Diastereoisomers of Platinum(II) Complexes with Chiral *N*-Substituted 1,2-Diamines. II. Structures of Dichloro[(*S*)-1-(2-amino-2-methylpropyl)amino-2-propanol]platinum(II)

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Square-planar complexes with the formula [PtCl$_2$(*S*-Hp-Mepn)], where *S*-Hp-Mepn is (*S*)-1-(2-amino-2-methylpropyl)amino-2-propanol, $CH_3CH(OH)CH_2NHCH_2C(CH_3)_2NH_2$, were synthesized and separated into three types of crystals: small imbricate crystals (**1**), needles (**2**), and plates (**3**). ^{1}H NMR spectroscopy has revealed that **1** and **2** are diastereoisomers each other but that **3** consists of both diastereoisomers in 1 : 1 composition. X-Ray crystallography has shown that the diastereoisomer **2** has the absolute configuration of *R* about the nitrogen atom of secondary amine and **3** is a quasi-racemic compound of *S*(*N*) and *R*(*N*) isomers: **2**; orthorhombic, space group $P2_12_12_1$ with a=10.447(1), b=13.017(2), c=8.764(2) Å, R=0.043, R_w=0.052: **3**; monoclinic, space group $C2$ with a=21.530(1), b=11.019(2), c=13.491(5) Å, β=125.73(1)°, R=0.042, R_w=0.054. But the conformations of *R*(*N*)-isomers in **2** and **3** were different. The analysis of the CD and ^{1}H NMR spectra of **1** and **2** shows that **1** has the absolute configuration of *S* about the secondary amine site. For both isomers, the major conformers in aqueous solution are those with equatorially substituted *N*-hydroxypropyl group and are different from those found in crystals where the packing force participates.

The chemical properties of Pt(II) complexes with *N*-alkyl substituted 1,2-alkanediamines are important for the development of the Pt(II) complexes in antitumor therapy.1) The stereochemistry of Pt(II) complexes with *N*-alkyl substituted 1,2-alkanediamines has been analyzed by use of methyl as the *N*-alkyl group and has been reported that a 1,2-alkanediamine forms a puckered five-membered chelate ring and the *N*-alkyl group takes either pseudo-axial or pseudo-equatorial disposition depending on the combination of the absolute configuration of the coordinated secondary amine and the conformation of the five-membered chelate ring.2—7) Several platinum(II) complexes have been prepared with 2-aminomethylazetidine and 2-aminomethylpyrrolidine as carrier ligands, which can be classified as *N*-alkyl-1,2-ethanediamines, and have been reported that their dichloro and cyclobutane-1,1-dicarboxylato complexes are effective as anticancer drugs.8) We have reported previously the structure of the Pt(II) complexes with a ligand which is potentially tridentate with three donor atoms and carries an asymmetric center at the *N*-alkyl group: (*R*)-2-(2-amino-2-methylpropyl)amino-1-butanol ($CH_3CH_2{}^*CH(CH_2OH)NHCH_2C(CH_3)_2NH_2$=*R*-Hb-Mepn).9) This ligand acts as a didentate 1,2-alkanediamine. The hydroxyl group enhances the solubility in aqueous solution and the presence of the enantiotropic center in the *N*-alkyl substituent facilitated the separation of the diastereoisomers of the [PtCl$_2$(*R*-Hb-Mepn)], and the structures of the both diastreoisomers have been determined by X-ray crystallography.9)

We have examined the structure of the Pt(II) complexes with analogous *S*-1-(2-amino-2-methylpropyl)-amino-2-propanol, $CH_3{}^*CH(OH)CH_2NHCH_2C(CH_3)_2NH_2$ (*S*-Hp-Mepn). This ligand is also a potentially tridentate and has the hydroxyl group bonded to the asymmetric carbon and is expected to reveal a more pronounced effect of the optically active center on the property of the Pt(II) complexes. The dichloroplatinum(II) complex with this ligand afforded three types of crystals which are different in the composition of the diastereoisomers derived from the absolute configuration of the coordinated secondary amine. In this report, we describe the synthesis, spectroscopic properties, and X-ray crystallography of the diastereoisomers of [PtCl$_2$(*S*-Hp-Mepn)].

Experimental

General. Specific rotation was measured using a JASCO DIP-4 polarimeter. Absorption spectra were measured with a Shimadzu UV 210-A spectrophotometer and CD spectra with a JASCO J600 spectropolarimeter. ^{1}H NMR spectra were recorded on a JEOL GSX-400 spectrometer with D_2O (containing 0.1 M DCl and 0.1 M KCl, 1 M=1 mol dm^{-3}) as solvent and sodium 3-(trimethylsilyl)propionate-2,2,3,3-d_4 (TSP) as an internal standard. 1-Amino-2-propanol was resolved according to the method of Yashiro.10) *S*-1-Amino-2-propanol was obtained from the less soluble L-(+)-tartarate. The ligand (*S*)-Hp-Mepn was prepared by Mannich reaction of (*S*)-1-amino-2-propanol with formaldehyde and 2-nitropropane, followed by hydrogenation of the corresponding nitro compound according to the procedure for preparation of

Table 1. Experimental Data for X-Ray Diffraction Study of Dichloro[(*S*)-1-(2-amino-2-methylpropyl)amino-2-propanol]platinum(II)

	Plate crystal, **3**	Needle crystal, **2**
Formula	$(PtCl_2O_2N_2C_7H_{20})_2$	$PtCl_2ON_2C_7H_{18}$
Mol wt	860.50	412.23
Crystal dimension/mm	0.24, 0.16, 0.13	0.34, 0.19, 0.18
Space group	$C\,2$	$P\,2_12_12_1$
a/Å	21.530(1)	10.447(1)
b/Å	11.019(2)	13.017(2)
c/Å	13.491(5)	8.764(2)
β/°	125.73(1)	
V/Å^3	2598(2)	1192.1(3)
Z	4	4
F(0,0,0)	1632	776
d_{calcd}/g cm^{-3}	2.20	2.30
d_{meas}/g cm^{-3}	2.19	2.28
Radiation (Å)	Mo $K\alpha$ (0.70930)	Mo $K\alpha$ (0.70930)
μ/cm^{-1}	113.1	123.2
$2\theta_{max}$/°	54.0	60.0
High peak in final diff.map/e Å^{-3}	0.87(18)	5.11(40)
Number of Reflections		
unique	4982	3504
included in calcn	4179(F_o>3.0σ(F_o))	2973(F_o>3.0σ(F_o))
R	0.042	0.043
R_w	0.054	0.052
Parameter refined	252	118

(*R*)-2-(2-amino-2-methylpropyl)amino-1-butanol.[9,11] $[\alpha]_D$=+30.4°(c=5.0,H_2O). Anal. Found: C, 37.94; H, 9.32; N, 12.67%. Calcd for $C_7H_{18}N_2O\cdot 2HCl$: C, 38.36; H, 9.20; N, 12.78%.

Preparation and Separation of [PtCl$_2$(*S*-Hp-Mepn)]. K_2PtCl_4 1.66 g (4.0 mmol), *S*-Hp-Mepn·2HCl 1.5 g (6.8 mmol), and $NaHCO_3$ 880 mg (5.24 mmol) were successively dissolved in 14 ml of water. The mixture was filtered and the filtrate was let to stand at room temperature for 5 d. Yellow crystals gradually separated. Most of them were plates of quasi-racemic [PtCl$_2$(*S*-Hp-Mepn)], **3**, but occasionally more stable needle crystals of *R*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)], **2**, were formed simultaneously.

The crude crystals (700 mg) obtained above were treated with 0.2 M aqueous $AgNO_3$ solution and separated AgCl was removed by centrifugation. The supernatant was divided into two portions of equal volume. On addition of about 1.3 ml of 1 M hydrochloric acid to one of the portions, small crystals of *S*(*N*)-isomer, **1**, were separated. These were collected on a filter and washed with water. Yield, 140 mg. Anal. Found: C, 20.25; H, 4.57; N, 6.84%. Calcd for $C_7H_{18}N_2Cl_2PtO$: C, 20.40; H, 4.40; N, 6.80%.

Into the other portion 1.5 ml of 1 M aqueous LiCl solution saturated with $NaHCO_3$ was added and the mixture was allowed to stand overnight at room temperature. The volume of this mixture was reduced to about 2/3 by heating on a steam bath and needles of *R*(*N*)-isomer, **2**, were separated on addition of 0.3 ml of 6 M hydrochloric acid. Yield. 170 mg. Anal. Found: C, 20.01; H, 4.44; N, 6.65%. Calcd for $C_7H_{18}N_2Cl_2OPt$: C, 20.40; H, 4.40; N, 6.80%.

The sample of **3** for X-ray work was obtained by the following procedure. The mixture of **1** (40 mg) and **2** (160 mg) was dissolved in a small amount of water. The mixture was treated with 0.2 M aqueous $AgNO_3$ solution and separated AgCl was removed by centrifugation. The supernatant

Table 2. Positional Parameters and Thermal Parameters (Å^2) of Non-H Atoms of the Plate Crystal (**3**) of [PtCl$_2$(*S*-Hp-Mepn)]H_2O with esd's in Parentheses

Atom	x	y	z	B
Pt(1)	0.26835(3)	0.351(0)	0.86837(4)	2.19(1)
Cl(11)	0.1445(2)	0.4219(5)	0.7310(3)	3.4(1)
Cl(12)	0.3166(3)	0.4975(5)	0.8079(4)	3.8(1)
O(1)	0.0922(6)	0.129(2)	0.872(1)	5.3(4)
N(11)	0.3738(7)	0.281(1)	0.982(1)	2.6(3)
N(12)	0.2355(7)	0.214(1)	0.935(1)	2.5(3)
C(11)	0.3797(9)	0.200(2)	1.081(1)	2.8(4)
C(12)	0.3057(8)	0.132(2)	1.012(1)	2.7(4)
C(13)	0.447(1)	0.113(2)	1.136(2)	4.4(6)
C(14)	0.390(1)	0.284(2)	1.182(1)	3.9(5)
C(15)	0.2022(8)	0.256(2)	1.003(1)	2.7(4)
C(16)	0.1173(9)	0.249(2)	0.925(1)	3.3(4)
C(17)	0.083(1)	0.283(2)	0.994(2)	4.5(5)
Pt(2)	0.23401(3)	0.14881(8)	0.65206(4)	1.910(9)
Cl(21)	0.3534(2)	0.0635(5)	0.7889(3)	3.12(9)
Cl(22)	0.1761(2)	0.0174(5)	0.7085(3)	2.94(9)
O(2)	0.4043(7)	0.383(2)	0.618(1)	4.9(4)
N(21)	0.1317(6)	0.233(1)	0.5303(9)	2.0(3)
N(22)	0.2761(6)	0.274(1)	0.592(1)	2.2(3)
C(21)	0.1349(7)	0.300(2)	0.437(1)	2.4(3)
C(22)	0.2152(7)	0.363(2)	0.511(1)	2.2(3)
C(23)	0.124(1)	0.209(2)	0.341(1)	3.5(4)
C(24)	0.072(1)	0.395(2)	0.379(2)	3.5(4)
C(25)	0.3184(9)	0.218(2)	0.545(1)	3.3(4)
C(26)	0.3566(9)	0.308(2)	0.512(1)	3.1(4)
C(27)	0.4030(9)	0.242(2)	0.480(1)	4.1(5)
O(3)	0.0042(7)	0.063(2)	0.625(1)	4.2(4)
O(4)	0.511(1)	0.447(2)	1.126(1)	7.5(6)

Table 3. Positional Parameters and Thermal Parameters (Å^2) of Non-H Atoms of the Needle Crystal (**2**) of *R*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] with esd's in Parenthses

Atom	x	y	z	B_{eq}
Pt	0.27467(4)	0.47894(3)	0.14788(4)	1.885(4)
Cl(1)	0.0656(3)	0.5135(3)	0.0762(3)	3.24(5)
Cl(2)	0.2242(3)	0.3149(2)	0.2280(3)	3.03(5)
O	0.3444(8)	0.7648(6)	0.388(1)	3.2(2)
N(1)	0.4603(9)	0.4538(6)	0.200(1)	2.2(2)
N(2)	0.337(1)	0.6227(6)	0.087(1)	2.6(2)
C(1)	0.545(1)	0.5333(8)	0.128(1)	2.5(2)
C(2)	0.475(1)	0.6339(7)	0.140(2)	2.7(2)
C(3)	0.674(1)	0.535(1)	0.206(2)	3.8(3)
C(4)	0.559(1)	0.5023(9)	−0.041(1)	3.3(2)
C(5)	0.260(1)	0.7109(8)	0.142(1)	2.6(2)
C(6)	0.241(1)	0.7121(7)	0.316(1)	2.3(2)
C(7)	0.113(1)	0.765(1)	0.363(2)	4.0(3)

was added with 1 ml of 1 M hydrochloric acid and the mixture was allowed to stand at room temperature. Plates, **3**, were grown with needles of **2**. Suitable plates were separated mechanically and washed with water and dried in air. Anal. Found: C, 19.10; H, 4.66; N, 5.98%. Calcd for $C_{17}H_{18}N_2Cl_2PtO\cdot H_2O$: C, 19.54; H, 4.69; N, 6.51%.

The sample of **2** for X-ray work was obtained by slow evaporation of a dilute aqueous solution of **2**.

Collection and Reduction of X-Ray Data. X-Ray data were collected and corrected by the procedure described previously.[9] The absorption correction was based on the azimuthal (ϕ) scan of 3 (for **3**) or 6 (for **2**) reflections. Both crystals showed the deviation of less than 1 % in intensity during the data collection period. Crystal and empirical data are summarized in Table 1.

Solution and Refinement of the Structures. The structures were solved and refined by the procedure described previously.[9] The absolute configurations were deduced from the refinement of the enantiomorphs at the stage with non-hydrogen atoms using anisotropic thermal factors: for **3**, R=0.047 vs. 0.057: for **2**, R=0.049 vs. 0.059. The enantiomorph with lower R factors was chosen as the correct solution. The molecular and crystal plots were produced by ORTEP.[12] The fractional coordinates for non-hydrogen atoms of **3** and **2** are listed in Tables 2 and 3 respectively. Tables of thermal factors (Tables S1 and S4), hydrogen atom parameters (Tables S2 and S5), and structure factors (Tables S3 and S6) are deposited as Document No. 9025 at the Office of the Editor of Bull. Chem. Soc. Jpn.

Results and Discussion

Separation of Isomers. Plate crystals, **3**, separated from the reaction mixture of K_2PtCl_4 and diamine dihydrochloride under basic conditions were found to contain the diastereoisomers in 1 : 1 ratio which have opposite configuration at the secondary amine. Under these conditions there seems no selectivity of the chiral hydroxypropyl substituent for particular configuration at the secondary amine site. Treatment of this diastereoisomer pair with $AgNO_3$ and addition of hydrochloric acid afforded small crystals, **1**, which contain *S*(*N*)-isomer as the less soluble fraction. On the other hand, needles, **2**, which contain the *R*(*N*)-isomer, were obtained on heating **3** under basic conditions. This isomer was obtained also by heating an aqueous solution of *S*(*N*)-isomer, **1**.

Structure of the Pt Complexes. The structure of the two types of crystals suitable for X-ray work was determined. The plate crystals, **3**, are found to belong to $C2$ and contain two diastereoisomers of [PtCl$_2$(*S*-Hp-Mepn)] and two water molecules. The needle crystals, **2**, were found to belong to $P2_12_12_1$ and contain [PtCl$_2$(*S*-Hp-Mepn)] with the absolute configuration of R at the secondary amine center. The dichloro(*S*-Hp-Mepn)-platinum(II) molecules found in **2** and **3** have typical square planar structures with two chlorine atoms in cis position and the ligand acts as a didentate chelate with two nitrogen atoms coordinated to platinum(II). The conformations of *R*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] determined by crystallography, however, differ from each other.

The molecule with *S*-configuration at the secondary amine site found in **3** is shown in Fig. 1. This molecule

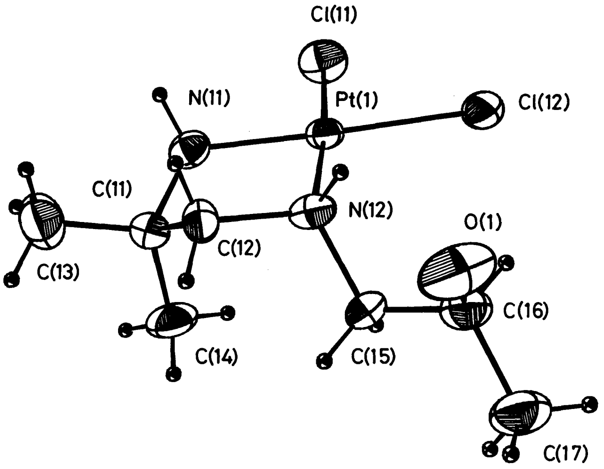

Fig. 1. ORTEP drawing of *S*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] of plate crystals, **3*S***.

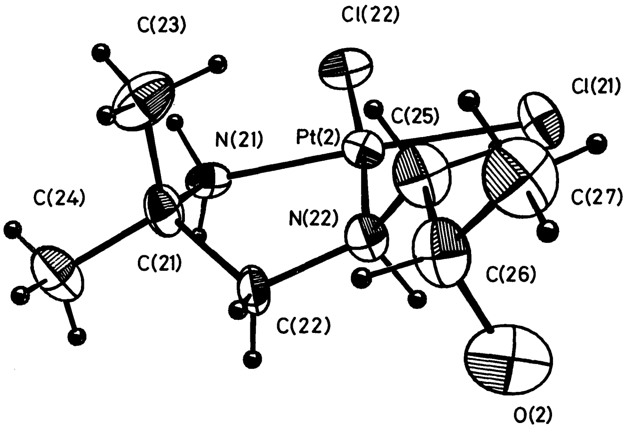

Fig. 2. ORTEP drawing of *R*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] of plate crystals, **3*R***.

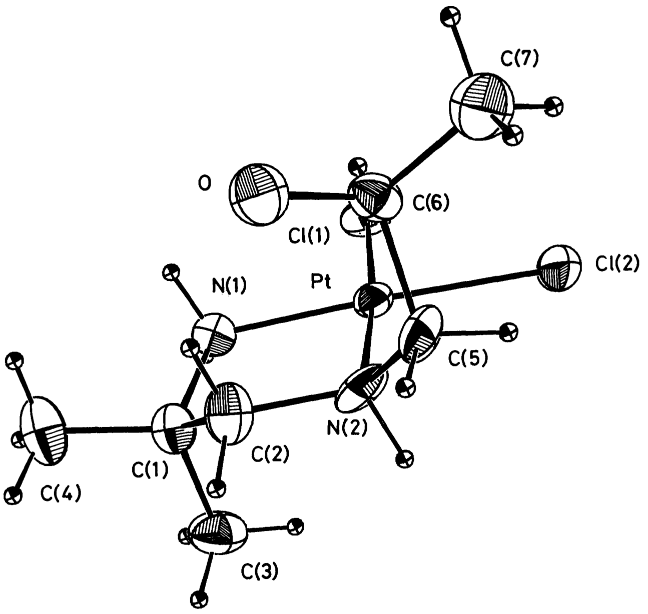

Fig. 3. ORTEP drawing of *R*(*N*)-[$PtCl_2$(*S*-Hp-Mepn)] of needle crystals, **2*R***.

has a λ conformation with respect to the five-membered chelate ring and will be denoted as **3*S*** hereafter where the *S*-2-hydroxypropyl substituent extends in the pseudo axial direction. The other molecule found in **3** shown in Fig. 2 has an *R* configuration at the coordinated nitrogen center and a δ conformation and will be denoted as **3*R***. In this isomer the substituent extends in the pseudo axial direction.

The molecule of **2** with *R*-configuration at the nitrogen center, shown in Fig. 3, has a λ conformation with the *N*-substituent extending in the pseudo equatorial direction and will be denoted as **2*R*** hereafter.

The comparisons of the bond lengths and bond angles among non-hydrogen atoms are listed in Table 4. The bond lengths between the platinum and chlorine which is trans to the primary amine (2.320(3)—2.315(3) Å) are larger than those between the platinum and chlorine trans to the secondary amine (2.309(2)—2.311(3) Å). The bond length of Pt–N(1) has the range between 2.01(1) and 2.045(9) Å and that of Pt–N(2) has the range between 2.051(7) and 2.076(9) Å.

The bite angles of N(1)–Pt–N(2) are not susceptible to the structure: 84.8(4), 84.1(3), and 84.4(3)°, for **3*S***, **3*R***, and **2*R***, respectively. The bond angles around N(2) show significant deviation from the tetrahedral value: Pt–N(2)–C(5) and C(2)–N(2)–C(5) angles are 116.0(7) and 113.1 (7)° for **3*S*** and 113.8(7) and 116.5(7)° for **3*R***, these complexes have axial substituents. For **2*R*** which has an equatorial substituent, the bond angles for Pt–N(2)–C(5) and C(2)–N(2)–C(5) are 116.9(6) and 110.0(7)°, respectively. The bond angles around C(5) for **3*R*** are deviated from the tetrahedral value: N(2)–C(5)–C(6), 115(1)°. This is probably due to the formation of the hydrogen bond between N(2) and O, i.e, N(2)–H(3)···O. Other bond lengths and bond angles are normal for this class of complexes.[4,5]

Table 4. Bond Lengths (Å) and Angles (°) of [$PtCl_2$-(*S*-Hp-Mepn)] with esd's in Parentheses

	Quasi-racemate(**3**)		**2**
	S(*N*),**3*S***	*R*(*N*),**3*R***	*R*(*N*),**2*R***
Pt–Cl(1)	2.320(3)	2.315(3)	2.317(2)
Pt–Cl(2)	2.310(3)	2.311(3)	2.309(2)
Pt–N(1)	2.01(1)	2.045(9)	2.019(8)
Pt–N(2)	2.076(9)	2.055(8)	2.051(7)
O–C(6)	1.45(2)	1.44(1)	1.43(1)
N(1)–C(1)	1.55(1)	1.50(1)	1.50(1)
N(2)–C(2)	1.53(1)	1.49(1)	1.52(1)
N(2)–C(5)	1.53(1)	1.51(1)	1.48(1)
C(1)–C(2)	1.49(2)	1.56(1)	1.50(1)
C(1)–C(3)	1.52(2)	1.54(2)	1.51(1)
C(1)–C(4)	1.55(1)	1.53(2)	1.54(1)
C(5)–C(6)	1.49(1)	1.52(1)	1.54(1)
C(6)–C(7)	1.54(3)	1.48(2)	1.56(1)
Cl(1)–Pt–Cl(2)	91.6(1)	92.5(1)	92.7(1)
Cl(1)–Pt–N(1)	176.8(3)	176.6(3)	176.7(2)
Cl(1)–Pt–N(2)	93.8(3)	92.6(2)	93.0(2)
Cl(2)–Pt–N(1)	89.9(3)	90.7(2)	90.0(2)
Cl(2)–Pt–N(2)	174.6(3)	174.8(3)	174.2(2)
N(1)–Pt–N(2)	84.8(4)	84.1(3)	84.4(3)
Pt–N(1)–C(1)	111.7(6)	109.9(6)	110.9(5)
Pt–N(2)–C(2)	105.8(6)	109.4(6)	108.0(5)
Pt–N(2)–C(5)	116.0(7)	113.8(7)	116.9(6)
C(2)–N(2)–C(5)	113.1(7)	116.5(7)	110.0(7)
N(1)–C(1)–C(2)	103.3(8)	105.1(7)	106.6(7)
N(1)–C(1)–C(3)	110.8(9)	109.3(9)	110.0(8)
N(1)–C(1)–C(4)	108.(1)	107.6(8)	106.6(8)
C(2)–C(1)–C(3)	111.(1)	112.9(8)	112.5(8)
C(2)–C(1)–C(4)	113.9(9)	110.(1)	110.2(8)
C(3)–C(1)–C(4)	109.8(9)	111.4(9)	110.7(8)
N(2)–C(2)–C(1)	113.(1)	110.4(9)	110.8(7)
N(2)–C(5)–C(6)	112.4(8)	115.(1)	113.5(7)
O–C(6)–C(5)	110.(1)	105.8(8)	110.1(7)
O–C(6)–C(7)	110.(1)	111.(1)	108.6(8)
C(5)–C(6)–C(7)	113.1(9)	109.9(9)	112.2(8)

Table 5. Torsion Angle (°)

	Quasi-racemate		Needle
	S(*N*),**3*S***	*R*(*N*),**3*R***	*R*(*N*),**2*R***
Pt–N(1)–C(1)–C(2)	41(2)	−42(2)	39(1)
N(1)–C(1)–C(2)–N(2)	−50(2)	50(2)	−48(2)
C(1)–C(2)–N(2)–Pt	−37(2)	33(2)	−34(2)
Pt–N(2)–C(5)–C(6)	101(2)	−175(1)	55(1)
Pt–N(1)–C(1)–C(3)	160(1)	79(1)	162(1)
Pt–N(1)–C(1)–C(4)	−80(2)	−160(2)	−78(1)
C(3)–C(1)–C(2)–N(2)	−169(1)	−69(1)	−169(1)
C(4)–C(1)–C(2)–N(2)	66(2)	165(2)	67(1)
C(2)–N(2)–C(5)–C(6)	−137(2)	57(2)	−69(2)
N(2)–C(5)–C(6)–C(7)	177(2)	174(2)	−151(1)
N(2)–C(5)–C(6)–O	53(2)	54(2)	88(1)

The comparison of the torsion angles among the non-hydrogen atoms is listed in Table 5. The torsion angles with regard to the five-membered chelate ring are normal as the five-membered chelate ring with gauche conformation.[4,5] The three molecules have the N(2)–

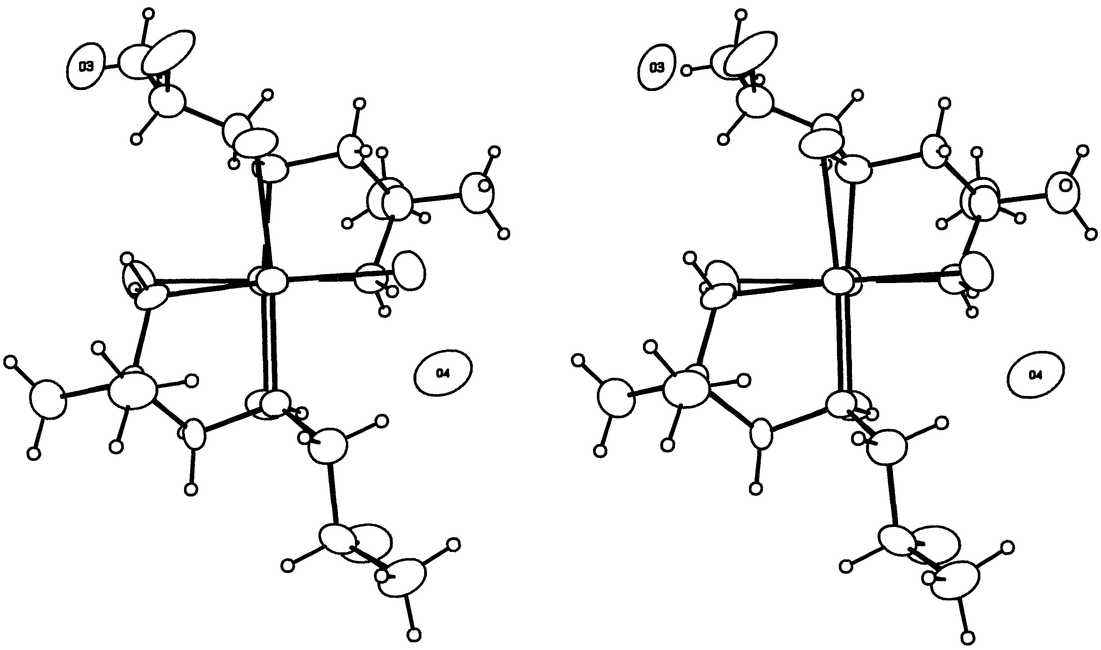

Fig. 4. Top view of the pseudo dimer of **3*S*** and **3*R***.

C(5)-C(6)-C(7) torsion angle of 177(2), 174(2), and −151(1)° and N(2)-C(5)-C(6)-O torsion angles of 53(2), 54(2), and 88(1)° for **3*S***, **3*R***, and **2*R***, respectively. A possible cause of the narrow torsion angles for **3*S*** and **3*R*** is the intramolecular hydrogen bond formation of N(2)-H(3)···O, because the distance between H(3) and O is 2.35 and 2.45 Å for **3*S*** and **3*R***, while H(3) and O in **2*R*** are located far from each other. The torsion angles of Pt-N(2)-C(5)-C(6) are 101(2), −175(1), and 55(1)° and those of C(2)-N(2)-C(5)-C(6) are −137(2), 57(2), and −69(2)° for **3*S***, **3*R***, and **2*R***, respectively. The *N*-alkyl substituents prefer the position where they are swung away from the chlorine atom in cis-position, Cl(2).

The plate crystals, **3**, contain diastereoisomers **3*R*** and **3*S*** and two water molecules. These diastereoisomers form a pseudo dimer unit shown in Fig. 4. The angle between the planes defined by platinum atom and four coordinated atoms is (3.0±3.6)°, thus these planes are parallel to each other. This dimer pair has an approximate inversion center at the middle of the two platinum atoms with Pt···Pt distance of 3.39 Å but the dihedral angles of Pt-N(2)-C(5)-C(6) destroy the symmetry of inversion. Four hydrogen bonds exist between N-H···Cl: N(11)-H(2)···Cl(21), 2.530(3); N(12)-H(3)···Cl(22), 2.526(3); N(21)-H(31)···Cl(11), 2.386(3); N(22)-H(33)···Cl(12), 2.735(3) Å. This type of dimer formation has been reported for the red form of [PtCl$_2$(bpy)]$^{13)}$ and dichloro[(*R*,*S*)-*N*,*N*′-bis(1-phenethyl)-1,2-ethanediamine)platinum(II).$^{14)}$ In these, Pt···Pt distances have been reported as 3.45 and 3.344(2) Å.

Structures in Solution. The X-ray crystallography revealed that the *N*-2-hydroxypropyl substituent can adopt both absolute configurations at the secondary amine center and also can adopt both pseudo axial and pseudo equatorial orientations. The pseudo axial orientation makes intramolecular hydrogen bonds possible to form. The two diastereoisomers different in the absolute configuration at the secondary amine site, **1** and **2**, were separated and their structures were exam-

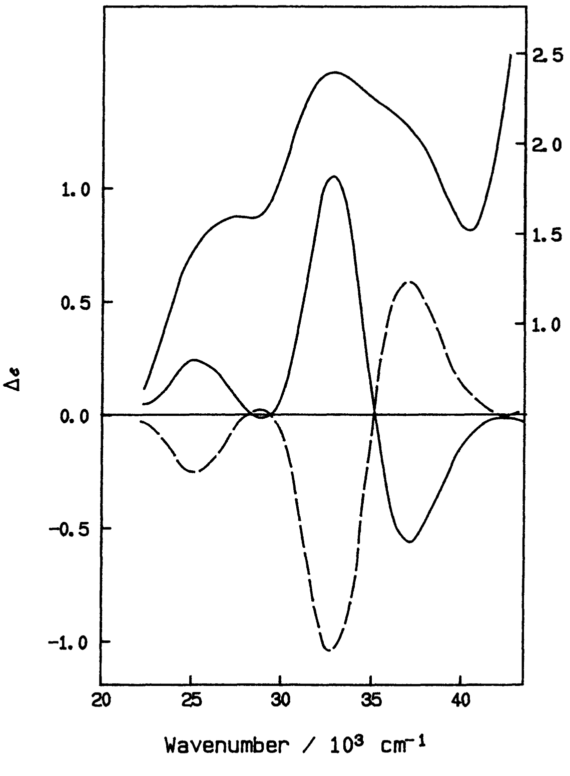

Fig. 5. UV and CD spectra of acidic aqueous solution of *S*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] (------) and *R*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] (——).

ined by UV-CD and ^{1}H NMR method with acidic aqueous solution of them.

UV-CD Spectra. The electronic and CD spectra of acidic aqueous solution of separated diastereoisomers are shown in Fig. 5. Dichloro(1,2-ethanediamine)platinum(II) shows strong singlet–singlet transitions around 33000 cm^{-1} ($d_{xy}\rightarrow d_{x^2-y^2}$) and 37500 cm^{-1} ($d_{xz},d_{yz}\rightarrow d_{x^2-y^2}$), or these originate from the split $d_{xz},d_{yz}\rightarrow d_{x^2-y^2}$ transitions.[3] The CD spectra of [PtCl$_2$(CH$_3$NHCH$_2$C*H(CH$_3$)NH$_2$=*N*$_2$-Me-*S*-pn)] have been analyzed by Bosnich and Sullivan and additivity of contributions from the configuration of the secondary amine and the conformation of the five-membered chelate ring has been found to hold.[3] Both the two isolated diastereoisomers of [PtCl$_2$(*N*$_2$-Me-*S*-pn)] have δ rings with equatorial C–CH$_3$ but the *R*(*N*)- and the *S*(*N*)-isomer has an equatorially and an axially orientated *N*-CH$_3$ group, respctively.[4,5] Due to the additivity of the two contributions the magnitudes of the CD peaks at 33000 and 37500 cm^{-1} are different between the *R*(*N*)- and *S*(*N*)-isomers.

In the present system of [PtCl$_2$(*S*-Hp-Mepn)], there seems to be little preference with regard to the conformation of the chelate ring because the optically active substituent is located at the side chain. The two CD spectra show almost the mirror image to each other, thus two isomers, **1** and **2**, have opposite configuration at the secondary amine site and the vicinal effect of the asymmetric carbon is small.

The CD spectrum of *R*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] is almost the same as that of *S*(*N*)-[PtCl$_2$(*N*$_2$-Me-*R*-pn)] and those of *S*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)] and *R*(*N*)-[PtCl$_2$(*N*$_2$-Me-*S*-pn)] are also similar. The CD spectra of these *N*-alkyl-1,2-alkanediamines have peaks with the same signs in spite of the opposite absolute configuration at the secondary amine. This is caused by the IUPAC rules for assignment of the absolute configuration of the secondary amine. The absolute configuration depends whether the order of the side chain is senior to the 1,2-ethanediamine segment. If the absolute configuration is determined on the order of platinum, the chelate ring, and the *N*-alkyl substituent, "*R*(*N*)"-isomer has negative and positive Cotton effects at 33000 and 37500 cm^{-1}, respectively, for all the dichloro(*N*-alkyl-1,2-alkanediamine)platinum(II) studied so far.[9]

The conformation of each isomer is not necessarily the same as those of solid states. The magnitudes of the CD peaks at 33000 and 37500 cm^{-1} are 1.06 and −0.57 for the *R*(*N*)-isomer and −1.05 and 0.59 for the *S*(*N*)-isomer. The contributions to the 33000 cm^{-1} Cotton effect of the absolute configuration of the secondary amine center and the chelate ring conformation are large and negligible respectively, because the same type complexes of optically active 1,2-propanediamine and 1,2-cyclohexanediamine which lack *N*-alkyl substituents show no CD features in this region.[15–18] The Cotton effect at 37500 cm^{-1} is a composite of both contributions.

Two conformers are possible for the *R*(*N*)-isomers for [PtCl$_2$(*N*$_2$-Me-*S*-pn)]: δ and λ conformations with the equatorial and axial *N*-methyl substituent respectively. If the population of conformers of *R*(*N*)-isomer is to be determined, the ratio of the magnitude at 37500 cm^{-1} to that at 33000 cm^{-1} will give an approximate estimation. Since the *S*(*N*)-[PtCl$_2$(*N*$_2$-Me-*S*-pn)] which is forced to take δ conformation has an axial *N*-methyl group, *S*(*N*)-[PtCl$_2$(*N*$_2$-Me-*R*-pn)] will have an equatorial *N*-methyl group, and its CD spectrum should be the mirror image of *R*(*N*)-[PtCl$_2$(*N*$_2$-Me-*S*-pn)]. The ratio of the magnitudes of CD peaks at 33000 and 37500 cm^{-1} is 1.593 and 0.208 for *S*(*N*)-[PtCl$_2$(*N*$_2$-Me-*S*-pn)] and *S*(*N*)-[PtCl$_2$(*N*$_2$-Me-*R*-pn)] respectively.

The ratio for *R*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)], **2**, and *S*(*N*)-[PtCl$_2$(*S*-Hp-Mepn)], **1**, is 0.537 and 0.562, respectively, thus, the fraction of the equatorial conformer (x) is calculated from the equation,

$$\text{observed ratio} = 1.593(1-x) + 0.208x$$

The fractions of the isomers with equatorially orientated *N*-2-hydroxypropyl substituent are 0.74 and 0.72 for the *R*(*N*)- and *S*(*N*)-isomer respectively. These results indicate that the preferred orientaion of 2-hydroxypropyl is equatorial for both isomers which are different from the structures in the crystals and the five-membered chelate ring adopts δ for the *S*(*N*)-, **1**, and λ for the *R*(*N*)-isomer, **2**. The ratio of the population of axial to equatorial conformers is larger for *N*-2-hydroxypropyl substituent than for *N*-2-hydroxybutyl substituent if the ratio of magnitudes of the two Cotton effect reflects the population.[9]

^{1}H NMR Spectra. The structure of both isomers in solution was evaluated by ^{1}H NMR spectroscopy using DCl–D$_2$O solution. Under the slightly acidic conditions, H–D exchange proceeded fast at O–H but amino protons were retained as broad signals and to couple with rest of the molecule. If coordinated amines dissociate from Pt(II), the H–D exchange would occur rapidly, therefore, any dissociation of the coordinated amines from central Pt(II) ion did not occur under the present conditions. The 400 MHz spectrometer pre-

Table 6. Chemical Shift/ppm and Coupling Constant/Hz of [Pt(*S*-Hp-Mepn)] in Acidic D$_2$O Solution

Nucleus	*S*(*N*)-, **1**	*R*(*N*)-, **2**
–CH(OH)–C*H*$_3$	1.179	1.170(6.4)
–C(C*H*$_3$)$_2$–	1.399	1.402
	1.497	1.514
–C(CH$_3$)$_2$–C*H*$_2$–	2.631(12.6, 9.5)	2.711(8.9)
	2.837(12.6, 5.2, 1.8)	2.714(6.4)
–CH(OH)–C*H*$_2$–	2.872(13.6, 8.0, 7.9)	2.952(14.0, 10.3, 1.9)
	3.355(13.6, 4.3, 2.5)	3.058(14.0, 9.3, 1.8)
–C*H*(OH)–	4.124(7.9, 6.4, 4.3)	4.286(10.3, 6.4, 1.8)
–N*H*$_2$	5.197	5.194
	5.309	5.340
–N*H*–	5.979	5.848

cludes the detection of couplings between ^{195}Pt and protons.[9] The numerical data of the chemical shifts and coupling constants based on the first-order analysis are listed in Table 6 and methylene and methine region traces are reproduced in Figs. 6 and 7 for **1** and **2** respectively along with those recorded under irradiation at several selected resonances.

^{1}H NMR spectra of **1** and **2** have different features in chemical shifts and coupling constants. The differences in chemical shift of the two methylene protons bonded to the same carbon at the chelate ring, C(2), and the N-2-hydroxypropyl substituent, C(5), are δ=0.206 and 0.483 for **1** but they are δ=0.003 and 0.106 for **2**, respectively. The vicinal coupling constants of the high field proton bonded to C(5) with secondary amino proton and with the methine proton are J=7.9 and 8.0 Hz respectively while those of the lower field proton are J=2.5 and 4.3 Hz respectively for **1**. On the other hand, those of the high field signal are J=1.9 and 10.3 Hz and those of the lower field signal are J=9.3 and 1.8 Hz respectively for **2**.

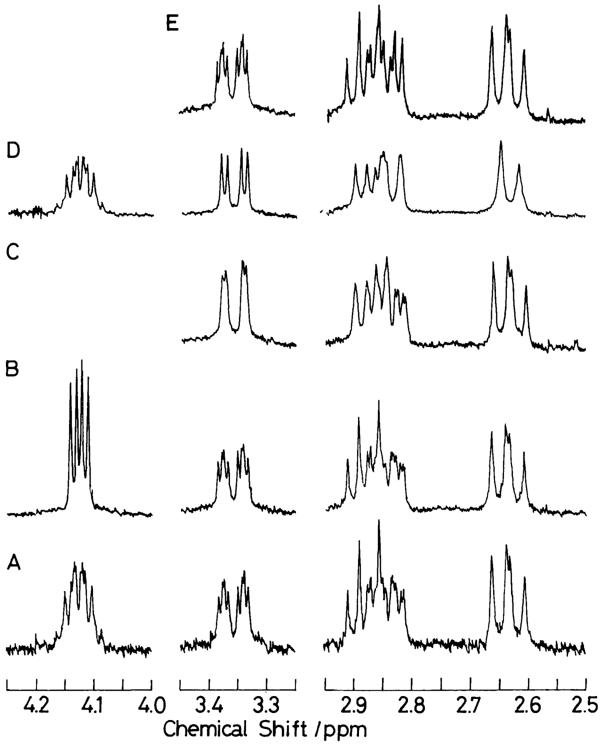

Fig. 6. Methylene and methine region of ^{1}H NMR spectra of S(N)-[PtCl$_2$(S-Hp-Mepn)]. A, non-irradiated; B, irradiated at methyl; C, irradiated at methine; D, irradiated at sec. N–H; E, irradiated at primary N–H.

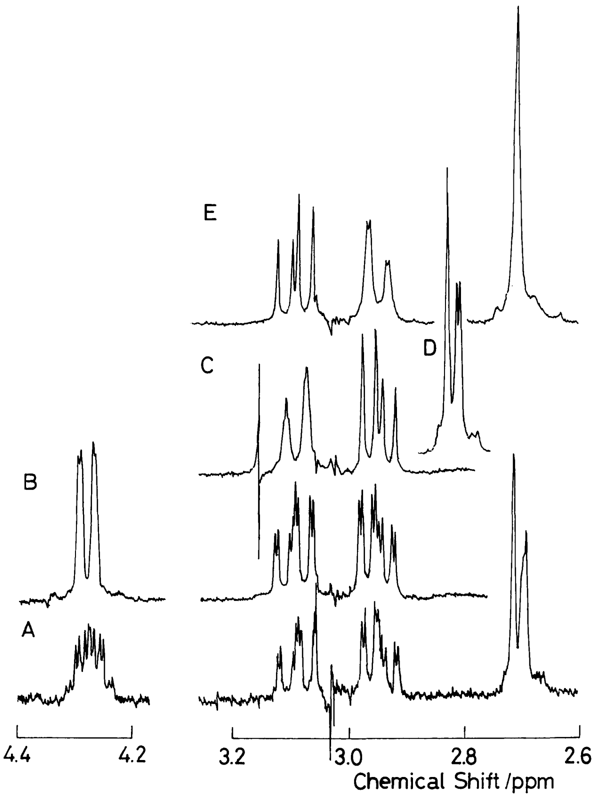

Fig. 7. Methylene and methine region of ^{1}H NMR spectra of R(N)-[PtCl$_2$(S-Hp-Mepn)]. A, non-irradiated; B, irradiated at methyl; C, irradiated at methine; D, irradiated at primary N–H; E, irradiated at secondary N–H.

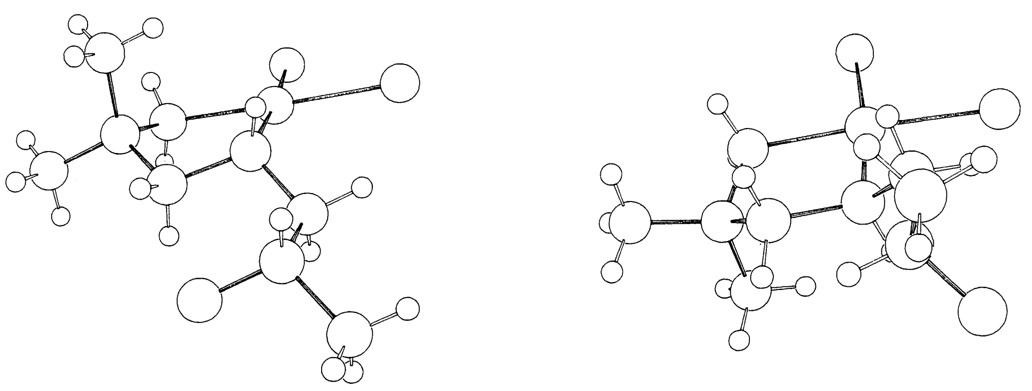

Fig. 8. Schematic representation of major conformers in aqueous solution: left, S(N)-[PtCl$_2$(S-Hp-Mepn)] (**1**); right, R(N)-[PtCl$_2$(S-Hp-Mepn)] (**2**).

The major conformers of **1** and **2** in solution are those which have equatorially substituted 2-hydroxypropyl group based on the results of the CD spectra. This requires the secondary amino proton to take the pseudo axial disposition for both **1** and **2**.

The conformation of 2-hydroxypropyl substituent is described by the combination of two torsion angles of Pt-N(2)-C(5)-C(6) (χ) and N(2)-C(5)-C(6)-C(7) (ω), these angles determine the torsion angles of C(2)-N(2)-C(5)-C(6) (ϕ). The schematic representations of the major conformations of **1** and **2** deduced from the CD and ^{1}H NMR spectroscopy are drawn in Fig. 8. The vicinal coupling constants of the two methylene protons bonded to C(5) of **1** with N-H and C-H are both large for the high-field proton and small for the low-field proton. A simple application of Karplus relationship between the vicinal coupling constant and torsion angle indicates the low-field proton to take a position anti to the secondary amine and χ is either 180° or 60°. In the latter case, the terminal methyl or hydroxyl group would be near to the chlorine atom (Cl(2)). In the former case, the substituent extends from the Pt coordination sphere and is expected to be sterically less hindered. Therefore, χ is expected to have a value of about 180°. The vicinal coupling constants with methine proton leads to the value of about 180° for ω.

For **2**, analogous analysis leads to the conformation in which either χ and ω has 180°. In this isomer, an intramolecular hydrogen bonding is possible because the hydroxyl oxygen and N-H locate near to each other. The stability of **2** is suggested by the synthesis and the conversion of the isomers although the precise analysis of the isomer distribution was not possible due to the decomposition of the complexes.

Comparison of the Conformation of Liqand between Crystal and Aqueous Solution. The chelate ring conformation and torsion angles of χ, ϕ, and ω found in the crystals and deduced from the spectroscopy of aqueous solutions are listed in Table 7. In plate crystals, the axial disposition of the *N*-2-hydroxypropyl substituent is assisted by hydrogen bondings between hydroxyl and N-H. Pucking force also plays an important role in determination of the orientation of flexible *N*-alkyl substituent. In an acidic aqueous solution, these hydrogen bonding will be destroyed and the equatorial disposition is favored. It will be noteworthy that χ has the value of about 180° irrespective to the state of the molecule.

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Table 7. Comparison of Cotton Effects and Structures of [$PtCl_2L$] Complexes

L	Cotton effect		Nitrogen configuration	Chelate ring conformation	Disposition of *N*-substituent	Torsion Angle/°		
	$^1A_1 \rightarrow {}^1A_2$	$^1A_1 \rightarrow {}^1E$				χ	ω	ϕ
R-pn[a]	(d)	+		λ				
S-Me-pn[b]	−	+	*R*	δ	Equatorial			
S-Me-pn[b]	+	−	*S*	δ	Axial			
R-Hb-Mepn[c]	+	−	*R*	λ	Equatorial			
R-Hb-Mepn[c]	−	+	*S*	δ	Equatorial			
S-Hp-Mepn								
Cryst,**3*S***			*S*	λ	Axial	101	177	−137
Solution	−	+	*S*	δ	Equatorial	180	180	−60
S-Hp-Mepn								
Cryst,**3*R***			*R*	δ	Axial	−175	174	57
Cryst,**2*R***			*R*	λ	Equatorial	55	−151	−69
Solution	+	−	*R*	λ	Equatorial	180	180	−60

a) Ref. 15. b) Ref. 3, 4. c) Ref. 9. d) Not observed.

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