P: ISSN No. 0976-8602 RNI No.UPENG/2012/4262 VOL.-8, ISSUE-2,(Part-1) April 2019

E: ISSN No. 2349-9443 Asian Resonance

Potential Antibacterial Oxidovanadium (IV) Complexes Containing Quinoline-8-olato and Hydroxamate Ligands: Synthesis and Characterization

Jitender Thakur
PhD Research Scholar
Deptt. of Chemistry,
Himachal Pradesh University,
Summer Hill, Shimla
India

Neeraj Sharma
Professor
Deptt. of Chemistry,
Himachal Pradesh University,
Summer Hill, Shimla
India

Abstract

The oxidovanadium (IV) complexes of composition $[VO(Q)(HL^{1-2})]$ with hydroxamate ligands(where Q= 8-hydroxyquinolate ion) (C_9H_6NO-); HL^1 = 2-chloro-4-nitrobenzohydraxamate (2-Cl-4-NO_2BzH); HL^2 =4-aminobenzohydroxamate (4-ABH) have been synthesized by the reactions of $VO(Q)_2$ with potassium hydroxamate ligands (2-Cl-4NO_2BzHK) and (4-ABHK) in 1:1 molar ratio in THF+MeOH. The complexes have been characterized by elemental analyses, molar conductivity, magnetic moment measurements, IR, mass spectrometry, electronic and ESR spectral studies. Bonding through hydroxamic and carbonyl oxygens (O, O coordination) has been inferred from IR spectra. The electrochemical behavior of complexes studied by cyclic voltammetric method has shown a quasi-reversible VO^{3+}/VO^{2+} redox couple. The antibacterial potential of complexes evaluated against some pathogenic Gram +ve bacteria (S.aureus, S.epidermidis) and Gram –ve bacteria (E.coli, S.typhi) by minimum inhibitory concentration (MIC) method has shown promising antibacterial activity relative to respective free ligands and standard drugs.

Keywords: Oxidovanadium (IV) complexes, 2-chloro-4-nitrobenzohydraxamate, 4-aminophenylhydroxamate, Spectral studies, Antibacterial activity.

Introduction

The coordination and biochemistry of vanadium, an important bioelement because of its pharmacological properties [1, 2] has been a subject of increasing research interest. The anionic form vanadate resembling phosphate and of the cationic forms, VO^{2+} in particular, have been of biological relevance [3-7]. The ability of vanadium to exhibit variable oxidation states especially the interconversion between vanadium (IV) and vanadium (V) in biological media has led to the synthesis of numerous complexes derived from organic ligands with varying donor atoms exhibiting broad coordination potentialities [3]. The antitumor [8], antimicrobial and insulin enhancing effects [9] of vanadium complexes are well-documented. There has also been a growing interest in the synthesis of vanadium complexes as models in haloperoxidation, phosphorylation, insulinmimicking [5, 10] and nitrogen fixation [11-13].

Review of Literature

Hydroxamic acids (-NHOH) an important class of organic bioligands have been of considerable chemical and biological importance [14, 15] because of exhibiting a wide spectrum of biological activities as antibiotics, antitumor [16]and antifungal agents and their involvement in processes such as microbial iron transport [17], inhibition of nickel-dependent urease enzymes [18, 19], the zinc-dependent matrix metalloproteinase [20, 21], the haem-dependent prostaglandin-H synthase and histone deacetylase inhibitors [22]. The versatility of bonding because of tautomerism exhibiting hydroxamic and hydroximic forms in their metal complexes is highly fascinating [23, 24]. Scattered reports describe the synthesis and biological activity of vanadium (IV, V) hydroxamic acid complexes [25, 26].The substituents at hydroxamate ligand have been found to exhibit a range of coordination possibilities depending on the metal ion involved & pH of reaction. The aminohydroxamic acids have been reported to coordinate to metal through (O, O) as a singly

deprotonated hydroxamate, through (N, N) of the amino and the deprotonated hydroxamic nitrogen or as a (N, N), (O, O) bridging bis chelating ligands [27].The complexes with electron withdrawing groups (-NO_2, -Cl) are known to exhibit higher activity than those with an electron releasing group (-NH_2). The -OH and –NH_2 substituted benzohydroxamic acids have been reported to inhibit mammalian ribonucleotidereductase and exhibit actineoplastic activity [7]. both acetylacetonate groups can be replaced with organic ligands. It is also aimed to study the coordination mode of the ligand and evaluate potential antibacterial activity of newly synthesized complexes

Objective of the Study

As a part of our research interest on the synthesis of oxidovanadium(IV)hydroxamates,[28-32] we report herein the synthesis of new Oxidovanadium (IV) Complexes containing quinoline-8-olato and hydroxamate ligands which has been reported to undergo ligand exchange reactions where one quinoline-8-olato group can be replaced with organic ligands.

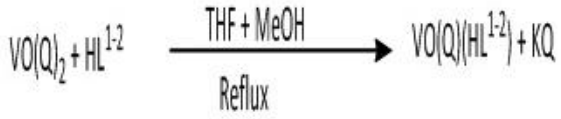
Experimental Details

Materials and physical measurements

All the reagent-grade solvents and chemicals were of reagent grade. The vanadium content in complexes was determined as V_2O_5. The carbon, hydrogen and nitrogen analyses were obtained on Eager 300 NCH System Elemental Analyzer. The molar conductance (10^{-3} M solutions in CH_3OH) was obtained at 25 ± 0.1^oC on an Elico Conductivity Bridge Type CM-82T. The room temperature magnetic susceptibilities were recorded by Guoy's method using $Hg[Co(NCS)_4]$ as calibrant. IR spectra were recorded as KBr pellets on Nicolet-5700 FTIR spectrophotometer. The pellets were prepared in a dry box to avoid the action of moisture.

Synthesis

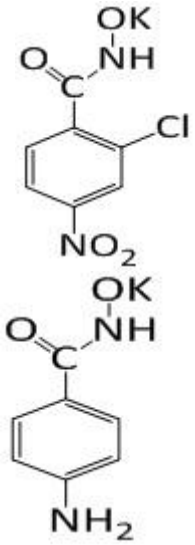
To a solution of [VO(Q)2) in THF+MeOH (20ml) were added equimolar amount of potassium hydroxamate ligands (2-Cl-4NO2BzHK) and (4-ABHK) in the same solvent in separate experiments. The reaction mixture was initially stirred for half an hour and was then refluxed for 16 h whereupon a change in color of reaction mixture from blue to brown was observed. The scheme of the reaction is as below



Structure of Ligands

Fig 1

Potassium-2-chloro-4-nitrobenzohydraxamate Potassium-4-aminobenzohydroxamate (2-Cl-4NO2BzHK) HL^1 (4-NH4BzHK) HL^2



Results and Discussion

The X-band ESR spectra of [VO(Q)HL^{1-2}] recorded at room temperature displayed the typical hyperfine splitting and anisotropic line shapes of vanadium(IV) chelates. The characteristic eight line ESR pattern is due to interaction between vanadium(IV) with its own nucleus I = 7/2 indicative of the presence of vanadium(IV). The nuclear magnetic quantum numbers corresponding to these lines are -7/2, -5/2, -3/2, -1/2, +1/2, +3/2, +5/2, +7/2 from low to high field. The g average values determined from the spectra are ≈1.98 close to the spin only value (free electron value of 2.00) suggesting a little spin-orbit coupling.

It therefore, follows that changes in characteristic infrared spectral bands from ligand to complexes, electronic spectral bands in the visible region, ESR and magnetic studies are consistent with the description of the metal center as vanadium(IV) and square-pyramidal geometry for complexes may tentatively be proposed as (Fig. 7, 8).

The UV-Vis spectra of [$VO(Q)_2$], $HL^{1-2}$and newly synthesized complexes have been recorded in CH_3OH. The electronic spectra of [$VO(Q)_2$] is known to exhibit bands at 390 573 and 769 nm a peculiar feature of vanadyl complexes [36,37]. The ligand KABH showed bands at 225, 257 nm attributed to intraligand π-π* transitions. The complexes [VO(Q)HL^{1-2}] displayed bands at 800-750 and 550-450 nm range ascribed to LMCT and d-d transitions respectively. These spectral observations are in agreement with those reported for square-pyramidal oxidovanadium (IV) complexes [33].

Mass spectra of complex 1 showed molecular ion peak at 425.23 and of complex 2 at 362.23, fragment ions supports the formation of complexes [VO(Q)HL^1] and [VO(Q)HL^2].

A comparison of IR spectra of ligands with those of complexes confirms the coordinate bonding

of hydroxamate ligands through carbonyl and hydroxyl oxygen atoms. The free ligand and the newly synthesized oxidovandium (IV) complexes were screened in-vitro for their antibacterial activity on selected gram +ve and gram -ve bacteria by MIC method. Complex [VO(Q)HL^1] has shown pronounced activity over [VO(Q)(HL^2)] and free ligands.

Fig 2. Mass Spectrum of [VO(Q)HL^1]

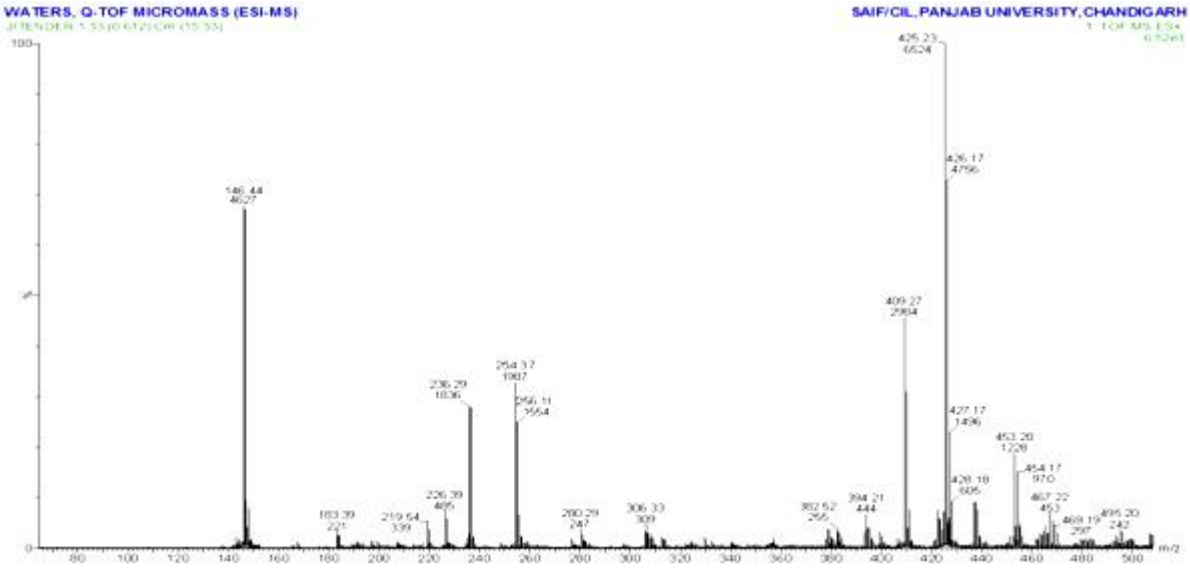


Fig 3. Mass Spectrum of [VO(Q)HL^2]

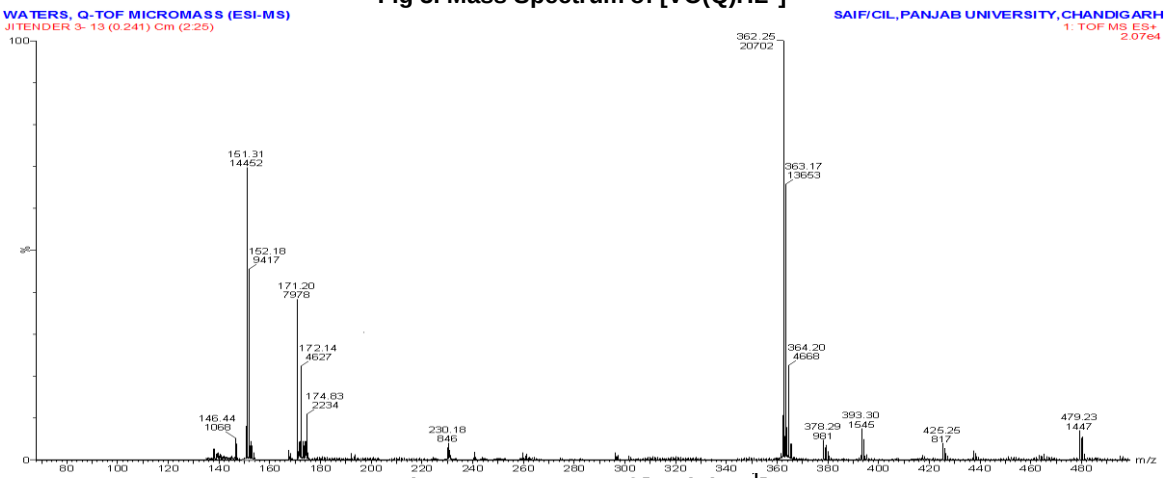


Fig 4. IR Spectrum of [VO(Q)HL^1]

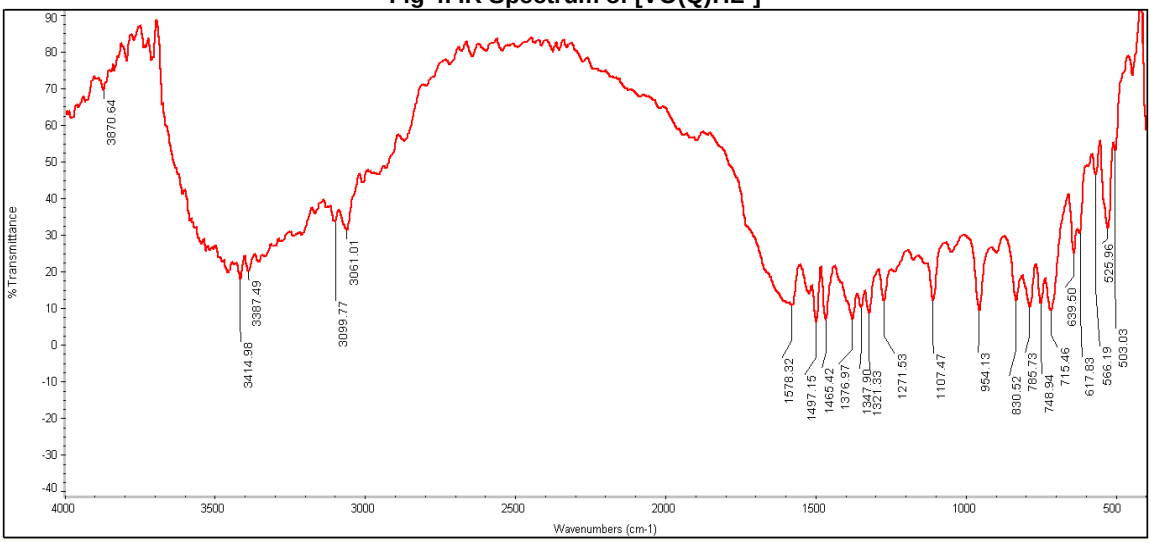


Fig 5. IR Spectrum of [VO(Q)HL^2]

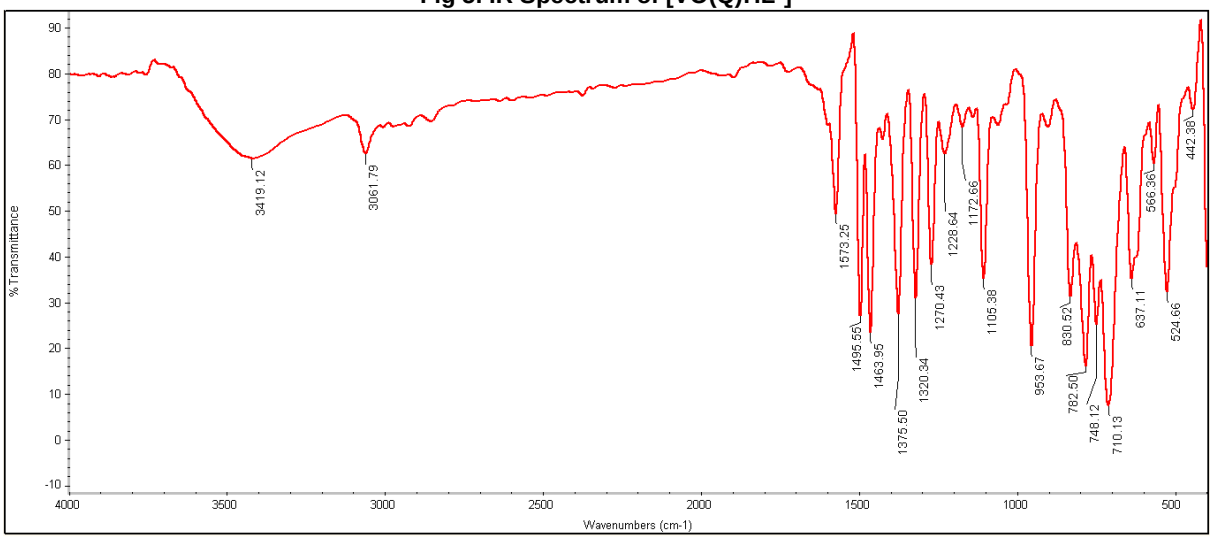


Fig 6. In vitro antibacterial spectrum of oxidovanadium(IV) complexes

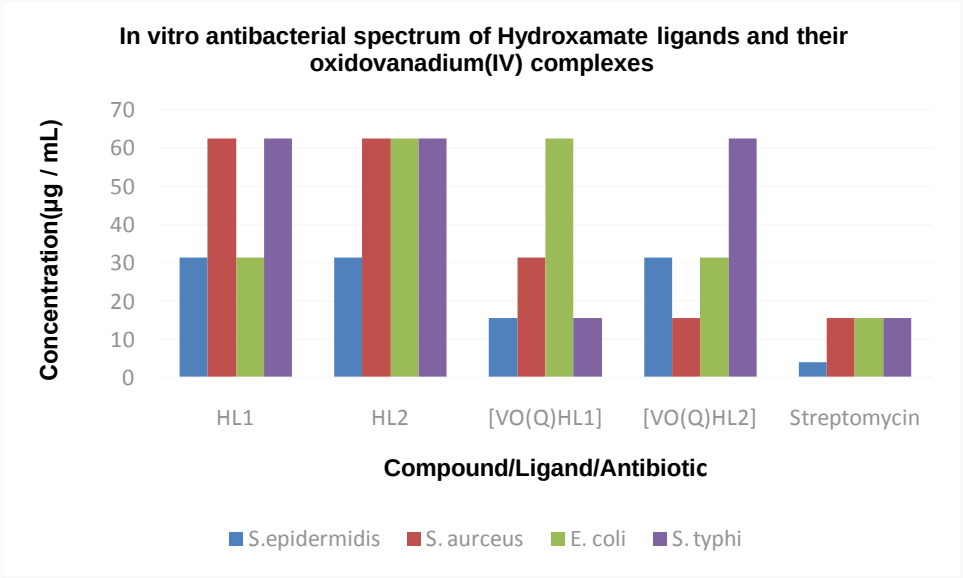


Fig 7. Structure of [VO(Q)HL^1]

Fig 8. Structure of [VO(Q)HL^2]

Conclusion

The mass spectra suggested these complexes to be mononuclear. Complexes displayed common base peak at m/z(%) 146(100) corresponding to the quinoline-8-olato ion. Hydroxamate ligands have displayed O, O coordination mode involving bonding through carbonyl and hydroxamic oxygen atoms excluding the involvement of amino and hydroxamic nitrogen atoms in bonding, has been inferred from IR spectra. Five coordinate square pyramidal geometry of complexes has initially been proposed from the spectroscopic studies. An assay of antibacterial activity of complexes has shown efficient antibacterial activity against the test organisms**.**

Acknowledgements

The authors wish to thank Department Of Science and Technology (DST) New Delhi, Govt. of India for providing financial assistance for FTIR and UV-Vis spectrophotometer facility to the department under its FIST program and UGC, New Delhi for cyclicvoltammeteric facility under UGC-SAP-II to the department, IIT Roorkee for magnetic susceptibility measurements, IIT Bombay for ESR spectra, Punjab University Chandigarh for recording mass specrtra and DepartmentOf Biosciences, Himachal Pradesh University Shimla for carrying out antibacterial activity study.

References

Ballhausan, C.J., Grey, H.B., Inorg. Chem., 1962. vol. 1, p. 111.

Botos, I., Scapozza, L., Zhang, D., et. al., Proc. Natl. Acad. Sci. U.S.A., 1996, vol. 93, p. 2749.

Crans, D.C., Yang, L., Alfano, J.A., et. al., Coord. Chem. Rev., 2003, vol. 237, p. 13.

Codd, R., Coord. Chem. Rev., 2008, vol. 252, p. 1387.

Crans, D.C., Smee, J.J., Gaidamauskas, E., Yang, L., Chem. Rev., 2004, vol. 104, p. 849.

Demuth, H.U., Stockel, A., Schierhorn, A., et. al., Biochem., Biophys. Acta., 1993, vol.1202, p.

Domingues, N., Pelletier, J., Ostenson, C.G., Castro, M.M., J. Inorg. Biochem., 2014, vol. 131, p. 115.

Geary, W.L., Coord. Chem. Rev., 1971, vol. 7, p. 81.
265.

Chem., 2004, vol. 15, p. 3003.

Haratake, M., Fukunaga, M., Ono, M., Nakayama, M., J. Biol. Inorg. Chem., 2005, vol. 10, p. 250.

Pasayat, S., Böhme, M., Dhaka, S., et. al., Eur. J. Inorg. Chem., 2016, p. 1604.

Sharma, N., Kumar, V., Sharma, R., et. al., Bull Chem. Soc. Japan., 2011, vol. 84, p. 855.

Sharma, N., Kanwar, S.S., Gupta, R., et. al., Bull. Chem. Soc. Japan., 2012, vol. 85, p. 1310.

Sharma, N., Kumari, M., Sharma, R., J. Therm. Anal. Calorim., 2012, vol. 107, p. 225.

Sharma, R., Sharma, N., J. Therm. Anal Calorim., 2012, vol. 110, p. 539.

Sharma, R., Sharma, N., J. Therm. Anal. Calorim., 2013, vol. 112, p. 25.

Rowe, R.A., Jones, M.M., Inorg. Synth., 1957, vol. 5, p. 114.

Hauser, C.R., Renfrow, W.B., Benzohydroxamic acid.

Farkas, E., Brown, D.A., Cittaro, R., Glass, W.K., J.Chem. Soc. Dalton Trans., 1993, p. 2803.

vol.199, p. 1442.

Grams, F., Crimmin, M., Hinnes, L., et. al., Biochemistry., 1995, vol. 34, no. 43, p. 14012.

Etcheverry, S.B., Leon, I.E., Di Virgilio, A.L., et. al., Dalton Trans., 2013, vo. 42, p. 11868.

Thompson, K.H., and Orvig, C., Coord. Chem. Rev., 2001, vol. 219-221, p. 1033.

Maurya, M. R., Coord. Chem. Rev., 2003, vol. 237, p. 163.

Maurya, M. R., J. Chem. Sci., 2006, vol. 118, no. 6, p. 503.

Molineuvo, M.S., Bario, D.A., Cortizo, A.M., Etcheverry, S.B., Chemother. Pharmacol., 2004, vol. 53, p. 163.

Marmion, C. J., Griffith, D., Nolan, K. B., Eur. J. Inorg.

Kawabe, K., Yoshikawa, Y., Adachi, Y., et. al., Life.Sci., 2006, vol. 78, p. 2860.

Sanna, D., Micera, G., Garribba, E., J. Biol. Inorg. Chem., 2010, vol.15, p. 825.

Ugwu, D. I., Ezema, B. E., Eze, F. U., et. al., Amer. J. Org. Chem., 2014, vol. 4, no. 2, p. 26.

Karmaker, S., Saha, T.K., Yoshikawa, Y., Sakurai, H., Afri. J. Pharm. Pharmacology., 2010, vol. 4, p. 235.

Sanna, D., Micera, G., Garribba, E., Inorg. Chem., 2010, vol. 49, p. 174.

Abakumova, O. Y., Podobed, O. V., Belayeba, N. F., Tochilkin, A. I., Biomed. Chem., 2012, vol. 6no. 2, p. 164.

Pawar, V., Joshi, S., Uma, V., Biokemistri., 2011, vol. 23 no. 1, p. 21.

Pal D, and Saha S., J. Adv. Pharm. Technol. Res., 2012, vol. 3, p.92.

Kehl (ed.), H., Chemistry And Biology of Hydroxamic Acids, Karger, New York., 1982.

Kobashi, K., Kumari, K., Hase, J., Biochim. Biophys. Acta., 1971, vol. 227, p. 429.

Odake, S., Morita, Y., Morikawa, T., et. al., Biochem. And biophy. Research. Comm., 1994,

Stankiewicz, P.J., Tracey, A.S., Crans, D.S., et. al., Metal ions in biological systems. 1995 p. 31. Organic Synthesis.Coll.Vol. II, Edi. A.H. Blatt and John Wiley and Sons, New York., 1967, p. 67.