Thermodynamic Characteristics of Vanadium(IV) Acetohydroxamate Complexes

K. ALI, N. FATIMA AND Z. T. MAQSOOD
Department of Chemistry, University of Karachi

(Received 16th September, 2002, revised 25th June, 2003)

Summary: Vanadium(IV) forms highly stable complexes with acetohydroxamate. In the determination of thermodynamic parameters such as ΔG, ΔH and ΔS of these Vanadium (IV) complexes, the data was processed and analyzed by computer program BEST for the refinement of the calculated log β values. Graphs were plotted with lnβ versus 1/T, which gave $-\Delta H/R$ as slope and $\Delta S/R$ as intercept. Enthalpy change for Vanadium(IV) with this simple hydroxamic acid was found to be -166.0, -83.0 and -86.0kJ/mole for ML_1, ML_2 and ML_3 respectively. Entropy change was 672.30, 475.38 and 567.12 J/mole for ML, ML_2 and ML_3 complexes respectively. While ΔG values calculated for these species were –372.3, -230.5 and -261.8 kJ/mole. The ΔS is most positive for a 1:1 complex while ΔG and ΔH are more negative for the same.

Introduction

The importance of vanadium complexes is worthwhile either in terms of its significance due to toxicity or its many useful applications in the treatment of various diseases like diabetes, anemia, tuberculosis and in cancer.

In biological system, vanadium exists in +3, +4 and +5 oxidation states[1]. Vanadium is present in specialized vacuoles in the ascidian blood in the form of complex of V(III) [2-6] having small fraction of Vanadium(IV) [7-15]. Fly agaric toadstool contains a low molecular weight V(IV) compounds (amavanadine) with an unknown function [16]. It has recently been found that hydroxamic acid conjugated to the tripyrrolepeptide, distamycin induced highly specific DNA cleavage in the presence of vanadyl ion [17].

The standard potential of the vanadate $(H_2VO_4)^-$ to vanadyl $(VO)^{2+}$ is 1.31 V [16]. Hence vanadyl undergoes auto-oxidation to vanadate in the presence of oxygen and vanadate is reduced by reductants such as glutathion, ascorbate and NADH. This facile change between V(V) and V(IV) has an interesting feature in the biological significance of vanadium. For instance, vanadium can act as competitor to phosphate $(HPO_4)^{2-}$. On the other hand it acts as a transition metal ion, which competes with other metal ions in coordination to biogenic compounds.

At 1M hydrogen ion concentration, aqueous solution of Vanadium(V) behaves like a moderately good oxidizing agent,

$$V(OH)_4^+ + 2H^+ + e^- \rightarrow VO^{2+} + 3H_2O \quad E^0 = 1.000\ V$$

In aqueous solution vanadyl ion exist either as VO^{2+} or as $[VO(H_2O)_5]^{2+}$, and the thermodynamic data reported is: [1].

$$\Delta H_f^\circ = -133\ K\ cal / mol$$

$$\Delta G_f^\circ = -109\ K\ cal / mol$$

$$\Delta S_f^\circ = -13.4\ cal / deg / mol$$

Vanadium is an essential trace element present in normal foods. The daily in take is about 2mg [18]. Spectrophotometric study indicates that concentration of vanadium in normal human blood is 0.18-0.22 ppm.

In the cancer patient's blood the average vanadium concentration is higher such as 5-2 ppm [19]. On the other hand vanadium salts (usually alkali metal salts either ortho or meta vanadic acid) have also been employed pharmacologically in the treatment of aneamia, tuberculosis and in various chronic diseases [19].

Vanadium has been used with great success as an oral treatment for animal model of diabetes [20]. Vanadate is 6-10 times more toxic then vanadyl [21,22] but excessive application of vanadyl is less effective than vanadate probably because of the fact that vanadate enters the living cells more rapidly [23].

Vanadyl permeability can be increased by complexing it with a naturally occuring water soluble

ligand such as hydroxamates analog [24,25] or Maltol [26]. The maximal effect of vanadyl in which is in the order of 20-30% of that of insulin is shifted towards 110-115% stimulation by hydroxamate chelation [27]. Recently the reaction chemistry of the potent insulin-mimetic agent bis(maltolato) oxo-vanadium(IV) has been reported [28]. Its vivo studies proves that it is at least three times more effective than uncomplexed vanadyl sulfate [29].

Generally phenolates are present in bacteria and the hydroxamates in higher living organism as fungi and Yeast [30,31]. The first hydroxamate type ligand was isolated in 1952 [32].

The aim of the present study is to have an insight of vanadium complexation with the simplest hydroxamte, acetohydroxamic acid (AHA).

Results and Discussion

The thermodynamic parameters of V(IV) complexes was studied with acetohydroxamate ligand. It is the simplest and basic hydroxamate analogue. The stability constant values were determined on different temperatures. The data was then treated on the basis of the following equation:

$$-RT\ln K = \Delta G$$

and

$$\Delta G = \Delta H - T\Delta S$$

Therefore,

$$-RT\ln K = \Delta H - T\Delta S$$

and then dividing both sides by RT,

$$\ln \beta_n = -\Delta H/RT + \Delta S/R$$

The titration curves of the V(IV) complex at different temperatures were found to have less depression but more twists which showed the low stability constant values with more species present at a time. The stability of these species present at lower pH was found to be more sensitive to temperature Fig I-IV.

Theoretical β values were calculated with the data obtained by these titrations and then it is subjected to computer program "BEST" for refining log β values. For 1:1 and 1:2 type of complexes when concentration of metal ions were assme to be equal to concentration of VO(IV). Prior to this refining, the theoretical β values were calculated for all species

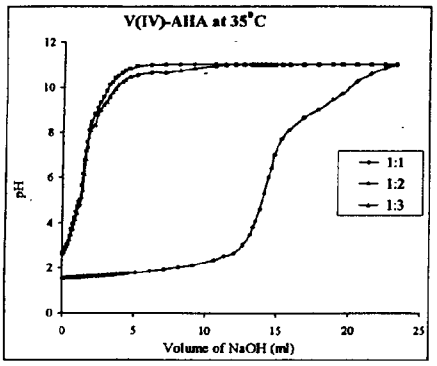

Fig. 1: pH variation of V(IV)-AHA Complex with Different L/M Ratio at 35°

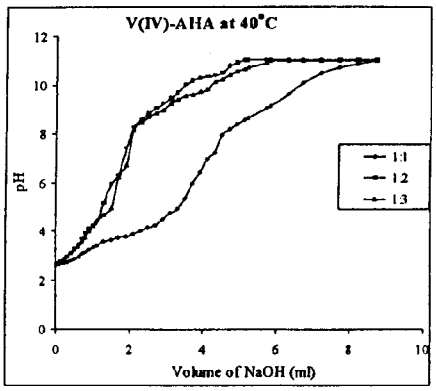

Fig. 2: pH variation of V(IV)-AHA Complex with Different L/M Ratio at 40°

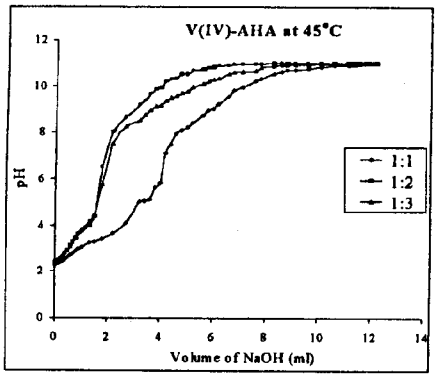

Fig. 3: pH variation of V(IV)-AHA Complex with Different L/M Ratio at 45°

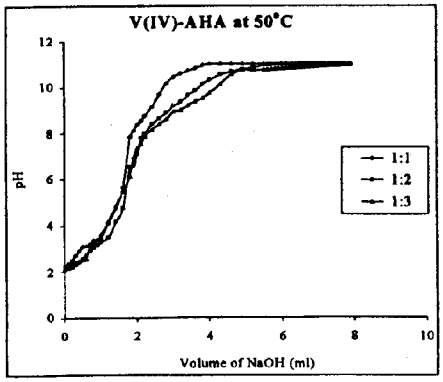

Fig. 4: pH variation of V(IV)-AHA Complex with Different L/M Ratio at 50°

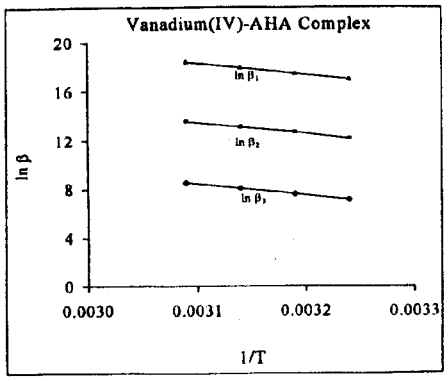

Fig. 5: Heat Energies of Vanadium(IV)-AHA Complex

from the titration curves and then the data file "FOR004.DAT" was written for each titration. These refined β values with least sigma fit were selected for each species (Table I). For further calculations, these log β values were converted into ln β values. These 1:1, 1:2 and 1:3 β values were also calculated by spectroscopic method.

Similarly, 1/T values were also calculated (Table II). The graphs were plotted against ln β and 1/T to calculate ΔH, ΔS and ΔG values (Fig V). The slope of the graph gave -ΔH/R values, which when multiplied by R gave ΔH values. The intercept was found to be equal to ΔS/R and again by multiplying with R, ΔS value was calculated and using the equation:

$$\Delta G = \Delta H - T\Delta S$$

Table-I: Log β Values for V(IV)-AHA Complexes at Different Temperature

S.No.	Complexes	35°C	40°C	45°C	50°C
1	$[VO(AHA)(H_2O)_3]^+$	3.10	3.30	3.50	3.70
2	$[VO(AHA)_2(H_2O)]^0$	5.30	5.50	5.70	5.90
3	$[V(AHA)_3]^+$	7.40	7.60	7.80	8.00

Table-II: ln β Values for V(IV)-AHA Complexes at Different Temperature

S. No.	T (Temp.)	1/T	$\ln \beta_1$	$\ln \beta_2$	$\ln \beta_3$
1	35°C	3.24×10^{-3}	7.1393	12.2059	17.0422
2	40°C	3.19×10^{-3}	7.5990	12.6660	17.5028
3	45°C	3.14×10^{-3}	8.0605	13.1271	17.9634
4	50°C	3.09×10^{-3}	8.5211	13.5877	18.4240

Table-III: Thermodynamic Properties for V(IV)-AHA Complexes

S. No.	Complexes	ΔH KJ/mol	ΔS J/mol	ΔG KJ/mol
1	$[VO(AHA)(H_2O)_3]^+$	-166.0	672.30	-372.3
2	$[VO(AHA)_2(H_2O)]^0$	-83.0	475.38	-230.5
3	$[V(AHA)_3]+$	-86.0	567.12	-261.8

ΔG for each species of Vanadium(IV) and Vanadium(V) acetohydroxamate complexes were also obtained (Table III).

All the ΔH and ΔG values calculated for Vanadium(IV) acetohydroxamic acid complexes were found to be negative showing high thermal stability. The 1:1 complex showed greater negative enthalpy value (-166 $kJmol^{-1}$), approximately double to that of 1:2 and 1:3 (-83 $kJmol^{-1}$ and -86 $kJmol^{-1}$ respectively), showing a high change in internal energy during formation of complex from aquo metal ions. Free energy change in case of each L/M ratio of V(IV)-AHA complexes were slightly different from each other but in the order 1:1 > 1:3 > 1:2. The ML_3 type complex showed greater negative ΔG value (-261 $kJmol^{-1}$) than ML_2 (-230 $kJmol^{-1}$). It may be due to the removal of vanadyl oxygen during the formation of hexadentate complex from simple bidentate ligand. For 1:1 it is (-372 $kJmol^{-1}$). Change in entropy values were also observed high and positive in all cases and in the same order as discussed in free energy case (672.3 $Jmol^{-1}$, 475.38 $Jmol^{-1}$ and 567.12 $Jmol^{-1}$ respectively). This can be easily proved from the following equations:

$$[VO(H_2O)_5]^{2+} + HL \rightleftharpoons [VO(H_2O)_3L]^+ + H^+ + 2H_2O \quad \text{(i)}$$

$$[VO(H_2O)_3L]^+ + 2HL \rightleftharpoons [VO(H_2O)L_2] + 2H^+ + 2H_2O \quad \text{(ii)}$$

or

$$[VL_3]^+ + OH^- + H_2O \rightleftharpoons [VO(H_2O)L_2] + HL \quad \text{(iii)}$$

$$[VO(H_2O)_5]^{2+} + 3HL \rightleftharpoons [VL_3]^+ + H^+ + 5H_2O \quad \text{(iv)}$$

Equations (i) & (iv) show that in case of 1:1 and 1:3 the entropy should be the same. Whereas in 1:2 there may be two types of mechanisms as shown in equations (ii) & (iii). According to equation (ii) the entropy of 1:1 and 1:2 complexes should be equal but in case of second mechanism, as it is in equation (iii), change in entropy should come in negative value. Result showed that formation of this specie may have both types of mechanisms occurring simultaneously, therefore, the value is in between these two.

Experimental

In the present research work, all reagents used were of A. R. grade supplied by different sources like Merck, Sigma and Aldrich Riedel-de- Haen and were employed without further purification. Doubly distilled and deionized water was used in the preparation of all stock / standard solutions.

For pH titration, CO_2 free water was prepared by boiling redistilled and deionized water for 10 minutes and then cooling it in air tight flask [33]. A 0.05 M solution of potassium hydrogen phthalate, which has the pH value 4.01 at 25°C was used to calibrate pH meter.

For these titrations 25 ml of 0.01M Vanadium(IV) solution was mixed with 25ml, 50ml, and 75ml of 0.01M (AHA) in order to get 1:1, 1:2 and 1:3 L/M respective ratios . Purified nitrogen gas was purged through the solution for half an hour. These titrations were carried out at 35°C, 40°C, 45°C and 50°C. The circulating water from the thermostat to the reaction cell controlled the temperature of the reaction mixture. The reaction mixture was stirred on a magnetic stirrer while the titration was carried out with standard 0.2M NaOH and the pH was measured by an Orion S. A model 720 pH meter having a resolution of + 0.001 pH unit.

Conclusions

The results are also supported by the literature values, showing that the complexes are highly stable thermodynamically, with greater ΔH and ΔG values with negative sign. High values for 1:3 shows that in normal conditions metal is generally chelated by AHA, satisfying all its coordination points having coordination number 6 while ligand behaves as a bidentate ligand. ΔS values were high and positive, again showing more stability. From these entropy, enthalpy and free energy changes, further mechanism of the complex formation can also be deducted as a future task. The order of stability is 1:1> 1:3> 1:2, which is justified with the suggested mechanism also.

References

1. R. J. H. Clark, *"The Chemistry of Titanium and Vanadium"*, Elsevier, Amsterdam (1968).
2. L.S. Ciezerko, E. M. Ciezerko, E.R. Harris, C.A. Lane, *Comp. Biochem. Physio.*, **8**, 137, (1963).
3. J.H. Swinehart, W.R. Biggs, D.J. Hallko, N.C. Schroeder, *Biol. Bull.*, **146**, 302 (1974).
4. W.E. Robinson, M.L. Aqu delo, K. Kustin, *Comp. Biochem. Physiol.*, **78A**, 667 (1984).
5. H. Mishibata, J. Hirata, U. Michiko, T. Namakumai, H. Sukurai, *J. Exp. Zool.*, **244**, 33 (1987).
6. D.H. Anderson, J. H. Swinehart, *Comp. Biochem. Physiol.*, **99A**, 585 (1991).
7. S. Lee, K. Kustin, W.E. Robinson, R.B. Frankel, K. Spartalin, *J. Inorg. Biochem.*, **33**, 183 (1988).
8. S.G. Brand, C.J. Hawkins, A.T. Marshal, G.W. Nette, L. Parry, *Comp. Biochem. Physiol.*, **93B**, 425 (1989).
9. E. Boeri, A. Ehrenberg, *Arch. Biochemistry, Biophys.*, **50**, 404 (1954).
10. L.T. Rezaeva, *Fed. Proc. Transl. Suppl.*, **24**, 836 (1964).
11. R.M.K. Karlson, *Proc. Natt. Acad. Sci. U.S.A.*, **72**, 2217 (1975).
12. T.D. Tullius, W.O. Gillium, R. M. K. Carlson, K.O. Hodgson, *J. Am. Chem. Soc.*, **102**, 5670 (1980).
13. P. Frank, B.Hedman, R.M.K.Carlson, A.L. Roc, K.O. Hodgson, *Biochem.*, **26**, 4975 (1987).
14. P. Frank, R.M.K. Carlson, K.O. Hodgson, *Inorg. Chem.*, 25, 470 (1980).
15. C.J. Hawkins, P. Kott, D.L. Parry, J.H. Swinhart, *Comp. Biochem. Physiol.*, **8**, 137 (1963).
16. D. Black, A. Hartshorn, *J. Coord. Chem. Rev.*, **9**, 219 (1972).
17. H. Shigeki, I. Takahiro, N. Yushin, *Chem. Pharm. Bull.*, **48**(5), 603 (2000).

18. H. A. Schroeder, J. J. Balassa, I. Tipton, *J. Chron. Dis.*, **16**, 1047 (1963).
19. Y. K. Grawal, *Bioinorganic Chemistry*, **9**, 369 (1978).
20. J. Mayerovish, P. Rolhenberg, Y. Shechter, W. Sussan. Bonner, C.R. Kahn, *J. of Chem. Invest.*, **87**, 1286 (1991).
21. M.D. Waters, *Toxicology of Vanadium*, In R.A. Goyer, A. Mehlman, Eds., *Toxicology of Trace metals*, John Wiley and Sons, New York, 147 (1977).
22. S. Ramandham, R.W. Brownsey, G. Cross, J. J. Mangold, J. H. McNeil, *Metabolism*, **38**, 1022 (1989).
23. M. N. Hughe, In "*Comprehensive Coordination Chemistry*", Wilkinson, G. Ed. Pergamon Press, Oxford, **6**, 666 (1987).
24. Y. Shechter, A. Shisheva, R. Lazar, J. Libmann, A. Shanzer, *Biochemistry*, **31**, 2063 (1992).
25. V. Kofman, S.A. Dikanov, A. Harn, J. Libman, A. Shanzer, D. Goldfarb, *J. Am. Chem. Soc.*, **117**, 383 (1995).
26. J.H. McNeil, V.G. Yuen, H.R. Hoveyda, C. Orvig, *J. Med. Chem.*, **35**, 1489 (1992).
27. L.R. Summerline, J.L. Ealy, *J. Chem. Demonstration*, ACS. Washington D.C. 105 (1985).
28. P. Caravan, G. Lucio, G. Nicholas, F, Geoffery Herring, Huali, H. M Li. John, J. R. Steven, A. S. IKA, Ed Shuter.; Sun. Yan S. T. Alan, G. Y. Violet, O. Chris, *J. Am. Chem. Soc.* **117**, 12759 (1995).
29. V. G. Yuen, C. Orvig, J. H. Can McNeill, *J. Physiol. Pharmacol.*, **73**, 55 (1995).
30. J.B. Neiland, "*Inorganic Biochemistry*" (Ed. G. Eishhorn), Elsevier, Amsterdam, 167 (1973).
31. K.N. Raymond, *Adv.Chem. Ser.*, **33**, 162 (1977).
32. J.B. Neiland, *Adv. Chem. Ser.*, **33**, 162 (1977).
33. "Vogel's Text Book of Quantitative Inorganic Analysis", 4th Ed. Longman, Inc., New York, (1978).