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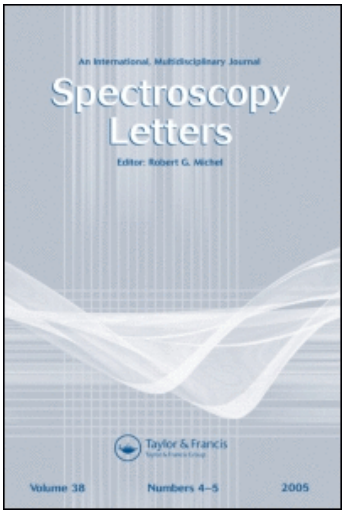

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A ^{1}H NMR Study of Palladium(II) Coordination Compounds with 2-Aminooxypropanoic Acid and Its Methyl Ester

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A ^{1}H NMR STUDY OF PALLADIUM(II) COORDINATION COMPOUNDS WITH 2-AMINOOXYPROPANOIC ACID AND ITS METHYL ESTER

Key words: ^{1}H NMR spectroscopy, 2-aminooxypropanoic acid, esters, hydrochlorides, complexes, palladium(II).

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ABSTRACT

The ^{1}H NMR spectra of 2-aminooxypropanoic acid, its methyl ester and their hydrochlorides have been inspected. The interaction of these ligands with palladium(II) has been investigated in deuterium oxide and in dimethyl sulfoxide. The metal has been found to form a chelate with the acid, whereas its esters coordinated to the metal through the nitrogen atom of the aminooxy group only. In dimethyl sulfoxide, also the methyl esters and hydrochlorides of 2-aminooxybutanoic, 2-aminooxy-3-methylpentanoic,as well as the ester of 2-aminooxyhexanoic and the hydrochloride of the ester of 2-aminooxy-3-phenylpropanoic acid have been studied.

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INTRODUCTION

There are many reports in chemical literature on pharmacologic activity of hydroxylamine derivatives. These compounds encompass also aminooxy acids of the general formula $RCH(ONH_2)CO_2H$. Compounds carrying the $-ONH_2$ group have been known as antibiotics, cancer inhibitors and antifungal agents[1,2]. 2-Aminooxyethanoic acid, for instance, exhibits distinct bacteriostatic activity against certain microorganisms[3]. It also inhibits transamination of β-alanine and ornithine in the liver and it is likely to inhibit γ-aminobutyric acid transamination in the brain[4-6]. A number of articles have been devoted to the synthesis and properties of peptides containing aminooxy acids[7-10].

Apart from the bioactivity of these compounds, also their physico-chemical properties have been studied[11-17].

Our preceding articles have been concerned with the coordination compounds of the aminooxy acid ligands with bivalent metal ions[16,17]. The purpose of this contribution is to study the interaction of 2-aminooxypropanoic acid and its methyl ester with palladium(II).

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EXPERIMENTAL

Reagents

2-Aminooxypropanoic acid, its hydrochloride and methyl ester were synthesized by the methods described by Testa et al.[18]. Commercially available amino acids were used as the starting reagents. The identity of the products was checked by elemental analysis and by mass spectrometry[14,17]. Sodium tetrachloropalladate was obtained from Alfa Products. A titration showed it to be of at least 99% purity.

Measurements

The ^{1}H NMR spectra were recorded on a Tesla BS-487C instrument operated at 80 MHz, using hexamethyldisiloxane as an internal reference. The compounds were dissolved in deuterium oxide and in dimethyl sulfoxide (DMSO), at 25°C.

RESULTS AND DISCUSSION

2-Aminooxypropanoic acid, its methyl ester, and the hydrochloride salts were chosen as model compounds for studying the -ONH_2 derivatives. The ^{1}H NMR spectra of the 2-aminooxypropanoic acid solution in D_2O and DMSO were inspected by Sohar et al[12]. Our results referring to systems containing Pd(II) are listed in Table 1.

A comparison of the ^{1}H NMR spectrum of 2-aminopropanoic acid in D_2O of pD 2.0 with that of the Pd(II)-containing solution of the acid reveals a slight displacement of the methyl proton peaks to lower fields (from δ 1.70 to 1.75). Further,a distinct broadening of the doublet can be noticed together with its distortion that resembles splitting into two doublets.

The peak of the methine group proton is shifted much more to lower fields (from δ 4.75 to 5.64),this indicating interaction of the Pd(II) ions with the ligand resulting in deshielding of the carbon backbone. This effect is most pronounced just with this group. The hydrogen atom of the methine group becomes more acidic and undergoes rapid exchange with the proton of water present in trace amounts in D_2O. This feature, together with the possibility of formation of conformers, might be responsible for the observed broadening and distortion of the resonance signals.

Similar effects are observed in solution of pD 4.0. Analogous tendency, though not so pronounced as previously, is noted with 2-aminooxypropanoic acid hydro-

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TABLE 1

^{1}H NMR Spectra of 2-Aminooxypropanoic Acid, its Hydrochloride, and the Hydrochloride of the Methyl Ester in D_2O (δ in ppm)

Compound	Ligand conc. $^{-3}$ (mol dm^{-3})	Pd(II) conc. $^{-3}$ (mol dm^{-3})	pD	δ (CH_3)	δ (CH)	δ (OCH_3)
2-Aminooxypropanoic	0.811	-	2.0	1.70d	4.75q	
	0.640	0.125	2.0	1.75db	5.64q	
acid	0.649	0.201	2.0	1.75db	5.64q	
	0.812	-	4.0	1.60d	4.54q	
	0.640	0.126	4.2	1.62db	4.65q	
	0.649	0.201	4.3	1.64db	5.00q	
	0.650	0.303	4.3	1.78db	5.10q	
2-Aminooxypropanoic	0.702	-	1.5	1.79d	5.09q	
	0.701	0.040	1.0	1.80d	5.13q	
acid hyrdochloride	0.700	0.185	1.0	1.83d	5.20q	
	0.702	-	3.5	1.68d	4.69q	
	0.701	0.040	3.5	1.70db	4.73q	
	0.700	0.185	3.4	1.72db	4.76qb	
	0.710	0.233	3.6	1.73db	5.03qb	
Methyl	0.521	-	1.8	1.78d	5.10q	4.09s
	0.449	0.098	1.5	1.82db	5.20q	4.10s
2-aminooxypropanoate	0.521	-	6.5	1.66d	4.68q	3.63s
	0.449	0.098	6.5	1.68db	4.72mb	3.65s
hydrochloride	0.521	0.272	6.4	1.72db	4 90mb	3.65s

Footnote: s-singlet, d- doublet, db-broadened doublet, qb-broadened quartet, mb-broadened multiplet.

chloride as a ligand (Table 1). The smaller shifts, in particular those of the methine proton, are understandable in view of protonation of the aminooxy moiety of the hydrochloride as compared to that of the free acid. It is worth noting that the basicity of the nitrogen atom in this group is by five orders of magnitude lower than that of analogous amino acids[18]. Hence, the tendency to form zwitterionic structure by 2-aminooxy acids is much weaker than is the case with amino acids.

This notwithstanding, protonation of the $-ONH_2$ group in the aminooxy acids is complete. Hence, the shifts of the resonance lines, especially that of the methine group, during coordination of the Pd(II) ion are less pronounced than in the case of free 2-aminooxy acids. In the spectrum of the hydrochloride of methyl 2-aminooxy-propanoate a new singlet of the ester group appears (Table 1). Upon addition of Pd(II) to the solution, the position of the singlet remains unaffected. However, distinct displacements of the remaining peaks reveal the coordination of the ligand to palladium(II) through the $-ONH_2$ group.

The complexation was also studied in the DMSO solution (Table 2). The proton peaks of the methyl and methine groups of 2-aminooxypropanoic acid emerge at δ 1.37 (doublet) and 4.22 (quartet) respectively. Moreover, at δ 7.40, a broad peak of the aminooxy protons appears (Fig.1,a). Upon addition of Pd(II) to the solution, the resonance lines of these protons are shifted to higher fields owing to their stronger deshielding (Fig.1,b,c). Peaks due to the methyl and methine protons are shifted only slightly toward lower fields owing to their deshielding caused by delocalization of electrons to the nitrogen atom.

Peaks of particular protons in solutions of the hydrochlorides appear at higher δ values (Table 2). The direction of their displacement remains, however, similar to that observed with the free acid. These findings, in particular the large shift of the $-ONH_2$ proton peaks, suggest that Pd(II) coordinates to the 2-aminooxypropanoic acid molecule through the nitrogen atom and probably also through the oxygen atom of the carboxylic group.

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TABLE 2

^{1}H NMR Spectra of 2-Aminooxypropanoic Acid, its Hydrochloride, and the Hydrochloride of the Methyl Ester in DMSO (δ in ppm)

Compound	Ligand conc. (10^{-3} mol dm^{-3})	Pd(II) conc. (10^{-3} mol dm^{-3})	δ (CH_3)	δ (CH)	δ (NH_2)	δ (OCH_3)
2-Aminooxypropanoic	0.650	-	1.37d	4.22q	7.40sb	
acid	0.650	0.223	1.38d	4.28q	6.90sb	
	0.650	0.330	1.40d	4.35q	6.43sbr	
2-Aminooxypropanoic	0.701	-	1.62d	4.98q	11.28sbr	
acid hydrochloride	0.616	0.165	1.61d	5.06q	10.10sbr	
	0.665	0.281	1.67db	5.21q	8.05sbr	
Methyl 2-aminooxypropanoate	0.444	-	1.59d	5.08q	9.90sbr	3.94s
hydrochloride	0.445	0.157	1.66d	5.10q	5.67sbr	3.95s

Footnote: q-quartet, sb-broadened singlet, sbr-broad singlet.

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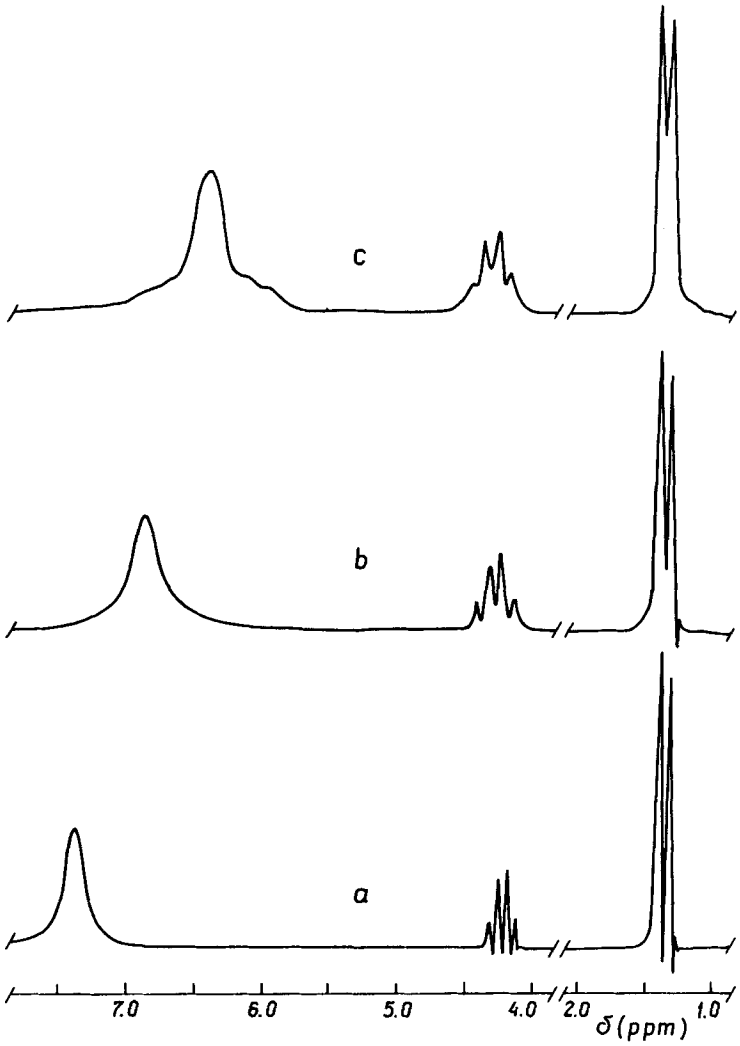

FIG. 1. ^{1}H NMR spectra of the DMSO solutions containing 2-amino-oxypropanoic acid and palladium(II). Acid concentration 0.650 M; Pd(II) concentrations; a-0.00 M, b-0.223 M, c-0.330 M.

The complexing capacity of the methyl ester of 2-aminooxypropanoic acid in DMSO was also investigated. The spectrum of the ester (Fig.2,a) shows a doublet of the methyl group at δ 1.39, a quartet of the methine proton at δ 4.33, and a singlet of the ester group at δ 3.83. Protons of the aminooxy group give a single, broadened peak at δ 6.22.

In the spectrum of the hydrochloride of the ester (Fig.2,b), the proton peaks of particular groups are shifted to higher δ values. Appearance of a positive charge on the aminooxy group in the hydrochloride moves the electron density toward the nitrogen atom thus weakening the shielding effect of the remaining protonated group. The strongest deshielding of the methine proton is observed with a peak at δ 5.10. It is shifted by δ 0.77 relative to the free ester. The smallest displacement is noted with the ester group protons, where the resonance line appears at δ 3.91.

The $-ONH_2$ proton peak is broadened owing to the quadrupole momentum of the nitrogen nucleus. In the case of the $-ONH_3^+$ group, the shift of the protons to the lower field is observed (down to δ 9.90) with simultaneous strong broadening of the peak as compared to that of the nonprotonated aminooxy group.

Addition of Pd(II) to the solution of the hydrochloride of methyl 2-aminooxypropanoate shifts the aminooxy proton peaks to higher fields similarly as is the case with the free acid and its hydrochloride. The shift is, however, distinctly larger in this case (Table 2). The methine proton peaks behave similarly as analogous ones of the free acid and its hydrochloride. The position of the ester proton peaks remains unaffected by Pd(II). It can thus be concluded that Pd(II) coordinates the hydrochloride of the ester only through the nitrogen atom of the aminooxy group.

There are no reports on the esters of 2-aminooxy acids in the literature. For this reason Table 3 lists ^1H NMR data of the esters synthesized by us and of the hydrochlorides of higher members of the 2-aminooxyalkanoic acid series. The direction of displacements of particular peaks in the spectra on going from the esters

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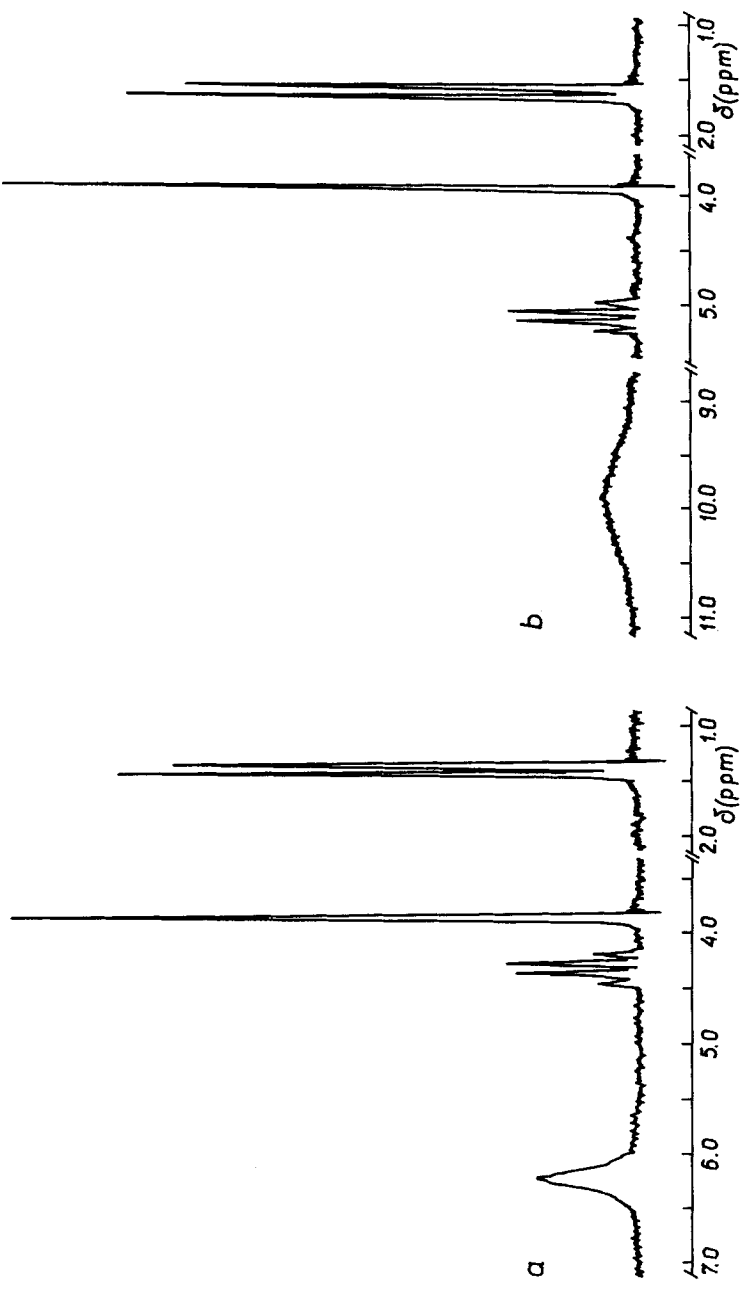

FIG.2. ^{1}H NMR spectra of the methyl 2-aminooxypropanoate (a) and its hydrochloride (b) in the DMSO.

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TABLE 3

^{1}H NMR Spectra of the Methyl Esters of some 2-Aminooxy Acids and their Hydrochlorides in DMSO (δ in ppm)

Compound	δ CH_3	δ CH	δ NH_2	δ OCH_3	δ CH_2	δ $CH-CH_2$	δ (CH_2)
Methyl 2-aminooxybutanoate	1.02t	4.15t	6.29sb	3.81s	1.77qi		
Methyl 2-aminooxybutanoate hydrochloride	1.10t	4.96t	9.30sbr	3.92s	1.99qi		
Methyl 2-aminooxy-3-methylpentanoate	1.02d	4.23t	6.15sb	3.80s	1.58m	1.82m	
Methyl 2-aminooxy-3-methylpentanoate hydrochloride	1.12db	5.02t	9.30sbr	3.94s		1.80m	
Methyl 2-aminooxyhexanoate	0.98t	4.16t	6.18sb	3.78s	1.90m		1.40m
Methyl 2-aminooxy-3-phenylpropanoate hydrochloride	7.43s^{ar}		5.19t	10.60sb	3.85s	3.37d	

Footnote: ar- signal of aromatic ring, t-triplet, qi-quintet, m-multiplet.

to their hydrochlorides is similar to that observed in the 2-aminooxypropanoic acid counterparts.

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