Determination of the Absolute Configuration of Bis(dipeptidato)-cobaltate(III) Complexes by ^{1}H Nuclear Magnetic Resonance Spectroscopy

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Summary In one diastereoisomer of [Co(L-phe–gly)$_2$]$^-$ both of the methylene protons of the *C*-terminal CH$_2$ group are shifted upfield by the ring current of the aromatic ring, whereas in the other diastereoisomer only one of the protons is shifted upfield: comparison of these results with models enables the absolute configuration of the diastereoisomers to be determined.

THE bis(dipeptidato)cobaltate(III) complexes have been studied by several groups of workers,[1–3] and although the crystal structure of [Co(gly–gly)$_2$]$^-$ has been reported,[1,2] there is so far no crystallographic work on any of the complexes containing an optically active amino-acid. The absolute configuration of these complexes is at present unknown, as for such complexes of polydentate ligands it is not possible to assign the absolute configuration from the c.d. spectrum. Indeed both diastereoisomers of all of the complexes containing only L-amino-acids,† [Co(L-α–gly)$_2$]$^-$, [Co-gly–L-α)$_2$]$^-$, and [Co(L-α–L-α)$_2$]$^-$, have a strong negative circular dichroism in the region of the lowest energy *d–d* band. The diastereoisomers can be separated by chromatography on anion exchange Sephadex, and the isomer which is eluted first, isomer (A), is distinguished by a negative circular dichroism at *ca.* 570 nm, whereas the more strongly adsorbed isomer (B) has either no c.d. in this region, or a positive band, the strength of which depends markedly on the peptide (see Figure).

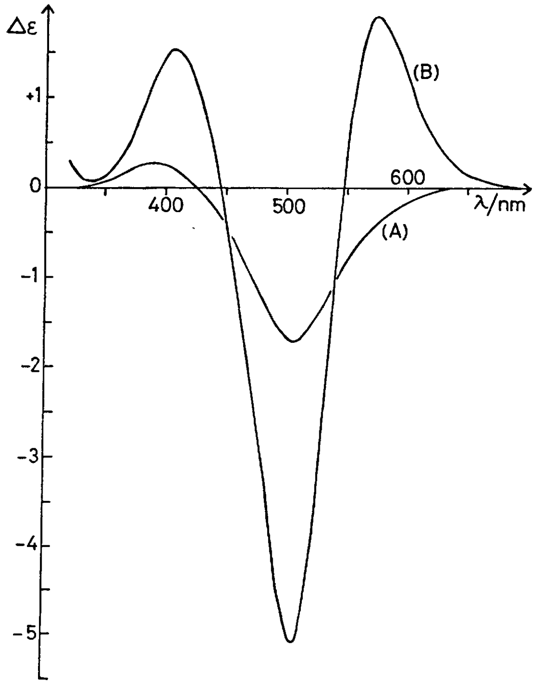
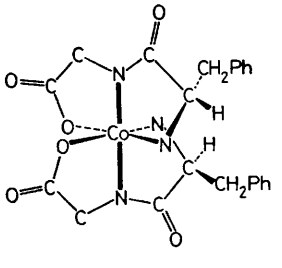
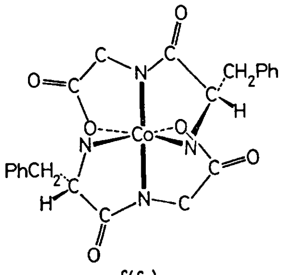


FIGURE. C.d. spectra of the diastereoisomers of [Co(L-phe–gly)$_2$]$^-$: (A), *S*(*C*$_2$) isomer, eluted first from QAE-Sephadex A-25; (B), *R*(C$_2$), more strongly adsorbed isomer.



R(*C*$_2$)



S(*C*$_2$)

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† L-α signifies any L-amino-acid.

Several interesting differences emerge from comparison of the ^{1}H n.m.r. spectra of the pairs of diastereoisomers of [Co(L-α–gly)$_2$]$^-$. The *C*-terminal methylene usually gives a singlet, although isomer (B) of [Co(L-ala–gly)$_2$]$^-$ shows slight inequivalence at 220 MHz. However although isomer (A) of [Co(L-phe–gly)$_2$]$^-$ has the typical sharp singlet, albeit somewhat upfield of the usual position, in isomer (B) the two methylene protons are very inequivalent (Δδ 0·21 p.p.m.): one of them is in a similar position to that observed for other complexes, whereas the other is shifted upfield. Examination of molecular models of the pair of diastereoisomers indicates that in the $R(C_2)$ isomer‡ only one of the glycyl methylene protons can be significantly influenced by the ring current of the phenylalanine aromatic ring, and thus be shifted upfield: from the approximate distance in the model, a shift of *ca.* 0·3—0·5 p.p.m. can be estimated by comparison with literature data for the upfield shifts caused by an aromatic ring.[4] The models suggest that for the $S(C_2)$ isomer both the methylene protons will be influenced by the aromatic ring to a similar extent. Thus the isomer more strongly adsorbed on anion exchange Sephadex, with the c.d. shown in curve (B) in the Figure, has the $R(C_2)$ configuration.

Further evidence confirms this assignment. There is only a small difference between the chemical shifts of the two protons of the phenylalanyl CH$_2$ group in isomer (B) (Δδ 0·09 p.p.m.) but a much larger difference in isomer (A) (Δδ 0·37 p.p.m.). Models indicate that in the $R(C_2)$ isomer neither proton is near to a carboxylate group, whereas in the $S(C_2)$ isomer one proton is close to a carboxylate group, and one is much further away.

The chemical shift of the *N*-terminal CH group in $R(C_2)$-[Co(L-phe–gly)$_2$]$^-$ (*i.e.* isomer B) is shifted 0·2 p.p.m. upfield compared with that of isomer (A); this is also true for the isomer (B) of all the [Co(L-α–gly)$_2$]$^-$ and [Co(L-α–L-α)$_2$]$^-$ complexes we have prepared; we thus conclude that for all these complexes isomer (B) has the $R(C_2)$ configuration. The c.d. of isomer (B) of all bis(dipeptidato)cobaltate(III) complexes of L-peptides has a positive configurational contribution in the 560 nm. region, and thus isomer (B) of [Co(gly–L-α)$_2$]$^-$ probably also has the $R(C_2)$ configuration.

Although the upfield shift of part of one ligand by an aromatic unit in another ligand has been used in several studies of ternary complexes in which the ligands stack with each other,[5] this is apparently the first report of the use of the shift due to the ring current in the determination of the absolute configuration of metal complexes, although it would seem to be equally applicable to many other complexes.

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‡ We designate the isomers by the helicity of the twofold axis, as the I.U.P.A.C. nomenclature ('Nomenclature of Inorganic Chemistry,' 2nd edn., Butterworths, London, 1970), using pairs of skew lines, fails to define an unambiguous label for bis(dipeptidato)cobaltate(III) complexes.

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