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# Studies on the Interactions between Potassium oxalato-oxodiperoxovanadate and Histidine by NMR and MS

Jian Liang YE[1], Xing Wang ZHOU[1,2], Zhong CHEN[1]*,
Zhi Wei CHEN[1], Pei Qiang HUANG[1]*

[1]Department of Chemistry, [2]Department of Biology, Xiamen University, Xiamen 361005

**Abstract:** Multi-nuclear NMR and ESI-MS have been applied to study the interactions between oxalato-oxodiperoxovanadate and histidine in neutral solution. Coordination between the complex and histidine was monitored by $^{51}V$ NMR. A pair of new isomers produced *via* vanadium atom binding separately to N1 and N3 of the imidazole ring of histidine was characterized by several spectroscopic methods. Experimental results show that the structure activity relationship of peroxovanadium complexes bearing organic ligands may be related to the specific recognition between peroxovanadium and histidine residue of tyrosine phosphatase.

**Keywords:** Oxalato-oxodiperoxovanadate, histidine, peroxovanadium, NMR, ESI-MS.

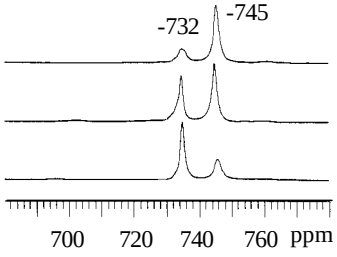
$K_3[VO(O_2)_2(C_2O_4)]\cdot 2H_2O$, (abbr. BpV (ox)) pertains to peroxovanadium (abbr. pV) complexes, which have been attracted considerable attention nowadays, since they are inhibitors of tyrosine phosphatase and may be developed into a new kind of drugs for the treatment of diabetes[1]. According to the evidence on water-biperoxovanadium, the molecular mechanism of insulin-like effects of pV involves in irreversibly oxidizing the catalytic cysteine at the active site of the target enzyme[2,3]. However, the study on the structure-activity relationship of pV complexes bearing organic ligands is scarce. Recently, we suggested that the structure-activity relationship is also related to the specific binding with some functional group in tyrosine phosphatase[4]. Considering strong affinity of histidine in acid phosphatase for vanadium atom[5] and the imidazole residue to be the essential groups of histidine for the activity of the tyrosine phosphatase[6], we selected histidine as the object of study on the interaction of histidine with bpV (ox).

All NMR spectra with $D_2O$ as solvent were recorded on a Varian Unity$^+$ 500 spectrometer. $^{51}V$ chemical shifts are referred to $VOCl_3$ as external standard at $\delta$ 0.00. ESI-MS spectra were performed on Finnigan MAT LCQ Instrument. The complex, bpV (ox), was synthesized and characterized as our latest paper[7] and its $^{51}V$ NMR peak locates at –732 ppm. All NMR and MS spectra were recorded after the samples were kept with various molar ratios of bpV (ox) and histidine in equilibrium *ca*. 1 h. $^{51}V$ NMR spectra with 1:3, 1:1 and 3:1 molar ratios of bpV (ox) and His are shown in **Figure 1**. Besides the peak of bpV (ox), there was a new peak at –745 ppm. According to the previous $^{51}V$ NMR report[8] on the interaction of water-biperoxovanadium toward His, it is reasonable to suggest that the new peak is attributed to new formed products *via*

vanadium binding to the imidazole of His. The peak of $K_3[pV(ox)\cdot(His)]\cdot 2H_2O$ and *m/z* 528.3 in ESI-MS of the mixtures provides the positive evidence for our suggestion.

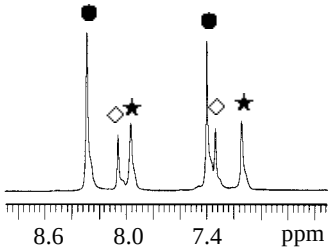
$^1$H NMR spectrum with 1:1 molar ratio of bpV (ox) and His is shown in **Figure 2**. The results revealed that the new formed complexes are a pair of isomers by the vanadium atom separately binding to N1 and N3 in imidazole ring. The six $^1$H peaks arose from the protons of the imidazole ring. These peaks are divided into three groups, *i.e.*, dominating N1 linkage isomer, N3 linkage isomer and free ligand of His.

**Figure 1** $^{51}$V NMR spectra ($D_2O$) with various molar ratios of bpV(ox) and histidine




(a) 1:3, (b)1:1, and (c) 3:1

**Figure 2** $^1$H NMR spectra with 1:1 molar ratio of bpV(ox) and His




●, dominating N1 linkage isomer; ◇, N3 linkage isomer; ★, free ligand

In addition, interactions between His and other bpV complexes of $[VO(O_2)_2L]^{n-}$, where L is 1,10-phenanthroline (abbr. phen), pyridine-2-carboxylic acid (abbr. pic) and bipyridine (abbr. bipy), respectively, were also studied. Experimental results indicated that similar situation occurs on bpV (pic) while there are no obvious interactions for complexes of bpV (bipy) and bpV (phen). The interaction results observed in this work showed parallel correlation with their biological activity[4]. In conclusion, the present paper provides the evidence that the structure-activity relationship of this class of bpV complexes may be related to the specific recognition between pV and histidine residue of the phosphatase. Detailed results will be presented in a full paper in the near future.

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