Notes

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Synthesis of 1-(Methylthio)phenazine Platinum(II) and Its S-demethylated Complexes

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1-(Methylthio)phenazine (mtph) reacts with platinum(II) and palladium(II) in acetone–water to give orange complexes. The mtph coordinates to metal through the sulfur and nitrogen atoms as a bidentate ligand, and the two halogen atoms of the complexes are in *cis*-configuration. When the orange complex, $PtCl_2$(mtph), was refluxed in N,N-dimethylformamide, a reddish violet S-demethylated complex was produced. On the other hand, $PdCl_2$(mtph) did not give any demethylated complexes under similar conditions.

Keywords——platinum complex, 1-phenazinethiol; palladium complex, 1-(methylthio)phenazine; 1-phenazinethiol, complex with heavy metal ions; 1-(methylthio)-phenazine, metal complexes; S-demethylation reaction of 1-(methylthio)phenazine; antitumor activity, 1-(methylthio)phenazine metal complexes

In the previous paper, the authors reported the preparation of 1-phenazinethiolates of Zn(II), Co(II), Pd(II), and Pb(II) by reaction of metal chlorides with 1-phenazinethiol,[2] but were unsuccessful in isolating Pt(II) phenazinethiolate because 1-phenazinethiol probably decomposed in the presence of Pt(II) ions. This paper describes the preparation of the Pt(II) complex of 1-(methylthio)phenazine (abbreviation; mtph) and Pt(II) phenazinethiolate through the S-demethylation reaction of the Pt(II) complex of mtph.

Experimental

Equimolar amounts of K_2PtCl_4 and mtph were mixed in 50% aqueous acetone and the solution was allowed to stand at room temperature for 12 hr. Orange crystals, $PtCl_2$(mtph) precipitated were collected and washed with water and acetone.

$PtBr_2$(mtph) was obtained by mixing K_2PtCl_4 and mtph in the presence of a large excess of KBr.

$PdCl_2$ (mtph) was prepared by the same method as $PtCl_2$(mtph) using K_2PdCl_4.

The S-demethylated complex was prepared by refluxing $PtCl_2$(mtph) in N,N-dimethylformamide (DMF).

Analytical data of these complexes are shown in Table I

TABLE I. Elemental Analyses of the Pt(II) and Pd(II) Complexes

Complexes	Calcd.			Found		
	C	H	N	C	H	N
$PtCl_2$(mtph)	31.7	2.0	5.7	31.9	1.8	5.7
$PtBr_2$(mtph)	26.9	1.7	4.8	27.1	1.9	4.9
$PdCl_2$(mtph)	38.7	2.5	6.9	38.5	2.3	6.4
$[PtCl(\text{phenazinethiolate})]_n$	32.6	1.6	5.8	32.8	1.9	6.5
$[PtBr(\text{phenazinethiolate})]_n$	29.6	1.4	5.8	29.7	1.3	5.7

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[2] K. Inagaki, Y. Kidani and H. Koike, *Chem. Pharm. Bull.* (Tokyo), **24**, 156 (1976).

Results and Discussion

From the analytical data and molecular model fo $PtCl_2$(mtph), the following three types of complexes are conceivable: (a) a complex in which mtph coordinates to Pt(II) through the sulfur and nitrogen atoms as a bidentate ligand and the two chloride atoms are in *cis*-configuration, (b) a magnus type complex containing $Pt(mtph)_2$ and $PtCl_4$, (c) a dinuclear halide-bridged complex in which mtph coordinates to Pt(II) as an unidentate ligand.

The electronic absorption spectrum of $PtCl_2$(mtph) shows absorption maximum at 385 nm (*p*-band due to ring nitrogen atoms)$^{3)}$ which is similar to that of the ligand cation (382 nm), and this suggests N-coordination. Infrared spectral bands due to the methyl group of $PtCl_2$ (mtph) shift to lower frequency than that of the ligand, [δ_{sym}: 1320(ligand)—1306 (complex), and δ_{asym}: 1043 (deuterated ligand)—1037 and 1026 (complex)], and this suggests S-coordination. Far-infrared spectrum of $PtCl_2$(mtph) exhibits three bands at 338, 323 and 287 cm^{-1}, and a shoulder at 310 cm^{-1}. The former two bands disappeared and a new band appeared at 247 cm^{-1} upon replacing the two chloride ions by two bromide ions, and therefore both the bands at 338 and 323 cm^{-1} are assigned to the Pt-Cl stretching modes. Occurrence of two Pt-Cl stretching vibration suggests the *cis*-configuration of both the chloride ions. Pt-S stretching vibrations$^{4)}$ of $PtX_2(Me_2S)_2$ (X=Cl, Br, and I) appeared at 311—135 cm^{-1}. Therefore the band at 310 cm^{-1} is assignable to the Pt-S stretching mode because the mtph itself exhibits only weak band at 290 cm^{-1}. From these spectral data, it is concluded that the $PtCl_2$(mtph) is the (a) type complex mentioned above.

TABLE II. Infrared Bands of Metal Complexes of 1-(Methylthio)phenazine

$PtCl_2$(mtph)	$PtBr_2$(mtph)	$PdCl_2$(mtph)	Assignments
338 s	—	336 s	ν_{M-Cl}
323 s	—	323 s	ν_{M-Cl}
310 sh	307 m	305 sh	ν_{M-S}
287 m	285 m	287 m	ligand
—	247 m	—	ν_{M-Br}

1-(Methylthio)phenazine exhibits a weak band at 290 cm^{-1}.

S-Demethylation of $PtCl_2$(mtph)

When $PtCl_2$(mtph) was refluxed in either N,N-dimethylformamide or cyclohexanone for 2 hr., a reddich violet complex was produced. It is considered that the reddish violet complex is a S-demethylated complex because its infrared spectrum dose not show any bands due to the methyl group. On the other hand, $PdCl_2$(mtph) did not give any S-demethylated complex under similar conditions. Livingstone, et al. reported that Pd(II) and Pt(II) complexes of 8-(methylthio)quinoline gave the corresponding complexes of 8-quinolinethiol as a result of the S-demethylation reaction, whereas the complexes of 2-methyl-8-(methylthio)quinoline did not give any S-demethylated complex because of steric hindrance due to the methyl group at the 2 position.$^{5,6)}$ A molecular model of $PtCl_2$(mtph) shows that the hydrogen atom at the 9-position of the phenazine ring and the halide ion which is in the *trans* position relative to the sulfur atom overlap each other in Van der Waals radius. It is of interest that the $PtCl_2$ (mtph) gives the S-demethylated complex, though it has steric hindrance and $PdCl_2$ (mtph) dose not give any S-demethylated complex.

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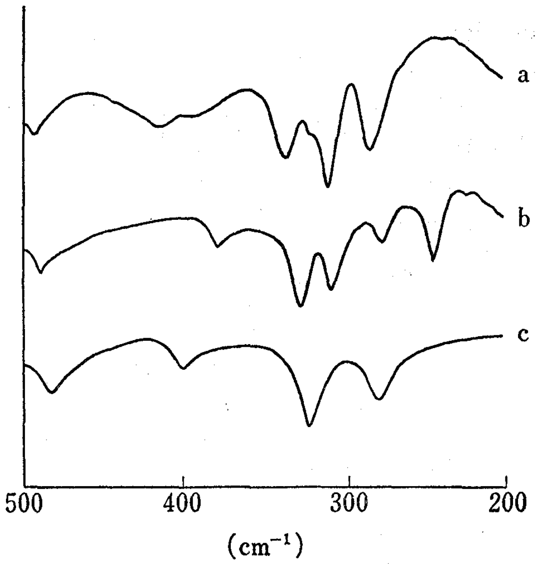

Fig. 1. Infrared Spectra of the Demethylated Complexes and Pd(II) bis-(phenazinethiolate)

a) [PtCl(phenazinethiolate)]$_n$;
b) [PtBr(phenazinethiolate)]$_n$;
c) Pd(phenazinethiolate)$_2$.

The reddish violet S-demethylated complex was not soluble in any of the following solvents; H_2O, DMF, dimethyl sulfoxide and $CHCl_3$. This suggests polymeric complex formation. Analytical data of this complex are consistent with the polymeric formula, [PtCl(phenazinethiolate)]$_n$. Demethylated chloro complex, [PtCl(phenazinethiolate)]$_n$, exhibits three bands at 336, 310, and 285 cm^{-1} in the far-infarared spectrum and the corresponding bromo complex, [PtBr(phenazinethiolate)]$_n$, four bands at 328, 310, 282, and 251 cm^{-1}. Unfortunately, the Pt-S stretching vibration of the chloro complex can not be distinguished from the Pt-Cl stretching vibration because of overlapping. Pd(phenazinethiolate)$_2$ exhibits Pt-S stretching vibration at 329 cm^{-1}.[7] In the case of the bromo complex, the vibration at 328 and 310 cm^{-1} may be assigned to Pt-S stretching mode because the Pt-Br stretching vibration appeared at 251 cm^{-1}.

From the analytical data, the molecular model, and the presence of two Pt-S stretching vibrations in the far-infrared spectrum, it seems likely that the demethylated complex is a polymeric one containing thiolo bridges.

Antitumor activity of various Pt(II) complexes has been the subject of investigation for the past few years. Unfortunately, screening result of antitumor activity for $PtCl_2$(mtph) showed that it was not active against Leukemia L-1210 in CDF_1 mice, *i.e.*, $T/C=105\%$ at a dose of 400 mg/kg by *i.p.* administration.

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7) Unpublished data.