Note

Nitrogen-15 NMR coordination shifts of β-alanine and glycine in cobalt(III) complexes

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Abstract

^{15}N NMR chemical shifts of β-alaninato chelates in cobalt(III) complexes were investigated in comparison to that of glycinato chelates, for the effect of *trans* influence and chelate ring size on amine nitrogen NMR coordination shifts. The coordination shifts of both chelates are found to be about 20 ppm larger for an amine group *trans* to the oxygen ligator than for one *trans* to the nitrogen ligator in a complex. It is also found that β-alanine exhibits on average 10 ppm smaller coordination shifts. Both effects may be considered as a consequence of N–Co bond strength changes.

Key words. ^{15}N NMR; Cobalt complexes; Amino acid complexes

Introduction

Large upfield ^{15}N NMR coordination shifts of amine nitrogen (−30 to −60 ppm) have been observed upon chelation of amino acids to cobalt(III) [1, 2] or binding to platinum(II) [3]. The ^{15}N coordination shift of glycine coordinated as the aminocarboxylato chelate to cobalt(III) was found to be very sensitive to the *trans* influence [1]. The effect of the amino acid composition on the coordination shifts was also studied, and observed to be the largest in transition from glycinato to β-alaninato chelates [2]. The general validity of this finding for transition metal aminocarboxylato chelates is yet to be proved, since the *trans* influence was studied only for the glycinato chelate, while the effect of amino acid composition was investigated only in one type of complex. The eventual general regularities of ^{15}N coordination shifts of amino acids in metal complexes will be important for analysis of metal binding to peptides.

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In the present study we undertook investigation of ^{15}N coordination shifts of β-alanine in comparison to that of glycine. Recently we reported the synthesis, and determined molecular geometries, of a complete series of $[Co(Gly)_{3-n}(\beta\text{-Ala})_n]$ complexes ($n=1$–3) [4]. The series allowed us to investigate the effects of both *trans* influence and chelate ring enlargement on ^{15}N coordination shifts of the chelated amino acids.

Results and discussion

For the natural abundance detection of ^{15}N chemical shifts the indirect detection via heteronuclear [^{1}H–^{15}N] multiple quantum coherence transfer (HMQC) [5] was applied. Nitrogen chemical shifts are obtained in the second dimension of the 2D spectrum (Fig. 1). The assignment of amine proton resonances has been done by correlating them with methylene protons through scalar coupling (Fig. 2). The methylene chemical shifts have been assigned previously [4].

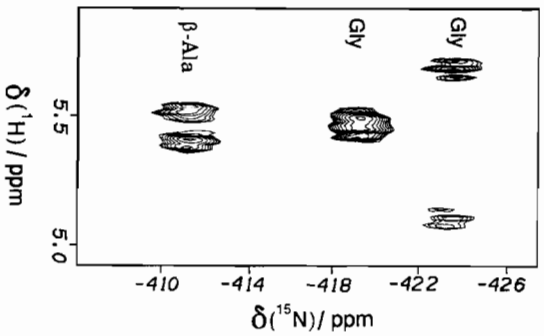

Fig. 1. Amine region in ^{1}H–^{15}N HMQC spectrum of *fac*-$[Co(Gly)_2(\beta\text{-Ala})]$.

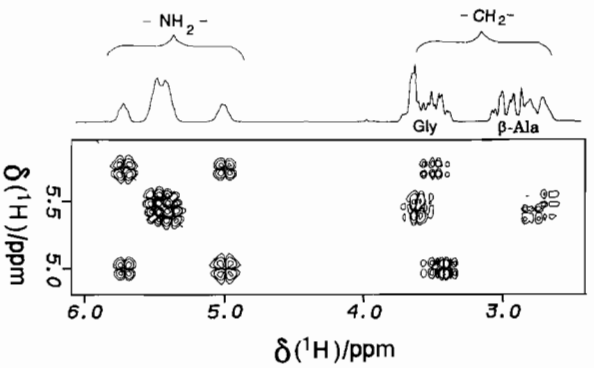

Fig. 2. Amine–methylene protons chemical shift correlation in a double quantum filter COSY spectrum of *fac*-$[Co(Gly)_2(\beta\text{-Ala})]$. Dashed line is drawn through the diagonal peaks.

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Obtained ^{15}N chemical shifts of glycine and β-alanine, coordinated as aminocarboxylato chelates, are presented in Table 1 in comparison with the chemical shifts they exhibit as free protonated amino acids. The corresponding coordination shifts are mainly sensitive to the *trans* influence. They are about 20 ppm larger for the amine group *trans* to the oxygen ligator than for one *trans* to the nitrogen ligator in a complex. In this respect β-alanine exhibits much the same behavior as glycine. However, the coordination shifts of β-alanine are smaller, on average, by about 10 ppm (see Fig. 3). Therefore, it may be concluded that the *trans* influence on ^{15}N coordination shifts of chelated amino acids is essentially the same for the six- and five-membered chelate rings, while the coordination shifts are affected by the chelate ring size to a small extent. Consequently, the eventual general regularity of the *trans* influence on ^{15}N coordination shifts of coordinated amino acids is further substantiated by the present study.

TABLE 1. ^{15}N chemical shifts (δ, ppm) of glycine (Gly) and β-alanine (β-Ala) chelates in cobalt(III) complexes and corresponding coordination shifts ($\Delta_c\delta$, ppm) from the free protonated amino acids (GlyH and β-AlaH). Ligators in *trans* position to amine nitrogen are presented in parentheses

Complex[a]	δ(^{15}N)		$\Delta_c\delta$	
	Gly	β-Ala	Gly	β-Ala
fac-[Co(Gly)$_3$]	−421 (O)		−59	
fac-[Co(Gly)$_2$(β-Ala)]	−423 (O)	−410 (O)	−61	−48
	−419 (O)		−57	
fac-[Co(Gly)(β-Ala)$_2$]	−426 (O)	−417 (O)	−64	−55
		−413 (O)		−51
fac-[Co(β-Ala)$_3$]		−418 (O)		−56
mer-[Co(Gly)$_3$]	−405 (N)		−43	
	−408 (N)		−46	
	−425 (O)		−63	
trans(O$_5$)-[Co(Gly)$_2$(β-Ala)]	−399 (N)	−398 (N)	−37	−36
	−421 (O)		−59	
trans(N$_5$)-[Co(Gly)$_2$(β-Ala)]	−406 (N)	−417 (O)	−44	−55
	−409 (N)		−47	
trans(N$_5$O$_5$)-[Co(Gly)$_2$(β-Ala)]	−399 (N)	−398 (N)	−37	−36
	−426 (O)		−64	
trans(O$_6$)-[Co(Gly)(β-Ala)$_2$]	−399 (N)	−402 (N)	−37	−40
		−418 (O)		−56
trans(N$_6$)-[Co(Gly)(β-Ala)$_2$]	−422 (O)	−391 (N)	−60	−29
		−393 (N)		−31
trans(N$_6$O$_6$)-[Co(Gly)(β-Ala)$_2$]	−401 (N)	−399 (N)	−39	−37
		−423 (O)		−61
mer-[Co(β-Ala)$_3$]		−392 (N)		−30
		−390 (N)		−28
		−424 (O)		−62
trans(N)-K[Co(ox)(Gly)$_2$][b]	−398 (N)		−36	
trans(N)-K[Co(CO$_3$)(β-Ala)$_2$]	−385 (N)			−23
GlyH (pH = 0)	−362			
β-AlaH (pH = 0)		−366		

[a]The geometrical isomers are labeled by *trans* pairs of ligators from the ring of the same kind (the ligator index denotes the chelate ring size). [b]oxH$_2$ = oxalic acid.

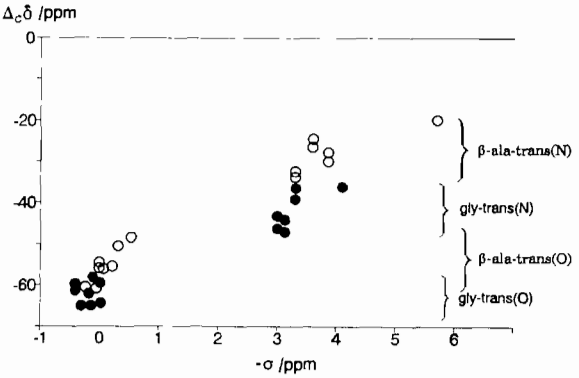

Fig. 3. Correlation of ^{15}N coordination shifts of glycine (●) and β-alanine (○) with amine nitrogen shielding due to cobalt(III) magnetic anisotropy. The shielding (σ) exerted by the magnetic anisotropy of cobalt(III) was calculated by the method described previously [9]

There has been a certain dispute in the literature on the nature of ^{15}N coordination shift changes with geometrical isomerism of a complex. In one approach to the problem the changes have been related to a through space influence of cobalt(III) magnetic anisotropy [6], although the anisotropy was calculated to be too small for the observed variations [7]. In the other approach, the changes have been related to metal–nitrogen bond strength [7, 8], and a through-bond effect on the coordination shifts of the right magnitude has been calculated [1]. An analysis of the here reported coordination shifts according to the two theories is presented in Fig. 3. It is seen that classification of coordination shifts according to the *trans* influence is running parallel to the cobalt(III) magnetic anisotropy influence. However, generally smaller coordination shifts of β-alaninato chelates cannot be accounted for by the magnetic anisotropy effect, because the amine nitrogens of both chelates are essentially at the same positions relative to the cobalt(III) magnetic anisotropy tensor [4]. It is well known that the β-alaninato chelate produces a weaker ligand field than the glycinato chelate [10], presumably due to the weaker metal–ligand bond. This then produces smaller ^{15}N coordination shifts by the through-bond effect. Therefore, the present results are in better accordance with the through-bond theory of coordination shifts [1].

Experimental

For synthesis of the complexes see ref. 4. For NMR measurements samples were prepared as 0.05 molar aqueous solutions (10% of D_2O) in 5 mm NMR tubes (about 30 mg of the samples). All the NMR spectra were measured on a 500 MHz spectrometer (Bruker

AMX-500). Proton chemical shifts are relative to TSP (3-(trimethylsilyl)tetradeuterato sodium propionate). Nitrogen chemical shifts are referenced to nitromethane via proton resonance of TSP internal standard using the resonance ratio $\omega(^{15}N)$nitromethane/$\omega(^{1}H)$TMS = 0.10136783 [11].

Direct coupling between amine protons and the amine ^{15}N nucleus (about 80 Hz for coordinated amine and 90 Hz for protonated amine group) of the amino acids was used for heteronuclear multiple quantum coherence transfer, according to the pulse sequence developed by Bax *et al.* [5]. The water signal was suppressed by pre-irradiation (1 s).

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