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# Determination of the Absolute Configuration of u-fac-$[Co(ida)(mdien)]^+$ by $^1H$ NMR Spectroscopy

Tomoharu AMA,* Sumio KAIZAKI,† Hiroshi KAWAGUCHI, and Takaji YASUI
Department of Chemistry, Faculty of Science,
Kochi University, Akebono-cho, Kochi 780
†Department of Chemistry, Faculty of Science,
Nara Woman's University, Nara 630

Iminodiacetic acid containing asymmetric carbon with S chirality ($H_2$ida($C_s$); $HOOCCH_2NHC^*HDCOOH$) was prepared by stereospecific deuteration of $(-)^{CD}_{563}$-mer(O)cis($N_c$)-[Co(ida)(edma)]. Using this $H_2$ida($C_s$), u-fac-$[Co(ida(C_s))(mdien)]^+$ was prepared and optically resolved. On the basis of the $^1H$ NMR spectra of the chelating ida($C_s$), the absolute configuration of the $(-)^{CD}_{550}$ isomer was assigned to ΔΛΔ.

In the previous papers,[1, 2)] the absolute configurations of the complexes containing facially chelated edma (edma: $NH_2CH_2CH_2NHCH_2COO^-$) were determined from $^1H$ NMR spectra of the optically active isomers with an asymmetric carbon-containing edma (obtained from stereospecifically deuterated $(-)^{CD}_{543}$-ΔΛΔ-$C_2$-trans(O)-$[Co(edma)_2]^+$). In the present letter, we report that the $^1H$ NMR method for determining the absolute configuration is applicable to the complex containing ida (ida: $NH(CH_2COO^-)_2$), namely u-fac-$[Co(ida)(mdien)]^+$ (mdien: $CH_3N(CH_2CH_2NH_2)_2$).

Since u-fac-$[Co(ida)(mdien)]^+$ was derived from $(-)^{CD}_{563}$-ΔΛΔ-mer(O)cis($N_c$)-[Co(ida)(edma)] ($N_c$ denotes central nitrogen) (Fig. 1) in this work, correct assignment of the $^1H$ NMR signals for ida in the latter complex is required.

Chemical environments of two glycinate-rings (G-rings) in the coordinating ida are different in mer(O)cis($N_c$)-[Co(ida)(edma)], as shown in Fig. 1 (o- and n-rings: the trans positions of two carboxyl groups are occupied by oxygen and nitrogen atoms of edma, respectively). The $^{13}C$ NMR resonances of the methylene carbons in these rings were observed at 57.8 and 59.3 ppm. In $^{13}C$ NMR studies of Co(III) complexes

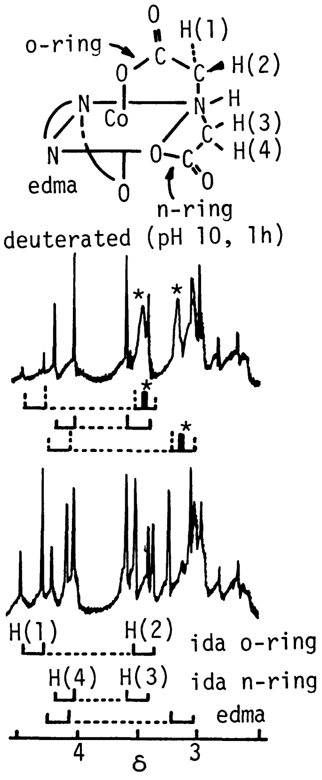

Fig. 1. $^1H$ NMR spectra (100 MHz) and structure of $(-)^{CD}_{563}$-ΔΛΔ-mer(O)cis($N_c$)-[Co(ida)(edma)]. (asterisked peaks: G-ring -C<u>H</u>D-).

containing G-rings, it has been reported that the methylene carbon lying in the environment similar to that of the o-rings resonates at a higher field than that of the n-rings.[4, 5] Accordingly, the $^{13}C$ NMR signal at 57.8 ppm can be assigned to the o-ring and that at 59.3 ppm to the n-ring. An H-C COSY NMR (correlation spectroscopy) of this complex showed that the $^{13}C$ NMR signal at 57.8 ppm (on the o-ring) was closely related to the $^{1}H$ NMR signals at 3.45 and 4.33 ppm (Fig. 1). Therefore, they can be assigned to the methylene protons on the o-ring. Similarly, the $^{1}H$ NMR signals at 3.50 and 4.07 ppm can be assigned to the n-ring protons.

The methylene protons of the chelating G-rings are deuterated in a basic $D_2O$ solution and the deuteration rate is affected by the other ligand in the complex.[1, 6] In $(-)^{CD}_{563}$-ΔΛΔ-mer(O)cis($N_c$)-[Co(ida)(edma)], the deuteration of the o-ring in ida was more rapid at pH 10 than that of the n-ring. Moreover, the spectrum of the deuterated complex indicated that the deuteration on the o-ring proceeded stereospecifically, that is, the $^{1}H$ NMR signal at 4.33 ppm disappeared but that at 3.45 ppm did not (Fig. 1). It is known that the deuteration rate of the proton which is blocked by another ring of the chelate is much slower than the proton which is not blocked.[1, 2, 7] Accordingly, we can assign the $^{1}H$ NMR signal at 3.45 ppm to H(2) (on the o-ring); this deuterated complex contains ida with an asymmetric carbon of <u>S</u> chirality (ida($C_s$)).[8] From this ida($C_s$) complex, we derived [Co(ida($C_s$))(mdien)]$^+$. The procedure is as follows. (An outline of the procedure is illustrated in Fig. 2.)

$(-)^{CD}_{563}$-ΔΛΔ-Mer(O)cis($N_c$)-[Co(ida)(edma)] (1.0 g) was dissolved in $D_2O$ and deuterated at 40°C (pH 10, 50 min). After the solution had been neutralized with 1 mol $dm^{-3}$ HCl, zinc powder (10 g) was added and the mixture was stirred for 5 min in order to reduce $Co^{III}$ to $Co^{II}$. Excess of zinc powder was filtered off, and then $PbO_2$ powder (7 g) was added to the filtrate to reoxidize $Co^{II}$ to $Co^{III}$. After stirring for 30 min, the insoluble material was filtered off and the filtrate was chromatographed on a QAE-Sephadex column ($ClO_4^-$ form; eluent: 0.5 mol $dm^{-3}$ $NaClO_4$) to obtain Na[Co(ida($C_s$))$_2$] (a mixture of trans(N) and cis(N)) and to remove [Co(ida($C_s$))(edma)] and [Co(edma)$_2$]$ClO_4$. The obtained Na[Co(ida($C_s$))$_2$] complex was dissolved in 20 $cm^3$ of water. Zinc powder (5 g) was added to the solution and then excess zinc was filtered off. To the solution, 1.5 g of mdien•3HCl, 0.9 g of $CoSO_4$•$7H_2O$, and 5 g of $PbO_2$ were added. After the pH of the

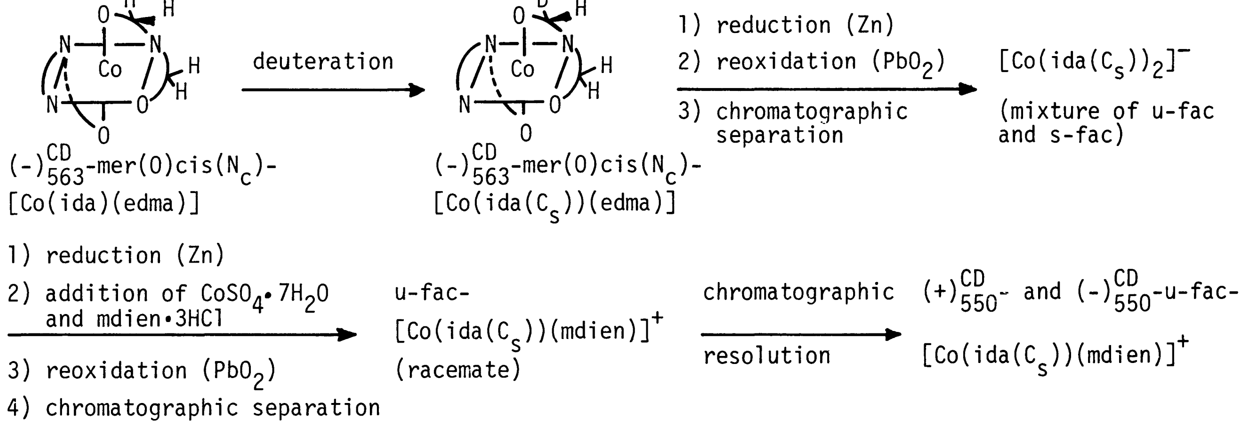

Fig. 2. The outline of the procedure to prepare $(+)^{CD}_{550}$- and $(-)^{CD}_{550}$-u-fac-[Co(ida($C_s$))(mdien)]$^+$.

solution had been adjusted to 7 with 2 mol dm$^{-3}$ NaOH, the solution was stirred for 30 min and filtered. The filtrate was chromatographed on an SP-Sephadex column (eluent: 0.1 mol dm$^{-3}$ KCl). The u-fac-[Co(ida(C$_s$))(mdien)]$^+$ complex obtained from the red eluate was optically resolved by the chromatographic method (eluent: 0.1 mol dm$^{-3}$ $K_2Sb_2$(d-tart)$_2$).3)

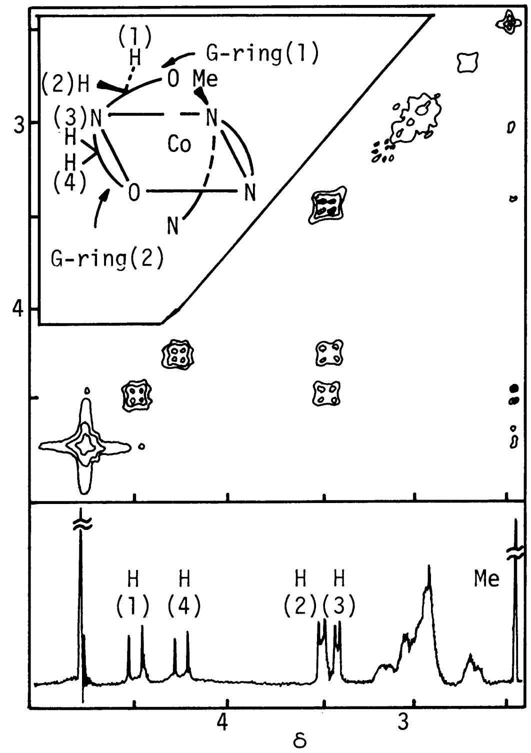

Fig. 3. Structure and NOESY NMR (270 MHz) of u-fac-[Co(ida)(mdien)]$^+$.

The $^1$H NMR spectrum of u-fac-[Co(ida)(mdien)]$^+$ is shown in Fig. 3, together with the H-H NOESY NMR (NOE correlation spectroscopy). The H(1) on the G-ring(1) is very close to the methyl group of mdien but the H(2), H(3), and H(4) are remote from the methyl. The NOESY NMR indicates that the proton resonating at 4.44 ppm (doublet) is closely related to the methyl protons of mdien. Accordingly, the signal is assigned to the H(1) proton in Fig. 3. In the case where the deuterated ida(C$_s$) was used, u-fac-[Co(ida(C$_s$))(mdien)]$^+$ provides four isomers whose $^1$H NMR spectra are different from each other (Fig. 4). It gives that the ΔΛΔ isomers (a mixture of two of the

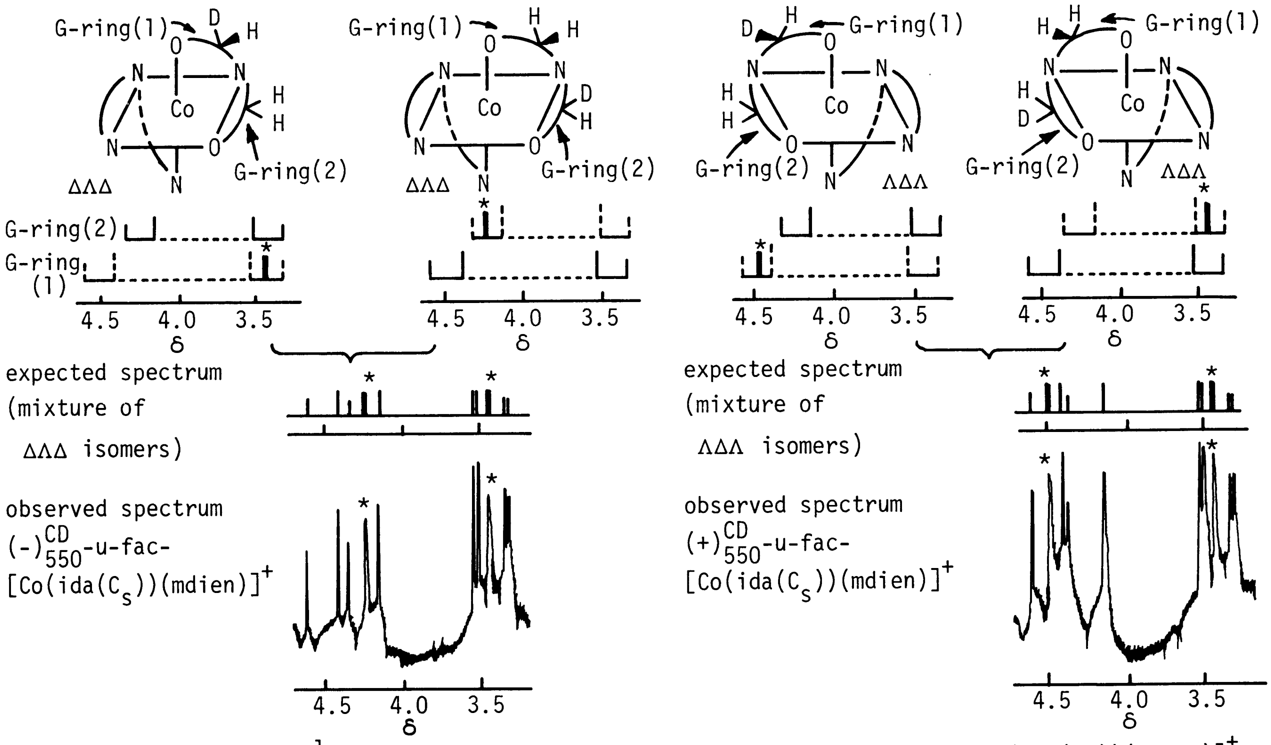

Fig. 4. Structures and $^1$H NMR spectra (100 MHz) of optically active u-fac-[Co(ida(C$_s$))(mdien)]$^+$ isomers. (Asterisked peaks: G-ring -CHD- of ida(C$_s$).)

four isomers) show signals of the G-ring -C$\underline{H}$D- at 4.21 and 3.40 ppm, while the ΛΔΛ isomers do the signals at 4.44 and 3.39 ppm. The NMR peaks arising from the G-ring -C$\underline{H}$D- were observed at 4.21 and 3.40 ppm in $(-)^{CD}_{550}$-u-fac-[Co(ida($C_s$))(mdien)]$^+$, while those were observed at 4.44 and 3.39 ppm in the $(+)^{CD}_{550}$ isomer (Fig. 4). These results lead to the following assignments: the absolute configurations of $(-)^{CD}_{550}$ and $(+)^{CD}_{550}$ isomers are ΔΛΔ and ΛΔΛ, respectively.

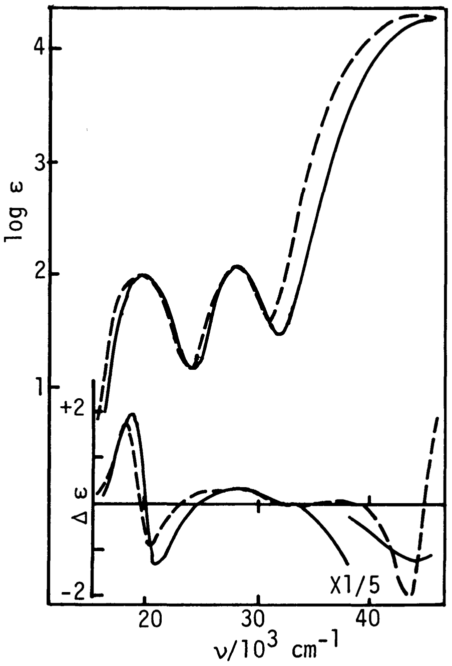

Fig. 5. Absorption and CD spectra of $(+)^{CD}_{550}$-u-fac-[Co(ida)(mdien)]$^+$ (– – –) and $(+)^{CD}_{538}$-u-fac-[Co(ida)(dien)]$^+$ (——).

The CD spectra of $(+)^{CD}_{538}$-u-fac-[Co(ida)(dien)]$^+$ and $(+)^{CD}_{550}$-u-fac-[Co(ida)(mdien)]$^+$ are illustrated in Fig. 5. These complexes show a CD pattern similar to each other. Since it is not likely that N-methylation of dien in ΛΔΛ-u-fac-[Co(ida)(dien)]$^+$ (giving ΛΔΛ-u-fac-[Co(ida)(mdien)]$^+$) brings about an inversion of the CD pattern, it can be concluded that the $(+)^{CD}_{538}$ dien and $(+)^{CD}_{550}$ mdien complexes have the same absolute configuration. Though the absolute configuration of the $(+)^{CD}_{538}$ dien complex has been assigned to ΔΛΔ on the basis of the CD behavior in the first absorption region,$^{9)}$ we propose that the $(+)^{CD}_{538}$ dien and $(+)^{CD}_{550}$ mdien complexes have the same ΛΔΛ configuration. The assignment based on the above NMR study will be more reliable than that based on the CD behavior, because the relationship between the CD pattern and the absolute configuration has not been made clear for Co$^{III}$ complexes containing terdentate ligands.

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