S.E. Kariper et al. / Hacettepe J. Biol. & Chem., 2014, 42 (3), 337–342

Theoretical Studies on Eight Oxovanadium(IV) Complexes with Salicylaldehyde and Aniline Ligands

Salisilaldehid ve Anilin Ligandlarını İçeren Sekiz Oksovanadyum(IV) Kompleksi Üzerine Teorik Çalışmalar

Sultan Erkan Kariper*, Koray Sayın, Duran Karakaş
Cumhuriyet University, Faculty of Science, Department of Chemistry, Sivas, Turkey

ABSTRACT

Eight oxovanadium(IV) complexes with five-coordinate consists of salicylaldehyde and anilines which their abbreviated representations are VO(sal-anl)$_2$ (1), VO(sal-clanl)$_2$ (2), VO(sal-mxyanl)$_2$ (3), VO(sal-ntranl)$_2$ (4), VO(brsal-anl)$_2$ (5), VO(brsal-clanl)$_2$ (6), VO(brsal-mxyanl)$_2$ (7), VO(brsal-ntranl)$_2$ (8) were optimized by using density functional theory (DFT) at B3LYP level with 6-31G and LANL2DZ basis sets in vacuum. Geometrical parameters, stretching frequencies and some quantum chemical parameters of all complexes were obtained from optimized structures. Bond distance and bond angle are not present in the literature were predicted with computational methods. The calculated V-O stretching frequencies of complexes were calculated at B3LYP method with 6-31G and LANL2DZ basis sets. The most compatible stretching frequencies with the experimental values were found with B3LYP/6-31G level. Some quantum chemical parameters were calculated to predict the biological activity ranking. Biological activity ranking of these complexes were found as (7) < (8) < (4) < (6) < (5) < (2) < (1) < (3)

Key words
Oxovanadium(IV) complexes, biological activity, computational chemistry

ÖZET

Kısaltılmış gösterimleri VO(sal-anl)2 (1), VO(sal-clanl)2 (2), VO(sal-mxyanl)2 (3), VO(sal-ntranl)2 (4), VO(brsal-anl)2 (5), VO(brsal-clanl)2 (6), VO(brsal-mxyanl)2 (7), VO(brsal-ntranl)2 (8) olan salisilaldehid ve anilin ligandlarını içeren beş koordinasyonlu sekiz oksovanadyum(IV) kompleksi gaz fazda B3LYP düzeyi 6-31G ve LANL2DZ temel seti içeren yoğunluk fonsiyon teorisi kullanılarak optimize edildi. Komplekslerin geometrik parametreleri, titreşim frekansları ve bazı kuantum kimyasal parametreleri optimize edilmiş yapılardan elde edildi. Literatürde deneysel bağ uzunlukları ve bağ açıları şimdiye kadar verilmediği için öngörüldü. Komplekslerin hesaplanan V-O bağ gerilmeleri frekansları B3LYP metodunda 6-31G ve LANL2DZ temel setleri ile hesaplandı. Deneysel verilerle en uyumlu bağ gerilme frekansları B3LYP/6-31G düzeyinde elde edildi. Bazı kuantum kimyasal parametreler biyolojik aktivite sırasını öngörmek için hesaplandı. Bu komplekslerin biyolojik aktiflik sıralaması (7)< (8) < (4) < (6) < (5) < (2) < (1) < (3) olarak belirlendi.

Anahtar Sözcükler: Oxovanadium(IV) kompleksleri, biyolojik aktivite, hesaplamalı kimya

Article History: Received: Jan 13, 2014; Revised: Jun 25, 2014; Accepted: Aug 24, 2014; Available Online: Sep 15, 2014.

Corresponding author: S.E. Kariper, Cumhuriyet University, Faculty of Science, Department of Chemistry, Sivas, Turkey
Tel: 0541 387 58 85 E-Mail: sultanerkan58@gmail.com

INTRODUCTION

Vanadium is an important element with regard to biological and pharmacological activity [1]. Vanadium complexes are the necessary for human body [2] and they are used for treating diabetes, low blood sugar, high cholesterol, heart disease and preventing cancer. Therefore vanadium complexes have attracted considerable interest in recent years. Especially, many varieties oxo-vanadium complexes with different coordination structures have been synthesized in order to reduce the side effects of drugs, increase the half-life of the compounds and prevent drug poisoning [3]. Furthermore, many clinical trials of vanadium compounds have also been reported [4–7]. In recent studies, quantum chemical methods related to chemical structures for their biological activities give information about drug design and medicinal chemistry [8-10]. Biological activities of the complexes are a function of quantum chemical descriptors. Quantum chemical parameter contributes to biological activities as negative or positive tendency.

Misra et al. have studied experimentally a series of oxovanadium(IV) complexes with Schiff bases ligand [11]. Five-coordinate oxovanadium(IV) complexes consists of salicylaldehyde (5-bromosalicylaldehyde) and anilines. The structures of these type complexes and their abbreviated representations were given in Figure 1.

The aim of this work for oxovanadium (IV) complexes given in Figure 1 is to determine the structural parameters, calculate stretching frequencies of V-O bonds and predict biological activity ranking by using some quantum chemical parameters, theoretically. Calculations were performed at B3LYP/6-31G and B3LYP/LANL2DZ levels in vacuum. The best optimized structures were determined according to V-O stretching frequencies. The structural parameters were obtained from these optimized structures. The quantum chemical descriptors which are highest occupied molecular orbital energy (E_{HOMO}), lowest unoccupied molecular orbital energy (E_{LUMO}), energy gap (ΔE), electronegativity (χ), electrophilicity (ω), chemical hardness (η), chemical potential (μ), chemical softness (σ) were used to determine the ranking of biological activities. Quantum chemical descriptors were calculated as below:

Energy gap (ΔE) $= E_{LUMO} - E_{HOMO}$

Electronegativity (χ) $= (E_{LUMO} + E_{HOMO})/2$

Electrophilicity (ω) $= \mu^2/2\eta$

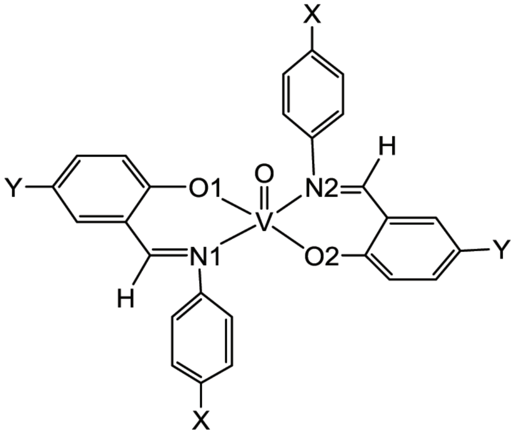
Chemical hardness (η) $= (E_{LUMO} - E_{HOMO})/2$

Chemical potential (μ) $= -\chi$

Chemical softness (σ) $= 1/\eta$

Computational method

The structures of all oxovanadium complexes were prepared with GaussView 5.0.8 [12]. The geometries were fully optimized by using Gaussian 09 Revision-A.02 [13] at DFT/B3LYP/6-31G and DFT/B3LYP/LANL2DZ levels for all atoms in the gas phase. DFT method is based upon a strategy of modeling electron correlation via general



(1) VO(sal-anl)$_2$	X=H	Y=H
(2) VO(sal-clanl)$_2$	X=Cl	Y=H
(3) VO(sal-mxyanl)$_2$	X=OCH_3	Y=H
(4) VO(sal-ntranl)$_2$	X=NO_2	Y=H
(5) VO(brsal-anl)$_2$	X=H	Y=Br
(6) VO(brsal-clanl)$_2$	X=Cl	Y=Br
(7) VO(brsal-mxyanl)$_2$	X=OCH_3	Y=Br
(8) VO(brsal-ntranl)$_2$	X=NO_2	Y=Br

Figure 1. Chemical structures of the oxovanadium (IV) complexes and abbreviated representations.

functionals of the electron density. The B3LYP Beke's three-parameter exchange-correlation hybrid functional with non-local correlation corrections, provided by Lee, Yang and Parr was used in calculations [14-17]. 6-31G basis set indicates that each inner shell STO is represented by a sum of six Gaussians and each valance shell STO is split into inner and outer parts described by three and one Gaussian primitives, respectively [18]. LANL2DZ basis set is used for post-third-row atoms. This basis set uses effective core potentials in calculations [19].

RESULT AND DISCUSSION

V-O stretching frequencies of complexes

Harmonic V-O stretching frequencies of oxovanadium complexes were calculated at B3LYP/6-31G and LANL2DZ levels in gas phase. This process was done to determine the structure compatible with experimental structure. Harmonic frequencies were scaled with 0.9620 for B3LYP/6-31G and 0.9257 for B3LYP/LANL2DZ levels [20]. Calculated stretching frequencies were listed in Table 1.

Table 1. The calculated and experimental V-O stretching frequencies (cm^{-1}) for studied complexes.

Complexes	Calc. Freq.		Exp. Freq.
	6-31G	LANL2DZ	
(1)	980	971	980
(2)	979	969	983
(3)	978	970	971
(4)	978	966	987
(5)	985	974	986
(6)	995	972	980
(7)	993	972	980
(8)	988	976	985

The calculated V-O stretching frequencies are compatible with experimental values. In other words, the harmony between experimental and theoretical values were determined with average differences (AD). Namely, the average differences decrease with increasing of harmony between the experimental and calculated values. The average difference is found as follows:

$$AD = \frac{\sum \left| \nu_{Calc} - \nu_{Exp} \right|}{n}$$

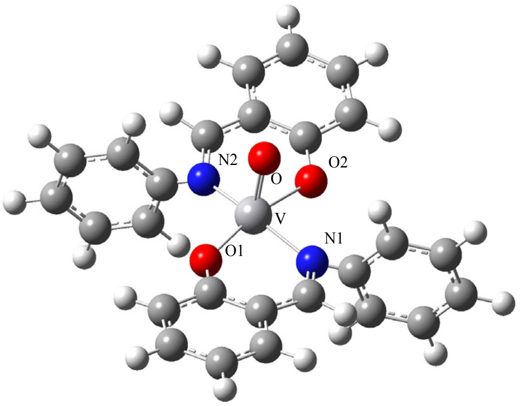


Figure 2. Optimized structure and atomic numbering scheme for complex (1).

where n is compound number. The average differences is 6.5 and 10.2 for 6-31G and LANL2DZ basis sets, respectively. Consequently, 6-31G basis set for optimized structures is more compatible than LANL2DZ.

Optimized Geometries

Structural parameters are not present in the literature for all complexes. Therefore, bond distances and bond angles for studied complexes were obtained with B3LYP/6-31G level from optimized molecular structures. Optimized molecular structure and atomic numbering scheme of complex (1) are presented in Figure 2.

Atomic numbering schemes are same and optimized molecular structures are similar for the other seven complexes. The selected structural parameters were listed in Table 2 for all complexes.

As shown in Table 2, V=O, V-O1 and V-O2 bond distances are 1.61, 1.91 and 1.91 Å for all complexes, respectively. Vanadium double-bonded oxygen is shorter than vanadium single-bonded oxygen. This is expected a situation because of theoretically double-bonded is shorter than single-bonded. V-N1 and V-N2 bond distances are 2.14 Å for all complexes.

O1-V-O2, N1-V-N2 bond angles are 180° in ideal square pyramidal geometry. Whereas these angles were approximately obtained as 127° and 163°, respectively. O1-V-N1, O2-V-N1, O2-V-N2 and O1-V-N2 angles are 90° in ideal square pyramidal geometry. These angles were approximately

Table 2. Structural parameters obtained at B3LYP/6-31G level for the type complexes $[VO(L)_2]$.

Distance(Å)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
V=O	1.62	1.62	1.62	1.62	1.61	1.61	1.61	1.61
V-O1	1.91	1.91	1.91	1.91	1.91	1.91	1.91	1.91
V-O2	1.91	1.91	1.91	1.91	1.91	1.91	1.91	1.91
V-N1	2.14	2.14	2.14	2.14	2.14	2.14	2.14	2.14
V-N2	2.14	2.14	2.14	2.14	2.14	2.14	2.14	2.14
Angle(°)								
O1-V-O2	126.6	126.7	126.2	127.0	126.8	126.8	126.4	127.4
N1-V-N2	162.7	162.9	163.2	162.7	162.6	162.9	163.1	162.6
O1-V-N1	85.9	85.9	86.0	85.9	85.9	85.9	86.0	86.0
O2-V-N1	86.3	86.4	86.4	86.4	86.3	85.9	86.4	86.4
O2-V-N2	85.9	85.9	86.0	86.4	85.9	85.9	86.0	86.0
O1-V-N2	86.3	86.0	86.4	86.4	86.3	86.4	86.4	86.4
O=V-O1	116.7	116.6	116.9	116.5	116.6	116.6	116.8	116.8
O=V-N1	98.7	98.5	98.4	98.6	98.7	98.6	98.4	98.4
O=V-O2	116.7	116.6	116.9	116.5	116.6	116.6	116.8	116.8
O=V-N2	98.6	98.5	98.4	98.6	98.7	98.6	98.4	98.4

found as 86° for all complexes. In addition, angles between atoms (O1, O2, N1 and N2) in square planer and V=O are 90° in ideal square pyramidal geometry. But O=V-N(1,2) and O=V-O(1,2) angles were obtained as 98° and 116°. These results indicate that vanadium(IV) center is not ideal square pyramidal. Namely, molecular geometries of all complexes are distorted square pyramidal.

When geometric parameters are examined, bond distances and bond angles of vanadium center are almost unchanged in all complexes. Whereas it is expected that bond distances and angles have changed with connecting the electron-withdrawing and electron-donor groups. Then, structural parameters do not effect biological activity of complexes. Because biological activities of complexes were found to be different.

Quantum chemical descriptors

Pharmacological activities of molecules depend on quantitative structure and this relationship is determined experimentally or computationally. Quantitative structure-activity relationships (QSAR) are expressed as a function of the molecular descriptors:

$$Activity = c_0 + c_1 d_1 + c_2 d_1^2 + c_3 d_2 + c_4 d_2^2 + \ldots$$

where d_i is the value of the descriptor and c_i is a coefficient calculated by fitting the data by regression analysis [18]. Quantum chemical descriptors are calculated with computational methods. In this study quantum chemical descriptors were obtained by using B3LYP/6-31G level in gas phase. They are listed in Table 3.

Experimental activity ranking (IC_{50} values) of oxovanadium (IV) complexes have been measured by Misra S. at all [11]. We know that biological activity is reduced with increasing of IC_{50} values. In that case, (3) and (4) have the highest and (7) has the lowest biological activity. Namely, biological activity ranking is as follows:

(7) < (8) < (5) < (2) < (1) < (3) = (4)

Biological activity ranking according to E_{LUMO}, (ΔE, η and $-\sigma$) and ω is as follows:

(8) < (4) < (6) < (5) < (7) < (2) < (1) < (3) (E_{LUMO})
(7) > (1) > (2) > (3) > (5) > (6) > (4) > (8) (ΔE, η, $-\sigma$)
(3) < (1) < (7) < (2) < (5) < (6) < (4) < (8) (ω)

The ranking of E_{HOMO}, χ and $-\mu$ for studied complexes are accordance with experimental ranking except for complex (4). The ranking of these descriptors is as follows:

(7) < (8) < (4) < (6) < (5) < (2) < (1) < (3)

Table 3. Quantum chemical descriptors* for all oxovanadium complexes.

Complex.	E_{HOMO}	E_{LUMO}	ΔE	χ	η	μ	σ	ω
(1)	-3.79	-1.89	1.90	-2.84	0.95	2.84	1.05	4.26
(2)	-3.93	-2.05	1.89	-2.99	0.94	2.99	1.06	4.74
(3)	-3.66	-1.81	1.85	-2.73	0.93	2.73	1.08	4.03
(4)	-4.68	-3.06	1.63	-3.87	0.81	3.87	1.23	9.22
(5)	-4.08	-2.24	1.84	-3.16	0.92	3.16	1.09	5.43
(6)	-4.34	-2.52	1.82	-3.43	0.91	3.43	1.10	6.45
(7)	-7.88	-2.15	5.73	-5.01	2.86	5.01	0.35	4.39
(8)	-4.86	-3.25	1.61	-4.05	0.80	4.05	1.24	10.22

*Quantum chemical descriptors are given in unit eV

This final ranking indicates that some descriptors are accordance with experimental ranking. A prediction was carried out for biological activity of complex (6) which its biological activity was not determined experimentally.

CONCLUSIONS

Eight oxovanadium (IV) complexes with salicylaldehyde and aniline ligands were studied at the B3LYP/6-31G and B3LYP/LANL2DZ levels in vacuum. Optimal basis set was determined as 6-31G level in terms of comparison the calculated stretching frequencies with experimental values. Bond distances and bond angles were calculated with optimal basis set. The structures of all oxovanadium complexes were found as distorted square pyramidal. Quantum chemical descriptors were calculated at the same basis set. The ranking for E_{HOMO}, $-\mu$ and χ was found to be consistent with experimental biological activity ranking.

ACKNOWLEDGMENTS

We are grateful the office of scientific research project of Cumhuriyet University (Project No: F-308 and F-372) for financial supports. This research was made possible by TUBITAK ULAKBIM, High Performance and Grid Computing Center (TR-Grid e-Infrastructure).

REFERENCES

1. D. S. Antal, C. A. Dehelean, C. M. Cancıu, M. Anke, Vanadium in medicinal plants: new data on the occurence of an element both esential and toxic to plants and man, Analele Universitii din Oradea, Fascicula Biologie, 2 (2009) 5.
2. B. Mukherjee, B. Patra, S. Mahapatra, P. Banerjee, A. Tiwari, M. Chatterjee, Vanadium – An Element of Atypical Biological Significance, Toxicology Letters, 150 (2004) 135.
3. H. Zhang, Y.Yi, D. Feng, Y.Wang, S. Qin , Hypoglycemic Properties of Oxovanadium (IV) Coordination Compounds with Carboxymethyl-Carrageenan and Carboxymethyl-Chitosan in Alloxan-Induced Diabetic Mice, Hindawi Publishing Corporation, 691067 (2011) 7.
4. A. B. Goldfine, D. C. Simonson, F. Folli, M.E. Patti, C.R. Kahn, Metabolic effects of sodium metavanadate in humans with insulin-dependent and noninsulin-dependent diabetes mellitus: in vivo and in vitro studies, The Journal of Clinical Endocrinology and Metabolism, 80 (1995) 3311.
5. N. Cohen, M. Halberstam, P. Shlimovich, Oral vanadyl sulfate improves hepatic and peripheral insulin sensitivity in patients with non-insulin dependent diabetes mellitus , Journal of Clinical Investigation, 95 (1995), 2501.
6. N. Cohen, , M. Halberstam, P. Shlimovich, C.J. Chang, H. Shamoon, L. Rossetti, Oral vanadyl sulfate improves hepatic and peripheral insülin sensitivity in patients with non-insulin dependent diabetes mellitus, J. Clin. Invest., 95 (1995) 2501.
7. K. Cusi, S. Cukier , R. A. DeFronzo , M. Torres, F. M. Puchulu, J. C. Redondo., Vanadyl sulfate improves hepatic and muscle insulin sensitivity in type 2 diabetes, Journal of Clinical Endocrinology and Metabolism, vol. 86 (2001) 1410.
8. D. Hadjipavlou-Litina, Review, reevaluation, and new results in quantitative structure-activity studies of anticonvulsants, Med. Res. Rev., 18 (1998) 91.
9. P. Gramatica, Principles of QSAR models validation: internal and external, QSAR Comb. Sci., 26 (2007) 694.
10. C. Hansch, A. Kurup, R. Garg, H. Gao, Chem-Bioinformatics and QSAR: A Review of QSAR Lacking Positive Hydrophobic Terms, Chem. Rev, 101 (2001) 619.

11. S. Misra, K.B. Pandeya, A.K. Tiwari, A.Z. Ali, T. Saradamani, S.B. Agawane, K. Madhusudana, Antihyperglycemic, α-glucosidase inhibitory and DPPH free radical scavenging activity of 5-bromosalicylaldehyde and Schiff bases, International J. Nut. Met., 4 (2011) 11.
12. K. Biernacki, A. Magalhães, C. Freire, M. Rangel, a DFT quantum mechanical study of 3-hydroxy-4-pyrone and 3-hydroxy-4-pyridinone based oxidovanadium(IV) complexes, Structural Chemistry, 22 (2011) 697.
13. C.D. Sherrill et. al, Advances in methods and algorithms in a modern quantum chemistry program package, Phys. Chem. Chem. Phys., 8 (2006) 3172.
14. A.D. Becke, Density-Functional Thermochemistry. III. The Role of Exact Exchange, J. Chem. Phys., 98 (1993) 5648.
15. A.D. Becke, Density-Functional Exchange-Energy Approximation With Correct Asymptotic-Behavior, Phys. Rev., 38 (1988) 3098.
16. C. Lee, W. Yang, R.G. Parr, Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density , Phys. Rev. B, 37 (1988) 785.
17. P.J. Stevens, F.J. Devlin, C.F. Chabalowski, M. J. Frisch, Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields, J. Chem. Phys., 98 (1994) 11623.
18. J.P. Lowe, K.A. Peterson, Elsevier, Quantum chemistry, third edition , Academic Press, 2006.
19. D. Karakaş, K. Sayın, DFT and TD-DFT studies on copper(II) complexes with tripodal tetramine ligands, Indian Journal of Chemistry, 52A (2013) 480.
20. D. Kumar, G.N. Sastry, S.P. de Visser, Steric Factors Override Thermodynamic Driving Force in Regioselectivity of Proline Hydroxylation by Prolyl-4-hydroxylase Enzymes, B. Karamzadeh, J. Phys. Chem. A, 114 (2010) 13234.