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네자리 리간드-황아미노산 금속착물의 산화반응에 의한 배위된 황원자의 sulfoxide 원자단으로의 전환*

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Conversion of Coordinated Sulfur Atom into Sulfoxide Group via Oxidation Reaction of Metal Complexes of Tetradentates and Sulfur Amino Acids

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요 약. 주게원자가 질소원자와 산소원자인 N_2O_2형 네자리 리간드 ethylenediamine-N,N'-S-α-isobutylacetic acid(SS-eniba)의 디클로로 로듐(III)[Rh(SS-eniba)Cl_2]$^-$의 합성에서 Δ-*s-cis* 및 Λ-uns-cis 이성체를 분리하였다. Δ-*s-cis*-[Rh(SS-eniba)Cl_2]$^-$ 착물과 S-methyl-*L*-cysteine(Smc)의 반응으로부터 Δ-*s-cis*-[Rh(SS-eniba)(Smc)]$^+$ 착물을 합성한 다음 H_2O_2를 이용한 산화반응으로부터 배위된 황원자가 sulfoxide 원자단으로 산화된 Δ-*s-cis*-[Rh(SS-eniba)(Smc-o)]$^+$(Smc-o=S-methyl-*L*-cysteine sulfoxide) 착물이 형성됨을 관찰하였다. 한편 S-methyl-*L*-cysteine을 H_2O_2와 반응시켜 sulfoxide 원자단으로 산화시킨 S-methyle-*L*-cysteine sulfoxide의 합성을 별도로 진행한 후 Δ-*s-cis*-[Rh(SS-eniba)Cl_2]$^+$ 착물에 배위시켜 표준착물인 Δ-*s-cis*-[Rh(SS-eniba)(Smc-o)]$^+$를 합성한 다음 Δ-*s-cis*-[Rh(SS-eniba)(Smc)]$^+$ 착물을 산화시켜 얻은 Δ-*s-cis*-[Rh(SS-eniba)(Smc-o)]$^+$ 착물과 비교하여 배위된 황원자가 sulfoxide 원자단으로 전환되었음을 또한 관찰하였다.

ABSTRACT. Reaction between the N_2O_2-type tetradentate ligand, ethylenediamine-N,N'-di-S-α-isobutylacetic acid (SS-emiba) and $RhCl_3 \cdot 3H_2O$ has yielded Δ-*s-cis*- and Λ-*uns-cis*-[Rh(SS-eniba)Cl_2]$^-$. Δ-*s-cis*-[Rh(SS-eniba)Cl_2]$^-$ has been utilized to react with S-methyl-*L*-cystcine(Smc) to give Λ-*s-cis*-[Rh(SS-eniba)(Smc)]$^+$. The oxidation of Δ-*s-cis*-[Rh (SS-eniba)(smc)]$^+$ using H_2O_2 has produced Δ-*s-cis*-[Rh(SS-eniba)(Smc-o)]$^+$, in which the coordinated sulfur has been converted into the sulfoxide group. In a separate series of experiments the S-methyl-*L*-cysteine is oxidized by H_2O_2 to give S-methyl-*L*-cysteine sulfoxide, which is then coordinated to Δ-*s-cis*-[Rh(SS-eniba)Cl_2]$^-$ to make the standard complet of Δ-*s-cis*-[Rh(SS-eniba)(Smc-o)]$^+$ for comparison with the complex obtained from the oxidation of Δ-*s-cis*-[Rh(SS-eniba)(Smc)]$^+$ by H_2O_2.

INTRODUCTION

Rhodium(III) ion, with its d^6 electronic configuration, is suitable to make variety of octahedral complexes. Though rhodium(III) complexes of quite a number of bidentate and/or tridentate ligands are long known, only a few tetradentate ligands have

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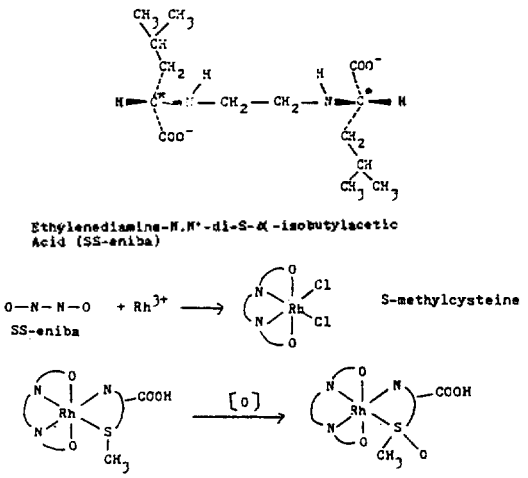

Fig. 1. Synthetic route to [Rh(SS eniba)(smc o)]$^+$.

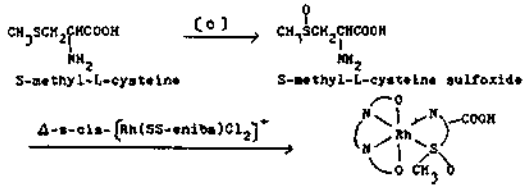

Fig. 2. Synthetic route to the standard complex of [Rh (SS eniba) (smc-o)]$^+$.

been utilized to prepare the octahedral rhodium(III) complexes.[1-6] The tetradentate ligands known so far to make rhodium(III) complexes are triethylene-tetraamine,[7-9] 1,4,7,10-tetraazacyclododecane,[10] 1,4,8,11-tetraazaundecane,[11] and recently ethylenediamine-N,N'-di-S-α-propionic acid.[12-15].

The purpose of this work is two-fold. First, using the N_2O_2-type tetradentate ligand, ethylenediamine-N,N'-di-S-α-isobutylacetic acid (SS-eniba), which has been synthesized recently in our laboratory,[16] we with to prepare the dichloro rhodium(III) complexes of SS-eniba, [Rh(SS-eniba)Cl_2]-(1), and second, we wish to convert the coordinated sulfur atom of the S-methyl-*L*-cysteine (smc) into the sulfoxide group via the oxidation reaction of [Rh(SS-eniba)(smc)]$^+$(2) obtained from the coordination of smc to the complex (1) as envisaged in *Fig.* 1.

In a separate series of experiments shown in *Fig.* 2 the S-methyl-*L*-cysteine is oxidized to S-methyl-*L*-cysteine sulfoxid (smc-o), which is then coordinated to the complex 1 to obtain the standard complex of [Rh(SS-eniba)(smc-o)]$^+$ for comparison with the complex 3.

EXPERIMENTAL

Chemical Reagents. *L*-Leucine, 1,2-dibromoethane, *L*-alanine, and rhodium(III) chloride hydrate were used as obtained from Aldrich Chemical Co. S-methyl-*L*-cysteine was purchased from Nutritional Biochemicals.

Physical Measurements. Proton nmr spectra were recorded on a 60 MHz Varian EM-360 L NMR spectrometer or a 8 MHz Varian FT-80A NMR Spectrometer. Electronic absorption spectra were obtained with a Shimadzu UV-240 Spectrophotometer, while infrared spectra were taken with a Shimadzu IR-435 Spectrophotometer. Elemental analyses were performed by Micro-Tech Analytical Laboratories, Skokie, Illinois, U.S.A. Circular dichroism spectra were obtained with a Jasco J-550 C Automatic Recording Spectropolarimeter.

Preparation of Ethylenediamine-N,N'-di-S-isobutylacetic Acid (SS-eniba). 8.0 g of NaOH in 20 m*l* of water was added to 26.2 g of *L*-leucine in 100 m*l* of water. 17.4 g of 1,2-dibromoethane and 10.6 g of Na_2CO_3 were added in portions to this solution while maintaining the system at 70°C. The reaction mixture was stirred for 30 hours at 70°C. The solution was cooled and acidified to pH 6 with conc HCl. The precipitated white product was collected on a filter, washed with water and petroleum ether, and dried in vacuo. Yiled. 11.0 g. Anal. Calcd for $C_{14}H_{28}N_4O_2$: C, 58.29; H, 9.80; N, 9.71. Found: C, 58.49; H, 9.77; N, 9.60.

Preparation of *s-cis* and *uns-cis* Isomers of Hydrogen Dichloro(ethylenediamine-N,N'-

di-S- isobutylacetato)rhodate(III). *s-cis-* and *uns-cis-H*[Rh(SS-eniba)Cl_2]·H_2O. To a solution of 0.20 g of LiOH·H_2O dissolved in 20 m*l* of water was added 1.10 g of SS-eniba. 0.82 g of $RhCl_3 \cdot 3H_2O$ was added, and the reaction mixture was refluxed for 2 hours. The pH of the solution was adjusted to 5.0 with dilute LiOH solution and the refluxing was continued for a additional 6 hours. The pH of the solution was adjusted again with LiOH·H_2O. The solution was cooled and filtered to remove traces of solids. The filtrate was chromatographed on a column of Dowex 1-X8 anion- exchange resin (100-200 mesh, Cl^- form) using a dilute HCl solution (0.01*M*) as an eluent. The solution was separated into two bands, with the *s- cis* isomer eluting before the *uns-cis* isomer. Yield. 0.33g (*s-cis* isomer) and 0.21 g (*uns-cis* isomer). Anal. Calcd for $RhC_{14}H_{27}N_2O_4Cl \cdot H_2O$: C, 35.09; H, 6.10; N, 5.84; Cl, 14.80. Found: For *s-cis* isomer: C, 34.95; H, 6.14; N, 6.91; Cl, 14.88. For *uns-cis* isomer: C, 35.14; H, 6.08; N, 5.89; Cl, 14.75.

Preparation of *s-cis*-Ethylenediamine-N,N'-di- S-isobutylacetato(S-methyl-*L*-cysteine)rhodium (III) Chloride, *s-cis*-Rh(SS-eniba)(smc)Cl·H_2O. 0.12 g of *s-cis-H*[Rh(SS-eniba)Cl_2]·H_2O was dissolved in 15 m*l* of water and heated on a steam bath. 0.03 g of S-metyl-*L*-cysteine was slowly added with stirring. The resulting solution was heated for 1 hour. The solution was cooled. Slow evaporation under moving air led to crystallization of the yellowish complex. The product was filtered and washed with ethanol and ether. Yield. 0.04 g. Anal. Calcd for $RhC_{18}H_{35}N_3O_6ClS \cdot H_2O$: C, 37.41; H, 6.45; N, 7.27. Found: C, 37.30; H, 6.39; N, 7.14.

Preparation of *s-cis*-Ethylenediamine-N,N'-di-S- isobutylacetato(S-methyl-*L*-cysteinesulfoxide) rhodium(III) Chloride. *s-cis*-[Rh(SS-eniba)(smc--o)]Cl·H_2O. 0.03 g of *s-cis*-[Rh(SS-eniba)(smc)]Cl·H_2O was dissolved in 10 m*l* of water. To this solution was added 2.0 m*l* of 8*N* HCl. 5 m*l* of methanol and 1.2 g of 30 % H_2O_2. The reaction mixture was cooled in water bath and let stand at room temperature for two hours. One gram of amylamine was added to neutralize the solution. The reaction mixture was filtered. Slow evaporation led to precipitation of the product, which was filtered and washed with ether. Yield. 0.01 g. Anal. Calcd for $RhC_{18}H_{35}N_3O_2ClS \cdot H_2O$: C, 36.40; H, 6.28; N, 7.07; Cl, 5.97. Found: C, 36.51; H, 6.27; N, 6.99; Cl, 6.01.

Preparation of S-methyl-*L*-cysteine sulfoxide. To a 50-m*l* aqueous solution of 5.25 g of S-methyl-*L*-cysteine was added 4.0 m*l* of 12*N* HCl, 50-m*l* of methanol, and 5.5 g of 30 % H_2O_2. The reaction mixture was cooled in a water bath and then let stand at room temperature for three hours. 5.0 g of amylamine was added which was followed by 50 m*l* of methanol. The reaction mixture was filtered. 500 m*l* of acetone was added and allowed to stand until the supernatant liquid was almost clear. The precipitated product was collected and washed with ether. Yield. 4.1 g. Anal. Calcd for $C_4H_9NO_3S$: C, 31.78; H, 5.99; N, 9.26. Found: C, 31.80; H, 6.06; N, 9.17.

Preparation of the Standard Complex of *s-cis*-Ethylenediamine-N,N'-di-S-isobutylacetato(S-methylcysteinesulfoxide)rhodium(III) Chloride. Standard *s-cis*-[Rh(SS-eniba)(smc-o)]Cl·H_2O. 0.12 g of *s-cis*-H[Rh(SS-eniba)Cl_2]·H_2O was dissolved in 15 m*l* of water and heated on a steam bath. 0.04 g of S-methyl-*L*-cysteine sulfoxide was slowly added with stirring and heating was continued for 2 hours. After cooling to room temperature the volume of the solution was reduced to one-half of the original volume upon evaporation under moving air. The solution was chilled in a refrigerator overnight. The product was collected on a Hirsh filter and rinsed with cold water and ether. Yield. 0.07 g. Anal. Calcd for Rh

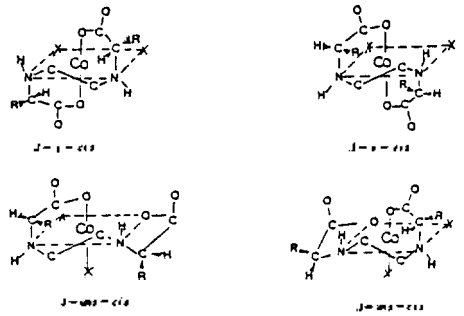

Fig. 3. The four possible isomers of $[Rh(SS\text{-}eniba)X_2]^+$ complex (X=Cl).

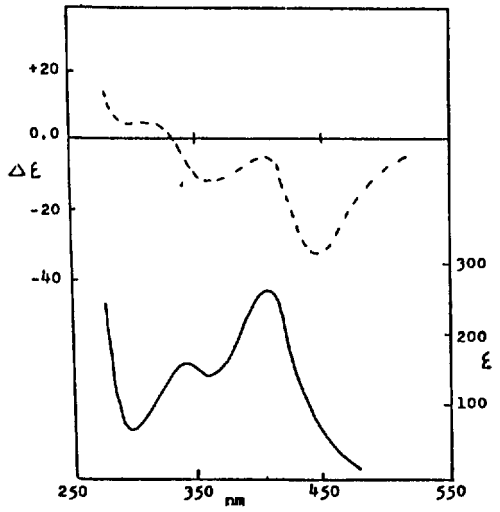

Fig. 4. Electronic absorption (——) and CD(----) spectra of s cis $[Rh(SS\text{-}eniba)Cl_2]$.

$C_{18}H_{35}N_3O_7ClS$: C, 36.40; H, 6.28; N, 7.07; Cl, 5.97. Found: C, 36.46; H, 6.25; N, 7.15; Cl, 5.91.

RESULTS AND DISCUSSION

The dichloro rhodium(III) complexes of SS-eniba were prepared by the reaction of the ligand with an aqueous solution of $RhCl_3 \cdot 3H_2O$. While the SS-eniba ligand yielded three isomers (*Δ-s-cis*, -uns-*cis* and *Λ*-uns-*cis* isomers) in the case of the diaqua cobalt(III) complexes,[17,18] only two isomers (*Δ-s-cis* and *Λ* -uns-*cis*) of the possible four isomers depicted in *Fig.* 3 were formed.

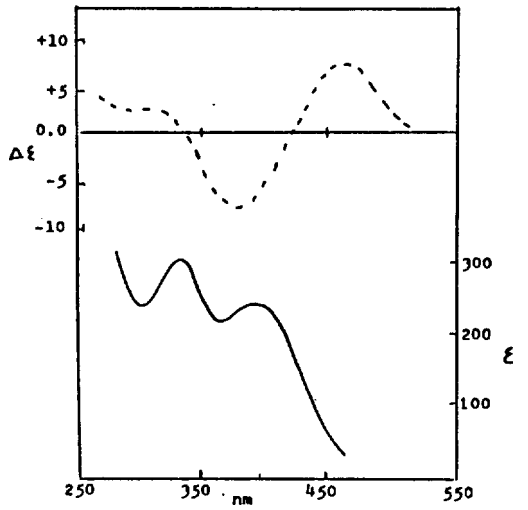

Fig. 5. Electronic absorption (——) and CD(----) spectra of uns cis $[Rh(SS\text{-}eniba)Cl_2]$.

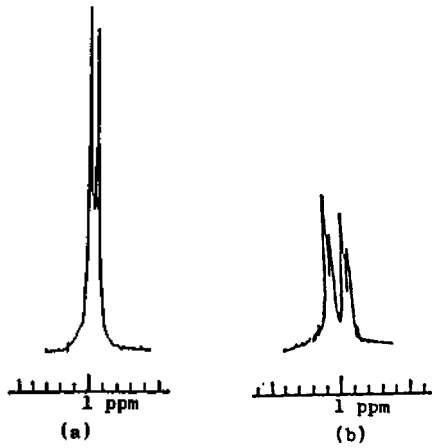

Fig. 6. ^1H nmr spectra of the methyl group region of the isobutyl arm in (a) s-cis-$[Rh(SS\ eniba)Cl_2]^-$ and uns-cis-$[Rh(SS\ eniba)Cl_2]^-$.

The distinction between the s-cis and uns-cis isomers of $[Rh(SS\text{-}eniba)\ Cl_2]^-$ can be made from the electronic absorption and proton nmr spectra shown in *Fig.* 4~6. The absorption peaks in the uns-cis are at slightly higher energy than the corresponding peaks in the *s-cis* isomer in the long wavelength region. Such band shifts are consistent witth those observed for $[\ Rh(SS\text{-}eddp)Cl_2\ ]^-$,[12] $[\ Rh(SS\text{-}eddp)en\ ]^+$,[13] and for the isomers of $[Co(SS\text{-}eddp)en]^+$ and $[\ Co(SS\text{-}edda)L\ ]^-$ series.[19-21]

The *s-cis* and *uns-cis* isomers have been clear-

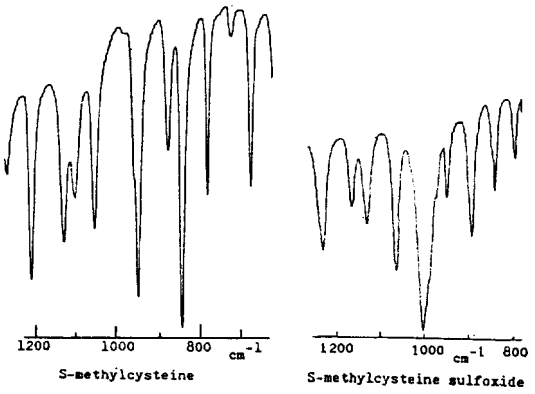

Fig. 7. Infrared spectra of S methylcysteine and S methylcysteine sulfoxide.

ly distinguished by their proton nmr spectra: while the *s-cis* isomer has shown a distinct methyl doublet (δ 1.0) of the isobutyl arm, two methyl doublets of the same isobutyl arm are shown in the *uns-cis* isomer (*Fig.* 6).

The Cotton effect signs for both *s-cis* and *uns-cis* isomer are shown in *Fig.* 4 and 5, respectively. The *s-cis* isomer shows the negative major CE and is assigned the absolutte configuration in agreement with the Δ-*s-cis*-[Co(SS-eddp)en]$^+$ and the Δ-$[Rh(en)_3]^{3+}$ and Δ-$[Rh(en)_2L]^{2+}$ complexes.[22-24] The *s-cis* rhodium(III) complex of SS-eniba retains the effective C_2 symmetry,[25] and a negative CE is expected for the *s-cis* isomer by analogy to the en comples. On the other hand, the *uns-cis* isomer shows a positive CE and absolute configuration is assigned.

The S-methyl-*L*-cysteine (smc) has been coordinated to the *s-cis*-$[Rh(SS\text{-eniba})Cl_2]^-$ to give complex (2) as shown in *Fig.* 1. The conversion of the coordinateed sulfure atom into thee sulfoxide group has then be accomplished via the oxidation by H_2O_2. The ir spectrum of the complex (2) shows the uncoordinated carbonyl at 1595 cm^{-1} indicating the fact that the S-methyl-*L*-cysteine has been coordinated via the nitrogen and sulfur donor atoms.

The conversion of the coordinated sulfur atom of the smc ligand into the sulfoxide group is con-

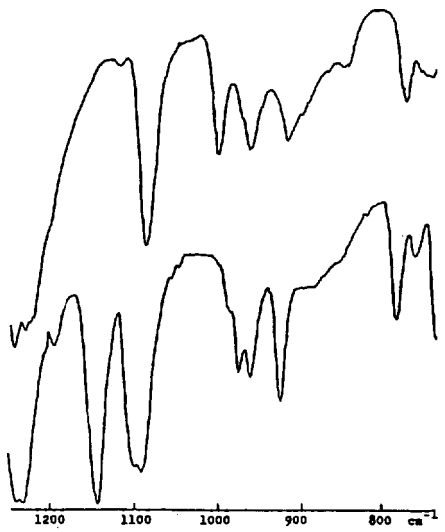

Fig. 8. Infrared spectra of s cis [Rh(SS eniba)(smc)]$^+$ and uns cis [Rh(SS eniba)(smc o)]$^+$

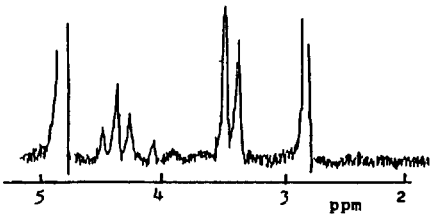

Fig. 9. ^{1}H nmr spectrum of S methylcysteine sulfoxide.

firmed by the ir spectral data of the ligands and complexes. *Fig.* 7 shows the ir spectra of smc and smc-o in the 1200-800 cm^{-1} region. While smc-o shows the S-O stretching frequency at 1006 cm^{-1}, smc doesn't have any absorption at near 1000 cm^{-1}. In *Fig.* 8 the S-O stretching frequency of the [Rh(SS-eniba)(smc-o)]$^+$ complex (3) has been shifted to 1140 cm^{-1}, which is like those found in [Pt(methioninesulfoxide)Cl_2] and complexes of Me_2SO.[26-29]

In a separate series of experiments the sulfur atom of smc has been oxidized to the sulfoxide group (smc-o) by H_2O_2 and the resultant smc-o ligand has been coordinated to complex (1) to give the standard complex of [Rh(SS-eniba) (smc-o)]$^+$ for comparison with complex (3). *Fig.* 9 shows the S-methyl group at δ2.8 for smc-o while the S-methyl group for smc is known to show at δ2.2.[30]

The standards complex of [Rh(SS- eniba)(smc-o)]$^+$ shows the S-O stretching frequency at 1140 cm^{-1} which is coincident as that for complex (3). The methyl grroup of complex (3) and the standard [Rh(SS-eniba) (smc-o)]$^+$ exhibits the chemical shieft at δ3.4. Thus, the conversion of the coordinated sulfur atom into the sulfoxide group is confirmed by comparison of complex (3) with the standard [Rh(SS- eniba)(smc-o)]$^+$ complex prepared separately. Upon formation of a sulfoxide group there is localization of one of the electron parirs of the sulfur in the free sulfide ligand into an S-O bond resulting in a greater chemical shift of the methyl group of the sulfoxide ligand. Tying up the second pair of electrons in a Rh-S bond causes a greater methyl chemical shift in the complex.

Upon conversion of the coordinated sulfur atom into the sulfoxide group the sulfur atom itself becomes an asymmetric center. There is possibility that the oxidation reaction can be proceeded stereoselectively. Although the absolute configuration of the asymmetric sulfur atom could not be determined from our current work, further studies such as X-ray crystallographic study on complex (2) should give some insight into any stereoselective nature of the oxidation reaction.

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