A Semi-Empirical Study on Metal Ion/Murexide Complexation

N. Zeynep ATAY and Tereza VARNALI
Boğaziçi University, FEF, Department of Chemistry,
Bebek 80815, Istanbul-TURKEY
e-mail: varnali@boun.edu.tr

Modeling of the metal ion/ligand complexation reactions between divalent metal cations (M^{2+}) and hydrophilic tridentate ligand murexide (Mu^-) in water, water+glycerol, and in glycerol was carried out. Kinetic studies showed that the rate of the reaction is very dependent on the metal ion, with $Zn^{2+} > Ni^{2+}$, but, reactions are slower in dispersed glycerol than in dispersed water. Theoretical calculations, which have shown a metal ion dependence, were consistent with the experimental observations. The entropy values calculated in all solvents were negative and were similar in value, indicating that these spontaneous reactions are enthalpy driven.

Key Words: Murexide, complexation, glycerol, metal ion.

Introduction

Computational chemistry has recently introduced the improved reaction field theory and now is capable of evaluating the bulk solvent effect quite accurately. It is time to expand this capability to mixed solvents, as it is often extremely useful through is still not well understood. For example, the determination of rates of complexations of divalent metal ions with a tridentate metal-ion indicator dye murexide (Figure 1) in water are greatly affected by the addition of glycerol. This empirical technique of using the mixed solvent water-glycerol in the determination of metal ion/ligand complexation rate constants has been used extensively. The kinetics of the complex formation have been explained in terms of an exchange of solvent molecules from the inner-coordination sphere of metal ions with the ligand in the outer sphere. It is not, however, clear how this exchange changes when mixed solvents are used. We undertook a preliminary study of the atomistic details of the ligand-solvent exchange equilibrium between the inner and outer coordination spheres of the metal ion by using a semi-empirical approach with the purpose of gaining guidelines to model the coordination sphere of solvation. Computational chemistry offers the opportunity to explain preferential solvation in terms of energetics.
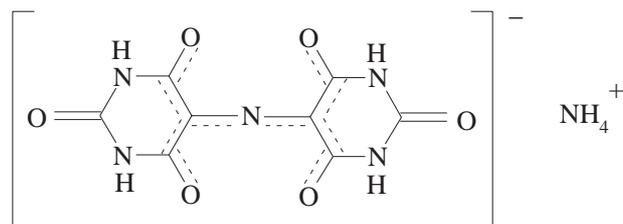
Figure 1. Murexide

In order to understand the effects of mixed solvation, the complexation reaction between divalent metal cations (M^{2+}) and the hydrophilic tridentate ligand murexide (Mu^-) were modeled in water, glycerol+water, and glycerol. Kinetics studies of this reaction in both bulk and dispersed media have been studied previously[1-10]. A schematic representation of metal ion/murexide complex is given in Figure 2. For aqueous systems, the reaction scheme, both in bulk water and in water droplets that are dispersed in an oil-continuous medium in the presence of a surfactant, has been shown to be consistent with the following mechanism[1-5]:
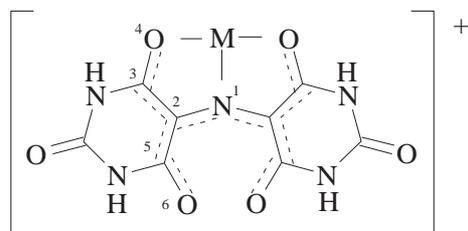
Figure 2. Model of a M^{2+}/Mu^- complex

$$M^{2+}(H_2O)_6 + Mu^- \xrightarrow{K_{as}} (M^{2+}(H_2O)_6/Mu^-) \xrightleftharpoons{K_{ex}} (M(H_2O)_5Mu)^+ + H_2O$$

$$\textbf{(1) outer-sphere complex} \qquad \textbf{(2) inner-sphere complex} \tag{1}$$
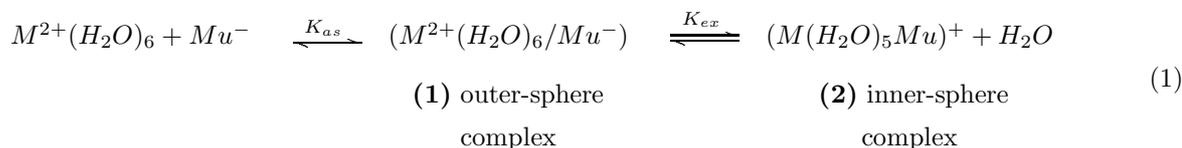
Step **(1)** is a rapid pre-equilibrium step, step **(2)** is rate limiting, with the result that

$$k_f = K_{os}k_{ex} \tag{2}$$

where $k_f/$ dm^{3}mol^{-1}s^{-1} is the second-order rate constant for the overall forward reaction, $k_b/$ s^{-1} is the rate constant for the back reaction (dissociation of murexide from $(MMu)^+$), $K_{os}/$ dm^{3}mol^{-1} is the association equilibrium constant for outer-sphere complex formation, and $k_{ex}/$ s^{-1} is identified with the rate constant for exchange of a solvent (water) molecule between the solvation shell of the metal ion and bulk water. Ring closure to form the inner-sphere complex is normally considered to be rapid. It is generally assumed that three water molecules are released during the formation of the final inner-sphere complex with murexide in water, with the release of the first one associated with k_{ex}.

Unfortunately, due to the high viscosity of glycerol, no comparable reactions (i.e. metal ion/murexide complexation) had been followed in bulk glycerol as solvent. It has been shown that the problems arising from the high viscosity of glycerol in studies of reaction kinetics in bulk glycerol can be successfully overcome if glycerol is dispersed in an oil-continuous medium[10]. It has also been shown that glycerol behaves in a

similar manner to water when dispersed in an alkane phase in the presence of a surfactant[11]. It can be assumed that one glycerol molecule, which solvates the metal ion as a tridentate ligand, is released during the formation of the final inner-sphere complex with murexide.

$$M^{2+}(Gly)_2 + Mu^- \rightleftharpoons (M^{2+}(Gly)_2/Mu^-) \longrightarrow (M(Gly)Mu)^+ + Gly \tag{3}$$
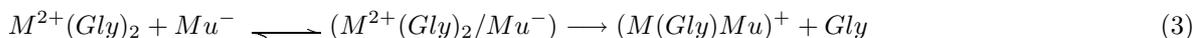
Similarly, reactions have been followed in "mixed" dispersions in which the reaction medium was a 1:1 v/v mixture of glycerol and water[10]. Amongst the possibilities are a) loss of three water molecules as a result of complex formation with murexide:

$$M^{2+}(H_2O)_3(Gly) + Mu^- \longrightarrow (M(Gly)Mu)^+ + 3H_2O \tag{4}$$

And
b) loss of one glycerol molecule:

$$M^{2+}(H_2O)_3(Gly) + Mu^- \longrightarrow (M(H_2O)_3Mu)^+ + Gly \tag{5}$$

Kinetic results seem to support the fact that the reaction mechanism in bulk and dispersed water, as well as dispersed glycerol and dispersed glycerol+water, is consistent with the Eigen-Tamm mechanism[1,2], in which the "solvated" metal ion and the ligand first form an outer-sphere complex in a fast pre-equilibrium step. This is then followed by the rate-determining solvent exchange from the metal ion. It has been observed that the rate of the reaction is very dependent on the metal ion, with $Zn^{2+} > Ni^{2+}$, in all the above systems[3]. Reactions have been found to be slower in dispersed glycerol when compared with dispersed water[10].

Bulk glycerol is assumed to act as a tridentate ligand when solvating metal ions[12]. Our calculations, however, are based on a model which allows glycerol to behave as a mono-, bi- or a tridentate ligand.

Modeling and Computational Details

Semiempirical molecular orbital calculations were carried out on all the species involved in this study using the HyperChem series of programs[13]. The method employed throughout was ZINDO/1, which is commonly used for the calculation of the energy states of transition metals. All structures were fully optimized.

Metal ions were solvated by six H_2O molecules, with the initial structure being a regular octahedron (Figure 3). Glycerol-solvated metal ions were modeled with glycerol acting as a tridentate ligand, occupying three positions of a regular octahedron around the metal ion (Figure 4). In the case of mixed solvation with both water and glycerol, glycerol was again placed in three positions of the octahedron, with H_2O molecules occupying the remaining three positions, $(H_2O)_3(Gly)$. The series with glycerol acting as a bidentate ligand, with four H_2O molecules around the metal ion, i.e. $(H_2O)_4(Gly)$, as well as glycerol as a monodentate ligand with five H_2O molecules around the metal ion, i.e. $(H_2O)_5(Gly)$, were also modeled to account for the reduced coordination of glycerol.

$$
\begin{array}{c}
\text{OH}_2 \\
\text{H}_2\text{O} \diagdown \quad | \quad \diagup \text{OH}_2 \\
\text{M} \\
\text{H}_2\text{O} \diagup \quad | \quad \diagdown \text{OH}_2 \\
\text{OH}_2
\end{array}
$$
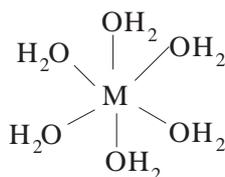
Figure 3. Model of a $M^{2+}(H_2O)_6$ complex
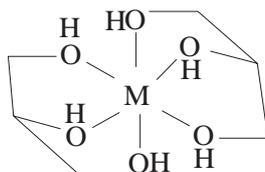
Figure 4. Model of a $M^{2+}(Gly)_2$ complex

The heat of the reactions, ΔH_R^0, have been calculated to be $(\Delta H_f^0)_{products}$ - $(\Delta H_f^0)_{reactant}$, where ΔH_f^0 is the standard heat of formation. Hence, a metal ion forming an inner-sphere complex with one Mu^- and three H_2O molecules can be calculated as in the following example:

$$\Delta H_R^0 = [\Delta H_f^0(M^{2+}Mu^-(H_2O)_3) + 3\Delta H_f^0(H_2O)] - [\Delta H_f^0(M^{2+}(H_2O)_3) + \Delta H_f^0(Mu^-)] \tag{6}$$

Results and Discussion

"Free" murexide delocalized π-electrons between the two rings and the bridging nitrogen (i.e. along the O_4-C_3-C_2-C_5-O_6-N_1 link in both rings). As mentioned previously, murexide takes the conformation seen in Figure 2 after complexation with a metal ion. Its geometrical parameters and Mulliken charges that undergo a significant change upon complexation are tabulated in Table 1. It was observed that Ni^{2+} received less electrons compared to Zn^{2+}, and hence acquired a more positive charge. There is an electron depletion of the oxygens on the 6-position (O_6), i.e. the ones that are not involved in the complexation, accompanied by a flow of electrons toward the "bonding" oxygens (O_4) and the nitrogen, (N_1). The most drastic change is observed on the central nitrogen where a positive charge is changed to negative. This delocalization of electrons is indicative of a complex formation. It is satisfying to see that the use of computational chemistry has allowed us to take a closer look at the complex at the molecular level, which one is unable to do under experimental conditions.

Table 1. Geometrical parameters (in Å) and Mulliken charges (q) of Mu^-, $(NiMu)^+$ and $(ZnMu)^+$

	Mu^-	$(NiMu)^+$	$(ZnMu)^+$
Geometrical parameters (in Å):			
C_3-O_4	1.22	1.33	1.34
C_2-C_3	1.46	1.43	1.46
N_1-C_2	1.34	1.41	1.45
M-N_1	-	1.84	2.02
O_4-M	-	1.87	2.07
Mulliken Charges:			
q_M	-	0.331	0.309
q_{N1}	0.276	-0.199	-0.270
q_{O4}	-0.390	-0.310	-0.295
q_{C3}	0.344	0.437	0.436
q_{C2}	-0.440	-0.065	-0.041
q_{C5}	0.344	0.335	0.340
q_{C6}	-0.385	-0.100	-0.095

The heats of formation, $\Delta H_f^0/\text{kcal mol}^{-1}$, of Mu^-, water, glycerol (Gly) and divalent metal ions Ni^{2+} and Zn^{2+}, as well as their coordinated forms, are given in Tables 2 and 3, respectively. Using these results,

the heat of the reactions, ΔH_R^0/kcal mol^{-1}, for all possible $M^{2+} + X \rightarrow M^{2+}X$ type reactions involving Ni^{+2} and Zn^{2+} with $X = H_2O$, Gly, and Mu^- were calculated and tabulated in Table 4. For both metal ions, the absolute value of ΔH_R^0 for the formation of the following products increases in the order:

$$M^{2+}(H_2O) < M^{2+}(Gly) < M^{2+}(Mu^-)$$
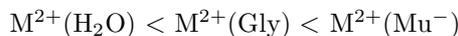
This indicates a favorable attraction of metal ion to glycerol compared to water. Complexation with the ligand is even more preferred.

Table 2. ΔH_f^0 values of all "single" species involved in modeling.

Molecule or Ion	ΔH_f^0/kcal mol^{-1}
Mu^-	-4956.6
H_2O	-207.9
Ni^{2+}	684.5
Zn^{2+}	653.1
Gly	-2100.5

Table 3. ΔH_f^0/kcal mol^{-1} values of complexes involved in modeling

Complex	$M^{2+} = Ni^{2+}$	$M^{2+} = Zn^{2+}$
$M^{2+}(H_2O)$	283.9	240.1
$M^{2+}(H_2O)_2$	-98.0	-162.9
$M^{2+}(H_2O)_3$	-435.4	-534.6
$M^{2+}(H_2O)_4$	-759.5	-879.2
$M^{2+}(H_2O)_5$	-1056.9	-1180.4
$M^{2+}(H_2O)_6$	-1334.7	-1473.4
$M^{2+}(Gly)$	-1871.6	-2023.0
$M^{2+}(Gly)_2$	-4268.7	-4512.4
$M^{2+}(Gly)(H_2O)_3$	-2806.2	-3019.4
$M^{2+}(Gly)(H_2O)_4$	-3077.1	-3321.1
$M^{2+}(Gly)(H_2O)_5$	-3365.6	-3603.6
$M^{2+}(Mu^-)$	-5118.9	-5282.8
$M^{2+}(Mu^-)(H_2O)$	-5416.8	-5659.5
$M^{2+}(Mu^-)(H_2O)_2$	-5686.1	-6051.9
$M^{2+}(Mu^-)(H_2O)_3$	-5946.2	-6546.5
$M^{2+}(Mu^-)(Gly)$	-7416.6	
$M^{2+}(Mu^-)_2$	-10572.7	

Table 4. ΔH_R^0/kcal mol^{-1} values of complex formation

Reaction	$M^{2+} = Ni^{2+}$	$M^{2+} = Zn^{2+}$
$M^{2+} + H_2O \rightarrow M^{2+}(H_2O)$	-192.7	-205.2
$M^{2+} + Gly \rightarrow M^{2+}(Gly)$	-455.5	-575.7
$M^{2+} + (Mu^-) \rightarrow M^{2+}(Mu^-)$	-846.7	-979.3

The ΔH_R^0 / kcal mol^{-1} values for the exchange of solvent at the metal ions are summarized in Table 5. Computational chemistry allows us to model mixed solvation of the metal ion by using different combinations of solvent binding with both water and glycerol molecules. Six water molecules, initially in

the inner coordination sphere, were replaced by a glycerol molecule that could act as a mono-, a bi-, or even a tridentate ligand, which are impossible to distinguish between under experimental conditions. Comparing the values of enthalpy in Table 5 suggests that the monodentate binding of glycerol in the case of mixed solvation is preferred.

Table 5. ΔH_R^0/kcal mol^{-1} values for solvent exchange at hexaquo or glyco metal complexes

Reaction	M^{2+} = Ni^{2+}	M^{2+} = Zn^{2+}
M^{2+}(H$_2$O)$_6$ + Gly → M^{2+}(H$_2$O)$_3$(Gly) + 3H$_2$O	5.5	-69.0
M^{2+}(H$_2$O)$_6$ + Gly → M^{2+}(H$_2$O)$_4$(Gly) + 2H$_2$O	-57.6	-162.8
M^{2+}(H$_2$O)$_6$ + Gly → M^{2+}(H$_2$O)$_5$(Gly) + H$_2$O	-138.2	-237.5
M^{2+}(H$_2$O)$_6$ + Mu$^-$ → M^{2+}(H$_2$O)$_3$(Mu$^-$) + 3H$_2$O	-278.4	-738.0
M^{2+}(Gly)$_2$ + Mu$^-$ → M^{2+}(Gly)(Mu$^-$)+ Gly	-291.8	

A further look at the results in Tables 3 to 5 confirms that the metal ion complexation with murexide is much more exothermic than that of metal ion/solvent complexations. In the case of a mixed solvent, ΔH_R^0 increases in the following order for both Ni^{2+} and Zn^{2+}:

$$M^{2+}(Gly)(H_2O)_5 < M^{2+}(Gly)(H_2O)_4 < M^{2+}(Gly)(H_2O)_3 < M^{2+}(Gly)_2$$
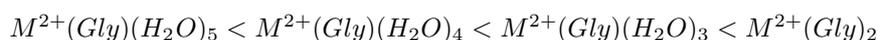
Hence, the loss of a H$_2$O molecule at a metal ion, solvated by both glycerol and H$_2$O, seems to be easier than the loss of a glycerol molecule.

It is not possible to compare the experimental and theoretical results directly. This is due to a) there are no empirical reaction enthalpies, and b) the quantum mechanical calculations refer to the gas phase. The presence of the solvent ligands in the complexes only partially accounts for the effects of the solvent medium.

Table 6. Calculation of ΔS_R^0 / cal K^{-1} mol^{-1} values for Ni^{2+}/Mu$^-$ complexation reaction in various solvent medium using theoretical ΔH_R^0 and experimental K results.

Solvent medium	K / dm^3 mol^{-1}	ΔG_R^0 / cal mol^{-1}	ΔS_R^0 /cal K^{-1} mol^{-1}
Bulk water	412	-3565	-922
Dispersed water	133	-2896	-923
Bulk water+glycerol	393	-3540	-919
Dispersed water+glycerol*	292	-3362	-920
Dispersed water+glycerol**	292	-3362	-941
Dispersed glycerol	1100	-4145	-962

* Three H$_2$O molecules are replaced by murexide in the end product.

** One glycerol molecule is replaced by murexide in the end product.

The thermodynamic equilibrium constants (K_{thermo}) for Ni^{2+}/Mu$^-$ complexation reactions have been observed and were found to be in good agreement with the kinetic equilibrium constant K_{kin} (K_{kin}= k_f/k_b)[10]. These values have been used in the calculations of Gibbs free energy of Ni^{2+}/Mu$^-$ complexation reactions, ΔG_R^0 (where ΔG_R^0 = -RTln$K$), in bulk and dispersed media. The empirical data for the Gibbs free energy automatically includes solvent effects. Consequently, combining the calculated enthalpies and empirical Gibbs free energies provides only crude entropy estimates. The values of experimental K and

theoretical ΔH_R^0 values were combined to calculate a series of ΔS_R^0 values (Table 6) in bulk and dispersed water and glycerol+water mixtures, as well as in dispersed glycerol. A rather surprising result is that all the ΔS_R^0 values calculated are negative and are very similar, with the average value being -931 $\pm$ 3% cal K^{-1} mol^{-1}. The complex formation seems to be independent of solvation with respect to entropy. Since in all cases ΔG_R^0 values are negative, Ni^{2+}/Mu^- complexation in any of these solvents seems to be enthalpy-driven. The reaction with the zinc ion is much faster to be measured by kinetic methods, and there is limited data on the rate constants. Hence, it has not been possible to create a similar table for the Zn^{2+}/Mu^- case.

Conlusion

Computational chemistry can successfully be applied to explain the mixed solvation of metal ions. In the case of glycerol and water mixtures, modeling of the replacement of water molecules by mono-, bi- and/or tridentate glycerol at the molecular level introduces new means to understand the solvation phenomena.

Electron delocalization in murexide confirms that a metal ion/murexide complexation, in fact, does take place. Both Zn^{2+} and Ni^{2+} have greater tendencies to complex with murexide when compared with either water or glycerol, or both. A similar value of ΔS_R^0 calculated for reactions in bulk and dispersed media suggests that the driving force behind complexation is enthalpy. The negative entropy values indicate an increase in order as the metal ion is surrounded by the tridentate murexide.

Acknowledgment

References

1. M. Eigen and K. *Z.* Tamm, **Elektrochem., Ber. Bunsenges, phys. Chem**., 1962, **66,93**, 107.

2. M. Eigen and R. G. Wilkins, **Mechanism of Inorganic Reactions**; Gould, R. F., Ed.; **Adv. in Chem. Ser**., Am. Chem. Soc., Washington, 1965; **Vol. 49**, p. 55.

3. B. H. Robinson, D. C. Steytler and R. D. Tack, **J. Chem. Soc. Farad. Trans. I.,** 1979, **75**, 481.

4. M. Fischer, W. Knoche, B. H. Robinson and J. H. Maclagan Wedderburn, **J. Chem. Soc. Farad. Trans. Trans. I**, 1979, **75**, 119.

5. M. Fischer, W. Knoche, P. D. I. Fletcher, B. H. Robinson and N. C. White, **Coll. Poly. Sci**., 1980, **258**, 733.

6. G. Geier, **Ber. Bunsenges. phys. Chem**., 1965, **69**, 617.

7. C. T. Lin and J. L. Bear, **J. Phys. Chem**., 1971, **75**, 3705.

8. A. Jost, **Ber. Bunsenges. phys. Chem**., 1975, **79**, 850.

9. D. J. Hewkin and R. H. Prince, **Coord. Chem. Rev.,** 1970, **5**, 45.

10. N. Z. Atay and B. H. Robinson, **Langmuir**, 1999, **Vol.15**, **No.15**, 5056.

11. P. D. I. Fletcher, M. F. Galal and B. H. Robinson, **J. Chem. Soc. Farad. Trans. I**, 1984, **80**, 3307.

12. E. F. Caldin and M. W. Grant, **J. Chem. Soc. Farad. Trans. I.,** 1973, 69, 1648.

13. **HyperChem 3**, developed by **Hypercube Inc**. 1993.