RESEARCH ARTICLE

Electrochemistry Study of Few Ru(II) and Zn(II)-Thione and Selone Complexes

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ABSTRACT

Hydrogen peroxide, as a byproduct of cellular respiration through incomplete reduction of oxygen yields deleterious free radicals through the Fenton reaction with iron (II/III) and Cu(I/II). Metals, such as ruthenium and zinc, are also capable of like- Fenton reaction and the production of the hydroxide radical responsible for oxidative DNA damage. This damage manifests itself through single-strand breaks in the DNA backbone corresponding to mutation and apoptosis of cells. Thus, recent research has focused on preventing this reaction through organometallic antioxidative methods. Sulfur and selenium antioxidant compounds like dmit, dmise, and methimazole coordinate to iron and other Fenton-like metal centers. Based on the electrochemistry study, the result of cyclic voltammetry can predict whether or not these metals compounds generate hydroxyl radicals when they meet hydrogen peroxide in body by figuring out their redox potentials. In this study, the electrochemical effects of these thione/selone ligands are determined through cyclic voltammetry with differing metal centers. Zinc complex redox activity was found to vary negligibly in changing solvent as well as scan speeds. In addition, ruthenium complexes from solvato complex precursors, their electrochemical peaks analyzed to prepare for reaction with hydrogen peroxide.

Keywords: Antioxidants, Cyclic voltammetry, Electrochemistry, Hydroxyl radical, Hydrogen peroxide. Redox potentials, Ruthenium complexes,

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INTRODUCTION

Recent antioxidant research has centered itself around the cellular phenomenon of metal-mediated oxidative DNA damage. Oxidation of iron ions can drive the reduction of cellular hydrogen peroxide to produce the hydroxide radical through the Fenton reaction.[1] When localized onto DNA, this reaction's impact is maximized through considerable oxidative DNA damage.[2] Other mimic iron metals capable of attaining multiple oxidation states such as chromium, cerium, zinc and ruthenium, are also capable of reducing hydrogen peroxide in a nearly analogous process to the Fenton reaction.[3,4] With that in context, these alternative systems can be used to better understand the mechanisms to prevent metal-mediated oxidative DNA damage.

On the other hand, sulfur and selenium and their compounds are responsible for multiple facets of healthy human physiology.[2,4] Both are found in several amino acids and derivatives such as cysteine and selenomethionine. When double bonded to a carbon atom as a thione/selone functional group in amino acids, these compounds have been utilized as thyroid medications.[2] In addition, research has utilized these compounds as antioxidants due to their scavenging of hydrogen peroxide as well as preventing metal-mediated oxidative DNA damage.[4,5] As shown in Figure 1 are three compounds of interest: dmit= N,N-dimethylimidazole thione, MMI= methimazole , and dmise, dmise = N,N-dimethylimidazole selone.

Ruthenium and zinc thione and selone complexes have been shown in previous studies to oxidize by hydrogen peroxide.[2,4,6,7] Though not related to free radical DNA damage, this reaction is intriguing as an analog to ruthenium and zinc thione and selone complexes reduction of hydrogen peroxide. Ruthenium solvato complexes, in which the metal is bound to a solvent such as acetonitrile, have been studied to simplify syntheses these complexes.[4, 8-10] In particular, acetonitrile –ruthenium

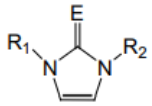

Figure 1: R_1, R_2, are $-CH_3$, E= S; dmit, E=Se; dmise, R_1= $-CH_3$, R_2= H, E= S; methimazole.

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complexes have received attention due to the simplicity of replacing the solvent ligands with various thione and selone compounds and vastly reducing the time incorporated with conventional synthesis.[9]

In this work, cyclic voltammetry studies can determine whether or not the redox potentials of the Ru(II/III/IV) in their complexes in or out the redox potentials range of the relative biomolecules (-0.32-0.460 V) such as NAD(P)H/NAD(P)$^+$ (-0.32 V versus NHE) and redox potential of hydrogen peroxide H_2O_2/OH + OH^-.[11] So, this study and based on the cyclic voltammetry studies results can suggest whether or not ruthenium as a mimic iron metal oxidized by hydrogen peroxide and generate hydroxyl radical and reduced by NADPH. In addition, and in order to determine the effects of changing scan speed, solvent system, and counter-ion that may contribute in redox potentials change, we also studied the cyclic voltammetry with various scan rates and in DMF and acetonitrile as solvents to figure out change on the redox potential values based on changing solvent, scan rate and changing the counter ions.

EXPERIMENTAL METHOD

Zinc thione and selone complexes that include $Zn(Dmit)_2Cl_2$ (**1**), $Zn(Dmise)_2Cl_2$ (2), $[Zn(dmit)_4][BF_4]_2$ (3), and $[Zn(demise)_4][BF_4]_2$ (4) have been synthesized and characterized according to the procedure that described by Stadelman *et al.*[2] $RuCl_2(DMSO_4)$ was synthesized as reported.[10] While $[Ru(NCCH_3)_6][BF_4]_2$ was synthesized as a description procedure by Abbas *et al.*[9] All the rest ruthenium thione and selone were synthesized based on the stoichmetric mole of ligand using $RuCl_2(DMSO_4)$, $[Ru(NCCH_3)_6][BF_4]_2$, and $RuCl_3.xH_2O$ as a starting materials with similar conditions of ruthenium thion and selone complexes.

Electrochemical measurements Cyclic voltammetry (CV) experiments were carried out electrode in chemistry department laboratory, Clemson university, Clemson, SC 29634-0973, USA. using CHI Electrochemical analyzer, employed a three-electrode cell consisting of a glassy carbon working electrode, an Ag/AgCl reference electrode, and a platinum wire auxiliary. zinc CV experiments were conducted in both acetonitrile and dimethylformamide with 1.0 mM complex and 10.0 mM tetra-n-butyl ammonium hexafluorophosphate (TBAPF6) as a supporting electrolyte at varying scan speeds (0.025, 0.05, and 0.1 V/s) from -1.60 to 1.60V. Ruthenium CV experiments were conducted in acetonitrile with 1.0 mM complex and 10.0 mM tetra-n-butyl ammonium hexafluorophosphate (TBAPF6) as a supporting electrolyte at a scan speed of 0.1 V/s from −1.60 to 1.60 V. Solutions were deoxygenated with dry nitrogen gas and maintained under a blanket of nitrogen during measurements. The measured potentials were corrected for junction potentials relative to ferrocenium/ferrocene (0.543 mV vs. Ag/AgCl).

RESULTS AND DISCUSSION

Cyclic Voltammetry of Zinc Complexes

Electrochemical shifts of previously synthesized zinc thione/selone complexes 1-4 were determined *via* cv with different scan rates in Figures 2-3. Additional analysis was conducted in order to determine the effects of changing scan speed, solvent system, and counter-ion. The results for each species are found in Table 1. In most trials, increasing scan speed did

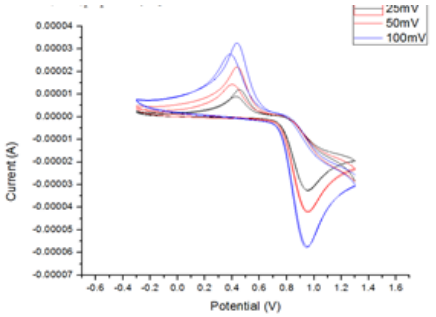

Figure 2: Cyclic voltammograms (in MeCN) vs. Ag/AgCl of $Zn(dmit)_2Cl_2$ (1mM). Scan window 1.1V to -0.5V. Sample Interval (V) = 0.001, Quiet Time (sec) = 5, Sensitivity (A/V) = 1e-5, 4 segments.

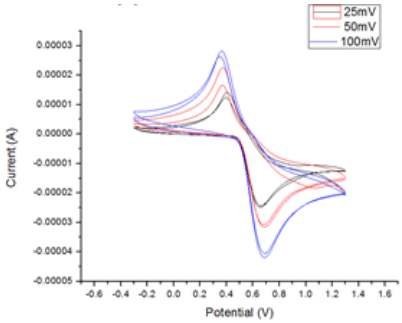

Figure 3: Cyclic voltammograms (in MeCN) vs. Ag/AgCl of $Zn(dmise)_2Cl_2$ (1mM). Scan window 1.1V to -0.5V. Sample Interval (V) = 0.001, Quiet Time (sec) = 5, Sensitivity (A/V) = 1e-5, 4 segments.

Table 1: Electrochemical potentials (vs. NHE) for the tested Zn (II) complexes.

Compound		*In DMF*			*InMeCN*		
		25 mV	*50 mV*	*100 mV*	*25 mV*	*50 mV*	*100 mV*
1.	Epc	0.489	0.48	0.473	0.453	0.437	0.435
	Epa	---	1.034	1.08	0.953	0.956	0.952
	E	---	0.554	0.607	0.500	0.519	0.517
	E1/2	---	0.757	0.776	0.703	0.696	0.694
2.	Epc	0.434	0.420	0.400	0.404	0.373	0.364
	Epa	0.800	0.826	0.831	0.660	0.686	0.685
	E	0.366	0.406	0.431	0.256	0.313	0.321
	E1/2	0.617	0.623	0.616	0.532	0.530	0.524
3.	Epc	0.490	0.469	0.447			
	Epa	1.025	1.032	1.047			
	E	0.535	0.563	0.600			
	E1/2	0.758	0.751	0.747			
4.	Epc	0.412	0.392	0.380			
	Epa	0.799	0.816	0.815			
	E	0.387	0.424	0.435			
	E1/2	0.606	0.606	0.598			

not greatly change the overall redox potential but did slightly alter the individual oxidation and reduction potentials. Overall, each complex shows a quasi-reversible redox couple for their respective ligand.

The CV for 1 exhibit mixed results, when examined by solvent system as the positive trend of potential with increasing scanning speed in DMF, is not matched by MeCN, perhaps owing to solubility constraints due to differing polarities of these solvents. Complex 2, however, does not show any trending at all, as, although the ΔE value increases with increasing scanning speed, the redox potential remains relatively unchanging at about 0.620 V in DMF and 0.528 V in MeCN. These differences in peak potential for the respective solvents, though greater for the dmise complex, likely amount to considerations of the nature of the given solvent. However, the nature of the ligand in solution may determine the electrochemical impact of the solvent system (Figure 4).

Complexes 1 and 3 are electrochemically comparable in DMF, their only difference being their stabilizing counter-ion. Overall, the data does not appear to indicate that either drastically alters the redox potential of the dmit ligand. The dichloro-bound complex 1 yielded a peak potential (though impacted by poor resolution at 25 mV) of around 0.767 V while the tetrafluoroborate-bound complex **3** exhibits a potential on average of 0.752 V. Though it is not a remarkable result, this discrepancy may indicate a change in ligand redox potentials in response to stoichiometric coefficients. This effect would be important to note in future trials, as the differing stoichiometry of the solvato precursors may need to be taken into account when analyzing the electrochemistry of its substituted derivatives (Figure 5).

Comparing the redox potential of the dmise ligand found in complexes 2 and 4, when assessing the impact of counter-ion, exhibits nearly parallel results. Once more, the dichloro complex exhibits a higher potential (0.618 V) than did the tetrafluoroborate complex (0.603 V). Interestingly, or perhaps coincidentally, the difference between the average potentials of each complex at the examined scan rates are equal. Though a small sample size, additional samples that repeated this trend could indicate a concrete relationship for standardizing results be-tween counter-ions. Though that seems unlikely given the differences between the dmit and dmise ligands, perhaps the metal coordination at C2 of each ligand negates the differing redox activities of sulfur and selenium. At any rate, given these results, no conclusions can be made regarding the effects of a differing counter-ion on either ligand's electrochemical potential.

Cyclic Voltammetry of Ruthenium Complexes

Electrochemical shifts of several ruthenium complexes formed from complexes produced from precursors were calculated by CV except Ru[NOCl](dmise)BF_4 and Ru[NOCl](dmit)BF_4 complexes that were studied before and mentioned just for comparison as shown in Table 2. Also, with different scan rates 50, 100, and 200 mV, cyclic voltmagrams for these complexes have been studied, Table 2. For multiple complexes, there

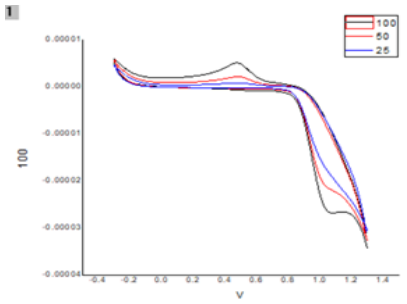

Figure 4: Cyclic voltammograms (in DMF) vs. Ag/AgCl of $Zn(dmit)_2Cl_2$ (1mM). Scan window 1.1V to -0.5V. Sample Interval (V) = 0.001, Quiet Time (sec) = 5, Sensitivity (A/V) = 1e-5, 4 segments.

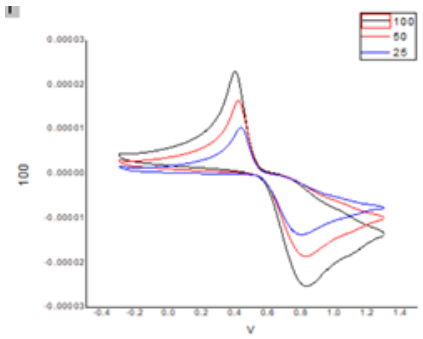

Figure 5: Cyclic voltammograms (in DMF) vs. Ag/AgCl of $Zn(dmise)_2Cl_2$ (1mM). Scan window 1.1V to -0.5V. Sample Interval (V) = 0.001, Quiet Time (sec) = 5, Sensitivity (A/V) = 1e-5, 3 segments.

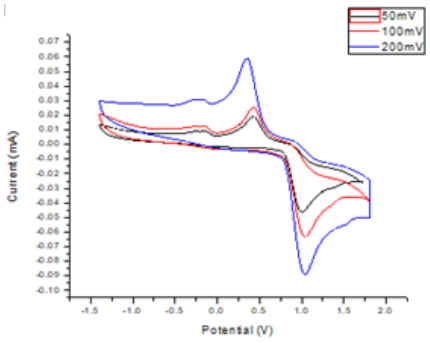

Figure 6: Cyclic voltammograms (in DMF) vs. Ag/AgCl of $Zn(dmit)_4(BF_4)_2$ (1mM). Scan window 1.1V to -0.5V. Sample Interval (V) = 0.001, Quiet Time (sec) = 5, Sensitivity (A/V) = 1e-5, 4 segments.

Table 2: Electrochemical potentials (vs. NHE) for the tested Ru[NOCl] $(dmit)_4]BF_4$(**5**), and Ru[NOCl]$(dmise)_4BF_4$ (**6**) complexes.

Compound		*In MeCN*		
		50 mV	*100 mV*	*200 mV*
5.	Epc	-0.689	-0.693	-0.704
	Epa	1.240	1.310	1.371
	E	1.929	2.003	2.075
	E1/2	0.965	1.001	1.037
6.	Epc	-0.440	-0.443	-0.457
	Epa	1.210	1.170	1.130
	E	1.646	1.613	1.587
	E1/2	0.823	0.806	0.793

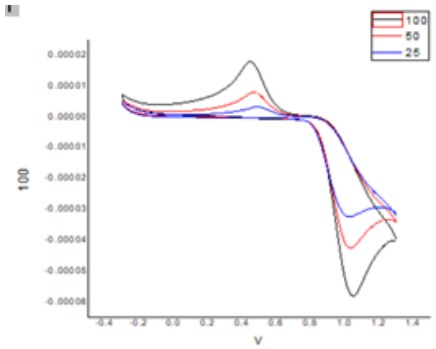

Figure 7: Cyclic voltammograms (in MeCN) vs. Ag/AgCl of Ru[NOCl](dmit)$_4$]BF_4 (1mM). Scan window 1.1V to -0.5V. Sample Interval (V) = 0.001, Quiet Time (sec) = 5, Sensitivity (A/V) = 1e-5, 4 segments.

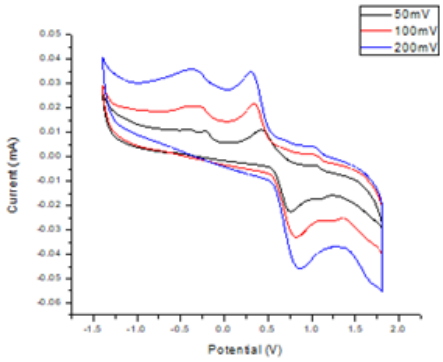

Figure 8: Cyclic voltammograms (in MeCN) vs. Ag/AgCl of Ru[NOCl](dmise)$_4$]BF_4 (1mM). Scan window 1.1V to -0.5V. Sample Interval (V) = 0.001, Quiet Time (sec) = 5, Sensitivity (A/V) = 1e-5, 4 segments.

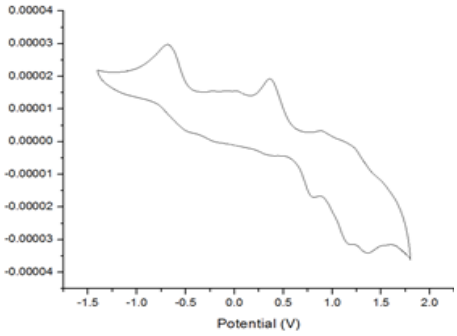

Figure 9: Cyclic voltammogram (CV) for [Ru(MMI)$_6$]Cl_3

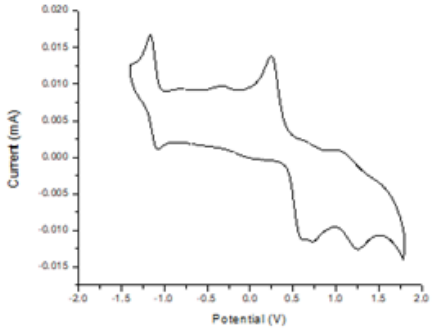

Figure 10: CV for $RuCl_2$(dmit)$_4$.

were indiscriminate peaks at potentials greater than 0.0 V Table 3. While it is assumed that these peaks are indicative

Table 3: Electrochemical potentials (vs. NHE) for the tested Ru complexes. Values shown indicate Ru(II)→Ru(III) redox cycling unless noted by ligand in the complex

Complex	*Epc*	*Epa*	*ΔE*	*E1/2*
	(V)	*(V)*	*(V)*	*(V)*
Ru[MeCN]$_6$(BF_4)$_2$	-0.599	-0.157	0.442	-0.378
Ru[NOCl](dmise)BF_4[4]	-0.457	-0.721	-0.264	-0.589
Dmise[2]	0.431	0.783	0.352	0.607
Ru[NOCl](dmit)BF_4[4]	-0.689	1.240	1.929	0.965
Dmit[2]	1.009	1.036	0.027	1.022
Ru(MMI)$_6Cl_3$	-0.579	-0.649	-0.070	-0.614
MMI	0.463	0.691	0.228	0.577
Ru[MeCN]$_5$(dmit)(BF4)$_2$	-0.509	-0.625	-0.116	-0.567
$RuCl_2$(dmit$_4$)	-0.569	-0.625	-0.056	-0.597
$RuCl_2$(DMSO)$_4$	-0.657	-0.683	-0.026	-0.670
Ru[MMI]$_6$(BF_4)$_2$	-0.605	---	---	---

of ligand redox cycling, differing amounts of secondary peak potentials are likely due to stoichiometric differences or possible ruthenium cycling at higher oxidation states. In certain compounds, high resolution peaks were observed through positive and negative DPV, and these peaks were assumed to indicate the ligand in complex. For these instances, the ligand electrochemical potentials were calculated (Figure 6).

Upon immediate review, the point of interest is the irreversibility of the ruthenium cycling. In all complexes, barring the hexakis acetonitrile complex used as a control of sorts, the $Ru^{3+/2+}$ reduction potential ranges between -0.670 V and -0.567 V. The extent of these complexes' irreversibility, when com-pared to the aforementioned "control" is much greater, yet no definitive conclusions as to the reasoning behind that can be made, as there are no direct hexaxis ligands (data for the final complex was marred by low resolution DPV peaks). However, knowing that the standard reduction potential of ruthenium is quasi-reversible, it can be reasoned that the coordination to each ligand has altered the metal such that its rate of electron transfer is much lower than as a free ion. Additional trials, particularly upcoming reactions with hydrogen peroxide, will develop a bet-ter understanding of whether this change in reduction potential is correspondent to a decreased ability to perform the Fenton-like reaction, or if the electrochemistry of ruthenium is such that the ligand does not completely prevent its propensity to redox cycle (Figure 7-10).

CONCLUSIONS

Previously studied zinc complexes and novel ruthenium thione/selone complexes synthesized from ruthenium solvato molecules through the displacement of solvent ligands were characterized, and their electrochemical shifts determined through cv. Zinc complex data indicates a slightly higher reduction potential for the dichloro complexes and shows a differing reduction potential on the basis of solvent system.

Cv data of the ruthenium complexes offer mixed results. In all complexes, the redox cycling of Ru(II) to Ru(III) was observed. However, in more intricate molecules, solvent

system interactions as well as the nature of the individual ligands in solution resulted in indiscriminate peak potentials that may either correspond to the redox cycling of the ligand, or perhaps an additional redox cycle for ruthenium, Ru (III) to Ru (IV), for instance. Further experiments will be pursued to fully understand the redox shifts present in the ruthenium and the bound ligands. Comparison values for each species will allow for an understanding of how these complexes alter the individual activity of their constituents in solution.

The substitution of solvent ligands with antioxidative ligands offers a variety of possibilities for further syntheses with varying ratios of solvent to a ligand. Additionally, improved syntheses of the substituted solvato complexes may yield higher resolution voltage potentials and negate the possible impacts of impurity or incomplete decomposition. Finally, further electrochemical analysis following reaction with hydrogen peroxide will elucidate the mechanisms behind Fenton-like reactions with oxometallates and assess the thione/selone ligands efficacy in preventing these reactions through the tuning mechanism when bound to ruthenium.

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REFERENCES

1. Angelé-Martínez C, Goodman C, Brumaghim J. Metal-mediated DNA damage and cell death: mechanisms, detection methods, and cellular consequences. Metallomics. 2014 Aug;6(8):1358-81.
2. Stadelman BS. Synthesis, Characterization, and Reactivity of Iron (II)-and Zinc (II) Complexes of Imidazole Thione and Selone Ligands: Investigations into Oxidation Mechanisms.
3. Bokare AD, Choi W. Review of iron-free Fenton-like systems for activating H2O2 in advanced oxidation processes. Journal of hazardous materials. 2014 Jun 30;275:121-35.
4. Abbas MA. Synthesis, Characterizations, and Study of the Antioxidant Activity of Novel Ruthenium-Thione and-Selone Complexes (Doctoral dissertation, Clemson University).
5. Battin EE, Zimmerman MT, Ramoutar RR, Quarles CE, Brumaghim JL. Preventing metal-mediated oxidative DNA damage with selenium compounds. Metallomics. 2011 May;3(5):503-12.
6. Chatterjee D, Ember E, Pal U, Ghosh S, van Eldik R. Kinetics and mechanism of the [Ru III (edta)(H 2 O)]−-mediated oxidation of cysteine by H 2 O 2. Dalton Transactions. 2011;40(41):10997-1004.
7. Underwood CC, Stadelman BS, Sleeper ML, Brumaghim JL. Synthesis and electrochemical characterization of [Ru (NCCH3) 6] 2+, tris (acetonitrile) tris (pyrazolyl) borate, and tris (acetonitrile) tris (pyrazolyl) methane ruthenium (II) complexes. Inorganica Chimica Acta. 2013 Aug 24;405:470-6.
8. Walker JM, McEwan A, Pycko R, Tassotto ML, Gottardo C, Th'ng J, Wang R, Spivak GJ. [Tris (pyrazolyl) methane] ruthenium complexes capable of inhibiting cancer cell growth.
9. Abbas MA, McMillen CD, Brumaghim JL. Synthesis, characterization, and structures of ruthenium (II) complexes with multiple solvato ligands. Inorganica Chimica Acta. 2017 Nov 1;468:308-15.
10. Pierre JL, Fontecave M. Iron and activated oxygen species in biology: the basic chemistry. Biometals. 1999 Sep 1;12(3):195.