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Potentiometric Investigation on Complexation of Divalent Transition Metal Ions with Some Zwitterionic Buffers and Triazoles

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The interaction between the zwitterionic buffers *N*-(2-acetamido)iminodiacetic acid (ADA), *N*-[tris(hydroxymethyl)methyl]glycine (tricine), and *N*,*N*-bis(2-hydroxyethyl)glycine (bicine) and 1,2,4-triazole (TRZ), 3-mercapto-1,2,4-triazole (TRZSH), and 3-amino-1,2,4-triazole (TRZAM) with the divalent transition metal ions, Cu^{2+}, Ni^{2+}, Zn^{2+}, and Co^{2+}, was investigated in aqueous media at 25 °C and ionic strength $I = 0.1$ $mol\cdot dm^{-3}$ $NaNO_3$ using the potentiometric technique. The acid−base properties of the ligands were investigated and discussed. The acidity constants of the ligands were determined and used for determining the stability constants of the different complexes formed in solution. The formation of the different 1:1 and 1:2 binary complexes and 1:1:1 ternary complexes is inferred from the corresponding titration curves. The ternary complex formation was found to occur in a stepwise manner. The order of stability of the complexes formed in solution was investigated in terms of the nature of the zwitterionic buffer, triazole, and metal ion used. The values of $\Delta\log K$, percentage of relative stabilization (% R.S.), and log *X* for the mixed-ligand complexes studied have been evaluated and discussed. The concentration distribution of the various species formed in solution was evaluated. The ionization processes of ADA and TRZAM and their interaction with Cu^{2+}, Ni^{2+}, and Co^{2+} were studied at different temperatures [(15, 25, 35, and 45) °C], and the corresponding thermodynamic parameters have been evaluated and discussed. In addition, the dissociation constants of ADA and TRZAM and stability constants of their 1:1 binary and 1:1:1 ternary complexes with Ni^{2+} in various water + dioxane mixtures at 25 °C were determined and discussed.

Introduction

Over the years, a variety of zwitterionic buffers that are suitable for biological systems have been developed.[1−4] The zwitterionic buffers *N*-(2-acetamido)iminodiacetic acid (ADA), *N*-[tris(hydroxymethyl)methyl]glycine (tricine), and *N*,*N*-bis(2-hydroxyethyl)glycine (bicine) have been used in the pH range of biological interest.[3,4] Metal complexes involving such compounds are of immense biological interest because of their role in the exchange and the transport mechanism of trace metal ions in the biological systems.[4−6] Studies involving metal ions in solution, which require pH control, are inevitably subjected to the possibility of buffer interferences because of complexation. These zwitterionic buffers are interesting chelating agents because of their flexibility to bind with metal ions forming unidentate, bidentate, and tridentate ionic structures.[5−12] This flexibility is established from the fact that these ligands contain various chelating centers.[13−18] In generating a series of more than 20 zwitterionic buffers for use in biological systems, Good et al.[1] listed the prevention of metal ion complexation as one of their desired goals. The zwitterionic buffers are presently used routinely in biochemical and speciation studies under the assumption that they undergo little if any interaction with biologically and environmentally important metal ions. However, there has been an increase in reports on buffer interferences when zwitterionic biological buffers are used in the presence of metal ions.[4−11] The importance of the metal complexes of triazoles in biological fields is well-recognized.[19] Triazole complexes are very important in pharmaceutical drug productions that are used to inhibit tumor growth and cancer in mammals.[19−22] In addition, triazole complexes are used to treat viral as well as bacterial infections.[23] The bioactivities of triazoles are correlated with their ability to form complexes with metal ions in the biological systems.[24,25] On the other hand, it was recognized that, in the biological systems, the metal ion is bound to two different ligands at various stages.[26,27] Thus, study of the ternary complexes of the ligands under investigation is an important effort to understand the zwitterionic buffer/metal ion binding in biological systems.

This work reports on the complexation of the divalent transition metal ions, Cu^{2+}, Ni^{2+}, Zn^{2+}, and Co^{2+} with the zwitterionic buffers, ADA, tricine, and bicine in the presence of 1,2,4-triazole (TRZ), 3-mercapto-1,2,4-triazole (TRZSH), and 3-amino-1,2,4-triazole (TRZAM) in aqueous solution at 25 °C and ionic strength $I = 0.1$ $mol\cdot dm^{-3}$ $NaNO_3$. The interaction of Cu^{2+}, Ni^{2+}, and Co^{2+} with ADA and TRZAM in aqueous media at different temperatures [(15, 25, 35, and 45) °C] and ionic strength $I = 0.1$ $mol\cdot dm^{-3}$ $NaNO_3$ is reported. The interaction of the Ni^{2+} ion with ADA and TRZAM in various water + dioxane mixtures at 25 °C and ionic strength $I = 0.1$ $mol\cdot dm^{-3}$ $NaNO_3$ is also reported. The present investigation is an extension of our earlier work on binary and ternary complexes of biologically important ligands in solution.[28−37]

Experimental Section

Materials and Solutions. The zwitterionic buffers, ADA, tricine, and bicine, were Sigma products and used without further purification. The triazoles, TRZ, TRZSH, and TRZAM were analytical-grade Fluka products. Stock solutions ($1\cdot 10^{-2}$ $mol\cdot dm^{-3}$) of zwitterionic buffers and triazoles were prepared by dissolving an accurate mass in the approporiate volume of

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Table 1. Summary of Experimental Parameters for the Potentiometric Measurements

system	dissociation processes of ligands: zwitterionic buffers (ADA, tricine, and bicine) and triazoles (TRZ, TRZSH, and TRZAM) binary: ADA/tricine/bicine, TRZ/TRZSH/TRZAM with Cu^{2+}, Ni^{2+}, Zn^{2+}, and Co^{2+} in aqueous media ternary: ADA/tricine/bicine and TRZ/TRZSH/TRZAM with the same metal ions mentioned above in aqueous media
solution composition	[ligand] range ($1\cdot10^{-3}$ to $4\cdot10^{-3}$ $mol\cdot dm^{-3}$), metal/ligand ratios ranging from 1:1 to 1:4 for binary systems and 1:1:1 and 1:2:2 for ternary systems ionic strength: 0.10 $mol\cdot dm^{-3}$ supporting electrolyte ($NaNO_3$)
experimental method	pH-metric titration of 50 cm^3 samples in the range of pH 2 to 11.5
instrument	SM 702 Metrohm automatic titrator with a combined pH glass electrode equipped with a 665 dosimat and a magnetic stirrer (Switzerland)
calibration	by titrating HNO_3 solution (0.10 $mol\cdot dm^{-3}$) against a standard NaOH solution at the same temperature and ionic strength as the solution under study
t (°C)	(15 to 45) °C
n_{tot}[a]	100 to 120
n_{tit}[b]	4 to 6
method of calculation	computer program based on unweighted linear least-squares fit

[a] Number of titration points per titration. [b] Number of titrations per titration curve.

CO_2-free deionized water, and the required volumes were used to prepare the investigated solutions. The solubility of free H_2ADA is very low in H_2O, and thus, the mono sodium salt (NaHADA) was prepared by dissolving 0.1902 g H_2ADA in 10 mL NaOH (0.1 $mol\cdot dm^{-3}$) and diluting to 100 mL with bidistilled water. Also, TRZAM is prepared in monoprotonated form. The metal salts were provided by BDH (England) as nitrates. Stock solutions of the metal salts were prepared in deionized water, and the metal ion concentration was obtained by standard analytical methods.[38] A carbonate-free sodium hydroxide (titrant, prepared in 0.1 $mol\cdot dm^{-3}$ $NaNO_3$) was standardized potentiometrically with KH phthalate (Merck AG). A nitric acid solution ($\approx$ 0.04 $mol\cdot dm^{-3}$) was prepared and used after standardization. Sodium hydroxide, nitric acid, and sodium nitrate were from Merck. Dioxane was of high purity (spectro grade product).

Apparatus and Procedure. Potentiometric pH titrations were performed using a Metrohm SM 702 titroprocessor equipped with a combined pH glass electrode and a 665 dosimat with a magnetic stirrer (Switzerland). The precision of the instrument was (± 0.001) pH unit. A computer program (GLEE, glass electrode evaluation[39]) has been used to calibrate the glass electrode by means of a strong acid/strong base titration under the same temperature and ionic strength used in the investigation. This program provides an estimate of the carbonate contamination of the base, the pseudo Nernstian standard potential, the slope of the electrode, and optionally, the concentration of the base and pK_w. The pH titrations were carried out in an 80 cm^3 commercial double-walled glass vessel. The ionic strength of all titrated solutions were maintained at 0.10 $mol\cdot dm^{-3}$ $NaNO_3$. The temperature of the titrated solutions was adjusted inside the titration cell at the desired temperature by circulating thermostatted water from a water thermostat with a temperature uncertainty of ± 0.1 °C. The investigated solutions were prepared (a total volume of 50 cm^3) and titrated potentiometrically against the standard NaOH solution. A stream of nitrogen was used to deaerate the investigated solutions, and magnetic stirring was used during all titrations. Each of the investigated solutions was thermostatted at the required temperature with a precision of ± 0.1 °C, and the solutions were left to stand at this temperature for about 15 min before titration. Three to four different metal-to-ligand ratios, ranging from 1:1 to 1:4 in binary systems, and the two ratios 1:1:1 and 1:2:2 for the ternary systems were used for all investigated solutions. The titrations repeated at least four times for each investigated system. About 100 to 120 experimental data points were available for evaluation in each system. The initial estimates of the ionization constants of the ligands and the stability constants of the binary and the ternary complexes were calculated by adopting the Irving and Rossotti technique.[40] These equilibrium constants were refined with a computer program based on an unweighted linear least-squares fit. Stoichiometries and stability constants of the different complex species formed in solution were determined by examining the possible composition models for all systems studied. The 1:1 and 1:2 complex models for binary complexes and 1:1:1 complex model for ternary complexes gave the best statistical fit for the systems investigated. The complexes are quite stable up to higher pH values. In all systems, no calculations were performed beyond precipitation points; hence, the hydroxy species likely to form after these points could not be studied.

Accounting for the differences in acidity, basicity, dielectric constant, and ion activities, the pH values for the Ni^{2+}−ADA−TRZAM system investigated in different water + dioxane ratios [(5 to 40) % (v/v) dioxane relative to pure aqueous ones] were corrected in accordance with the method of Douhe'ret.[41] A summary of the experimental details, for the potentiometric measurements, is given in Table 1.

Results and Discussion

Dissociation Constants of the Free Ligands. The structural formulas of the investigated ligands are given in Chart 1. The proton dissociation constants of the ligands investigated have been redetermined in an aqueous medium at 25 °C and I = 0.10 $mol\cdot dm^{-3}$ $NaNO_3$ and the pK_a values obtained for the ligands (Table 2) were in good agreement with literature values.[14−18] The zwitterionic buffers, ADA, tricine, and bicine (HA), are protonated at low pH at the carboxylic group producing the protonated form $(H_2A)^+$. Also, TRZ and its TRZSH and TRZAM derivatives (HL) are considered to be protonated at low pH at the imidiazolic nitrogen atom (N_4) producing the protonated form $(H_2L)^+$; such compounds are expected to have two ionization constants relevant to the following ionization steps[16,17] (eqs 1 to 4):

$$(H_2A^{\pm})^+ \rightleftharpoons HA^{\pm} + H^+ \tag{1}$$

$$HA^{\pm} \rightleftharpoons A^- + H^+ \tag{2}$$

$$(H_2L)^+ \rightleftharpoons HL + H^+ \tag{3}$$

$$HL \rightleftharpoons L^- + H^+ \tag{4}$$

However, the first ionization constants for the zwitterionic buffers, ADA, tricine, and bicine,[17] and the triazoles, TRZ

Chart 1

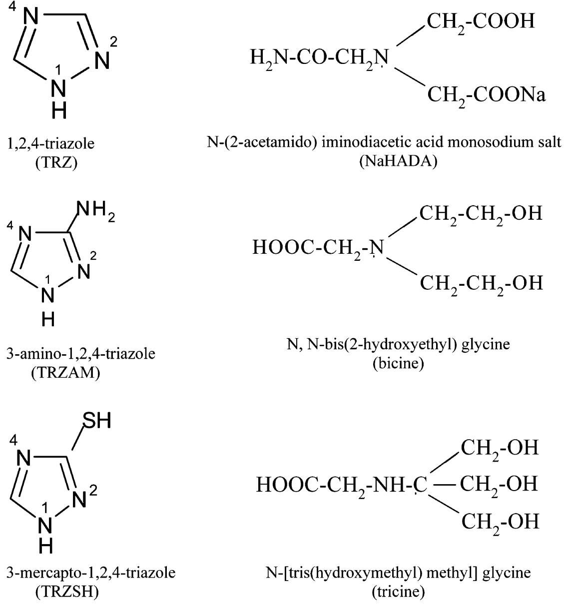

Table 2. Dissociation Constants of Zwitterionic Buffers (ADA, Tricine, and Bicine) and Triazoles (TRZ, TRZSH, and TRZAM) in Aqueous Media at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} NaNO$_3$

	pK's of ligands	
ligand	pK_{a1}	pK_{a2}
ADA		6.84 ± 0.02
tricine		8.20 ± 0.03
bicine		8.30 ± 0.01
TRZ		10.20 ± 0.01
TRZSH		7.16 ± 0.01
TRZAM	4.17 ± 0.02	10.82 ± 0.02

and TRZSH,[16,24,42] are very low (≤ 2.4); therefore, they could not be determined and were not used in the calculations. The concentration distribution diagram of tricine (Figure 1) shows that the zwitterionic buffer forms the HA$^{\pm}$ species up to pH 6. Above pH 6, the concentration of this species decreases, and the ligand anion A^{-} starts to form and reaches its maximum concentration of 100 % at pH 10.50. The HA$^{\pm}$ and A^{-} species are predominant in the physiological pH range.

Stability Constants of Binary Metal Complexes. Potentiometric pH-metric titrations of Cu^{2+}, Ni^{2+}, Zn^{2+}, and Co^{2+} with the ligands were performed according to the procedures described in the Experimental Section. A representative set of potentiometric pH-metric titration curves for the Zn^{2+} + tricine + TRZSH system investigated are displayed in Figure 2. Analyses of the complexed ligand curves indicate that the addition of metal ion to the free ligand solutions shifts the buffer regions of the ligands to lower pH values. This shows that complex formation reactions proceed by releasing protons from such ligands. The binary complexes observed for zwitterionic buffers begin to form in the pH range of 2.6 to 4.8. With respect to the titration curves of the binary metal ion/triazole complexes, one may deduce that these complexes start to form in the pH range of 3.1 to 4.9. These values obtained from the appearance of a divergence of the binary complex titration curves from that of the free ligands.

The stability constants of 1:1 binary complexes of zwitterionic buffers have been redetermined in an aqueous medium at 25 °C and I = 0.10 mol·dm^{-3} NaNO$_3$ (Tables 3, 4, 5, and 6) and were found to agree well with the reported literature values.[14,15,17,18,34] The stability constants of the 1:2 binary complexes of the investigated zwitterionic buffers were determined, and there is no available literature data for comparison. The stability constants of 1:1 binary complexes of the investigated triazoles with Cu^{2+}, Ni^{2+}, and Co^{2+} have also been redetermined in aqueous medium at 25 °C and I = 0.10 mol·dm^{-3} NaNO$_3$ (Tables 3 to 6) and were found to agree well with the reported literature values.[16] However, a survey of the literature revealed that no measurements have been done on Zn^{2+} ions with the investigated triazoles. Also, no literature data are available for the 1:2 binary complexes of the investigated metal ions and triazoles. It is observed that the stability constants of the different 1:2 metal−ligand complexes are lower than the corresponding 1:1 systems (Tables 3 to 6), as expected from statistical considerations.[43] This is the normal trend in neutral ligands where the enthalpy is more favorable for a 1:1 species (exothermic) as compared to a 1:2 species, and thus, for stepwise coordination in the binary complexes of the investigated ligands, the entropy contribution to the free energy change becomes less favorable

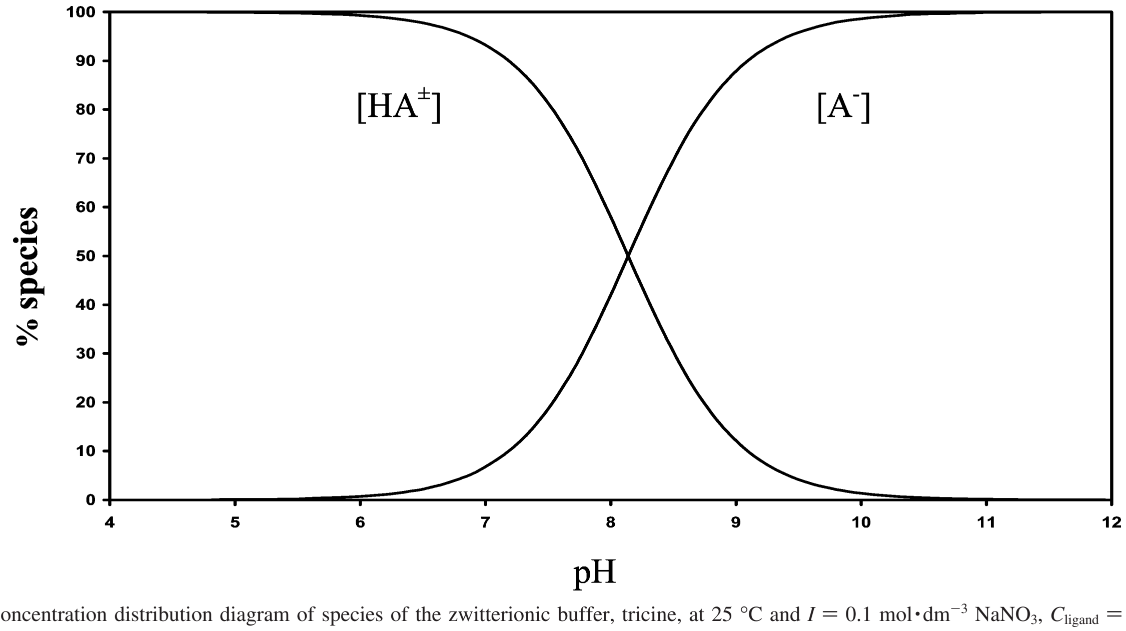

Figure 1. Concentration distribution diagram of species of the zwitterionic buffer, tricine, at 25 °C and I = 0.1 mol·dm^{-3} NaNO$_3$, $C_{\text{ligand}} = 1 \cdot 10^{-3}$ mol·dm^{-3}.

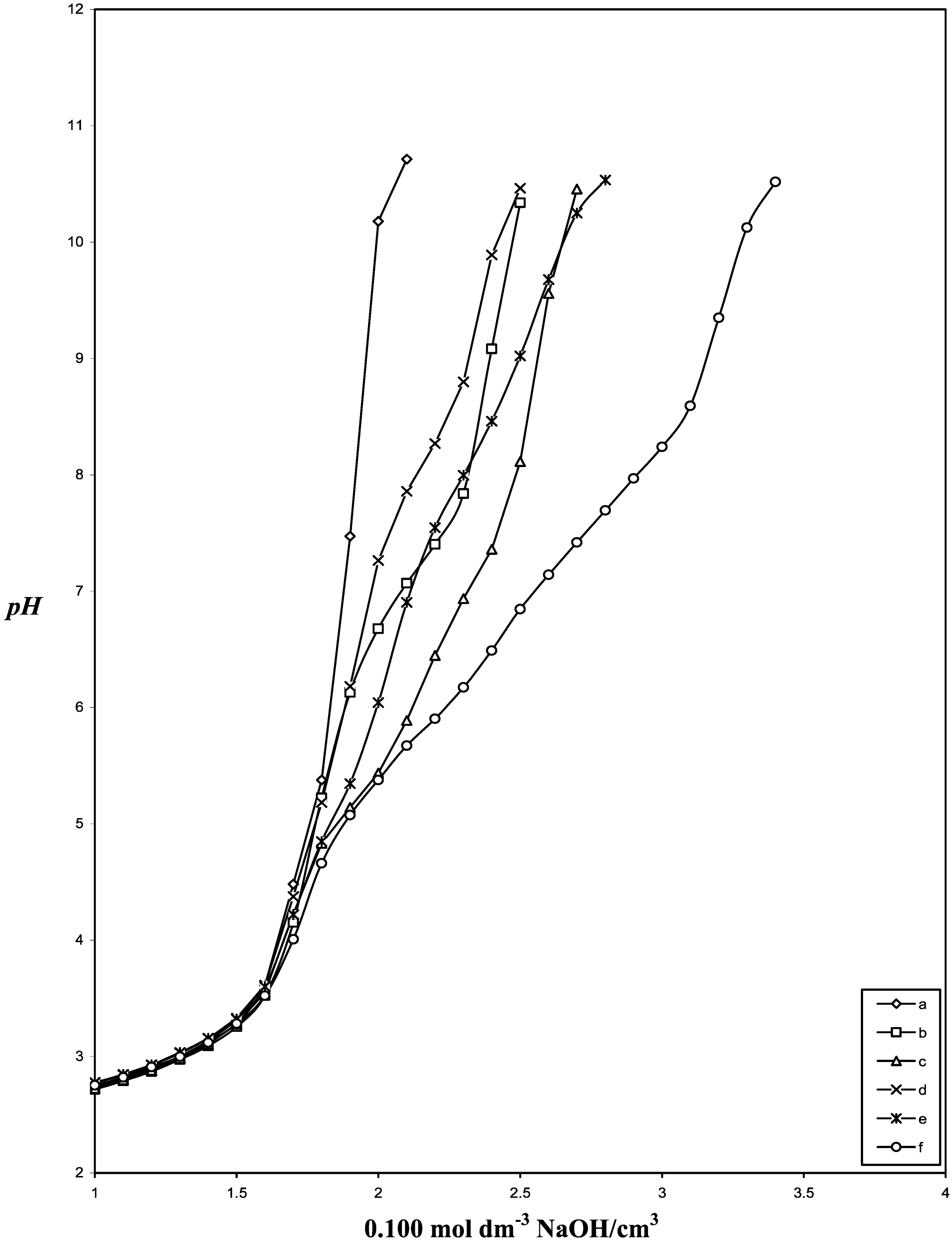

Figure 2. Potentiometric titration curves for the Zn^{2+} + tricine + TRZSH system at 25 °C and $I = 0.1$ mol·dm^{-3} $NaNO_3$: (a) 0.004 mol·dm^{-3} HNO_3 + 0.1 mol·dm^{-3} $NaNO_3$, (b) solution a + 0.001 mol·dm^{-3} TRZSH, (c) solution b + 0.00025 mol·dm^{-3} Zn^{2+}, (d) solution a + 0.001 mol·dm^{-3} tricine, (e) solution d + 0.00025 mol·dm^{-3} Zn^{2+}, and (f) solution a + 0.001 mol·dm^{-3} tricine + 0.001 mol·dm^{-3} TRZSH + 0.0005 mol·dm^{-3} Zn^{2+}.

from one coordination step to the next. Examination of the stability constants of the binary complexes (Tables 3 to 6) reveals the following:

(a) The observed order of stability of binary systems with respect to the zwitterionic buffer ligands is ADA > bicine > tricine; this behavior does not follow the basicities of the ligands (bicine and tricine ligands are highly basic relative to ADA). This observed stability order can be attributed to the formation of one five-membered chelate ring in the case of bicine and tricine. In the case of ADA, two five-membered chelate rings are formed, and ADA acts as a tridentate dianion ligand (NOO^- donor).[18]

(b) The stability constants of the binary triazole complexes of TRZAM and TRZ do not follow their basicities as expected. This behavior can likely be ascribed to the electrostatic repulsive interactions established during the formation of the binary complexes of TRZAM $\{M^{2+} + H_2L^+ \rightleftharpoons (ML)^+ + 2H^+\}$, compared to those in the formation of the binary complex of TRZ $\{M^{2+} + HL \rightleftharpoons (ML)^+ + H^+\}$.[16]

Stability Constants of the Ternary Complexes. A representative set of experimental titration curves for the Cu^{2+} + bicine + TRZ system are displayed in Figure 3. The existence of a ternary complex is proved by comparison of the mixed ligand titration curve with the composite curve obtained by graphical

Table 3. Stability Constants for Cu^{2+} Binary and Ternary Complexes in Aqueous Media at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} $NaNO_3$

			$\log K^{MA}_{MAL}$			$\log \beta^{M}_{MAL}$		
	$\log K_1$	$\log K_2$	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	8.30 ± 0.01	5.00 ± 0.01	9.55 ± 0.01	c[a]	11.03 ± 0.01	17.85		19.33
tricine	7.40 ± 0.02	4.11 ± 0.01	8.58 ± 0.01	c	8.01 ± 0.01	15.98		16.82
bicine	8.24 ± 0.03	4.82 ± 0.03	8.40 ± 0.01	c	7.72 ± 0.01	16.64		16.53
TRZ	9.19 ± 0.01	7.03 ± 0.03						
TRZSH	c	c						
TRZAM	8.81 ± 0.01	5.03 ± 0.02						

	$\Delta\log K$			% R.S.			$\log X$		
	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	0.36		2.22	3.92		25.23	6.18		11.52
tricine	−0.61		0.61	−6.64		8.24	4.23		8.01
bicine	−0.79		−0.52	−8.60		−6.31	4.00		8.16

[a] c: could not be determined because of precipitation.

Table 4. Stability Constants for Ni^{2+} Binary and Ternary Complexes in Aqueous Media at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} $NaNO_3$

			$\log K^{MA}_{MAL}$			$\log \beta^{M}_{MAL}$		
	$\log K_1$	$\log K_2$	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	6.90 ± 0.02	4.81 ± 0.02	9.17 ± 0.05	5.12 ± 0.02	10.59 ± 0.02	16.07	12.02	17.49
tricine	6.27 ± 0.04	3.80 ± 0.01	7.58 ± 0.06	4.12 ± 0.02	6.23 ± 0.03	13.85	10.39	12.29
bicine	6.56 ± 0.03	4.01 ± 0.03	6.86 ± 0.04	3.93 ± 0.01	6.18 ± 0.03	13.42	10.49	12.24
TRZ	7.01 ± 0.02	4.56 ± 0.05						
TRZSH	3.58 ± 0.01	2.35 ± 0.02						
TRZAM	6.06 ± 0.02							

	$\Delta\log K$			% R.S.			$\log X$		
	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	2.16	1.54	4.53	30.80	43.01	74.75	8.86	6.40	
tricine	0.57	0.54	−0.04	8.13	15.08	−0.63	6.06	4.78	
bicine	−0.15	0.35	−0.38	−2.14	9.77	−5.79	4.70	4.48	

Table 5. Stability Constants for Zn^{2+} Binary and Ternary Complexes in Aqueous Media at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} $NaNO_3$

			$\log K^{MA}_{MAL}$			$\log \beta^{M}_{MAL}$		
	$\log K_1$	$\log K_2$	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	6.71 ± 0.03	4.58 ± 0.03	8.93 ± 0.04	6.32 ± 0.03	10.51 ± 0.02	15.64	13.03	17.22
tricine	5.11 ± 0.01	3.67 ± 0.02	6.73 ± 0.02	5.16 ± 0.03	5.49 ± 0.01	11.84	8.35	11.59
bicine	5.71 ± 0.02	3.54 ± 0.03	5.94 ± 0.04	5.06 ± 0.03	5.40 ± 0.02	11.65	8.25	11.30
TRZ	6.41 ± 0.02	4.24 ± 0.03						
TRZSH	3.19 ± 0.03	2.33 ± 0.02						
TRZAM	5.98 ± 0.01							

	$\Delta\log K$			% R.S.			$\log X$		
	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	2.52	3.13	4.53	39.31	98.11	75.75	9.34	9.25	
tricine	0.32	0.05	0.38	4.99	0.97	7.43	4.25	2.40	
bicine	−0.47	−0.65	−0.31	−7.33	−11.38	−5.43	3.40	1.73	

Table 6. Stability Constants for Co^{2+} Binary and Ternary Complexes in Aqueous Media at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} $NaNO_3$

			$\log K^{MA}_{MAL}$			$\log \beta^{M}_{MAL}$		
	$\log K_1$	$\log K_2$	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	6.66 ± 0.05	4.17 ± 0.04	8.44 ± 0.03	4.46 ± 0.06	10.35 ± 0.04	15.10	11.12	17.71
tricine	4.58 ± 0.04	3.48 ± 0.03	6.52 ± 0.05	3.97 ± 0.02	5.22 ± 0.03	11.10	8.55	10.70
bicine	5.52 ± 0.03	3.44 ± 0.01	5.16 ± 0.04	3.90 ± 0.01	4.75 ± 0.03	10.68	9.42	10.23
TRZ	6.18 ± 0.01	4.14 ± 0.03						
TRZSH	3.09 ± 0.03	2.27 ± 0.02						
TRZAM	5.48 ± 0.02							

	$\Delta\log K$			% R.S.			$\log X$		
	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM	TRZ	TRZSH	TRZAM
ADA	2.26	1.37	4.87	36.57	44.33	88.86	9.05	6.05	
tricine	0.34	0.88	0.64	5.50	28.47	13.97	3.82	3.68	
bicine	−1.02	0.81	−0.77	−16.50	26.21	−13.95	2.09	4.52	

addition of the secondary ligand (TRZ) titration data to that of the 1:1 metal/primary ligand (bicine) titration curve. Therefore, it is assumed that, in the presence of both ligands, the zwitterionic buffer (A) interacts first with the metal ion forming a 1:1 MA binary complex which is then followed by interaction of the triazole (L); that is, the ternary complex formation could be considered in stepwise equilibria (eqs 5 and 6):

$$\mathrm{M} + \mathrm{A} \leftrightharpoons \mathrm{MA} \qquad K^{\mathrm{M}}_{\mathrm{MA}} = \frac{[\mathrm{MA}]}{[\mathrm{M}][\mathrm{A}]} \qquad (5)$$

$$\mathrm{MA} + \mathrm{L} \leftrightharpoons \mathrm{MAL} \qquad K^{\mathrm{MA}}_{\mathrm{MAL}} = \frac{[\mathrm{MAL}]}{[\mathrm{MA}][\mathrm{L}]} \qquad (6)$$

The overall stability constant $\beta^{\mathrm{M}}_{\mathrm{MAL}}$ may be represented by eq 7:

$$\mathrm{M} + \mathrm{A} + \mathrm{L} \leftrightharpoons \mathrm{MAL} \qquad \beta^{\mathrm{M}}_{\mathrm{MAL}} = \frac{[\mathrm{MAL}]}{[\mathrm{M}][\mathrm{A}][\mathrm{L}]} = K^{\mathrm{MA}}_{\mathrm{MAL}} \cdot K^{\mathrm{M}}_{\mathrm{MA}} \qquad (7)$$

The $\beta^{\mathrm{M}}_{\mathrm{MAL}}$ constant expresses the stability of the mixed-ligand species; it does not represent the binding strength between L and M^{2+} ions directly in the presence of A. This effect is much better reflected by the equilibrium constant, $K^{\mathrm{MA}}_{\mathrm{MAL}}$, calculated according to eq 8:

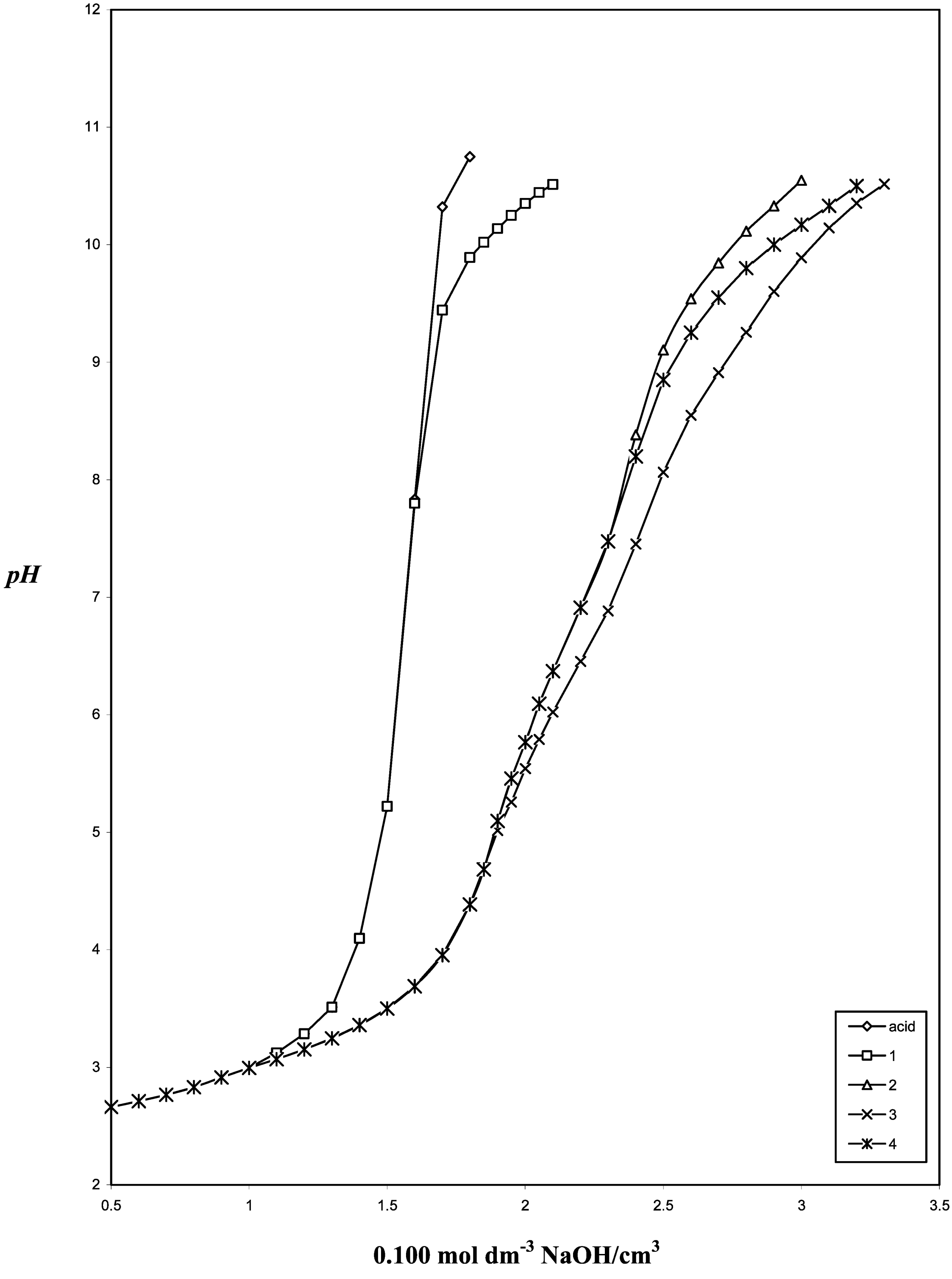

Figure 3. Potentiometric pH titration curves for the Cu^{2+}−bicine−TRZ system at 25 °C and $I = 0.1\ \mathrm{mol \cdot dm^{-3}}$ ($\mathrm{NaNO_3}$): 1, TRZ; 2, Cu^{2+}−bicine (1:1); 3, Cu^{2+}−bicine−TRZ (1:1:1); 4, composite curve.

$$\log K^{\mathrm{MA}}_{\mathrm{MAL}} = \log \beta^{\mathrm{M}}_{\mathrm{MAL}} - \log K^{\mathrm{M}}_{\mathrm{MA}} \qquad (8)$$

This latter reaction constant (the reaction is shown as in eq 6) indicates how tightly L is bound to the simple MA binary complex.

However, in case of the ternary systems, Zn^{2+} + tricine + TRZSH, Zn^{2+} + bicine + TRZSH, M^{2+} + tricine + TRZAM, and M^{2+} + bicine + TRZAM, ($\mathrm{M}^{2+} = \mathrm{Cu}^{2+}, \mathrm{Ni}^{2+}, \mathrm{Zn}^{2+}$, or Co^{2+}) the primary ligand is the triazole derivative.

On the basis of the ternary complexes' stability constant values, the following conclusions could be drawn:

(a) Stabilities of ternary complexes with respect to the zwitterionic buffer ligands follows the order: ADA < tricine < bicine. This behavior is expected because of the formation of two five-membered chelate rings by ADA compared to one five-membered chelate ring in the case of bicine or tricine. However, the participation of the hydroxyl groups of the bicinate or tricinate anion

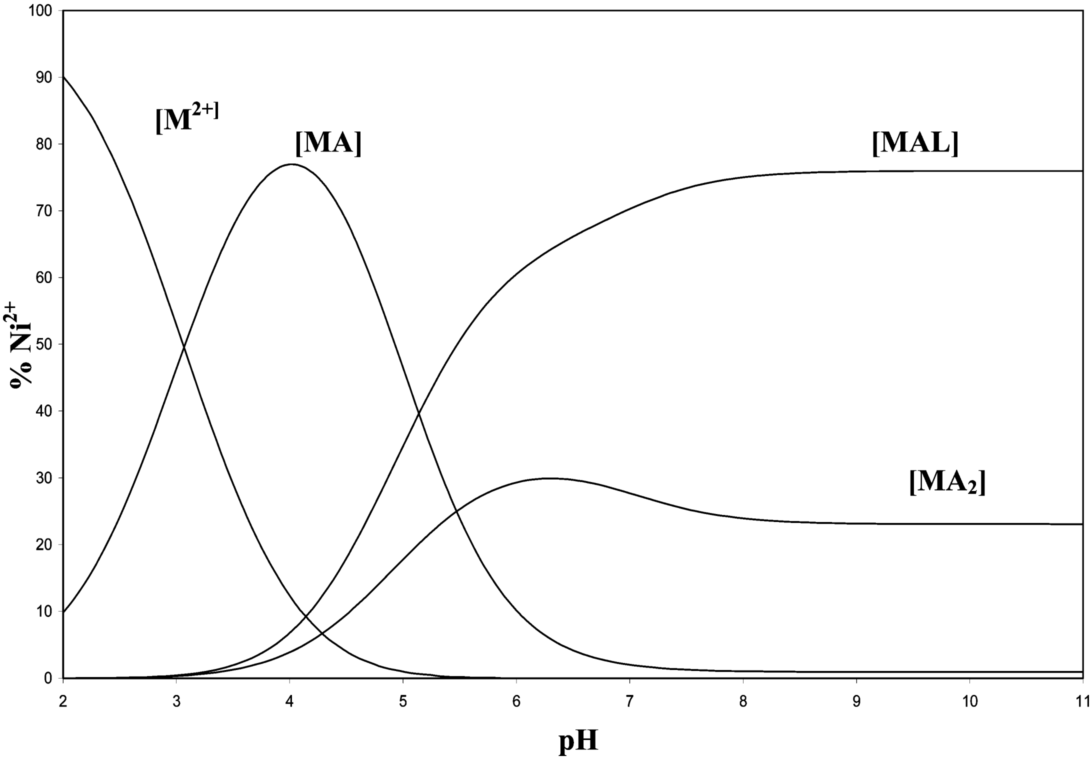

Figure 4. Representative concentration distribution curves as a function of pH calculated for Ni^{2+}−ADA−TRZSH system in the ratio 1:2:2 at 25 °C, $I = 0.10\ \mathrm{mol \cdot dm^{-3}}$ ($\mathrm{NaNO_3}$), and $C_{\mathrm{ligand}} = 1 \cdot 10^{-3}\ \mathrm{mol \cdot dm^{-3}}$.

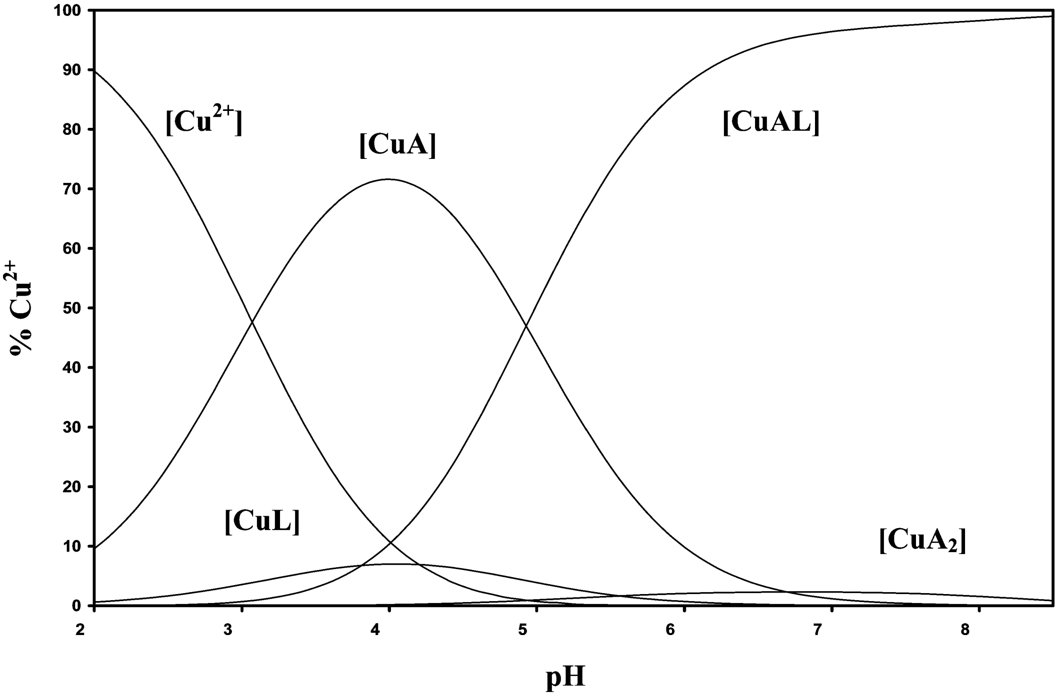

Figure 5. Representative concentration distribution curves as a function of pH calculated for Cu^{2+}−bicine−TRZ system in the ratio 1:2:2 at 25 °C, $I = 0.10\ \mathrm{mol \cdot dm^{-3}}$ ($\mathrm{NaNO_3}$), and $C_{\mathrm{ligand}} = 1 \cdot 10^{-3}\ \mathrm{mol \cdot dm^{-3}}$.

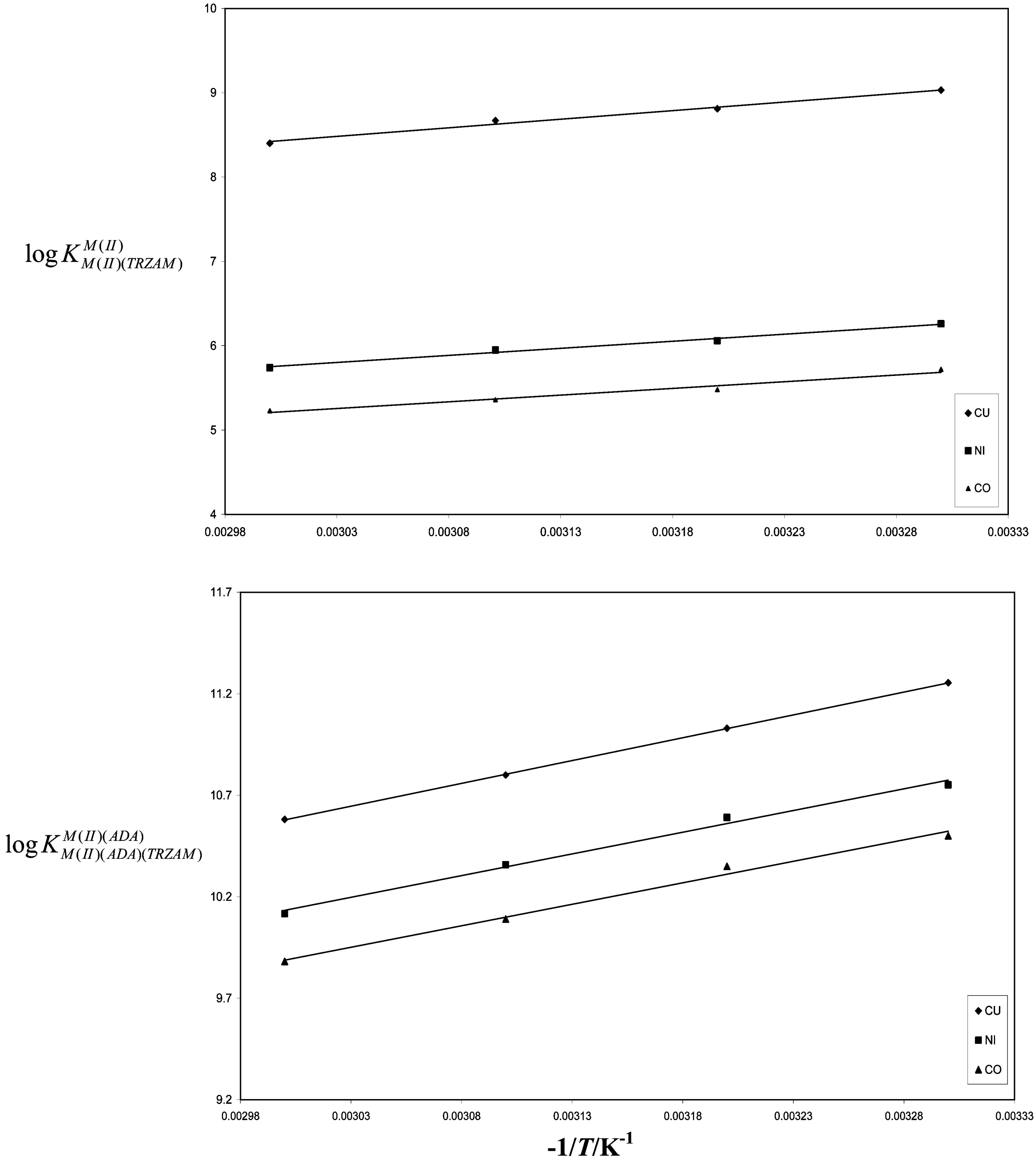

Figure 6. Plot of log $K^{\mathrm{M(II)}}_{\mathrm{M(II)(TRZAM)}}$ and log $K^{\mathrm{M(I)(ADA)}}_{\mathrm{M(II)(ADA)(TRZAM)}}$ vs $-1/T$ at $I = 0.10$ mol·dm^{-3} (NaNO$_3$).

during the formation of the mixed ligand complexes may also enhance the stability of the resulting species.[15]

(b) Stabilities of ternary complexes of the same metal ion that containing ADA decrease according to the following order: TRZAM < TRZ < TRZSH; this behavior can be explained in terms of the decrease in basicity of triazoles in the same direction.

(c) The complex stability of the binary and ternary complexes with respect to the metal ion present follows the order: $Zn^{2+} > Cu^{2+} < Ni^{2+} < Co^{2+}$ which is in accordance with the Irving−Williams series.[43]

Different methods are used to estimate the formation and the relative stability of the different ternary complexes formed in solution.[44] In most cases, the relative stability of the mixed-ligand species [MAL] is expressed in terms of the Δlog *K* parameter (the constant due to the equilibrium [MA] + [ML] = [MAL] + [M]), which is a way to characterize the tendency toward formation of mixed-ligand complexes. The Δlog *K* expresses the effect of the bound primary ligand (A) toward an incoming secondary ligand (L). Generally, positive Δlog *K* values are obtained (Tables 3 to 6) for the systems indicating favored formation of the ternary complexes over the corresponding binary complexes. This can be ascribed to interligand interactions or some cooperation between the primary and the secondary ligands such as H-bond formation. Also, Δlog *K* is negative for some systems, which is likely to be due to the smaller number of sites available for bonding on the binary MA complex than on the aquated M^{2+} ion. Another parameter, the percent relative stabilization (% R.S.), used to quantify stability of a ternary complex[45] may be defined as:

$$\%\ \mathrm{R.S.} = [(\log K^{\mathrm{MA}}_{\mathrm{MAL}} - \log K^{\mathrm{M}}_{\mathrm{ML}})/\log K^{\mathrm{M}}_{\mathrm{ML}}]\cdot 100 \quad (9)$$

and the values obtained (Tables 3 to 6) agree well with the Δlog *K* values. A third parameter, known as log *X*, is frequently used

Table 7. Dissociation Constants of ADA and TRZAM Ligands and Stability Constants of Their Binary and Ternary Complexes with Cu^{2+}, Ni^{2+}, and Co^{2+} at 1:1 and 1:1:1 Molar Ratios in Aqueous Media and $I = 0.10\ mol \cdot dm^{-3}$ $NaNO_3$ at Different Temperatures

		pK's or log K			
ligand or complex	cation	t/°C = 15	25	35	45
ADA	H	7.11 ± 0.02	6.84 ± 0.02	6.60 ± 0.02	6.44 ± 0.03
(1:1) binary complex of ADA	Cu^{2+}	8.44 ± 0.02	8.30 ± 0.01	8.04 ± 0.02	7.76 ± 0.01
	Ni^{2+}	7.15 ± 0.01	6.90 ± 0.02	6.70 ± 0.01	6.56 ± 0.02
	Co^{2+}	6.82 ± 0.02	6.66 ± 0.05	6.47 ± 0.03	6.23 ± 0.01
TRZAM	H	4.24 ± 0.02	4.17 ± 0.02	4.11 ± 0.03	4.04 ± 0.01
	H	10.99 ± 0.01	10.82 ± 0.02	10.69 ± 0.02	10.52 ± 0.03
(1:1) binary complex of TRZAM	Cu^{2+}	9.03 ± 0.01	8.81 ± 0.01	8.67 ± 0.01	8.40 ± 0.03
	Ni^{2+}	6.26 ± 0.03	6.06 ± 0.02	5.95 ± 0.01	5.74 ± 0.02
	Co^{2+}	5.72 ± 0.02	5.48 ± 0.02	5.36 ± 0.04	5.23 ± 0.01
(1:1:1) ternary complex of ADA and TRZAM	Cu^{2+}	11.25 ± 0.01	11.03 ± 0.01	10.80 ± 0.01	10.58 ± 0.04
	Ni^{2+}	10.75 ± 0.02	10.59 ± 0.02	10.35 ± 0.01	10.03 ± 0.02
	Co^{2+}	10.50 ± 0.04	10.35 ± 0.04	10.09 ± 0.02	9.88 ± 0.02

Table 8. Thermodynamic Quantities Associated with the Dissociation of ADA and TRZAM Ligands and Their Interaction with Cu^{2+}, Ni^{2+}, and Co^{2+} at 1:1 and 1:1:1 Molar Ratios in Aqueous Media at 25.0 ± 0.1 °C and $I = 0.10\ mol \cdot dm^{-3}$ $NaNO_3$

ligand or complex	cation	$\Delta H°$ $kJ \cdot mol^{-1}$	$\Delta G°$ $kJ \cdot mol^{-1}$	$\Delta S°$ $J \cdot mol^{-1} \cdot K^{-1}$
ADA	H	34.54	39.02	−18.20
(1:1) binary complex of ADA	Cu^{2+}	−43.55	−47.35	17.22
	Ni^{2+}	−37.72	−39.36	11.67
	Co^{2+}	−37.43	−38.00	7.27
TRZAM	H	12.68	23.79	−39.31
	H	29.60	61.73	−112.69
(1:1) binary complex of TRZAM	Cu^{2+}	−38.90	−50.26	44.40
	Ni^{2+}	−33.00	−34.57	13.97
	Co^{2+}	−30.45	−31.26	8.23
(1:1:1) ternary complex of ADA and TRZAM	Cu^{2+}	−43.04	−62.93	72.72
	Ni^{2+}	−40.90	−60.57	70.81
	Co^{2+}	−40.51	−59.05	66.98

Table 9. Dissociation Constants of ADA and TRZAM Ligands and Stability Constants of Their 1:1 Binary and 1:1:1 Ternary Complexes with Ni^{2+} in Different Water + Dioxane Mixtures at 25.0 ± 0.1 °C and $I = 0.1\ mol \cdot dm^{-3}$ $NaNO_3$

		ADA (A)	TRZAM (L)				
solvent composition % (v/v)	dielectric constant of medium (ε)	pK_{a1}	pK_{a1}	pK_{a2}	$\log K^{Ni(II)}_{Ni(II)A}$	$\log K^{Ni(II)}_{Ni(II)L}$	$\log K^{Ni(II)A}_{Ni(II)AL}$
0.00	78.54	6.84 ± 0.02	4.17 ± 0.02	10.82 ± 0.02	6.90 ± 0.02	6.06 ± 0.02	10.59 ± 0.02
5.00	77.71	6.88 ± 0.02	4.30 ± 0.01	11.03 ± 0.03	7.15 ± 0.01	6.22 ± 0.02	10.79 ± 0.03
10.00	76.80	6.92 ± 0.01	4.36 ± 0.01	11.20 ± 0.02	7.24 ± 0.02	6.43 ± 0.03	10.87 ± 0.01
20.00	74.74	7.04 ± 0.01	4.44 ± 0.02	11.46 ± 0.03	7.37 ± 0.01	6.69 ± 0.03	11.00 ± 0.02
30.00	72.24	7.16 ± 0.03	4.60 ± 0.02	11.69 ± 0.03	7.47 ± 0.02	6.84 ± 0.02	11.15 ± 0.03
40.00	69.19	7.25 ± 0.04	4.66 ± 0.01	11.80 ± 0.02	7.55 ± 0.03	6.90 ± 0.03	11.20 ± 0.02

to characterize the stability of ternary or mixed-ligand complexes. It measures the tendency of one mole each of the binary complexes MA_2 and ML_2 to disproportionate forming two moles of MAL as follows:

$$MA_2 + ML_2 \leftrightharpoons 2MAL \qquad X = \frac{[MAL]^2}{[MA]^2[ML]^2} \tag{10}$$

It is therefore calculated by:

$$\log X = 2 \log \beta_{MAL} - (\log \beta_{MA_2} + \log \beta_{ML_2}) \tag{11}$$

The value of the constant X expected on statistical grounds is 4. Whenever it deviates from this value, it must be the result of interligand electronic and/or steric interactions. [46] The log X values were calculated, and the results (Tables 3 to 6) show that the values are always greater than the statistically expected ones.

Estimation of the concentration distribution of various complex species in solution provides a useful picture of metal ion binding in biological systems. A species distribution diagram obtained for the Ni^{2+} + ADA + TRZSH system (Figure 4) shows that the formation of MA starts at pH < 2, reaches a maximum concentration (80 % total Ni^{2+}) at pH 4.3, and decreases to 2 % when MA_2 and MAL become predominant. Also, for the Cu^{2+} + bicine + TRZ system (Figure 5), the formation of MA starts at pH < 2, reaches a maximum concentration (70 % total Cu^{2+}) at pH 4.2, and decreases to a minimum when MAL becomes predominant. The concentration distribution of various complex species existing in solution as a function of pH was obtained using the SPECIES program.[47]

The effect of temperature of the medium on the dissociation of the ADA and TRZAM ligands and the stability of their 1:1 binary and 1:1:1 ternary complexes with Cu^{2+}, Ni^{2+}, and Co^{2+} metal ions was also investigated in aqueous media at $I = 0.10\ mol \cdot dm^{-3}$ ($NaNO_3$). The values of the stability constants of binary (1:1) and ternary (1:1:1) metal ion complexes for ADA and TRZAM were found to be linearly dependent on the inverse of temperature (Figure 6), indicating negligible change in heat capacity for these complexation reactions.[48] The equilibrium constants have been evaluated at four different temperatures [(15, 25, 35, and 45) °C], and the values obtained are reported in Table 7. The thermodynamic quantities associated with the dissociation processes of ADA and TRZAM and with the formation of their 1:1 binary and 1:1:1 ternary complexes were evaluated at 25 °C and are given in Table 8. The values of $\Delta H°$ for the ionization

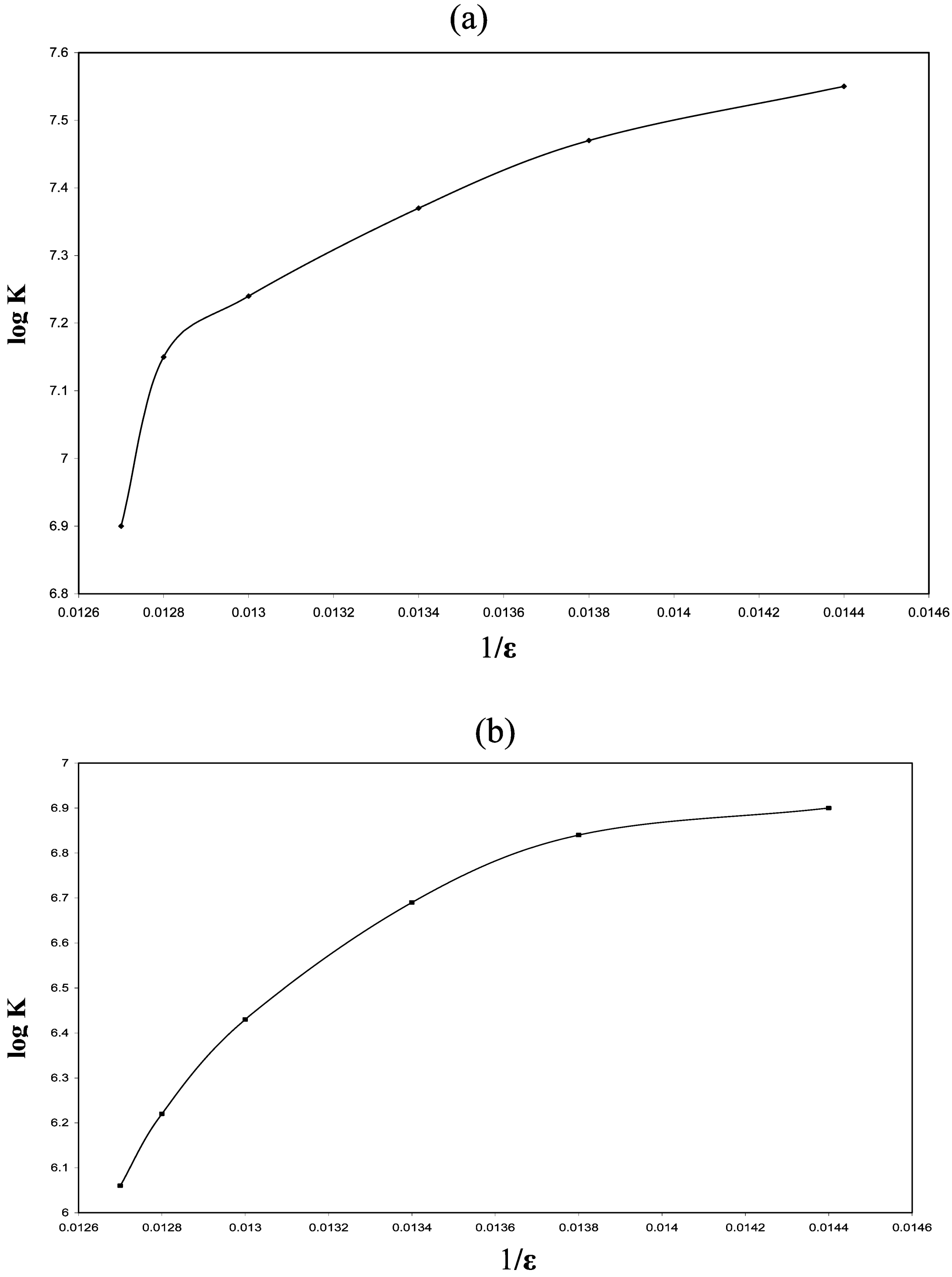

Figure 7. Variation of log K of the 1:1 binary complexes: a, Ni^{2+} +ADA; b, Ni^{2+} + TRZAM; with $1/\varepsilon$ of various water + dioxane mixtures at 25 °C and $I = 0.10\ mol \cdot dm^{-3}$ $NaNO_3$.

of the ligands were found to be positive indicating the endothermic nature of the deprotonation processes. The positive values of the standard free energy change ($\Delta G°$) for the dissociation processes of the ligands denote that these processes are not spontaneous. In addition, the negative values of $\Delta S°$ are pointing to increased ordering due to association. The values of the formation constants decrease with temperature because the formation reactions are exothermic (Le Chatelier's principle). This indicates that the complexation reactions investigated are favored at lower temperatures. The values of enthalpy changes ($\Delta H°$) for the binary and ternary systems investigated are negative. It is of great interest to note that the $\Delta H°$ values for the ternary systems studied are more negative as compared to those of the corresponding binary ones and ensure that despite the steric hindrance due to the primary ligand, ADA, the bond is stronger in the ternary complex formation. In addition, the relatively high negative values of $\Delta H°$ for ternary complexes may be due to less competition faced by a secondary ligand at this step from a water molecule.[49] Thus, the complex formation process is spontaneous in nature, as characterized by the negative $\Delta G°$ values. The values of $\Delta S°$ substantiate the suggestion that the different binary and ternary complexes are formed because of coordination of the ligand anion to the metal cation. Furthermore, the positive values of $\Delta S°$ suggest also a desolvation of the ligands, resulting in weak solvent−ligand interactions, to the advantage of the metal ion/ligand interaction.[50]

To shed more light on both the dissociation processes of ADA and TRZAM and, consequently, its complex-forming process in various water + organic solvent mixtures, dioxane (an aprotic nonionizing coorganic solvent) was chosen for the investigation. The dielectric constant,[51] hydrogen bonding, solvent basicity, dispersion forces, and proton−solvent interaction effects are commonly recognized as influencing factors in the ionization constants of ligands in partial aqueous media.[52] The ionization constants of ADA and TRZAM in different aqueous dioxane mixtures are shown in Table 9. The observed increase in the pK's of ADA and TRZAM as the medium is enriched in the aprotic nonionizing dioxane solvent may be attributed to the fact that the release of the protons from the ligands is rendered more difficult in the presence of this cosolvent because of a decrease in the dielectric constant (77.71, 76.80, 74.74, 72.24, and 69.19 for 5 %, 10 %, 20 %, 30 %, and 40 % (v/v) aqueous dioxane solutions, respectively), which increases, in turn, the fraction of associated ions to form Bjerrum ion pairs and higher aggregates such as triple ions and dipole aggregates[53,54] in the mixed solvents compared to that of pure aqueous media. In addition, the concentration of free ions is very low, and the complexes are governed largely by ionic association reactions. The change in the relative permittivity of the medium (ε) influences the activity coefficient of the charged species, as reported previously by Coetzee and Ritchie.[52] Thus, the activity coefficient of the metal ions or the ligand will increase with an increasing amount of dioxane in the aqueous medium, and hence, the complex stability constants will increase. It is concluded that electrostatic effects, established from the change in the relative permittivity of the medium, play the major role in the increased complex stability, and the interactions between the metal ion and the ligand are predominately ionic. However, the variation in the values of log k_1 for the 1:1 binary complex systems with the reciprocal of the dielectric constant of the mixed solvent (ε) is not linear (Figure 7). This behavior shows that other solvent effects, although mainly governed by the electrostatic effect, influence the increase in the stability constant of the 1:1 binary complex. Also, Mui et al.[55] provided evidence suggesting the presence of the probable important interactions with solvent in the overall reactions of complex formation. Water molecules have a high tendency to develop H-bonds compared with other solvents.[56] Thus, the ligand anion is less stabilized by hydrogen-bonding interactions as the amount of the organic solvent increased in the medium, leading to an increase in the association of the anion with the positive metal ion, forming the metal complexes. The stability constants for the 1:1 binary and 1:1:1 ternary complex species in aqueous dioxane media for the interaction of Ni^{2+} with ADA and TRZAM at 25 °C and $I = 0.10$ mol·dm^{-3} $NaNO_3$ are cited in Table 9.

Conclusion

The present work describes complexation of the divalent transition metal ions Cu^{2+} Ni^{2+}, Zn^{2+}, and Co^{2+} with some zwitterionic buffers and triazoles in an aqueous medium. The complex formation equilibria were investigated to ascertain the composition and stability constants of the complexes. The concentration distribution diagrams of the complexes were evaluated. The effect of the temperature of the medium on the dissociation of the ligands and complex formations for the M^{2+}−ADA−TRZAM ($M^{2+} = Cu^{2+}$, Ni^{2+}, and Co^{2+}) ternary systems has been studied along with the thermodynamic parameters. In addition, the dissociation constants of ADA and TRZAM and stability constants of their 1:1 binary and 1:1:1 ternary complex with Ni^{II} in various water + dioxane mixtures at 25 °C were evaluated.

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