y. Yoshikawa and H. Yamatera, Chem. Lett., (1975) 473.
97 M. Fujita and H. Yamatera, Bull. Chem. Soc. Jpn., 49 (1976) 1301.
98 M. Fujita, Y. Yoshikawa and H. Yamatera, Chem. Commun., (1975) 941.