

Speciation of protonated and nonprotonated complex species in biologically important mixed-ligand systems of dopamine (DOPM)

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ABSTRACT

Equilibrium studies on mixed ligand and mixed metal systems of biological relevance is the most fascinating area of research for inorganic chemists. This can be attributed to the interesting results generated from such studies. Present paper deals with the pH-metric equilibrium investigation on Ni(II)-DOPM-ala/phe/asp/glu ternary systems. The systems were investigated keeping the metal and ligands in equimolar ratio at three different ionic strengths (i.e. 0.05M, 0.10M and 0.15M (NaNO₃)) at 20±1°C and 30±1°C in aqueous medium.

Values of formation constants of protonated and nonprotonated complexes were calculated by algebraic method of Chaberek & Martell as modified by Dey et. al. and refined by SCOGS computer program. Various thermodynamic parameters were determined and percentage distribution of each complex species as a function of pH was obtained.

Key words : Equilibrium studies, Ternary systems, Formation constant.

INTRODUCTION

Dopamine acts as neurotransmitter in central nervous system (CNS)¹. Lack of dopamine causes 'Parkinson's disease' in which a person loses its ability to move controlled and smooth actions²⁻⁵. Transition metal ions Cu(II), Ni(II), Co(II), Ni(II) and Mg(II) etc. play vital role in biological systems⁶⁻⁸. Some hitherto unreported equilibrium studies were carried, using dopamine. In the present communication results obtained for Ni(II)-DOPM-Ala/Phe/Asp/Glu (1:1:1) systems are discussed (where, DOPM = dopamine, ala = L-alanine, phe = L-phenylalanine, asp = L-aspartic acid and glu = L-glutamic acid).

MATERIAL AND METHODS

All the reagents used were of highest purity and solutions were prepared in CO₂-free double distilled water having pH ≈6.9.

Following sets of titration mixtures were prepared at three different ionic strengths (μ = 0.05M, 0.10M and 0.15M (NaNO₃)) at two different temperatures (20±1°C and 30±1°C), keeping total volume 50mL and titrated against 0.10M NaOH solution :

1. Acid titration : HNO₃ (2.0×10^{-3} M)
2. Proton-Ligand 'A' System : HNO₃ (2.0×10^{-3} M) + ligand 'A' (1.0×10^{-3} M)

3. Metal-Ligand 'A'(1:1) Binary System: HNO_3 (2.0×10^{-3} M) + nickel nitrate (1.0×10^{-3} M) + ligand 'A' (1.0×10^{-3} M)
4. Proton-Ligand 'B' System : HNO_3 (2.0×10^{-3} M) + ligand 'B' (1.0×10^{-3} M)
5. Metal-Ligand 'B' (1:1) Binary System: HNO_3 (2.0×10^{-3} M) + nickel nitrate (1.0×10^{-3} M) + ligand 'B' (1.0×10^{-3} M)
6. Metal- Ligand 'A'- Ligand 'B' (1:1:1) Ternary System HNO_3 (2.0×10^{-3} M) + nickel nitrate

Table 1" protonation constants of ligands ($\log \beta_{\mu \rightarrow 0}$) and thermodynamic Formation constants of binary complexes of nickel(II) in equimolar systems

Parameter	DOPM		Alanine		Ligand Phenyl alanine		Aspartic acid		Glutamic acid	
	20°C	30°C	20°C	30°C	20°C	30°C	20°C	30°C	20°C	30°C
	20°C	30°C	20°C	30°C	20°C	30°C	20°C	30°C	20°C	30°C
$\log \beta_{\text{HA}}$	12.01	1.70	10.25	10.01	9.31	9.12	10.57	10.26	10.33	10.07
$\log \beta_{\text{H}_2\text{A}}$	22.65	22.05	-	-	-	-	15.05	14.69	14.90	14.54
$\log \beta_{\text{H}_3\text{A}}$	31.65	30.94	-	-	-	-	-	-	-	-
$\log \beta_{\text{MAH}_2}$	27.09	26.44	-	-	-	-	-	-	-	-
$\log \beta_{\text{MAH}}$	18.23	17.8	-	-	-	-	14.53	14.16	14.23	13.92
$\log \beta_{\text{MA}}$	9.31	9.01	6.26	6.20	5.86	5.62	8.40	8.23	7.60	7.44
$\log K_{\text{MAH}}^{\text{M}}$	4.44	4.39	-	-	-	-	3.96	3.90	3.90	3.84
$\log K_{\text{MAH}}^{\text{M}}$	6.22	6.10	-	-	-	-	6.14	5.93	6.63	6.48

† Thermodynamic formation constants were obtained by extrapolating the $\log \beta$ vs. $\sqrt{\mu}$ plot to zero ionic strength.

† Ala, Phe, Asp and Glu become the ligand 'B' in ternary systems.

Representative pH vs. 'a' curves

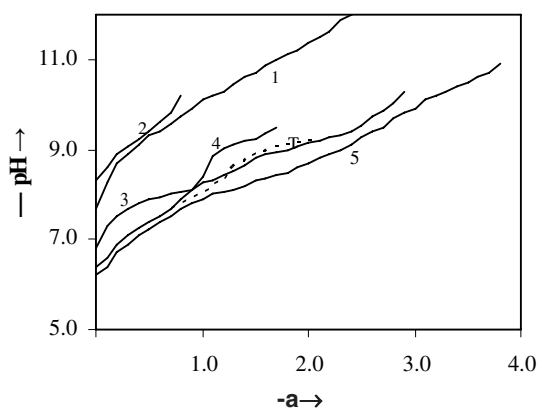


Fig. 1.1: pH vs 'a' curves for Ni(II)-DOPM-Phe (1:1:1) system at $20 \pm 1^\circ\text{C}$ ($\mu=0.10\text{M}(\text{NaNO}_3)$)

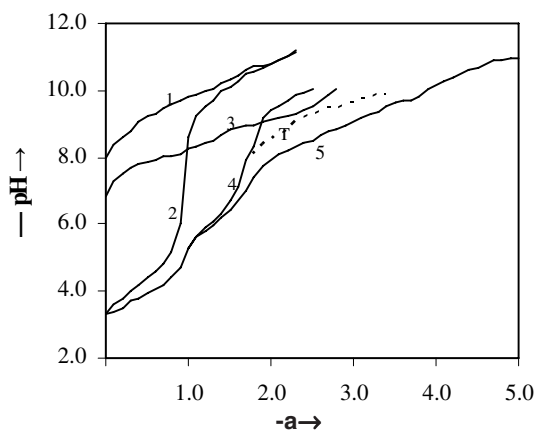


Fig. 1.2: pH vs 'a' curves for Ni(II)-DOPM-Asp (1:1:1) system at $20 \pm 1^\circ\text{C}$ ($\mu=0.10\text{M}(\text{NaNO}_3)$)

Where, Curve 1 represents Ligand 'A' (DOPM) Titration Curve
 Curve 2 represents Ligand 'B' (Ala/Phe/Asp/Glu) Titration Curve
 Curve 3 represents Metal-Ligand 'A' (1:1) Titration Curve
 Curve 4 represents Metal-Ligand 'B' (1:1) Titration Curve
 Curve 5 represents Mixed-Ligand (1:1:1) Titration Curve
 Curve 'T' represents Theoretical Composite Curve

Table 2: thermodynamic formation constants and other thermodynamic Parameters of nickel(II)-tyrosine-ligand 'b' ternary complexes in equimolar systems

Table 2.1: Ni(II)-DOPM-Alanine system

Parameter	20°C		30°C		$\Delta H^\circ \text{kJ mol}^{-1}$	$\Delta S^\circ \text{JK}^{-1} \text{mol}^{-1}$
	$\log K_{\mu \rightarrow 0}$	$\Delta G^\circ \text{kJmol}^{-1}$	$\log K_{\mu \rightarrow 0}$	$\Delta G^\circ \text{kJmol}^{-1}$		
$\log \beta \text{MABH}_3$	33.40	187.38	32.65	189.42	127.49	204.40
$\log \beta \text{MABH}_2$	24.62	138.12	23.95	138.95	113.89	82.70
$\log K_{\text{MAB}}^{\text{M}}$	14.54	81.57	14.10	81.80	74.79	23.13
$\log K_{\text{MAH2BH}}^{\text{M}}$	10.74	60.25	10.51	60.97	39.10	72.20
$\log K_{\text{MAH2BH}}^{\text{MAH2}}$	6.37	35.74	6.31	36.58	11.05	84.26
$\log K_{\text{MAH2BH}}^{\text{MB}}$	4.91	27.55	4.85	28.14	10.20	59.20
$\log K_{\text{MAH2B}}^{\text{M}}$	12.61	70.74	12.26	71.13	59.50	38.39
$\log K_{\text{MAHB}}^{\text{MAH}}$	6.45	36.19	6.40	37.13	8.50	94.49
$\log K_{\text{MAHB}}^{\text{MB}}$	6.35	35.62	6.20	35.97	25.50	34.56
$\log K_{\text{MAB}}^{\text{MA}}$	5.23	29.34	5.10	29.56	22.10	24.72
$\log K_{\text{MAB}}^{\text{MB}}$	8.28	46.45	8.03	46.59	42.50	13.50

Table 2.2 : Ni(II)-DOPM-Phenylalanine system

Parameter	20°C		30°C		$\Delta H^\circ \text{kJ mol}^{-1}$	$\Delta S^\circ \text{JK}^{-1} \text{mol}^{-1}$
	$\log K_{\mu \rightarrow 0}$	$\Delta G^\circ \text{kJmol}^{-1}$	$\log K_{\mu \rightarrow 0}$	$\Delta G^\circ \text{kJmol}^{-1}$		
$\log \beta \text{MABH}_3$	32.36	181.15	31.52	182.89	141.26	137.39
$\log \beta \text{MABH}_2$	23.83	133.69	23.21	134.65	105.39	96.58
$\log K_{\text{MAB}}^{\text{M}}$	13.63	76.44	13.19	76.52	73.94	8.51
$\log K_{\text{MAH2BH}}^{\text{M}}$	9.71	54.48	9.48	55.05	38.61	54.17
$\log K_{\text{MAH2BH}}^{\text{MAH2}}$	5.27	29.54	5.20	30.19	10.37	65.42
$\log K_{\text{MAH2BH}}^{\text{MB}}$	3.82	21.45	3.78	21.93	7.48	47.69
$\log K_{\text{MAH2B}}^{\text{M}}$	11.82	66.31	11.51	66.75	53.38	44.15
$\log K_{\text{MAHB}}^{\text{MAH}}$	5.59	31.33	5.54	32.13	7.99	79.67
$\log K_{\text{MAHB}}^{\text{MB}}$	5.91	33.18	5.77	33.48	24.48	29.69
$\log K_{\text{MAB}}^{\text{MA}}$	4.37	24.52	4.24	24.61	21.76	9.41
$\log K_{\text{MAB}}^{\text{MB}}$	7.77	43.56	7.52	43.63	41.65	6.54

(1.0×10^{-3} M) + ligand 'A' (1.0×10^{-3} M) + ligand 'B' (1.0×10^{-3} M).

Where, Ligand 'A' = dopamine

Ligand 'B' = L-alanine/L-phenylalanine/L-aspartic acid/L-glutamic acid.

For each system titration curves were obtained by plotting pH against 'a' (where, a = moles of alkali added per mole of metal/ligand).

Fig 1 and 2 represent representative titration curves for Ni(II)-DOPM-ala/phe and Ni(II)-DOPM-asg/glu systems respectively.

The values of formation constants for proton-ligand, metal-ligand and mixed-ligand complexes were calculated by algebraic method of Chaberek and Martell^{15,16} as modified by Dey *et al.*¹⁷. These values were refined by SCOGS

Table 2.3: Ni(II)-DOPM-Aspartic acid System

Parameter	20°C		30°C		-ΔH°kJ mol ⁻¹	ΔS°JK ⁻¹ mol ⁻¹
	logK _{μ→0}	-ΔG°kJmol ⁻¹	logK _{μ→0}	-ΔG°kJmol ⁻¹		
log βMABH ₃	43.13	241.96	42.11	244.36	173.39	234.05
log βMABH ₂	34.93	195.96	34.07	197.66	146.19	169.87
log βMABH	25.66	143.96	25.01	145.1	110.49	114.21
log K _{MAB} ^M	15.02	84.26	14.64	84.94	64.59	67.13
log K _{MAH2BH} ^M	9.91	55.60	9.80	56.86	18.70	125.93
log K _{MAH2BH} ^{MAH2}	5.47	30.69	5.41	31.39	10.20	69.93
log K _{MAH2BH} ^{MBH}	5.95	33.38	5.90	34.23	8.50	84.92
log K _{MAH2B} ^M	12.28	68.89	12.01	69.68	45.90	78.48
log K _{MAHBH} ^M	12.36	69.34	12.12	70.29	41.65	94.52
log K _{MAH2B} ^{MAH2}	7.84	43.98	7.63	44.27	35.70	28.28
log K _{MAHBH} ^{MAH}	6.14	34.45	6.02	34.9	21.25	45.04
log K _{MAHBH} ^{MBH}	8.40	47.15	8.21	47.6	33.83	45.46
log K _{MAH2B} ^{MB}	3.88	21.77	3.79	21.99	15.30	22.08
log K _{MAHB} ^M	13.65	76.58	13.31	77.22	57.80	64.10
log K _{MABH} ^M	15.09	84.68	14.75	85.54	59.33	86.53
log K _{MAHB} ^{MAH}	7.43	41.68	7.21	41.83	37.4	14.63
log K _{MABH} ^{MBH}	11.12	62.41	10.85	62.92	47.43	51.13
log K _{MABH} ^{MA}	5.77	32.39	5.74	33.27	6.63	87.93
log K _{MAHB} ^{MB}	5.25	29.45	5.08	29.47	28.9	1.90
log K _{MAB} ^{MA}	5.71	32.03	5.63	32.66	13.6	62.92
log K _{MAB} ^{MB}	6.63	37.17	6.42	37.22	35.7	5.02

Table 2.4 : Ni(II)-DOPM-Glutamic acid System

Parameter	20°C		30°C		-ΔH°kJ mol ⁻¹	ΔS°JK ⁻¹ mol ⁻¹
	logK _{μ→0}	-ΔG°kJmol ⁻¹	logK _{μ→0}	- ΔG°kJmol ⁻¹		
log βMABH ₃	42.33	237.48	41.38	240.07	161.49	259.35
log βMABH ₂	33.97	190.58	33.12	192.15	144.49	157.29
log βMABH	24.61	138.06	24.01	139.3	101.99	123.12
log K ^M _{MAB}	14.11	79.16	13.76	79.83	59.50	67.11
log K ^M _{MAH2BH}	9.35	52.45	9.25	53.66	17.00	121.01
log K ^{MAH2} _{MAH2BH}	4.91	27.55	4.86	28.20	8.50	65.00
log K ^{MBH} _{MAH2BH}	5.45	30.58	5.40	31.33	8.33	75.92
log K ^M _{MAH2B}	11.32	63.51	11.07	64.22	42.50	71.71
log K ^M _{MAHBH}	11.62	65.19	11.38	66.02	40.80	83.25
log K ^{MAH2} _{MAH2B}	6.88	38.60	6.68	38.73	34.85	12.80
log K ^{MAH} _{MAHBH}	5.40	30.27	5.27	30.6	20.57	33.10
log K ^{MBH} _{MAHBH}	7.72	43.28	7.52	43.65	32.47	36.91
log K ^{MB} _{MAH2B}	3.72	20.87	3.63	21.08	14.79	20.75
log K ^M _{MAHB}	12.60	70.69	12.31	71.39	50.15	70.11
log K ^M _{MABH}	14.28	80.11	13.94	80.87	57.80	76.17
log K ^{MAH} _{MAHB}	6.38	35.79	6.21	36.03	28.90	23.53
log K ^{MBH} _{MABH}	10.38	58.20	10.10	58.6	46.75	39.11
log K ^{MA} _{MABH}	4.97	27.89	4.93	28.63	6.46	73.15
log K ^{MB} _{MAHB}	5.01	28.13	4.86	28.2	26.18	6.66
log K ^{MA} _{MAB}	4.81	26.98	4.75	27.53	11.05	54.39
log K ^{MB} _{MAB}	6.51	36.54	6.33	36.7	32.13	15.07

Representative speciation curves

Where,

Curve1: [M], 2 : [MB], 3 : [MAH₂], 4 : [MAH], 5 : [MA], 6 : [MABH₂], 7 : [MABH], 8 : [MAB]

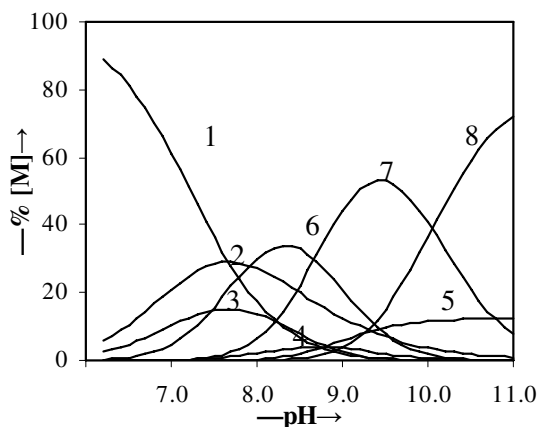


Fig. 2.1: Speciation curves for Ni (II)-DOPM-Ala (1:1:1) system at 20±1°C ($\mu=0.10\text{M}(\text{NaNO}_3)$)

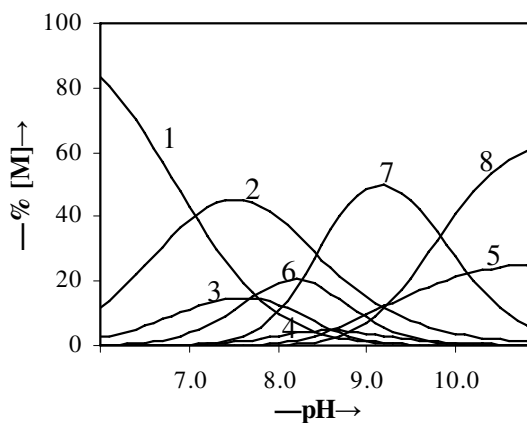


Fig. 2.2: Speciation curves for Ni (II)-DOPM-Phe (1:1:1) system at 20±1°C ($\mu=0.10\text{M}(\text{NaNO}_3)$)

where,

Curve 1: [M], 2: [MBH], 3: [MB], 4: [MABH₃], 5: [MABH₂], 6: [MABH], 7: [MAB], 8: [MAH₂], 9: [MAH], 10: [MA]

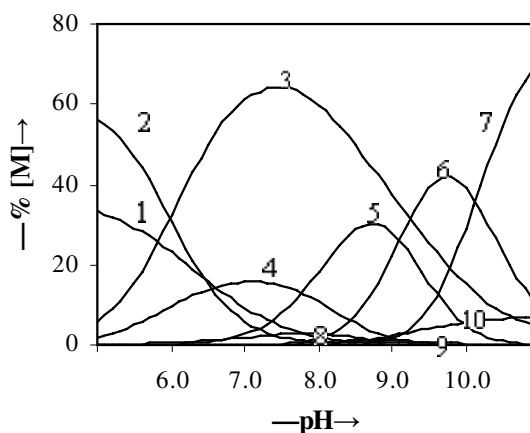


Fig. 2.3: Speciation curves for Ni (II)-DOPM-Asp (1:1:1) system at 20±1°C ($\mu=0.10\text{M}(\text{NaNO}_3)$)

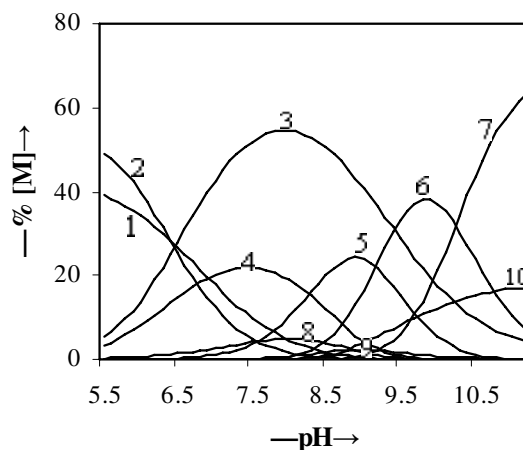


Fig. 2.4: Speciation curves for Ni (II)-DOPM-Glu (1:1:1) system at 20±1°C ($\mu=0.10\text{M}(\text{NaNO}_3)$)

computer program¹⁸⁻²⁰ and plotted against $\sqrt{\mu}$ (where, μ is the ionic strength) and extrapolated to zero ionic strength in order to obtain thermodynamic formation constants. The values are given in Table 1 & 2.

RESULTS AND DISCUSSION

Analysis of representative pH vs. 'a' curves (Fig. 1 and 2) reveals that in the ternary systems involving alanine/phenylalanine mixed ligand complex is formed by simultaneous interaction of both the ligands with metal, whereas stepwise equilibria is observed in Ni(II)-DOPM-aspartate/glutamate systems, where aspartate/glutamate behaves as primary ligand.

Speciation curves for Ni(II)-DOPM-alanine/phenylalanine systems (Fig. 3 & 4) show that NiB, and NiABH₂ are formed as dominating species in the initial stage, while the concentration of NiAH₂ is comparatively low. Concentrations of NiABH₂ and NiABH increase almost parallel up to pH 8.0 thereby showing the formation of both these species almost simultaneously but above pH 8.0, concentrations of NiABH₂, NiB and free metal decrease and that of NiABH increases up to pH 9.3; above which the concentration of the latter species decreases continuously while that of NiAB increases which shows formation of NiAB by dissociation of NiABH.

Percentage distribution of metal in complex species for Ni(II)-DOPM-aspartate/glutamate system show that after the formation of NiB as a major species up to pH $\approx$ 5.5, concentrations of NiB and free metal are decreased and those of NiB and NiABH₃ are increased and NiB is formed as major species which also shows that all the protons in the ternary

complex species (except NiABH₃) are attached to the DOPM site.

Further, no sharp inflection is observed in mixed-ligand titration curve, suggesting that none of the protonated and non-protonated ternary complex species is formed as dominating one.

The nature of speciation curves show that in these systems, above pH 8.0, NiABH₂ is formed by combination of NiB and H₂A as well as by dissociation of NiABH₃. Simultaneously NiABH and NiAB species are also formed by two paths; i.e. by combination of ligand 'A' with NiB and dissociation of higher protonated ternary complexes.

Dopamine coordinates with metal ion in pyrocatechol mode, whereas all the other selected ligands form chelate compound in glycine like manner²¹. All the selected ligands bear structural similarities. Hence values of formation constants for these systems are found to be comparable. Higher stability of alanine complexes is attributed to the electron withdrawing nature of phenyl group of phenylalanine. The values of thermodynamic parameters show that complexes of aspartic acid are more stable than those of glutamic acid, which is due to the presence of additional –CH₂– group in latter ligand.

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REFERENCES

1. Voet D., Voet J.G. & Pratt. C.W., 'Fundamentals of biochemistry Upgrade Edition', John Wiley & Sons, Inc., 91 (2001).
2. Zubay G., 'Biochemistry', 4th ed., Wm. C. Brown Pub., 711 (1998).
3. Choi H., Kim S.W., *et al.*, *J. Neurochem.*, **86**(1): 143 (2003).
4. Teismann P., Tieu K., *et al.*, *Proc. Natl. Acad. Sci., U.S.A.*, **100**(9): 5473 (2003).
5. Draus P.H. & Reichmann H., *J. Neuropsychiatry clin. Neurosci.*, **17**: 214 (2005).

6. Thornalley, P. J., *Biochem. Soc. Trans.*, **31**: 1343, (2003).
7. Szilagyi, R. K. Bryngelson, P. A., Maroney, M. J., Hedman, B., Hodgson, K. O., Solomon, E. I., *J. Am. Chem. Soc.*, **126**: 3018, (2004).
8. Jaouen, G., Ed. Bioorganometallics: Biomolecules, Labeling, Medicine, Wiley-VCH: Weinheim (2006).
9. Kiss T. & Gergely A., *J. Inorg. Biochem.*, **25**(4): 247 (1985).
10. Kiss T., Sóvágó I. & Martin R.B., *J. Am. Chem. Soc.*, **111**: 3611 (1989).
11. Nair M.S., Arasu P.T., Mansoor S.S., Shenbagavatti P. & Neelkantan M.A., *Indian J. Chem.*, **34**(A): 365 (1995).
12. Nair M.S., Arasu P.T. & Neelkantan M.A., *Indian J. Chem.*, **36**(A): 879 (1997).
13. Lamarque L., Navarro P., Miranda C., Aran V.J., Dchoa C., Escarti F., Garcia-Espana E., Latorre J., Luis S.V. & Miravet J.F., *J. Am. Chem. Soc.*, **123**(43): 10560 (2001).
14. Pathak T. V., Mehta J.P., Bhatt P.N. & Ramachandraiah G., *Trans. SAEST*, **38**(3), 107 (2003).
15. Chaberek S. & Martell A.E., *J. Am. Chem. Soc.*, **74**: 5052 (1952).
16. Chaberek S. & Martell A.E., *J. Am. Chem. Soc.*, **77**: 1477 (1955).
17. Ram Nayan & Dey A.K., *Indian J. Chem.*, **14**(A): 892 (1976).
18. Sayce I.G., *Talanta*, **15**, 1397 (1968).
19. Sayce I.G., *Talanta*, **18**, 653 (1971).
20. Sayce I.G. & Sharma V.S., *Talanta*, **19**: 831 (1972).
21. Nair M.S. & Subbalakshmi G., *J. Indian Chem. Soc.*, **77**: 26 (2000).