COOPERATIVE EFFECT OF NH BOND ORIENTATION AND TRIAMINE SIX-MEMBERED CHELATE RING RIGIDITY IN STEREOSPECIFIC FORMATION OF *exo*-((1,6-DIAMINE-3-AZAHEXANE)-(*S*)-ASPARTATO)COBALT(III) ISOMERS

František JURSÍK and Jana ONDRÁČKOVÁ

Department of Inorganic Chemistry,
Prague Institute of Chemical Technology, 166 28 Prague 6

Received April 4th, 1988
Accepted May 24th, 1988

Dedicated to the memory of Dr Karel Bláha.

Of the six isomers possible, only *exo-sym-fac*(*S*), *exo-unsym*$_1$*-fac*(*S*) and *exo-Δ-unsym*$_2$*-fac*(*R*)-[Co(1,6-dah)(*S*)-Asp]$^+$ (1,6-dah = 1,6-diamine-3-azahexane) isomers were prepared and characterized by electronic absorption and circular dichroism spectra. Isomers formation is stereospecific due to the linear triamine NH bond orientation which causes that of the three sites in *mer*(*R* or *S*)-[Co(1,6-dah)$(H_2O)_3$]$^{3+}$ intermediates, only two are available for initial coordination of aspartic acid as bidentate ligand. In addition to this, 1,6-dah six-membered chelate ring precludes the necessary movement of the five-membered chelate ring backbone so that the linear triamine isomerization is stereospecific. Any *mer* → *fac* intramolecular rearrangemeмt involves the six-membered chelate ring part of 1,6-dah. Stereospecificity is also controlled by the aspartic acid chirality.

Stereochemistry of octahedral metal complexes containing bidentate or tridentate amines was extensively studied and several conclusions concerning the sterochemical behaviour of these systems were made (cf. ref.[1]). Despite of this no systematic studies of terdentate octahedral mixed ligand metal complexes were done, so that stereochemical variables determining structure, isomerism, stereospecificity, chiroptical properties, conformational interconversions and intramolecular rearrangements of these complexes in relation to ligand structural diversity are not fully understood. To elucidate these factors, an investigation of cobalt(III) ternary complexes containing both stereochemically rigid and flexible ligands, i.e. linear triamine (ABA) and aspartic acid (Asp), was undertaken. Results obtained[2] show that the methylation of the secondary N atom of triamine has a pronounced effect both on isomers formation and their circular dichroism spectra pattern. Furthermore, several factors including donor atoms deviations from the defined plane (ascertained by

X-ray structural study of the *sym-fac*-[Co(1,7-dah)(*S*)-Asp]$^+$ isomer[3])*, contribute to optical activity of isomers when linear triamine coordinates forming two six-membered fused chelate rings. The rotational strength of the T_{1g} CD band corresponding to the configurational effect is of low intensity and to the CD spectra of [Co(1,7-dah)(*S*)-Asp]$^+$ isomers vicinal effect from (*S*)-aspartic acid dominates[4]. To ascertain if the presence of a six-membered chelate ring, when combined with a five-membered one, influences rotational strength of the II component of the CD spectra in the same manner as does 1,7-dah, the [Co(1,6-dah)(*S*)-Asp]$^+$ complex of closely related ligand to both 1,5-dap (its cobalt(III) complex with aspartic acid was already characterized[5]) and 1,7-dah, which coordinates forming one five- and one six-membered chelate ring is studied in this paper. Preliminary results revealed[6] similar CD spectra patterns with [Co(1,6-dah)(*S*)-Asp]$^+$ isomers. Inapplicable CD spectra for [Co(1,6-dah)(*S*)-Asp]$^+$ isomers differentiation led us to the determination of the molecular structure of two of the isolable isomers[7,8] as references for absolute configuration assignments. In order to evaluate the factors responsible for the stereospecific coordination of 1,6-dah, we desribe in this paper stereochemistry of [Co(1,6-dah)(*S*)-Asp]$^+$ isomers in more details.

EXPERIMENTAL

Methods: Electronic absorption spectra were measured on a Specord (C. Zeiss, G.D.R.) spectrophotometer and circular dichroism spectra were recorded on a Roussel Jouan Dichrograph.

Preparative Procedure: The [Co(1,6-dah)(*S*)-Asp]ClO_4 isomers were prepared and separated using ion exchange chromatography (DOWEX 50 WX 8, 100–200 mesh, Na^+ cycle, 0.1 M-$NaClO_4$ as eluting agent) as described by Legg and Cooke[5]. For $C_9H_{20}N_4O_8ClCo$ (406.7) calculated: 26.58% C, 4.95% H, 13.77% N; found: 1st eluted isomer 26.60% C, 4.97% H, 13.48% N, 2nd eluted isomer 26.44% C, 4.90% H, 13.21% N, 3rd eluted isomer 25.95% C, 4.90% H, 13.73% N.

RESULTS AND DISCUSSION

Structure of Isomers

In comparison with the analogous [Co(1,5-dap)(*S*)-Asp]$^+$ system, the [Co(1,6-dah)(*S*)-Asp]$^+$ cation displays, due to the stereoheterotopic character of linear triamine and sec-N atom chirality, six stereoisomers designated according to Legg and Cooke[5]: *sym-fac*(*R*), *sym-fac*(*S*), *unsym*$_1$*-fac*(*R*), *unsym*$_1$*-fac*(*S*), *unsym*$_2$*-fac*(*R*), *unsym*$_2$*-fac*(*S*) (nitrogen atom chirality is given in parenthesis). In spite of this, only three isomers in the ratio 50 : 25 : 25 (prolonged reaction

* Abbreviations: 1,5-dap = 1,5-diamine-3-azapentane, 1,6-dah = 1,6-diamine-3-azahexane, 1,7-dah = 1,7-diamine-4-azaheptane.

time) were obtained by the reaction of *mer*-[Co(1,6-dah)Cl_3] isomer with Ag_2-(*S*)-Asp in the presence of charcoal. Isomers obtained were separated using ion-exchange chromatography and designated in order of elution as *sym-fac*, *unsym*$_1$*-fac* and *unsym*$_2$*-fac* (Fig.1). The structure assignments of isomers isolated is based on their X-ray structural analysis determinations[7,8], electronic, CD spectra, molecular models and stereochemical course of their synthesis. As expected, all isomers have facial geometry forced by the coordination of rigid aspartic acid. Their absorption spectra (band locations and intensities are given in Table I) consist of two symmetrical bands shifted in comparison with structurally related [Co(1,5-dap)(*R*)-Asp]$^+$ isomers[5] to lower energy due to the presence of six-membered chelate rings of triamine. In addition to this, the

TABLE I
Electronic absorption and CD spectra of [Co(1,6-dah)(*S*)-Asp]$^+$ isomers

Isomer	Absorption λ_{max}, nm (ε, mol l^{-1} cm^{-1})	CD λ_{max}, nm ($\Delta\varepsilon$)
sym-fac(*S*)	495 (102)	560 (−0.71)
		485 (+1.86)
	362 (101)	369 (+0.30)
		320 (+0.06)
Λ-unsym$_1$*-fac*(*S*)	498 (51)	540 (+0.70)
		480 (−0.24)
	360 (81)	354 (+0.21)
Δ-unsym$_2$*-fac*(*R*)	501 (90)	550 (+1.56)
		480 (−1.13)
	361 (102)	354 (+0.43)

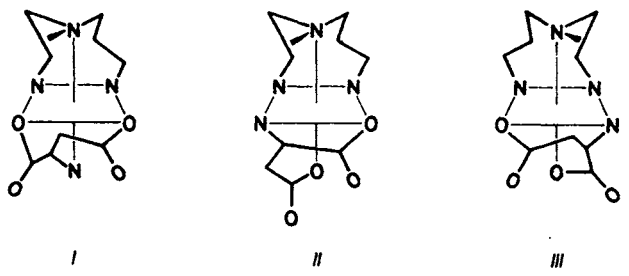

FIG. 1
[Co(1,6-dah)(*S*)-Asp]$^+$ isomers: *I exo-sym-fac*(*S*), *II exo-Λ-unsym*$_1$*-fac*(*S*), *III exo-Δ-unsym*$_2$*-fac*(*R*)

unsymmetrical character of 1,6-dah and the possibility to coordinate in two different ways with either *R* or *S* chirality of sec-N atom cause that the absorption band maxima of both unsymmetrical isomers somewhat differ from each other (not observed in the case of both [Co(1,5-dap)(*S*)-Asp]$^+$ and [Co(1,7-dah)(*S*)-Asp]$^+$ isomers containing symmetrical triamine[4,5]).

As far as CD spectra od isomers isolated are concerned (Fig. 2, Table I), they show the presence of two components which are opposed in sign in the low-frequency band region (*cis*-CoN_4O_2 chromophore) irrespective of the isomer symmetry and thus they do not provide a reliable basis for assignments of absolute configuration. The complexicity of the CD spectra and the fact that they do not reflect the expected configurational chirality differences, can be ascribed, similarly as in other complexes of this type[4], to the presence of an angle-expanding triamine six-membered chelate ring which deviates donor atoms from Cartesian coordinates. This, together with sec-N atom chirality, conformational and C-vicinal effects, makes different contributions to the overall shape and intensities of CD curves. The CD curves of *unsym*$_1$-*fac* and *unsym*$_2$-*fac*-[Co(1,7-dah)(*S*)-Asp]$^+$ isomers were interpreted[4] as being dominated by the vicinal effect from (*S*)-aspartic acid. However, from the comparison of CD spectra pattern of [Co(1,5-dap)(*R*)-Asp]$^+$ (ref.[5]), [Co(1,7-dah)(*S*)-Asp]$^+$ (ref.[4]) and [Co(1,6-dah)(*S*)-Asp]$^+$ isomers, it appears that in the latter ones, when at least one six-membered chelate ring is a part of coordinated linear triamine, vicinal effects predominate. This is particularly noticable in the case of

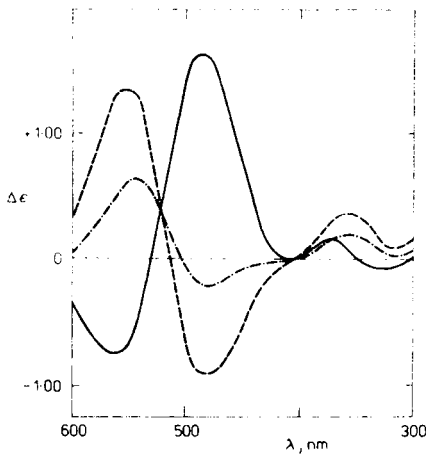

FIG. 2
Circular dichroism spectra of *exo-sym-fac*(*S*) – – –, *exo-Λ-unsym*$_1$-*fac*(*S*) – · – · –, *exo-Λ-unsym*$_2$-*fac*(*R*) – – – – isomers

the eluted isomer identified by X-ray analysis as *sym-fac* one[7] with the contribution to optical activity arising from the α-CH atom of (*S*)-aspartic acid, *S* sec-N atom and λ conformation of a five-membered triamine chelate ring (six-membered one assumes achiral chair conformation). CD spectrum of this isomer consists of two components with a sign sequence − + (from the lower-frequency side). The lowest energy components showing a negative Cotton effect can be ascribed to N-vicinal effect contribution from *S* sec-N atom of triamine, which has for structurally related $[Co(NH_3)_3(S)\text{-Alamp}]^+$ cation (Alamp = α-alaninato-N-monopropionate) a negative sign[9]. On the other hand, more intense component exhibiting a positive Cotton effect positioned at 480 nm corresponds both to the C-vicinal effect from (*S*)-aspartic acid[4] and the N-vicinal contribution from triamine sec-N atom[9] as both are in this region positive. Furthermore, as can be seen in Fig.2, differences in rotational strength between unsymmetrical isomers exist. These arise from the superposition of CD bands of different signs. For *unsym*$_1$*-fac* isomer which is *Λ*-(*S*) (vide infra) both configurational and N-vicinal contributions are partly compensated while for *unsym*$_2$*-fac* (*Δ*-(*R*)) both contributions have the same sign.

As mentioned, two bands of different signs associated with $A_{1g} \rightarrow T_{1g}$ *d–d* transition are observable in the CD spectra of *unsym*$_1$*-fac* and *unsym*$_2$*-fac* isomers (Fig. 2). Their CD spectral pattern does not reflect, similarly as in the

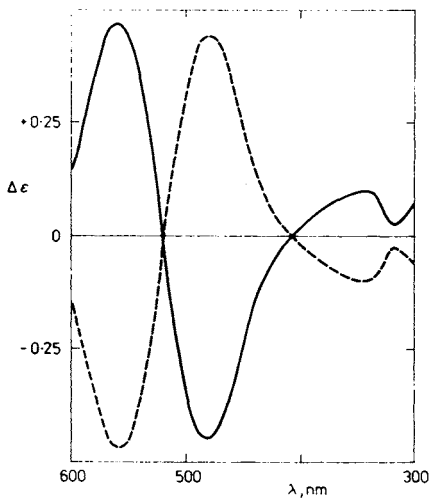

FIG. 3

Configurational chirality curves. – – – – *Λ-unsym*$_1$*-fac* (*S*): $\{(\Delta\varepsilon$ *unsym*$_1$*-fac*$(S)) - (\Delta\varepsilon$ *unsym*$_2$*-fac*$(R))\}/2$; ····· *Δ-unsym*$_2$*-fac*(R): $\{(\Delta\varepsilon$ *unsym*$_2$*-fac*$(R)) - (\Delta\varepsilon$ *unsym*$_1$*-fac*$(S))\}/2$

case of [Co(1,7-dah)(*S*)-Asp]$^+$ unsymmetrical isomers[4], chirality differences between them. The molecular structure of the *unsym$_1$-fac* isomer established by the X-ray method[8] shows that the absolute configuration of this isomer corresponds to *Λ* chirality tentatively assigned by Legg and Cooke[5] to *unsym$_1$-fac*-[Co(1,5-dap)(*R*)-Asp]$^+$ isomer (taking different aspartic chiralities into account) relating helicity to the sign of Cotton effect of the *E* component of the CD spectra. To assign the structure of the remaining *unsym$_2$-fac* isomer two possibilities arise depending on the position of the linear triamine chelate rings. Accordingly, isomer *unsym$_2$-fac* should be either *Λ*-(*R*) or *Λ*-(*S*). As follows from the study of the Dreiding molecular models, *Λ* isomer can be formed only when sec-N atom of 1,6-dah assumes *R* configuration (vide infra). This prediction, especially as far as configurational chirality is concerned is supported by calculation of configurational contributions from the CD spectra of unsymmetrical isomers. Subtracting CD curves of *unsym$_1$-fac* and *unsym$_2$-fac* isomers the resulting curves which bear enantiomeric character (Fig. 3) correspond to both configurational and N-vicinal contributions. Though the enantiomeric character of these curves estimates *Λ* chirality of the *unsym$_2$-fac* isomer* absolute configuration assignment must be considered tentative, however, until the configuration of the *unsym$_2$-fac* isomer will be established by the X-ray method.

While these novel [Co(1,6-dah)(*S*)-Asp]ClO_4 complexes exhibit many features which are similar to the previously studied ones[4,5], some differences can be noted. For example *sym-fac*-[Co(1,6-dah)(*S*)-Asp]$^+$ isomer does not undergo charcoal catalyzed isomerization. This is in sharp contrast with both [Co(1,5-dap)(*S*)-Asp]$^+$ and [Co(1,7-dah)(S)-Asp]$^+$ *sym-fac* isomers which isomerize easily in the presence of charcoal to a mixture of isomers, the relative ratio of which parallels thos obtained during the preparative procedure[13]. These results clearly demonstrate that the ability of [Co(ABA)(*S*)-Asp]$^+$ isomers to isomerize, depends only on the nature of linear triamine. According to Searle et al.[14] charcoal catalyzed isomerization of related [Co(1,5-dap)$_2$]$^{3+}$ and [Co(1,5-dap)(3-methyl-1,5-dap)]$^{3+}$ complexes containing linear triamine ligand, involves chelate ring opening. The same mechanism should operate in the case of *sym-fac*-[Co(1,6-dah)(*S*)-Asp]$^+$ isomer. Since complexes of linear triamines forming five- and six-membered fused chelate rings are thermodynamically more stable than those which coordinate with two five- or two six-membered chelate rings[15,16], the observed stability of the *sym-fac* isomer towards

* If chelate rings are neglected the unsymmetrical isomers have tetragonal holohedrized symmetry under which the first absorption band splitted into A_{2g} and E_g components[10]. The energy level of the E_g component which can be used for correlation of optical activity with absolute configuration[11] is higher for the *cis*-CoN_4O_2 than for the A_{2g} one (ref.[12]) Since the E_g component is negative for the *unsym$_2$-fac* isomer, it should have *Λ* chirality[11].

isomerization is thus of thermodynamic origin. In addition to this no structural changes were observed when the *sym-fac*-[Co(1,6-dah)(*S*)-Asp]$^+$ isomer was equilibrated in basic solution. Since the sec-N atom proton under conditions is exchanged rapidly, we conclude that the N—H proton is in facially coordinated 1,6-dah stereospecifically oriented with N—H bond pointed away from 1,6-dah chelate rings (*exo* position) (Fig. 1) This is in accordance with the observed stereospecific isomerization of 1,6-dah in described isomers (vide infra).

Stereospecificity

The isolation of three instead of six isomers expected suggests that there are appreciable stereospecific effects which control isomer formation. Stereospecificity might arise in [Co(1,6-dah)(*S*)-Asp]$^+$ complexes for several reasons. Some of them include steric and bonding effects. As inferred from molecular models, steric interactions are not so serious to restrict isomer formation and possible differences between isomers, as far as bond strains are concerned, are difficult to assess from models. It must be emphasized, however, that the *mer*-[Co(1,6-dah)Cl_3] isomer used as starting material for the isomer preparation is racemic at the sec-N atom. Thus two synthetic routes including both N(*R*)- and N(*S*)-*mer*-Co(1,6-dah)Cl_3] isomers must be considered (Fig. 4). Both these isomers differ from each other in the relative position of linear triamine chelate rings. On the other hand, a common feature of both N(*R*) and N(*S*) isomers consists in their inability to isomerize to *fac* isomers with N—H bond oriented towards the 1,6-dah chelate rings (*endo* position). This causes that of three labile sites in *mer*-Co(1,6-dah)$(H_2O)_3]^{3+}$ cation, only two are in fact available for initial coordination of aspartic acid as bidentate ligand (Fig. 4). An explanation of the results described here can be obtained by involving that the mechanism of the formation of: *sym-fac*, *unsym$_1$-fac* and *unsym$_2$-fac* isomers requires the edge displacement of one of the two linear triamine arms concomitant chelation of aspartic acid as terdentate ligand. Assuming that the 1,6-dah six-membered chelate ring is in the *mer*-[Co(1,6-dah)$(H_2O)_3]^{3+}$ isomers locked into a fairly rigid chair conformation (proved only in the case of *mer*-[Co(1,5-dap)(1,6-dah)]$^{3+}$ isomers[17]), the above mentioned step is crucial in the stereochemical course of reaction. An examination of the Dreiding molecular models show that rigid 1,6-dah conformation in any of the *mer*-[Co(1,6-dah)] intermediates precludes the movement of the five-membered chelate ring backbone so that the linear triamine isomerization is stereospecific. This requires on the other hand that any *mer* → *fac* intramolecular rearrangement must involve only the six-membered chelate ring end (Fig. 4) (the first indirect evidence of conformational influence of fused chelate ring on both isomerization and substitution reaction). Other possibilities which arise, are the

formation of pentacoordinated intermediates with facially coordinated 1,6-dah. However, owing to the strong stereorestrictive influence of six-membered 1,6-dah chelate ring, only the reaction pathway involving unsymmetrical trigonal bipyramid would be equivalent to edge displacement. An alternative stereochemical route through symmetrical bipyramid which leads to six isomers can be therefore omitted.

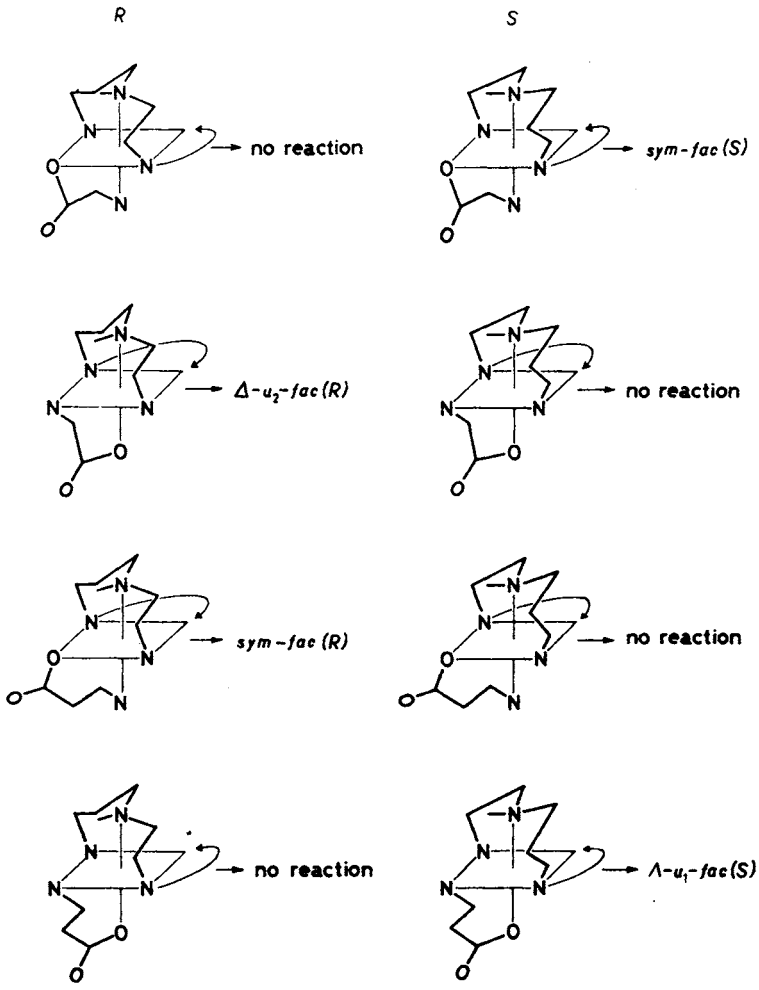

FIG. 4

Isomerization and edge displacement substitution paths of (*R*) -and (*S*)-*mer*-[Co(1,6-dah)(*S*)-Asp]$^+$ intermediates with aspartic acid coordinated as bidentate ligand

We can conclude, in accordance with experimental results obtained, that *exo-sym-fac*(*S*), *exo-Λ-unsym*$_1$*-fac*(*S*) and *exo-Λ-unsym*$_2$*-fac*(*R*) isomer are the only isomers possible. The absence of *exo-sym-fac*(*R*) isomer in the reaction mixture can be substantiated assuming that 1,6-dah fused chelate rings adopt both in *exo-sym-fac*(*S*) and *exo-sym-fac*(*R*) isomers the same conformations (*Λ*, chair). Buckingham et al.[18] pointed out that the sec-N atom of N-methylenediamine in $[Co(NH_3)_4(N\text{-Meen})]^{3+}$ cation coordinates with *S* chirality only when N-Meen five-membered chelate ring asssumes stable *λ* conformation. The same arguments can be applied to 1,6-dah complexes in which $-(CH_2)_3-NH_2$ arm represents "substituent" protruding from the sec-N atom of ethylenediamine, similarly as does CH_3 group in N-Meen. Because the position of this "substituent" is fixed by coordination, stereospecificity in comparison with $[Co(NH_3)_4(N\text{-Meen})]^{3+}$ is pronounced.

The complexes studied here are inert ones, so that their initial relative ratio in the preparative mixture depends on their relative rates of formation (time dependent experiments revealed that the isomer ratio changes with increasing reaction time 93 : 5 : 2 to 50 : 25 : 25). The relative abundance of the *exo-sym-fac*(*S*) isomer is in accordance with the kinetically preferred attack at the most labile site trans to sec-N atom in *mer*-$[Co(1,6\text{-dah})(H_2O)_3]^{3+}$ isomer by the aspartic acid nitrogen atom with simultaneous five-membered chelate ring closure. Lability of this is demonstrated by the unique formation of amino acid (AB) *mer*-$[Co(ABA)(AB)X]^{2+}$ isomers[19] with oxygen atom *trans* to X.

The authors are indebted to Dr P. Maloň, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, for the CD *spectra measurements.*

REFERENCES

1. Hawkins C.J.: *Absolute Configuration of Metal Complexes*. Wiley, New York 1971.
2. Jursík F., Ondráčková J., Hájek B.: Collect. Czech. Chem. Commun. *51*, 1039 (1986).
3. Jursík F., Ondráček J., Soldánová J., Archer R. D.: Unpublished results.
4. Jursík F., Archer R. D.: Inorg. Chem., submitted.
5. Legg J. I., Cooke D. W.: J. Am. Chem. Soc. 89, 6854 (1967).
6. Ondráčková J., Jursík F., Hájek B.: *Proc. 11th Conf. on Coord. Chem., Smolenice 1987*; p. 287.
7. Kratochvíl B., Ondráček J., Ondráčková J., Soldánová J., Jursík F., Hájek B.: Collect. Czech. Chem. Commun. *52*, 949 (1987).
8. Kratochvíl B., Ondráček J., Ondráčková J., Jursík F.: Unpublished results.
9. Okamoto K., Hidaka J., Shimura Y.: Bull. Chem. Soc. Jpn. *46*, 3134 (1973).
10. Dwyer F. P., Garvan F. L. Shulman A.: J. Am. Chem. Soc. *81*, 290 (1959).
11. McCaffery A. J., Mason S. F., Norman B.J.: J. Chem. Soc. *1965*, 5094.
12. Yamatera H.: Bull Chem. Soc. Jpn. *31*, 95 (1958).
13. Jursík F.: Unpublished results.
14. Searle G. H., Keene F. R. Lincoln S. F.: Inorg. Chem. *17*, 2362 (1978).

15. Anderegg G., Podder N. G., Blauenstein P., Hangartner M., Stünzi H.: *Proc. 16th I.C.C.C., Dublin 1974*; 2.30 b.
16. Paoletti P., Fabrizzi L., Barbucci R.: Inorg. Chim. Acta Rev. *7*, 43 (1973).
17. Ishi M.: Bull. Chem. Soc. Jpn. *57*, 3088 (1984).
18. Buckingham D. A., Marzilli L. G., Sargeson A. M.: J. Am. Chem. Soc. *89*, 825 (1967).
19. Ohkawa K., Fujita J., Shimura Y.: Bull. Chem. Soc. Jpn. *45*, 161 (1972).

Translated by the author (F.J.).