Isotopic Multiplets in the Carbon-13 Nuclear Magnetic Resonance Spectra Due to Partial Deuteriation of Co-ordinated NH_2 and NH Groups of Cobalt(III) Complexes containing an N-Glycoside. Importance of Sugar Ring Oxygen Atoms in the Long-range Isotope Shifts

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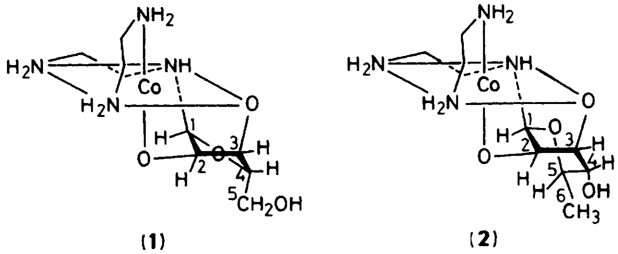
Carbon-13 n.m.r. measurements have been made in H_2O–D_2O solutions of cobalt(III) complexes containing an N-glycoside derived from ethylenediamine and an aldose (D-ribose or L-rhamnose). Partial deuteriation of exchangeable protons on the co-ordinated nitrogen atoms permits direct observation of the individual isotopomers and the resonances are observed as a series of multiplets, which can be analysed in terms of the two-bond and three-bond isotope effects that contribute to the deuterium-induced isotope shifts. The C–N bond formation between ethylenediamine and an aldose in the cobalt(III) complexes has been unambiguously confirmed by the information derived from the isotopic multiplets together with complete assignments of ^{13}C signals from the sugar units by means of two-dimensional n.m.r. spectroscopy. An extra doublet originating from the four-bond isotope effect is observed for the D-ribosyl residue, which suggests that the sugar ring takes the furanose form. The importance of sugar ring oxygen atoms in the long-range deuterium isotope shifts is discussed including an examination by use of C^1-methine proton deuteriated aldoses.

Inter-ligand reactions in transition-metal complexes accompanied by the formation of new C–N bond(s), such as the so-called 'template' reactions,[1] intramolecular imine or carbinolamine formation reactions with cobalt(III) complexes,[2] and so-called 'cage' complex-formation reactions,[3] have been of much interest in macrocyclic chemistry, co-ordination chemistry, and bioinorganic chemistry.

During the past decade, we have extensively studied the synthesis and characterization of nickel(II) complexes with N-glycoside(s) derived from a diamine and a sugar[4] and those of cobalt(III) complexes with a sexidentate geminal diamine derivative obtained from 3,7-diazanonane-1,9-diamine and α-aminomalonate.[5] Identification of the new C–N bond formation, which is one of the major problems in these studies, has been studied by *X*-ray crystallography in most cases. Therefore, it is desirable to develop a method to identify the C–N bond formation unambiguously and easily. Although n.m.r. spectroscopy is a powerful tool in the characterization of diamagnetic complexes with organic molecules, it has been difficult to identify C–N bond formation in metal complexes by means of conventional n.m.r. techniques. There is considerable uncertainty in estimation by vicinal ^{1}H–^{1}H spin–spin couplings (H–N–C–H) and by ^{1}H or ^{13}C n.m.r. chemical shifts. Observation of ^{15}N–^{13}C spin–spin couplings commonly requires preparations of ^{15}N-enriched samples.

Recent reports[6–17] have demonstrated that deuterium isotope effects on ^{13}C n.m.r. chemical shifts are very helpful in spectral assignments and molecular structure determination. Partial deuteriation of exchangeable protons in amines,[6–9] amides,[10] alcohols,[11,12] carbohydrates,[13–16] phenols,[17] and nucleosides[9] leads to isotopic multiplets in ^{13}C n.m.r. spectra observed under slow-exchange conditions between the protio- and the deuterio-isotopomer. In the spectra of amides[10] and cobalt(III)–amine complexes[9] isotopic multiplets corresponding to individual isotopomers of amide groups and co-ordinated amino groups were observed even in neutral H_2O–D_2O mixtures, since proton exchange in these systems is generally slow on the n.m.r. time-scale. Furthermore, isotopic multiplet patterns in the ^{13}C n.m.r. spectra of amines and amine derivatives contain information about the types of amino groups in the vicinity of the observed carbon atoms,[6,9] since the number of isotopomers produced by partial deuteriation of an NH_2 group is different from that of an NH group. Therefore, the multiplicities can give fingerprints of the polyamine structure.



(1) (2)

Figure 1. Structures of $[CoL^1(en)]^+$ (1) and $[CoL^2(en)]^+$ (2)

Recently, we reported the first synthesis and characterization of cobalt(III) complexes containing an N-glycoside derived from ethylenediamine (en) and an aldose as shown in Figure 1.[18] In that report, the formation of a new C–N bond was presumed according to the chemical shifts of the ^{13}C signals originated from the en units in their routine ^{13}C n.m.r. spectra, which were not unequivocal. In this paper, we assigned the ^{13}C n.m.r. signals of the sugar units of the cobalt(III)–N-glycoside complexes by two-dimensional n.m.r. spectroscopy, and applied the method of direct observation of isotopic multiplets in ^{13}C n.m.r. spectra to the cobalt(III) complexes in order to obtain direct evidence of C–N bond formation. A preliminary report on this work[19] has appeared.

During this work, an extra four-bond deuterium isotope effect has been observed on C^4 of the D-ribosyl residue in $[CoL^1(en)]^+$ (**1**) $[H_2L^1$ = 1-(2-aminoethylamino)-1-deoxy-D-ribose] which is the carbon atom in the position through the ring oxygen atom from the partially deuteriated glycosidic NH site. Long-range isotope effects such as three- and four-bond isotope effects can serve as useful information for elucidation of molecular structure details as reported for saturated organic molecules.[7,9,11,14–17,20–22] As further studies, therefore, we have examined deuterium isotope effects on ^{13}C chemical shifts of C^1-methine-proton deuteriated aldoses as model systems to obtain information about factors that contribute to the extra long-range isotope effect.

Experimental

Materials.—The complexes $[CoL^1(en)]ClO_4{\cdot}2H_2O$ (**1**) and $[CoL^2(en)]Br{\cdot}H_2O$ (**2**) $[H_2L^2$ = 1-(2-aminoethylamino)-1,6-dideoxy-L-mannose] were prepared by the methods described previously.[18] Deuterium oxide (99.8 atom % D), lithium aluminium deuteride (99 atom % D), non-deuteriated sugars, and aldonolactones were obtained from commercial sources and were used without further purification. Aldoses deuteriated at the C^1 methine proton were derived from aldonolactones according to the methods of Bhattacharjee *et al.*[23] modified by use of $LiAlD_4$ instead of $LiAlH_4$. $[1-^2H]$D-Galactose and $[1-^2H]$D-glucose were purified by recrystallization from ethanol and methanol–2-propanol (1:6), respectively. The satisfactory purity and deuterium contents were confirmed by their ^1H and ^{13}C n.m.r. spectra.

N.M.R. Spectroscopy.—Carbon-13 and ^1H n.m.r. spectra were recorded at 100.40 and 399.65 MHz, respectively, on a JEOL GX-400 spectrometer.

Two-dimensional n.m.r. measurements were performed as follows. Solutions of *ca.* 15% (w/v) in D_2O were prepared for complexes (**1**) and (**2**). Chemical shifts were determined by use of sodium $[2,2,3,3-^2H_4]$3-(trimethylsilyl)propionate (δ 0) and 2-methyl-2-propanol (δ 31.9 p.p.m.) for ^1H and ^{13}C, respectively, as internal references. Two-dimensional measurements were performed without internal references at ambient temperatures. The ^1H–^1H correlation spectroscopy (COSY) spectrum of complex (**1**) was obtained as follows. An initial data matrix ($t_1 \times t_2$) of 256 × 1 024 points represented a spectral width of 2 000 Hz in both dimensions. Sixteen transients were accumulated for each value of t_1. The delay before each acquisition was 1 s. The data were apodized by a sine-bell function, zero-filled to 512 × 2 048 points, and Fourier-transformed, and the absolute value was taken and symmetrized. The ^{13}C–^1H COSY spectrum of complex (**1**) was obtained as follows. An initial data matrix ($t_1 \times t_2$) of 256 × 2 048 points represented spectral widths ($F_1 \times F_2$) of 2 000 Hz × 8 000 Hz. The two fixed delays were 3.4 ms. Sixty-four transients were accumulated for each value of t_1. The delay before each acquisition was 1 s. The data were apodized by a trapezoidal function for the t_2 dimension, zero-filled to 256 × 4 096 points and Fourier-transformed, and the absolute value was taken. The two-dimensional n.m.r. spectra of complex (**2**) were obtained similarly.

Observation of isotopic multiplets of cobalt(III)*-N-glycoside complexes.* Solutions of *ca.* 10% (w/v) in H_2O–D_2O (*ca.* 1:1) were prepared for complexes (**1**) and (**2**), and were allowed to stand for 10 d at ambient temperatures. 100.40-MHz ^{13}C N.m.r. spectra were obtained at 306 ± 1 K under low-power broad-band decoupling conditions using these samples. Typically, 18 000 pulses were recorded at a recycle time of 1.5 s (45° pulse, 32 k data points, sweep width 10 000 Hz) and were calculated with adequate digital resolution (3 p.p.b. $point^{-1}$ after zero filling).

Observation of isotope shifts in ^{13}C *n.m.r. spectra of aldoses by deuteriation at* C^1. Solutions of *ca.* 15% (w/v) in D_2O were prepared for 2:1 and 1:1 mixtures of the deuteriated and non-deuteriated aldoses. 100.40-MHz ^{13}C N.m.r. spectra were obtained at 306 ± 1 K under low-power broad-band decoupling conditions. Typically, 8 000 pulses were recorded at a recycle time of 1.5 s (45° pulse, 32 k data points, sweep width 5 000 Hz) and were calculated with adequate digital resolution (1.5 p.p.b. $point^{-1}$ after zero filling). Chemical shifts were determined using 1,4-dioxane (δ 67.4 p.p.m.) as an internal reference.

Results and Discussion

Two-dimensional N.M.R. Spectra of Complexes (**1**) *and* (**2**).—Figures 2 and 3 present the ^1H–^1H and ^{13}C–^1H COSY two-dimensional n.m.r. spectra of complexes (**1**) and (**2**). In a previous paper[18] the ^1H signals from the sugar units were assigned by employing double- and triple-resonance techniques. At this time, the assignments were completely confirmed by means of the two-dimensional n.m.r. spectroscopy. The ^1H signals from the D-ribosyl residue were assigned by tracing correlation peaks from the H^1 signals with the highest chemical shift value (δ 4.327) and from the H^5 methylene proton signals correlating with the same methylene ^{13}C signal in the ^{13}C–^1H COSY spectrum. No correlation peak appears between the H^3 and H^4 signals, which indicates that the value of $^3J(H^3H^4)$ is nearly zero.[18] The ^1H signals from the L-rhamnosyl residue were assigned by tracing correlation peaks successively from the H^6 methyl proton signal. The ^{13}C signals from the sugar units of complexes (**1**) and (**2**) were unambiguously assigned from correlation with the ^1H signals in the ^{13}C–^1H COSY spectra.

Outlines of Isotopic Multiplets in the ^{13}C *N.M.R. Spectra due to Partial Deuteriation of Co-ordinated* NH_2 *and* NH *Groups.*—Partial deuteriation of co-ordinated NH_2 or NH groups is easily achieved in a neutral H_2O–D_2O mixture. Generally, hydrogen exchange of co-ordinated amino groups on cobalt(III) complexes in aqueous solutions is expected to be slow on the n.m.r. time-scale.[9] As a result, the isotope effects on the ^{13}C resonances of the α- (two-bond effect, $^2\Delta$) and β- (three-bond effect $^3\Delta$) carbons to the co-ordinated nitrogens should give rise to distinct ^{13}C resonances for the individual isotopomers due to upfield deuterium isotope effects on ^{13}C n.m.r. chemical shifts.[9] The magnitudes of the reported isotope shifts for the two-bond effects are in the range of 91 to 128 p.p.b. per deuteron, while those for the three-bond effects vary from 0 to 85 p.p.b. per deuteron.[9] In the ^{13}C n.m.r. spectra of complexes (**1**) and (**2**) in a H_2O–D_2O (*ca.* 1:1) mixture ^{13}C resonances were observed as a series of multiplets with clear spacings or shoulders as shown in Figure 4.

Partial deuteriation of a co-ordinated NH_2 group produces four species, NHH, NHD, NDH, and NDD, which cause ^{13}C resonances of α- and β-carbons to appear as quartets or triplets.[9] The latter is commonly observed, because, in many cases, isotope effects corresponding to the two ways of monodeuteriation are almost equivalent. Partial deuteriation of a co-ordinated NH group produces two species, NH and ND, which cause ^{13}C resonances of α- and β-carbons to appear as doublets.[9] Partial deuteriation of a hydroxyl group in H_2O–D_2O also gives two species, OH and OD. However, the neighbouring carbons appear not as doublets but as singlets, since hydrogen exchange of hydroxyl protons in aqueous solutions is fairly fast on the n.m.r. time-scale. Direct

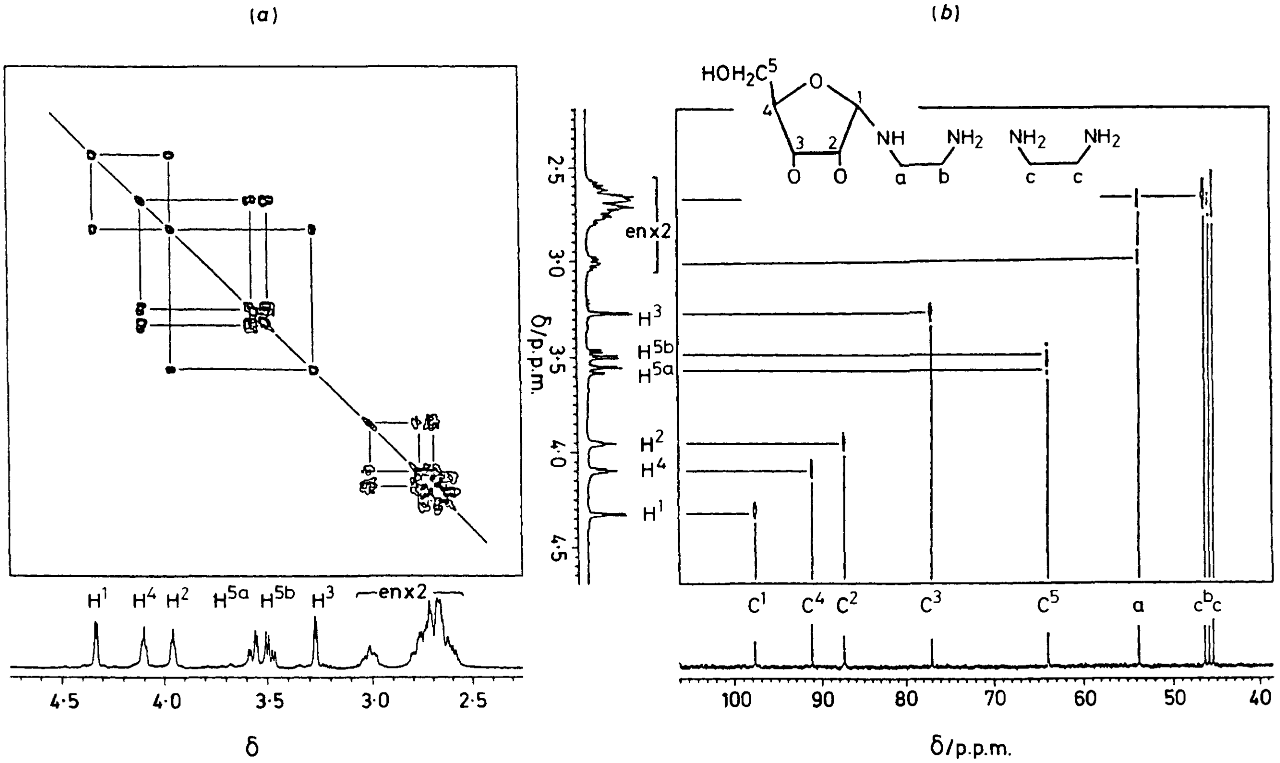


Figure 2. (*a*) ^1H–^1H COSY two-dimensional n.m.r. spectrum of complex (**1**) in D_2O; (*b*) corresponding ^{13}C–^1H COSY two-dimensional n.m.r. spectrum

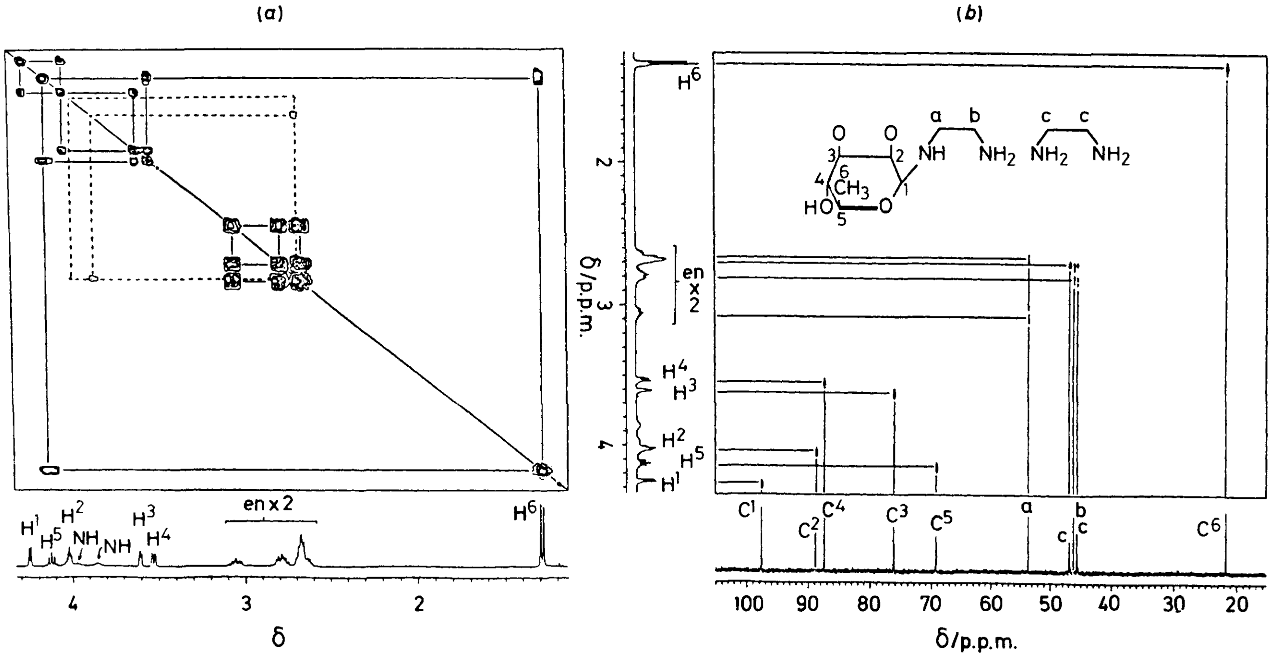


Figure 3. (*a*) ^1H–^1H COSY two-dimensional n.m.r. spectrum of complex (**2**) in D_2O; (*b*) corresponding ^{13}C–^1H COSY n.m.r. spectrum

observation of isotope effects on ^{13}C chemical shifts originating from deuteriation of hydroxyl protons is achieved by using aprotic solvent solutions desiccated carefully after partial deuteriation[11–17] or by using a dual co-axial n.m.r. cell separated by a water solution and a D_2O solution.[24] In the present work, consequently, hydroxyl groups in the sugar residues can be neglected in the analyses of isotopic multiplet patterns. The resonances of carbon atoms with two possible isotope effects exhibit multiplicities analogous to those due to spin–spin couplings because of the additivity of n.m.r. isotope shifts. Therefore, the individual carbons give characteristic multiplets corresponding to the types of amino groups in the vicinity of the observed carbons.

Evidence for N-Glycoside Bond Formation.—The isotopic multiplet patterns in the ^{13}C n.m.r. spectrum of complexes (**1**) or (**2**) are expected to be as follows on the basis of the empirical rules described above. Each ^{13}C signal from the bidentate en [en

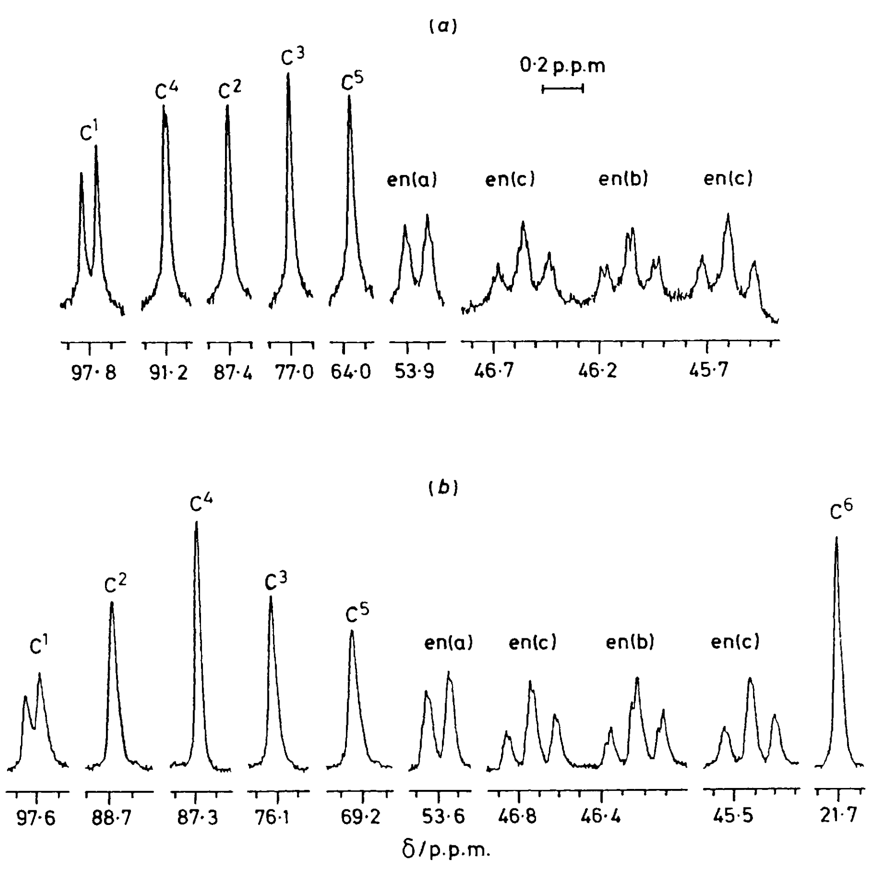


Figure 4. Isotopic multiplets in the ^{13}C n.m.r. spectra of (*a*) complex (**1**) and (*b*) complex (**2**) in neutral H_2O–D_2O (*ca.* 1 : 1) mixtures

Table 1. Characteristics of ^{13}C n.m.r. signals of cobalt(III)–N-glycoside complexes in H_2O–D_2O

	Expected isotope effect[a]		Multiplicity of ^{13}C signal[b]	
Carbon	$^2\Delta$	$^3\Delta$	Expected	Observed
C^1	NH	—	d	d
C^2	—	NH	d	s
en (a)	NH	NH_2	d × t	d × t
en (b)	NH_2	NH	t × d	t × d
en (c) [c]	NH_2	NH_2	t × d	t × t

[a] Types of amino groups with contribution to isotope effects are shown; the carbon has no amino group that contributes to the isotope effect. [b] s = Singlet, d = doublet, d × t = doublet of triplets, t × d = triplet of doublets, and t × t = triplet of triplets. [c] Unequivalent two carbons of bidentate en behave similarly according to their multiplicities.

(c)] may be observed as a triplet of triplets corresponding to the two-bond effect of one NH_2 group and the three-bond effect of the other NH_2 group. In contrast, of the two co-ordinated amino groups of the quadridentate N-glycoside ligand, one is an NH_2 group and the other is an NH group, which can give fingerprints of the N-glycoside bond formation. The carbon adjacent to the NH group of the en unit [en (a)] may appear as a doublet of triplets due to the two-bond effect of the NH group and the three-bond effect of the NH_2 group. The carbon adjacent to the NH_2 group of the en unit [en (b)] may appear as a triplet of doublets corresponding to the two-bond effect of the NH_2 group and the three-bond effect of the NH_2 group. The C^1 of the sugar units may be observed as a doublet corresponding to the two-bond effect of the NH group, and C^2 as a doublet due to the three-bond effect of the NH group. The other carbons in the sugar units, which are in positions more than three bonds away from the glycosidic N–H protons, are expected to give singlets due to no isotope shift. Table 1 presents possible two- and three-bond isotope effects for carbon atoms and isotopic multiplet patterns (expected and observed) for complexes (**1**) or (**2**). The assignments of the isotope effects are summarized in Table 2. The resonances of C^1 of the sugar units and the carbons of the en units of the N-glycoside ligands exhibit multiplet patterns originating from the presence of the glycosidic NH group as expected. These results reveal evidence for the presence of the C^1–NH–C–C–NH_2 moiety. In the previous paper[18] the N-glycoside bond formation was presumed according to the chemical shifts of the ^{13}C signals from the en units. One of the signals assigned to the en carbons, which presumably corresponds to the carbon atom adjacent to the glycosidic nitrogen atom, appears 7—8 p.p.m. downfield from the other three. Thus, the C–N bond formation on the cobalt(III) complexes was unambiguously demonstrated by the appearance of the isotopic multiplets in the ^{13}C n.m.r. spectra.

Magnitudes of Two- and Three-bond Isotope Effects.—The magnitudes of the two-bond isotope effects on the methylene carbons in the en units are in the range of 106 to 121 p.p.b. per deuteron, which are consistent with those reported for the methylene carbons in cobalt(III)–amine systems (91—128 p.p.b. per deuteron).[9] The magnitudes of the two-bond isotope effects on C^1-methine carbons in the sugar units are about 70 p.p.b. per deuteron, obviously smaller than those on the methylene carbons. The magnitudes of the three-bond isotope effects on the methylene carbons (15—27 p.p.b. per deuteron) are in the range of 0 to 40 p.p.b. per deuteron reported for the methylene carbons.[9] The C^2 methine carbons give no significant three-bond isotope shift by deuterium substitution of the glycosidic NH protons.

Table 2. Carbon-13 chemical shifts[a] (in p.p.m.), multiplicities,[b] and deuterium isotope effects ($^n\Delta$)[c] (in p.p.b. per deuteron) for sugar units and ethylenediamine units in cobalt(III)–N-glycoside complexes

Complex	C^1	C^2	C^3	C^4	C^5	C^6	en (a)	en (b)	en (c)	
(1)	97.83	87.40	77.00	91.20	63.96		53.92	46.20	46.70	45.74
	$^2\Delta$, d; 67	—	—	$^4\Delta$, d; 12	—		$^2\Delta$, d; 106	$^2\Delta$, t; 121	$^2\Delta$, t; 119	$^2\Delta$, t; 121
							$^3\Delta$, t; <15	$^3\Delta$, d; 27	$^3\Delta$, t; <21	$^3\Delta$, t; <15
(2)	97.65	88.68	76.12	87.27	69.24	21.70	53.67	46.38	46.88	45.57
	$^2\Delta$, d; 70	—	—	—	—	—	$^2\Delta$, d; 106	$^2\Delta$, t; 119	$^2\Delta$, t; 119	$^2\Delta$, t; 121
							$^3\Delta$, t; <20	$^3\Delta$, d; <24	$^3\Delta$, t; <18	$^3\Delta$, t; <15

[a] For the protio-isotopomers (lower-field components). [b] The magnitudes of all the isotope effects are negative (upfield shifts). Digital resolution is 3 p.p.b. [c] No isotope effect.

Table 3. Carbon-13 n.m.r. chemical shifts[a] (in p.p.m.) and deuterium isotope shifts by C^1 deuteration[b] (in p.p.b.) of aldopyranoses

Aldopyranose	C^{1c}	C^2	C^3	C^4	C^5	C^6
α-D-galacto	97.28	69.20	70.02	70.15	71.27	62.02
(3)	357	90	0	0	21	0
β-D-galacto	93.11	72.75	73.64	69.59	75.92	61.82
(4)	407	68	0	0	18	0
α-D-gluco	92.90	72.32	73.61	70.51	72.26	61.49
(5)	355	91	0	0	21	0
β-D-gluco	96.72	74.98	76.60	70.46	76.74	61.63
(6)	401	70	0	0	18	0

[a] Signal assignments are based on ref. 24. Chemical shift values are given for the protio-isotopomers (lower-field components). [b] All isotope effects are negative (upfield shifts). Digital resolution is 1.5 p.p.b., 0.16 Hz. [c] $^1J_{CD}$ couplings observed for the deuterio-isotopomers; 25.5, 24.2, 25.6, and 24.1 Hz for (3), (4), (5), and (6), respectively.

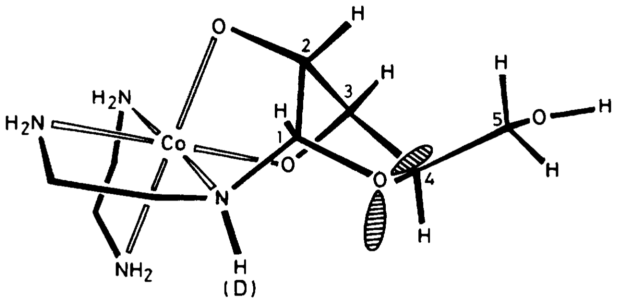


Figure 5. Estimated structure of complex (1). The sugar unit is drawn on the basis of the atomic co-ordinates optimized by the AM1 calculations[25]

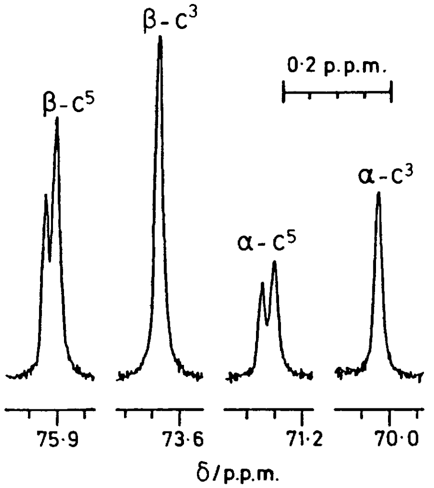
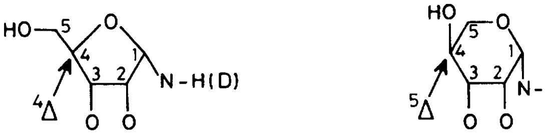


Figure 6. Three-bond isotope effects upon deuterium substitution of C^1 methine protons of D-galactopyranose; ^{13}C resonances of C^3 and C^5 observed for a D_2O solution of a deuteriated–non-deuteriated (*ca.* 2:1) mixture

These results are compatible with the known tendencies that the magnitudes of two-bond isotope effects are greater than those of three-bond isotope effects, and that the two- and three-bond isotope shifts for more-substituted methine carbons are smaller than those for less-substituted methylene carbons.[7,9,11,14]

Influence of the Sugar Ring Oxygen Atoms in Long-range Isotope Effects.—The C^4 signal of the D-ribosyl residue in complex (1) exhibits as an extra doublet (Δδ 12 p.p.b.) corresponding to the four-bond isotope effect upon partial deuteriation of the glycosidic NH proton. In contrast, neither the three-bond effect for C^2 nor the four-bond effect for C^3 is observed. We have analyzed the sugar unit structures of the cobalt(III)–N-glycoside complexes by means of semiempirical AM1 calculations considering n.m.r. parameters.[25] In the optimized structure of complex (1) (Figure 5) the distance from the glycosidic nitrogen atom to C^4 (3.14 Å) is longer than that to C^2 (2.53 Å) and is approximately as long as that to C^3 (3.04 Å). Commonly, the magnitude of the isotope effect becomes smaller as the number of the bonds and the direct distance from the deuteriated site to the observed nucleus increase. Accordingly, the four-bond isotope effect on C^4 seems to be due to another factor besides those of simple structural features.

From such a viewpoint, we have focused our attention on the presence of the sugar ring oxygen atom in complex (1). Sugar ring oxygen atoms play a role in the anomeric effect[26] which is well known in carbohydrate chemistry. The anomeric effect refers to the tendency of an electronegative substituent at C^1 of the pyranoid ring to adopt the axial rather than the equatorial orientation. This phenomenon has been explained on the basis of the electronic interactions between the ring oxygen lone pairs and the electronegative substituent at C^1.[26] Such electronic interaction which originates from the sugar ring oxygen atom is also expected to contribute to isotope effects. Then, in order to examine the contribution from the sugar ring oxygen atoms, we have investigated three-bond isotope effects due to deuteriation of methine protons at C^1 in D-galactose and D-glucose as model systems. Comparison between the three-bond isotope shifts for C^5 and C^3 will be appropriate regarding the influence of the ring oxygen atoms by reference to known empirical rules for the magnitude of the three-bond effect.[7,9,11,14–17,20–22] Since the pyranose rings adopt the typical chair conformation, C^5 and C^3 are similar as to their geometrical environment. Hence, the comparison will provide useful information concerning the influence of the ring oxygen atom. Observed isotope effects on ^{13}C chemical shifts in these systems are summarized in Table 3. The magnitudes of the isotope effects observed for C^5 signals (Δδ *ca.* 20 p.p.b.) are clearly greater than those for C^3 (less than



(*a*) (*b*)

Figure 7. The sugar ring structure of complex (**1**) and the assignment of the long-range isotope effect observed for C^4. (*a*) Furanose form; (*b*) pyranose form

the limit of detection) as shown in Figure 6. According to crystallographic data, the average of C^1–O(ring) and C^5–O(ring) bond lengths (1.43 Å) in α- and β-galactopyranose and glucopyranose is only about 9% shorter than that of C^1–C^2 and C^2–C^3 bond lengths (1.52 Å).[27] Therefore, the novel difference between the isotope effects for C^5 and C^3 could not be explained satisfactorily by considering that the direct C–H(D) dipole interaction with the electrons surrounding the ^{13}C nucleus is inversely proportional to the cube of the distance between the dipole and the electrons, but might be explained by taking into account the electronic influence of the ring oxygen atom on the deuterium isotope effect. Thus, it is confirmed that the presence of the ring oxygen atom significantly contributes to the isotope effects. In addition, four-bond isotope shifts should be interpreted by taking account of the through-space electronic interactions.[20] Hence, in the case of complex (**1**), the extra four-bond effect may be mainly attributable to the change of electronic environment surrounding the C^4 nucleus due to the through-space interaction between the lone pairs on the ring oxygen and the N–H(D) dipole in a specific direction (Figure 5). Conversely, in the free aldose system, deuteriation of the hydroxyl proton at C^1 gives no significant four-bond isotope shift through the H(D)–O–C^1–O(ring)–C bond sequence.[13–16] We feel that this fact is related to the orientations of O–H(D) bonds in free sugars which cannot be fixed, while in the case of complex (**1**) the N–H(D) bond is fixed in a specific direction. Furthermore, the N–H bond and one of the ring oxygen lone pairs are oriented nearly parallel,[25] and two dipoles seem to have much electronic interaction. In contrast, the C^5 signal of complex (**2**), the sugar ring of which has been proposed to take the pyranose form in the skew-boat conformation unlike that of complex (**1**),[18] exhibits no four-bond isotope shift. The N–H bond and the ring oxygen lone pairs of complex (**2**) are not oriented parallel as are those of complex (**1**).[25] These results indicate that the influence of the sugar ring oxygen atoms on the long-range isotope effects depends on the molecular geometrical properties.

From the viewpoint of stereochemistry, it is important that the extra isotope effect in complex (**1**) is observed not on C^5 but on C^4. This result should be interpreted as not the five-bond isotope effect through the H(D)–N–C^1–O–C^5–C^4 sequence in the pyranose ring [Figure 7(*b*)], but the four-bond isotope effect through the H(D)–N–C^1–O–C^4 sequence in the furanose ring [Figure 7(*a*)], which suggests that the sugar ring adopts the furanose form as proposed previously.[18] Thus the observation of the long-range isotope effects will serve as a useful tool for the determination of the ring structure (pyranose or furanose form) of sugar derivatives and complexes with sugar derivatives.

Our new finding concerning the importance of the sugar ring oxygen atoms should enhance the understanding of long-range isotope effects observed in other ring heteroatom systems.

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References

1 N. F. Curtis, *Coord. Chem. Rev.*, 1968, **3**, 3; D. H. Busch, K. Farmery, V. L. Goedken, V. Katovic, A. C. Melnyk, C. R. Sperati, and N. Tokei, *Adv. Chem. Ser.*, 1971, **100**, 44; J. J. Christensen, D. J. Eatough, and R. M. Izatt, *Chem. Rev.*, 1974, **74**, 351.
2 A. R. Gainsford, A. R. Pizer, A. M. Sargeson, and P. O. Whimp, *J. Am. Chem. Soc.*, 1981, **103**, 792; P. J. Lawson, M. G. McCarthy, and A. M. Sargeson, *ibid.*, 1982, **104**, 6710; N. E. Dixon and A. M. Sargeson, *ibid.*, p. 6716.
3 A. M. Sargeson, *Chem. Br.*, 1979, **15**, 23; J. M. Harrowfield, A. J. Herlt, and A. M. Sargeson, *Inorg. Synth.*, 1980, **20**, 85; L. R. Gahan, T. W. Hambley, A. M. Sargeson, and M. R. Snow, *Inorg. Chem.*, 1982, **21**, 2699; I. I. Creaser, R. J. Geue, J. M. Harrowfield, A. J. Herlt, A. M. Sargeson, M. R. Snow, and J. Springborg, *J. Am. Chem. Soc.*, 1982, **104**, 6016; H. A. Boucher, G. A. Lawrance, P. A. Lay, A. M. Sargeson, A. M. Bond, D. F. Sangster, and J. C. Sullivan, *ibid.*, 1983, **105**, 4652; J. M. Harrowfield, A. J. Herlt, P. A. Lay, and A. M. Sargeson, *ibid.*, p. 5503; R. J. Geue, T. W. Hambley, J. M. Harrowfield, A. M. Sargeson, and M. R. Snow, *ibid.*, 1984, **106**, 5478; R. J. Geue, M. G. McCarthy, and A. M. Sargeson, *ibid.*, p. 8282; P. Comba, I. I. Creaser, L. R. Gahan, J. M. Harrowfield, G. A. Lawrance, L. L. Martin, A. W. H. Mau, A. M. Sargeson, W. H. F. Sasse, and M. R. Snow, *Inorg. Chem.*, 1986, **25**, 384; D. J. Bull, I. I. Creaser, A. W. Sargeson, B. W. Skelton, and A. H. White, *ibid.*, 1987, **26**, 3040.
4 S. Takizawa, H. Sugita, S. Yano, and S. Yoshikawa, *J. Am. Chem. Soc.*, 1980, **102**, 7969; T. Tsubomura, S. Yano, K. Toriumi, T. Ito, and S. Yoshikawa, *Polyhedron*, 1983, **2**, 123; H. Shioi, S. Yano, K. Toriumi, T. Ito, and S. Yoshikawa, *J. Chem. Soc., Chem. Commun.*, 1983, 201; T. Tsubomura, S. Yano, K. Toriumi, T. Ito, H. Ito, and S. Yoshikawa, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 1833; S. Yano, Y. Sakai, K. Toriumi, T. Ito, H. Ito, and S. Yoshikawa, *Inorg. Chem.*, 1985, **24**, 498; T. Tsubomura, S. Yano, K. Toriumi, and S. Yoshikawa, *ibid.*, p. 3218; T. Tanase, K. Kurihara, S. Yano, K. Kobayashi, T. Sakurai, and S. Yoshikawa, *J. Chem. Soc., Chem. Commun.*, 1985, 1562.
5 M. Yashiro, A. Shimada, T. Usui, S. Yano, K. Kobayashi, T. Sakurai, and S. Yoshikawa, *J. Am. Chem. Soc.*, 1985, **107**, 4351.
6 J. J. Reuben, *J. Am. Chem. Soc.*, 1985, **107**, 1433.
7 J. J. Reuben, *J. Am. Chem. Soc.*, 1987, **109**, 316.
8 J. J. Reuben, *J. Am. Chem. Soc.*, 1986, **108**, 1082.
9 M. Yashiro, S. Yano, and S. Yoshikawa, *J. Am. Chem. Soc.*, 1986, **108**, 1096.
10 J. Feeney, P. Partington, and G. C. K. Roberts, *J. Magn. Reson.*, 1974, **13**, 268; R. A. Newmark and J. R. Hill, *ibid.*, 1976, **21**, 1; G. E. Hawkes, E. W. Randall, W. E. Hull, D. Gattegno, and F. Conti, *Biochemistry*, 1978, **17**, 3986.
11 J. Reuben, *J. Am. Chem. Soc.*, 1985, **107**, 1756.
12 R. A. Newmark and J. R. Hill, *Org. Magn. Res.*, 1980, **13**, 40.
13 D. Gagnaire and M. Vincendon, *J. Chem. Soc., Chem. Commun.*, 1977, 509; K. Bock and R. U. Lemieux, *Carbohydr. Res.*, 1982, **100**, 63; J. C. Christofides and D. B. Davies, *J. Chem. Soc., Chem. Commun.*, 1983, 324; J. Reuben, *J. Am. Chem. Soc.*, 1983, **105**, 3711.
14 J. C. Christofides and D. B. Davies, *J. Am. Chem. Soc.*, 1983, **105**, 5099; J. Reuben, *ibid.*, 1984, **106**, 6180; 1985, **107**, 1747, 5867.
15 J. C. Christofides and D. B. Davies, *J. Chem. Soc., Chem. Commun.*, 1982, 560.
16 J. C. Christofides and D. B. Davies, *J. Chem. Soc., Perkin Trans. 2*, 1984, 481; J. Reuben, *J. Am. Chem. Soc.*, 1984, **106**, 2461.
17 J. Reuben, *J. Am. Chem. Soc.*, 1986, **108**, 1735.
18 K. Ishida, S. Yano, and S. Yoshikawa, *Inorg. Chem.*, 1986, **25**, 3552.
19 K. Ishida, M. Yashiro, S. Yano, M. Hidai, and S. Yoshikawa, *J. Am. Chem. Soc.*, 1988, **110**, 2015.
20 Z. Majerski, M. Zuanic, and B. Metelko, *J. Am. Chem. Soc.*, 1985, **107**, 1721.
21 J. L. Jurlina and J. B. Stothers, *J. Am. Chem. Soc.*, 1982, **104**, 4677; R. Aydin and H. Gunther, *ibid.*, 1981, **103**, 1301; *Z. Naturforsch., Teil B*, 1979, **34**, 528; D. Doddrell, W. Kitching, W. Adcock, and P. A. Wiseman, *J. Org. Chem.*, 1976, **41**, 3036; L. Ernst, *Liebigs Ann. Chem.*, 1981, 376.

22 F. A. L. Anet and A. H. Dekmezian, *J. Am. Chem. Soc.*, 1979, **101**, 5449; L. Ernst, S. Eltamany, and H. Hopf, *ibid.*, 1982, **104**, 299; D. G. Morris and A. M. Murray, *J. Chem. Soc., Perkin Trans. 2*, 1976, 1579.

23 S. S. Bhattacharjee, J. A. Schwarcz, and A. S. Perlin, *Carbohydr. Res.*, 1975, **42**, 259.

24 P. E. Pfeffer, K. M. Valentine, and F. W. Parrish, *J. Am. Chem. Soc.*, 1979, **101**, 1265.

25 K. Ishida, S. Nonoyama, S. Yano, T. Hirano, M. Hidai, and S. Yoshikawa, *J. Am. Chem. Soc.*, in the press.

26 R. U. Lemieux, 'Molecular Rearrangements,' ed. P. de Mayo, Interscience, Alberta, 1964, **2**, 709; S. Wolfe, M. H. Whangbo, and D. J. Mitchell, *Carbohydr. Res.*, 1979, **69**, 1.

27 B. Sheldrick, *Acta Crystallogr., Sect. B*, 1976, **32**, 1016; G. M. Brown and H. A. Levy, *ibid.*, 1979, **35**, 656; S. S. C. Chu and G. A. Jeffrey, *ibid.*, 1968, **24**, 830.

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