Inorganica Chimica Acta, 210 (1993) 167–171

Preparation, X-ray structure and solution behavior of $[Ag(9\text{-}EtGH\text{-}N7)_2]NO_3 \cdot H_2O$ (9-EtGH = 9-ethylguanine)

Stephan Menzer, Edda C. Hillgeris and Bernhard Lippert*
Fachbereich Chemie, Universität Dortmund, D-4600 Dortmund (Germany)

(Received March 3, 1993; revised April 26, 1993)

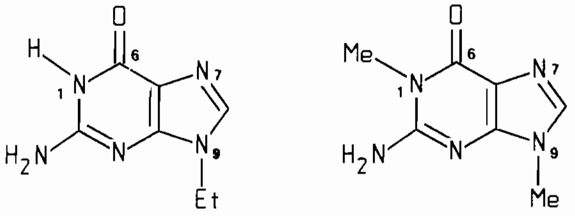
Abstract

The preparation and X-ray structure of $[Ag(9\text{-}EtGH\text{-}N7)_2]NO_3 \cdot H_2O$ (9-EtGH = neutral 9-ethylguanine) is reported. The compound crystallizes in the triclinic system, space group $P\bar{1}$ with $a = 7.063(6)$, $b = 7.153(3)$, $c = 11.306(10)$ Å, $\alpha = 83.36(6)$, $\beta = 76.66(7)$, $\gamma = 81.44(6)°$. The cation is centrosymmetric with Ag(I) coordinated via two N7 positions and Ag–N7 bond lengths of 2.11(1) Å. Applying ^{109}Ag NMR spectroscopy, complex formation constants for both the 1:1 complex (log $\beta_1 = 0.6$) and the title compound (log $\beta_2 = 1.6$) in Me_2SO have been determined.

Introduction

Among studies on the interaction of metal ions with nucleic acids, dinucleotides or models thereof, those of Ag(I) have played a major role, see ref. 1 for literature review. Despite this, molecular details of these reactions are still controversial and/or unclear. Structural work on Ag(I) nucleobase complexes in most cases has been restricted to binary systems (1-methylcytosine [2], 1-methylthymine [3], 1-methyluracil [4], 9-methyladenine [5], 9-methylhypoxanthine [6]). In one instance only the X-ray structure of an Ag(I) compound containing two different nucleobases (1-methylcytosine and 9-methyladenine) has been reported [1]. On its basis, we have put forward a novel proposal concerning the interaction of Ag(I) with a base pair in DNA, which involves the insertion of an $Ag–OH_2$ entity into an existing base pair.

In this report we describe the binary 2:1 complex of 9-ethylguanine (9-EtGH) with Ag(I), which represents the first structurally characterized guanine complex with this metal ion. The poor solubility of both guanine and guaninato complexes probably explains the lack of structure data in the literature. The corresponding compound with 1,9-dimethylguanine (1,9-DiMeG) was also prepared but not structurally characterized (Scheme 1).



Scheme 1.

Experimental

Chemicals

9-EtGH, 1,9-DiMeG (Chemogen, Konstanz (FRG)) and ethanediole (FLUKA) were used as received. The water used was deionized twice. Me_2SO (FLUKA) and $Me_2SO\text{-}d_6$ (Merck) were dried using CaH_2 and 0.3 Å molecular sieves, respectively.

Preparation

Attempts to obtain analytically pure samples of Ag(9-EtGH)X, $[Ag(9\text{-}EtGH)_2]X$ or Ag(9-EtG) (with 9-EtGH = neutral 9-ethylguanine, 9-EtG = deprotonated 9-ethylguanine, X = variable anion) from water were largely unsuccessful and gave compounds of variable stoichiometries, depending on reaction conditions and anions used, e.g. $(9\text{-}EtGH)_2 \cdot nAgNO_3 \cdot mH_2O$ ($n = 1–1.3$; $m = 1.5–2.5$); $9\text{-}EtGH \cdot 1.1AgNO_3$; $9\text{-}EtGH \cdot 0.85AgBF_4$; $9\text{-}EtGH \cdot 0.55Ag_2SO_4$. Poor solubility of these compounds in water and the multifunctional character of guanine probably explains this behavior. The title compound **1** was finally isolated in crystalline

---

*Author to whom correspondence should be addressed.

0020-1693/93/$6.00

form applying a gel growth procedure: 9-EtGH (0.11 mmol) was dissolved in ethanediole (5 ml), put into a test tube and solidified by cooling with dry ice. After putting a filter paper on the solid alcohol, the sample was layered with an aqueous solution (5 ml) of $AgNO_3$ (0.11 mmol) and allowed to warm to room temperature. The yield of **1** depended on the reaction time. High yields (>80%) of an analytically pure powder were obtained if the mixture was allowed to stand for 14 days or more, while single crystals could be produced within 1 or 2 days in low yields. Powder and crystals are identical on the basis of their IR spectra.

Anal. Calc. for $[Ag(9\text{-}EtGH)_2]NO_3 \cdot H_2O$, $C_{14}H_{20}N_{11}AgO_6$ (**1**): C, 30.8; H, 3.7; N, 28.2; Ag, 19.7. Found: C, 29.4; H, 3.9; N, 27.3; Ag, 20.4%.

IR data (KBr, cm^{-1}): 3420s, 3330s, 3120s, 2780w, 1690vs, 1650vs, 1600s, 1570s, 1530s, 1480s, 1360vs, 1180w, 950w, 810w, 780w, 710w, 690w.

The corresponding compound with 1,9-dimethylguanine instead of 9-ethylguanine $[Ag(1,9\text{-}DiMeG)_2]NO_3 \cdot H_2O$ (**2**) was prepared by reaction of 0.23 mmol $AgNO_3$ (39.2 mg) and 0.4 mmol 1,9-DiMeG (70.4 mg) in water (20 ml, pH=4). The solution was warmed to 40 °C and allowed to cool to room temperature. Crystallization started after few minutes. The product was filtered, washed with water and dried over P_4O_{10} in a desiccator, yield 80%.

Anal. Calc. for $C_{14}H_{20}N_{11}AgO_6$ (**2**): C, 30.8; H, 3.7; N, 28.2; Ag, 19.7. Found: C, 30.7; H, 3.6; N, 28.0; Ag, 20.5%.

IR data (KBr, cm^{-1}): 3320s, 3180s, 1690vs, 1640vs, 1580vs, 1520vs, 1440w, 1400vs, 1240w, 1050s, 820s, 670s.

Instruments

IR spectra were recorded on a Perkin-Elmer 580-B spectrometer using KBr pellets. There was no evidence for the formation of AgBr. ^1H (300.13 MHz), ^{13}C NMR (75.5 MHz) and ^{109}Ag NMR (13.9 MHz) spectra were recorded using an AM300 instrument (25 °C, 10 mm tubes, 95% Me_2SO, 5% $Me_2SO\text{-}d_6$). Chemical shifts are given in ppm with TMS as internal reference and 0.1 M $AgNO_3/Me_2SO$ as external reference, respectively.

Calculation of the complex formation constants log β_1 and log β_2* was performed by a least-squares fit analysis of the chemical shift data based on formula (1) [7]:

$$\delta_{obs} = \frac{\delta_{11}\beta_1[L] + \delta_{12}\beta_1\beta_2[L]^2}{1 + \beta_1[L] + \beta_1\beta_2[L]^2} \qquad (1)$$

This formula was derived on the assumption that both 1:1 and 1:2 complexes are present in solution. The program used was a modified version of the program NL-Regr 3 [8] and was adapted for use on an ATARI ST computer.

X-ray crystallography

The crystal structure of $[Ag(9\text{-}EtGH)_2]NO_3 \cdot H_2O$ (**1**) was determined on a Nicolet R3m/V diffractometer with graphite monochromated Mo $K\alpha$ radiation ($\lambda = 0.71073$ Å). Crystallographic data are as follows: $C_{14}H_{20}N_{11}AgO_6$, $M_r = 546.28$, triclinic system, space group $P\bar{1}$, $a = 7.063(6)$, $b = 7.153(3)$, $c = 11.306(10)$ Å, $\alpha = 83.36(6)$, $\beta = 76.66(7)$, $\gamma = 81.44(6)$, $V = 547.7(7)$ Å^3, $Z = 2$, $D_{calc} = 1.656$ g cm^{-3}, $F(000) = 274$, $\mu = 0.976$ mm^{-1}, $T = 20$ °C, final $R = 0.0761$ for 1443 unique reflections observed ($F_o \geq 4\sigma(F_o)$). Data were corrected for absorption effects. The largest peak in the final difference Fourier map was 1.85 e Å^{-3}. Although the crystal quality was poor, repeated attempts to obtain better samples of **1** failed. Atomic scattering factors for neutral atoms and real and imaginary dispersion terms were taken from the International Tables for X-ray Crystallography [9]. The programs used were PARST [10] and SHELXTL PLUS [11]. Atomic coordinates of the non-H atoms are given in Table 1. H atoms were not located. See also 'Supplementary material'.

Results

Structure of $[Ag(9\text{-}EtGH\text{-}N7)_2]NO_3 \cdot H_2O$ (1)

Figure 1 depicts the molecular cation of **1**. Selected interatomic distances and angles are listed in Table 2.

TABLE 1. Atomic coordinates ($\times 10^{-5}$) of the non-H atoms and equivalent isotropic displacement of **1** (Å$^2 \times 10^4$)[a]

	x	y	z	U_{eq}
Ag(1)	0	0	0	566(4)
C(2)	78742(107)	−35980(107)	−10426(76)	400(12)
C(4)	55408(103)	−27875(103)	5786(74)	365(12)
C(5)	41817(102)	−21012(105)	−904(79)	401(12)
C(6)	46400(111)	−21338(114)	−13564(82)	452(13)
C(8)	27975(118)	−17016(119)	17824(89)	547(13)
C(10)	56237(132)	−31089(141)	28223(85)	717(13)
C(11)	43690(158)	−24016(164)	39425(109)	1077(13)
N(1)	65854(93)	−29231(97)	−17881(65)	455(12)
N(2′)	96897(99)	−42868(108)	−16243(71)	560(12)
N(3)	74259(89)	−35675(92)	1563(61)	389(12)
N(7)	24269(93)	−14071(96)	6793(69)	477(12)
N(9)	46662(93)	−25455(100)	17658(68)	479(12)
N(10)	10619(176)	36659(174)	47450(144)	819(20)
O	−9420(127)	4255(125)	35720(90)	361(17)
O(6′)	35828(94)	−15604(104)	−20876(62)	740(12)
O(10)	4964(172)	37823(169)	59590(137)	997(20)
O(20)	18534(136)	22846(134)	43086(98)	467(18)
O(30)	821(164)	50308(164)	41606(130)	863(20)

[a] Equivalent isotropic U is defined as one third of the trace of the orthogonalized U_{ij} tensor.

---

*$\beta_1 = [ML]/[M][L]$, $\beta_2 = [ML_2]/[ML][L]$, $\delta_{11} = \delta_{ML} - \delta_{M(free)}$; $\delta_{12} = \delta_{ML_2} - \delta_{M(free)}$.

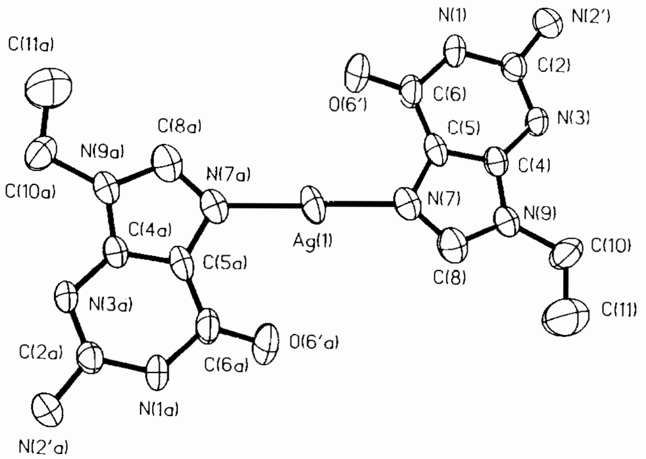


Fig. 1. View of $[Ag(9\text{-}EtGH\text{-}N7)_2]^+$ cation with atom numbering scheme.

TABLE 2. Selected bond distances (Å) and bond angles (°) in **1**

Ag(1)–N(7)	2.111(7)	N(1)–C(2)	1.379(11)
C(2)–N(3)	1.321(11)	C(2)–N(2′)	1.348(9)
N(3)–C(4)	1.364(9)	C(4)–C(5)	1.358(12)
C(5)–C(6)	1.395(13)	N(1)–C(6)	1.403(9)
C(6)–O(6′)	1.235(12)	C(5)–N(7)	1.400(9)
N(7)–C(8)	1.320(13)	C(8)–N(9)	1.364(10)
N(9)–C(4)	1.361(11)	N(9)–C(10)	1.492(13)
C(10)–C(11)	1.464(14)	O(10)–N(10)	1.347(22)
O(20)–N(10)	1.163(16)	O(30)–N(10)	1.315(18)
C(4)–N(9)–C(8)	106.8(7)	C(4)–N(9)–C(10)	125.2(6)
C(8)–N(9)–C(10)	128.0(7)	C(2)–N(1)–C(6)	123.7(7)
N(3)–C(2)–N(2′)	120.8(8)	N(3)–C(2)–N(1)	124.0(6)
N(2′)–C(2)–N(1)	115.2(7)	Ag(1)–N(7)–C(8)	133.0(5)
Ag(1)–N(7)–C(5)	122.2(6)	C(8)–N(7)–C(5)	104.4(7)
O(6′)–C(6)–N(1)	119.6(8)	O(6′)–C(6)–C(5)	128.6(7)
N(1)–C(6)–C(5)	111.9(7)	N(3)–C(4)–N(9)	126.0(8)
N(3)–C(4)–C(5)	127.2(8)	N(9)–C(4)–C(5)	106.8(6)
N(9)–C(8)–N(7)	112.1(7)	N(9)–C(10)–C(11)	110.9(8)
N(7)–C(5)–C(6)	129.4(8)	N(7)–C(5)–C(4)	109.8(8)
C(6)–C(5)–C(4)	120.8(7)	C(2)–N(3)–C(4)	112.4(7)
O(10)–N(10)–O(20)	123.1(13)	O(10)–N(10)–O(30)	110.7(11)
O(20)–N(10)–O(30)	122.8(16)		

The cation is centrosymmetric with Ag in the inversion center. The Ag–N(7) distance of 2.11(1) Å compares well with Ag–N distances in other nucleobase complexes containing neutral purine nucleobases [5, 6]. It is shorter than that in $Ag_2(1\text{-methylcytosine})_2(NO_3)_2$ (2.225(2) Å), which forms a macrocycle, but longer than Ag–N in compounds containing deprotonated nucleobases (2.08(1) Å [3], 2.08(3) Å [4]).

Bond lengths and angles of the guanine rings do not differ significantly from those of the free ligand [12].

The two guanine rings in the cation are coplanar. In the crystal lattice guanine rings stack efficiently, with the imidazole part of one base overlapping with the pyrimidine part of the other one and vice versa (Fig. 2). The intermolecular separation is 3.6 Å. The nitrate anion is disordered in such a way that the two disordered ions (50% occupancy) are on positions related by an inversion center.

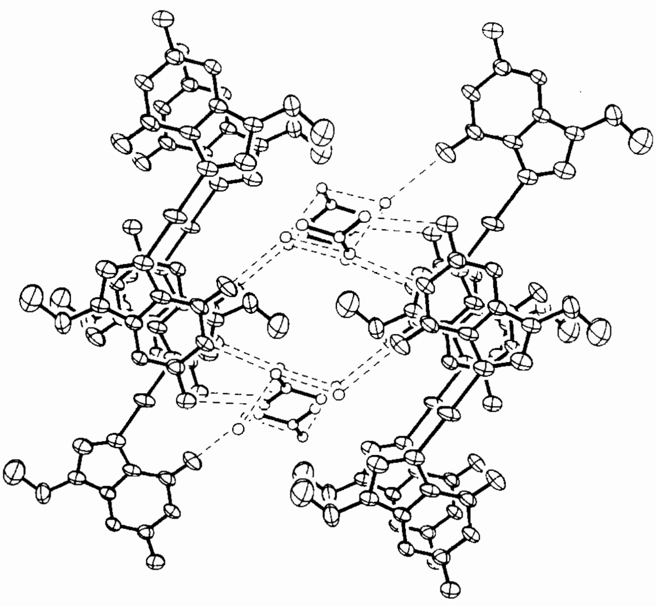


Fig. 2. Packing diagram of **1**. The view is along the *y* axis with H bonds indicated.

The water molecule forms a hydrogen bond with O6 of guanine (2.76 Å) and a nitrate oxygen (2.92 Å). In addition H bonds are formed between guanine N1–H and guanine–NH_2 with nitrate oxygens (2.82, 2.94 Å, respectively). A comparable H-bonding pattern has been found in $[Cu(9\text{-}MeG)_2(H_2O)_4]^{2+}$ [13].

Solution studies of $[Ag(9\text{-}EtGH)_x]^+$ in Me_2SO

Addition of increasing amounts of Ag^+ to solutions of 9-EtGH and 1,9-DiMeG (≈0.1 M) in Me_2SO led to smooth shifts in the ^{13}C NMR spectra. The C8 of the guanine ligands was affected most by the presence of Ag^+, e.g. $\delta = 2.48$ ppm for $r = [c(9\text{-EtGH})/c(Ag^+)] = 0.25$; $\delta = 1.7$ ppm for $r = [c(1{,}9\text{-DiMeG})/c(Ag^+)] = 0.5$. For the ^{109}Ag NMR spectra, to solutions of $AgNO_3$ (0.1 M) were added increasing amounts of 9-EtGH up to the point of oversaturation. Chemical shifts of the ^{109}Ag resonance were in the range of 250 ppm relative to 0.1 M $AgNO_3/Me_2SO$. The NMR behavior in all cases was consistent with a labile system (ligand exchange fast on ^{13}C and ^{109}Ag NMR time scale), leading to averaged signals between free components and metal species.

^{109}Ag NMR chemical shift data were used to determine the complex formation constants log β_1 and log β_2. Following a procedure of Henrichs *et al.* [14] and plotting ^{109}Ag NMR chemical shifts versus the ratio $r = [c(9\text{-EtGH})/c(Ag^+)]$ two almost linear segments

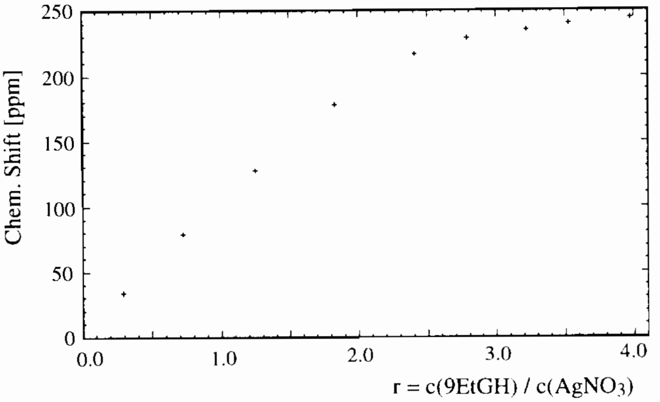


Fig. 3. ^{109}Ag NMR chemical shifts plotted vs. the ratio $r=c$(9-EtGH)/c(Ag$^+$).

were obtained which intersect at $r \approx 2.1$ (Fig. 3). This behavior suggested the presence of 1:1 and 2:1 complexes in solution. Analysis according to eqn. (1) gave log $\beta_1 = 0.6$ and log $\beta_2 = 1.6$ with $\delta_{11} = 181$ ppm and $\delta_{12} = 300$ ppm (c_0(Ag$^+$) = 0.1 M). The maximum chemical shift difference δ_{12} could not be observed in the experiment due to solubility problems.

The finding, that the [Ag(9-EtGH)$_2$]$^+$ complex is thermodynamically more stable than the corresponding 1:1 complex is consistent with stability data of other Ag$^+$ complexes as compiled in ref. 15. The magnitude of log β_1 and log β_2 is probably due to the relatively weak basicity of the guanine-N7 donor atom.

As to the possible structure of the 1:1 complex (Fig. 4) arrangements with a (nearly or ideal) linear coordination geometry (a), a chelating fashion (b) as seen in a tetraindene complex [16], or cyclic structures (c, d) are feasible. In the latter cases marked deviation from strict linearity about Ag(I) is to be expected and hence an increase in coordination number from 2 to 3 or 4 [1, 2]. Finally, it is feasible that a 1:1-stoichiometry is derived from adding an Ag(I) to the 2:1 complex, e.g. with the two nucleobases in a head–head orientation and the second Ag(I) bound to two O6 oxygens (e), or from a polymeric structure derived directly from the title compound (**1**) (f). A modification of the principle of (f) is realized in the 2:2 complexes of Ag(I) with 1-methylthymine [3] and 1-methyluracil [4] and has been discussed also for anionic 6-oxopurines [6, 17].

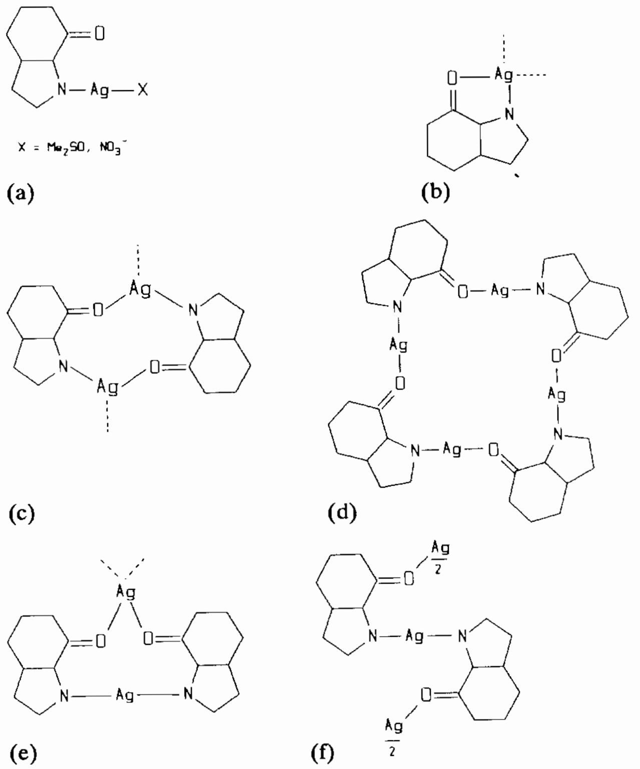


Fig. 4. Possible structures for [Ag(9-EtGH)]$^+$.

[Ag(1,9-DiMeG)$_2$]NO$_3$·H$_2$O (2)

Unlike **1**, the 1,9-dimethylguanine analogue **2** is soluble in water. Although its composition was not determined by X-ray crystallography, we assume that a structure analogous to that of **1** is present. As with **1**, the C8 resonance of 1,9-DiMeG is more affected (deshielded) than any of the other resonances in the ^{13}C NMR. Virtually no effect of Ag$^+$ on the ν(CO) vibration of the 1,9-DiMeG is seen in the IR spectrum.

Supplementary material

Positional parameters and anisotropic temperature factors of **1**, a listing of observed and calculated structure factors and experimental details of the structure determination can be obtained from the Fachinformationszentrum Karlsruhe, D-7514 Eggenstein-Leopoldhafen 2 under CSD 57072 on request. Requests should be accompanied by the complete literature citation.

Acknowledgements

This work has been supported by the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft. We thank A. Schimanski for his assistance.

References

1 S. Menzer, M. Sabat and B. Lippert, *J. Am. Chem. Soc., 114* (1992) 4644.

2 (a) L.G. Marzilli, T.J. Kistenmacher and M. Rossi, *J. Am. Chem. Soc., 99* (1977) 2797; (b) T.J. Kistenmacher, M. Rossi and L.G. Marzilli, *Inorg. Chem., 18* (1979) 240.

3 F. Guay and A.L. Beauchamp, *J. Am. Chem. Soc., 101* (1979) 6260.
4 K. Aoki and W. Saenger, *Acta Crystallogr., Sect. C, 40* (1984) 775.
5 (a) C. Gagnon and A.L. Beauchamp, *Inorg. Chim. Acta, 14* (1975) L52; (b) *Acta Crystallogr., Sect. B, 33* (1977) 1448.
6 F. Belanger-Gariepy and A.L. Beauchamp, *J. Am. Chem. Soc., 102* (1980) 3461.
7 K.A. Connors, *Binding Constants,* Wiley, New York, 1987, p. 200.
8 K. Ebert and H. Ederer, *Computeranwendungen in der Chemie,* VCH, Weinheim, 2nd edn., 1985, p. 322.
9 *International Tables for X-ray Crystallography,* Vol. IV, Kynoch, Birmingham, UK, 1974.
10 M. Nardelli, *Comput. Chem., 7* (1983) 95.
11 G.M. Sheldrick, *SHELXTL PLUS* (Release 3.4) for Nicolet R3m/V crystallographic systems, University of Göttingen, Göttingen, Germany, 1987.
12 R. Destro, T.J. Kistenmacher and R.E. Marsh, *Acta Crystallogr., Sect. B, 30* (1974) 79.
13 E. Sletten and N. Flogstad, *Acta Crystallogr., Sect. B, 32* (1976) 461.
14 P.M. Henrichs, J.J.H. Ackerman and G. Maciel, *J. Am. Chem. Soc., 99* (1979) 2544.
15 R.J. Lancashire in G. Wilkinson, R.D. Gillard and J.A. McCleverty (eds.), *Comprehensive Coordination Chemistry,* Vol. 5, Pergamon, Oxford, 1987, p. 775.
16 D.L. Smith and H.R. Luis, *Photogr. Sci. Eng., 20* (1976) 184.
17 Y.A. Shin and G.L. Eichhorn, *Biopolymers, 19* (1980) 539.