Asian Journal of Chemistry Vol. 18, No. 2 (2006), 1183–1190

Nickel(II) and Copper(II) Complexes of Schiff Base Derived from Isatin with 4-Ethylaniline

AYSE ERÇAĞ*, FATMA TURAK†, MAHMURE Ü. ÖZGÜR† and
ABDÜRREZZAK BOZDOĞAN†
Department of Chemistry, Engineering Faculty, Istanbul University
34320, Istanbul, Turkey
Fax: (90)(212)5911997; Tel: (90)(212)4737000/17703;
E-mail: ercaga@istanbul.edu.tr, mozgur@yildiz.edu.tr

Ni(II) and Cu(II) complexes of Schiff base ligand derived from 4-ethylaniline with isatin (1H-indole-2,3-dione) were prepared. The chemical structures were confirmed by means of analytical and spectroscopic (IR, UV-Vis, FAAS, Mass) techniques as well as magnetic and thermal measurements. The complexes have 1 : 2 metal : ligand ratios and are paramagnetic. The IR spectra indicate that the ligand coordinates as bidentate through metal(II) ions *via* the carbonyl oxygen and the azomethine nitrogen. The complexes with the molecular formula $[Cu(HL)_2Cl_2]$, $[Ni(HL)_2]Cl_2$ are non-electrolyte and 1 : 2 electrolyte, respectively. Solid state conductivities of synthesized compounds were measured using four-probe technique on a compressed pellet at room temperature. The ligand and Ni(II), Cu(II) complexes were studied potentiometrically in different aqua-organic solvent mixtures and temperatures. Protonation constants of the ligand and overall formation constants of the complexes were calculated from potentiometric data using the program TITFIT.

Key Words: **Isatin-anilines, Schiff bases, Ni(II) and Cu(II) complexes, Potentiometric titration.**

INTRODUCTION

The synthetic versatility of isatin has led to extensive use of this compound in organic synthesis. It has stemmed from the interest in the biological and pharmacological properties of the derivatives[1, 2]. Isatin and its derivatives have been used as reagents in dye industry as well. Although, it was first synthesized in the last century and recently it was discovered in mammalian tissues and body fluids. It was observed that monoamine oxidase was inhibited by isatin and its derivatives by *in vitro* studies[3].

As Schiff bases contain different donor atoms, they are an important class of ligands in coordination chemistry, being reported widely[4]. Schiff bases of isatin

---

†Department of Chemistry, Faculty of Arts and Sciences, Yildiz Technical University, 34210, Davutpasa, Istanbul, Turkey.

were reported to possess antibacterial[5], antifungal[6], antiviral[7], anti-HIV[8], antiprotozoal[9] and anthelmintic[10] activities. They also exhibit significant anticonvulsant activity, apart from other pharmacological properties[11]. Schiff base complexes incorporating two metal ions are of special interest, they are similar to those found in living organisms, *e.g.*, enzymes and proteins, and develop their activity in the presence of two or more metal ions[12]. Stability constants or equilibrium constants for metal complex formation have long been employed as an effective measure of the affinity of a ligand for a metal ion in solution and have served as a quantitative indication of success or failure of ligand design. Stability constants are needed to determine the nature of the metal complex formed under a wide variety of conditions for many applications in diverse areas of science and industry.

The object of the present study is to investigate the complexes formed by the reaction of nickel and copper ions with Schiff base (ISE or HL) derived from isatin and 4-ethylaniline. Further insight into the bonding and possible geometric structures were made by elemental analyses, magnetic moment measurements, solid-state and molar conductivities, thermal analyses, IR, UV-Vis, and mass spectra of the complexes. Formation constants of the proton-ligand and metal-ligand complexes were also calculated from potentiometric data using the program TITFIT developed by Zuberbühler and Kaden[13].

EXPERIMENTAL

Isatin (1H-indole-2,3-dione), 4-ethylaniline and phosphorus pentoxide were purchased from E. Merck and Aldrich. Metal chlorides were obtained from Fluka. All other chemicals used in this investigation were of reagent grade purity. Ethanol was distilled and dried prior to use.

The microanalyses of carbon, hydrogen, and nitrogen were carried out on a Carlo-Erba 1106 elemental analyzer. Nickel and copper were determined on a Unicam Solaar 929 atomic absorption spectrometer. Chloride ions were determined by a Jenway 3040 ion analyzer multimeter. The IR spectra were recorded with a Unicam Mattson 1000 FTIR spectrometer (in the range 4000–400 cm^{-1}) using KBr disc (1 mg/100 mg) technique. The electronic spectra were recorded on a Philips PU 8700 spectrophotometer (in the 190–700 nm region). ^1H, ^{13}C NMR spectra of the Schiff base were recorded with a Bruker Ac-200 instrument using TMS as internal standard and DMSO-d_6 as solvent. Fast atom bombardment FAB-mass spectra were measured on a micromass Zabspec mass spectrometer.

Molar conductances of the compounds were measured in DMSO on a WPA CMD750 conductivity meter. Solid-state electrical conductivity measurements were performed with the films removed from electrode surface on a Keithley 617 electrometer connected to a four-probe head with gold tips and calculated from the following equation:

$$\sigma = V^{-1} I \left(\ln \frac{2}{\pi d_n} \right)$$

where V is the potential in volts, I is current in A and d_n is the thickness in cm.

Schiff base and the complexes were prepared in the form of tablets with thicknesses of *ca.* 0.05 cm at a pressure of *ca.* 10 tons[14]. Magnetic measurements were performed on a Sherwood Scientific apparatus at room temperature by Gouy's method using $CuSO_4{\cdot}5H_2O$ as the calibrant and corrected for diamagnetism by applying Pascal's constants. Thermal analyses of the complexes were done on a Shimadzu 50 model TGA. Melting points were measured on a Büchi melting point B-545 instrument. Potentiometric titrations were carried out using Metrohm E-415 Dosimate and Metrohm E-510 pH-meter. A Metrohm 6.0204.000 combined glass electrode was used for pH measurements. The microelectrode was standardized from calculated acid concentrations in titrations covering the pH range 2.0–12.0. The instrument was calibrated before and after each series of pH readings under the same conditions using two buffer solutions at 4.0 and 7.0.

Preparation of Schiff Base

The free ligand, Schiff base, was synthesized by usual condensation reaction[15, 16]. For the preparation of HL, a solution of isatin (1 mmol) in absolute EtOH (25 mL) was added to a stirred solution of 4-ethylaniline (1 mmol) in absolute EtOH (25 mL). The mixture was refluxed for 4 h on water bath and kept for one day at room temperature. The solid product was filtered, washed with cold EtOH and Et_2O and then dried *in vacuo* (over P_4O_{10}). HL: yield 85%, deep orange crystals, m.p. 212°C. Anal. Found: C 76.80, H 5.60, N 11.20. Calcd. for $C_{20}H_{22}N_2O$: C 76.77, H 5.63, N 1.19. IR spectral data (KBr, cm^{-1}): 3234–3182 ν(NH), 2927–2851 ν(—CH_3—, CH_2), 1753 ν(C=O), 1650 ν(C=N), 1625 ν(C=C). ^1H NMR (DMSO-d_6): 1.23 (m, 3H, CH_3), 2.50 (m, 2H, —CH_2), 6.43–6.65 (two symmetric m, 2H, Ar-H), 7.00–7.40 (two m, 6H, Ar-H), 11.09 (s, 1H, NH). ^{13}C NMR: 15.57 (—CH_3), 27.63 (—CH_2—), 115.28, 117.45, 119.74, 122.53, 125.15, 127.49, 128.73, 134.26, 140.56, 146.82, 148.01 (benzenoid and indole ring C atoms), 154.65 (C=N), 163.58 (C=O).

Preparation of the complexes

A solution of $CuCl_2{\cdot}2H_2O$ (0.179 g, 1 mmol) in absolute EtOH (10 mL) was added, under continuous stirring, to the solution of the ligand (1 mmol). HL (0.250 g) in absolute EtOH (40 mL). The mixture was stirred and heated to 80°C for 1 h and turned to a brown coloured solution. The mixture was left to stand overnight at room temperature. The precipitated complex was filtered off, washed with cold EtOH several times and Et_2O and then dried *in vacuo* over P_4O_{10}. Yield 85%. Red-brown crystals. m.p.: 252°C. Anal. Found: C 60.12, H 4.50, N 8.33, Cl 10.10, Cu 10.40. Calcd. for $C_{40}H_{44}N_4O_2Cl_2Cu$: C 60.49, H 4.44, N 8.82, Cl 11.16, Cu 10.10%. λ_{max}, cm^{-1}: 17980. IR spectral data (cm^{-1}, KBr): 3175 ν(NH), 2927–2851 ν(—CH_3—, CH_2), 1702 ν(C=O), 1620 ν(C=N), 1625 ν(C=C). μ_{eff}: 2.10 B.M. Molar conductance (in Ω^{-1} cm^2 mol^{-1}) of a 10^{-3} M solution in DMSO at 25°C: 17.8.

Nickel(II) complex of ligand was prepared by a procedure analogous to the copper(II) complex using $NiCl_2{\cdot}6H_2O$ and absolute EtOH as solvent. Yield 82%. Brown microcrystals. m.p.: 369°C. Anal. Found: C 59.91, H 4.53, N, 8.45, Cl 10.85, Cu 9.18. Calc. For $C_{40}H_{44}N_4O_2Cl_2Cu$: C 60.98, H 4.48, N 8.89, Cl 1.25, Cu 9.31%. λ_{max}, cm^{-1}: 20300. IR spectral data (cm^{-1}, KBr): 3310–3100, ν(NH), 2927–2851 ν(—CH_3—, CH_2), 1702 ν(C═O), 1615 ν(C═N), 1625 ν(C═C). μ_{eff}: 3.45 B.M. Molar conductance (in Ω^{-1} cm^2 mol^{-1}) of a 10^{-3} M solution in DMSO at 25°C: 155.3.

Potentiometric Titrations

The potentiometric studies were performed in water-acetone, water-dioxane, and water-ethanol (25–75%, v/v) due to the low solubility of the ligand of water. The experimental procedure employed to determine the protonation constants by potentiometric measurements of hydrogen concentration has been described in detail elsewhere. The ionic strength of the medium was kept virtually constant at 0,1 M $NaClO_4$ as background electrolyte. All titration solutions were prepared in a total volume of 50 mL thermostated at different temperatures (10, 25, 30, 40° ± 0.1°C). Purified nitrogen gas was bubbled through the titrated solution to ensure stirring and neutral inert atmosphere. Furthermore, the solution was stirred magnetically to mixing.

The titration solution, in 50% volume organic solvent-aqua medium, were prepared under the following conditions:

Solution A: $HClO_4$ (2.5 mL, 0.1 M), $NaClO_4$ (5 mL, 0.1 M), water (17.5 mL), organic solvent (ethanol, acetone, dioxane) (25 mL).

Solution B: $HClO_4$ (2.5 mL, 0.1 M), $NaClO_4$ (5 mL, 0.1 M), solution of ISE in organic solvent (ethanol, acetone, dioxane) (5 mL, 0.01 M), water (17.5 mL), organic solvent (ethanol, acetone, dioxane) (20 mL).

Solution C: $HClO_4$ (2.5 mL, 0.1 M), $NaClO_4$ (5 mL, 0.1 M), solution of ISE in organic solvent (ethanol, acetone, dioxane) (5 mL, 0.01 M), aqueous solution of metal salt (*i.e.*, $CuCl_2 \cdot 2H_2O$, $NiCl_2 \cdot 6H_2O$) (5 mL 0.01 M), water (12.5 mL), organic solvent (ethanol, acetone, dioxane) (20 mL).

The solutions were titrated with 0.1 M NaOH in increments of 0.1 mL. The corresponding change in the pH value of the solution was measured. For each protonation constant two separate titrations were performed, each of 50 data points, covering a pH-range 2–12. The data obtained were analyzed on PC equipped with the program TITFIT[13].

RESULTS AND DISCUSSION

The solid complexes were synthesized using 1 : 1 mole ratio of all reactants but complexes indicate 1 : 2 metal-to-ligand stochiometry. The complexes are airstable, non-hygroscopic and are also characterized by high melting points. The complexes are insoluble in H_2O and *n*-hexane and sparingly soluble in common organic solvents, but soluble in DMF and DMSO.

The IR spectra of the free ligand shows a broad band around 3200 cm^{-1}, which can be attributed to NH streching vibration of isatin moiety. The position of this band remains at nearly the same frequency in the spectra of both complexes, suggesting the non-coordination of this group. Bands at 1753 and 1650 cm^{-1}, respectively, due to C═O and C═N group stretching frequencies in the ligand, shift towards lower values in the complexes, indicating that the carbonyl oxygen atom of isatin moiety and the azomethine nitrogen atom are coordinated[17].

According to measurements of the magnetic susceptibility, the isolated complexes are paramagnetic.With account of obtained values of μ_{eff}, $[Cu(HL)_2Cl_2]$ has octahedral, while $[Ni(HL)_2]Cl_2$ tetrahedral ligand environment which correlates with the positions of absorption bands in their electronic absorption spectra[18].

TGA and DTG analyses of Ni(II) and Cu(II) complexes were conducted in air within the range 25–700°C at 10°C/min rate. TGA and DTG curves show that the Ni(II) and Cu(II) complexes have great stability up to 310 or 216°C, above which point weight loss begins. For complexes $[Ni(HL)_2Cl_2]$ and $[Cu(HL)_2]Cl_2$ decomposition proceeds in two main steps. The first step includes elimination of chlorine atoms in the 316–355°C and 216–249°C ranges, respectively. The second step includes decomposition of the Isatin-Schiff base moiety; the thermal decomposition finishes with the formation of metal oxides (NiO or CuO) as the final product (Figs. 1 and 2)[19]

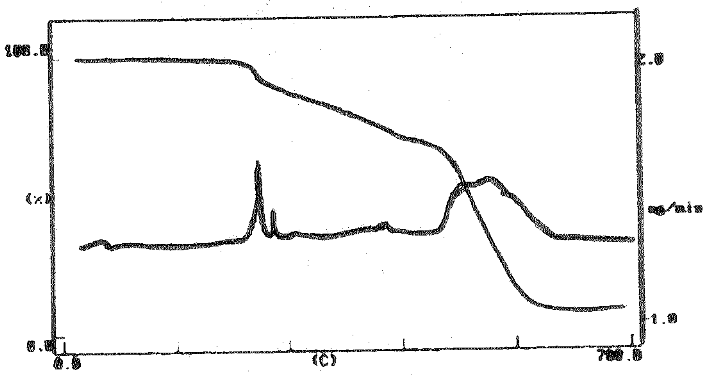

Fig. 1. TGA and DTG curves for the $[Ni(HL)_2Cl_2]$ complex

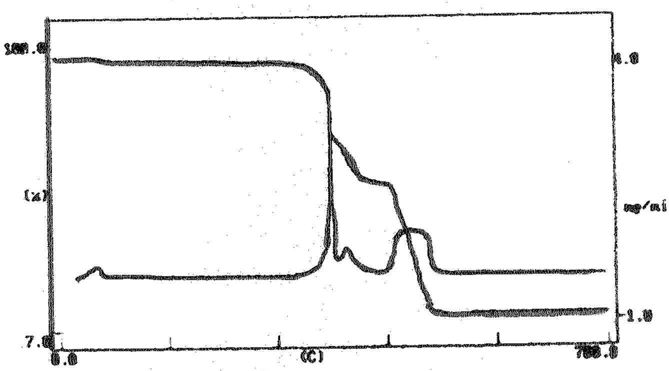

Fig. 2. TGA and DTG curves for the $[Cu(HL)_2]Cl_2$ complex

The molar conductivity measurements in DMSO (freshly prepared 10^{-3} M solutions) indicate that the Cu(II) complexes behave as non-electrolytes. Chloride ions are inside the coordination sphere. High molar conductance of the Ni(II) complex supports the fact that this compound is 1 : 2 electrolyte[20].

The conductivity range for semi-conducting materials is known[21] to be 10^{-7}–10^{2} s cm^{-1}. The solid-state electrical conductances (δ) at room temperature of HL and $[Cu(HL)_2Cl_2]$, $[Ni(HL)_2]Cl_2$ complexes are 1.17×10^{-5}; 5.05×10^{-6}; 5.35×10^{-6} s cm^{-1}, respectively. Both Schiff base and its complexes are found be semi-conducting, but Schiff base shows a higher conductivity than the parent complexes, which can be attributed to partial destruction of strong delocalization in the ligand by complexation.

The FAB-mass spectrum of the $[Cu(HL)_2Cl_2]$ complex does not display the expected molecular ion peak but instead exhibits peaks at m/z = 251.1, 503.2, 563.2, attributable to the $[HL + 1]^+$, $[2HL + 2]^+$ and $[2HL + Cu]^+$ fragment ions, respectively. The FAB-mass spectrum of the $[Ni(HL)_2]Cl_2$ complex, similar to that of the $[Cu(HL)_2Cl_2]$ complex, also shows a strong peak, m/z = 251.2, due to the $[HL + 1]^+$ ion.

The structural formulas of Cu(II) and Ni(II) complexes shown in Fig. 3 are consistent with the above mentioned data. The illustrated single crystal structure of copper complexes of hexyl derivative of ISE also supports the following suggested formula [unpublished data].

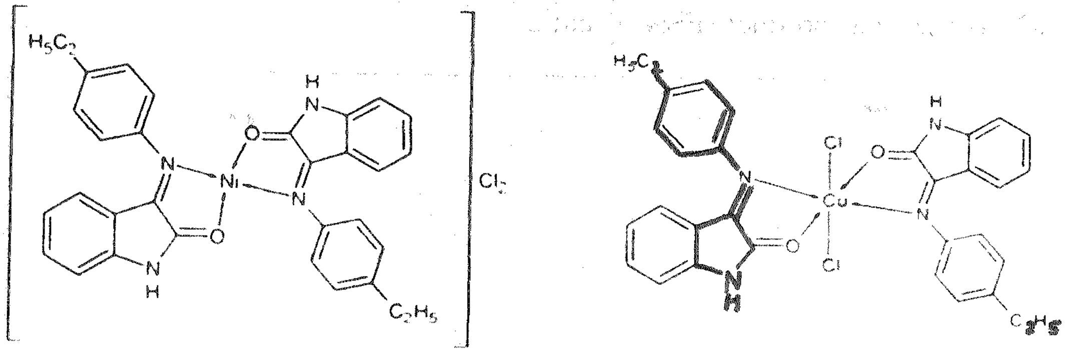

Fig. 3. Suggested structure of the complexes

The protonation behaviour and overall formation constant of ISE and its metal [Ni(II), Cu(II)] complexes were studied in 0.1 M $NaClO_4$ solution at 250.1°C temperature. The experiments were conducted in organic solvent mixture; 25–75% volume ethanol-water, dioxane-water, acetone-water [Table-1]. The ligand solution was titrated with standard sodium hydroxide to give the potentiometric equilibrium curve. A maximum number of two protons can be liberated from the ligand HL in the pH range 2.0–12.0. The distribution diagrams of ISE indicate that the doubly protonated species of ligand H_2L^+ predominate at pH = 4 and HL show a maximum around pH = 5–7. Free ligands (L^-) of ISE appear to dominate above pH = 9.

The titration data obtained for ISE in the presence of Ni(II) and Cu(II) ions were processed by the program TITFIT to observe the neutral and protonated complexes. Cumulative formation constants of the species encountered with all two metal ions are summarized in Table-1.

The numerical log β values determined in ethanol-water, dioxane-water, acetone-water mixtures increase with increasing ethanol, dioxane and acetone content in the solvent mixture, then the log β values decrease. We preferred the best solvent mixture 50% volume ethanol-water and the tests were conducted in ethanol-water 50–50% (volume) environment with I = 0.1 ($NaClO_4$) at different temperatures (10, 30, 40 ± 0.1°C).

Protonation and overall formation constants for the ligand and its metal (Cu(II), Ni(II)) complexes at different temperatures (10–40°C) are summarized in Table-2.

TABLE-1
PROTONATION AND OVERALL FORMATION CONSTANTS FOR ISE AND THEIR METAL Ni(II), Cu(II) COMPLEXES AT 25 ± 0.1°C FOR DIFFERENT SOLVENT MIXTURES

Solvent mixture	Species	log β*	Δ
25% E + 75% W	HL	5.08	0.021
	H_2L	13.41	0.021
50% E + 50% W	HL	8.03	0.0172
	H_2L	13.16	0.0172
75% E + 25% W	HL	7.74	0.017
	H_2L	11.05	0.017
25% A + 75% W	HL	4.86	0.0104
	H_2L	7.33	0.0105
50% A + 75% W	HL	10.52	0.025
	H_2L	14.58	0.025
75% A + 25% W	HL	8.14	0.0078
	H_2L	10.58	0.0078
25% D + 75% W	HL	10.39	0.0134
	H_2L	13.22	0.0135
50% D + 50% W	HL	10.04	0.1073
	H_2L	14.93	0.1670
75% D + 25% W	HL	9.03	0.028
	H_2L	11.13	0.028

* For computational purposes, the equilibria of the generalized algorithm will be set up in terms of overall constants, designated by β, in place of the more popular and more readily visualized stepwise constants (K).

Solvent mixture	Metal ion	Species	log β*	Δ
25% E + 75% W	Cu^{2+}	CuL	5.56	0.0025
		CuHL	8.70	0.0025
	Ni^{2+}	NiL	7.89	0.0053
		NiHL	11.00	0.0053
50% E + 50% W	Cu^{2+}	CuL	6.05	0.0160
		CuHL	12.40	0.0160
	Ni^{2+}	NiL	9.50	0.0290
		NiHL	13.00	0.0290
75% E + 25% W	Cu^{2+}	CuL	5.008	0.0160
		CuHL	10.02	0.0160
	Ni^{2+}	NiL	3.13	0.0154
		NiHL	9.82	0.0154
25% A + 75% W	Cu^{2+}	CuL	9.78	0.0396
		CuHL	15.20	0.0396
	Ni^{2+}	NiL	9.78	0.0395
		NiHL	15.20	0.0395
75% A + 25% W	Cu^{2+}	CuL	6.98	0.0136
		CuHL	11.64	0.0136
	Ni^{2+}	NiL	5.81	0.0206
		NiHL	7.63	0.0207
25% D + 75% W	Cu^{2+}	CuL	5.69	0.0094
		CuHL	8.31	0.0096
	Ni^{2+}	NiL	5.27	0.0141
		NiHL	7.66	0.0142

E: Ethanol, A: Acetone, D: Dioxane and W: Water, HL: 0.001 M,
log β = Mean value of two determinations, Δ = Standard deviation

TABLE-2
PROTONATION AND OVERALL FORMATION CONSTANTS FOR ISE AND ITS METAL (Cu(II), Ni(II)) COMPLEXES AT DIFFERENT TEMPERATURES (10–40°C) IN 50% (V/V) ETHANOL-WATER MEDIUM

Metal ion	Species	Log β* (Δ)		
		10°C	30°C	40°C
H^+	HL	8.49 (0.1203)	8.14 (0.1637)	8.95 (0.2046)
	MHL	13.74 (0.0156)	13.79 (0.2084)	3.53 (0.2622)
Cu^{2+}	CuL	5.40 (0.0714)	5.08 (0.0035)	6.05 (0.0086)
Ni^{2+}	NiL	7.15 (0.1397)	5.79 (0.187)	5.97 (0.1380)
	NiHL	14.04 (0.1193)	13.73 (0.1191)	12.73 (0.1196)

REFERENCES

1. J.F.M. Silva, S.J. Garden and A.C. Pinto, *J. Braz. Chem. Soc.*, **12**, 3 (2001).
2. R.T. Pardasani, R. Ghosh, D. Sherry and T. Mukherje, *Heteroatom. Chem.*, **10**, 381 (1999).
3. V. Glover, A.E. Medvedov and M. Sandler, *Vop. Med. Khim.*, **43**, 6 (2001).
4. G. Fachinetti, C. Floriani and P. Zanozzi, *Inorg. Chem.*, **18**, 3469 (1979).
5. S.N. Pandeya and D. Sriram, *Acta Pharm. Turc.*, **40**, 33 (1998).
6. S.N. Pandeya, D. Sriram, G. Nath and E. De Clercq, *Indian J. Pharm. Sci.*, **61**, 358 (1999a).
7. R.S. Varma and W.L. Nobles, *J. Med. Chem.*, **10**, 972 (1967).
8. S.N. Pandeya, P. Yogeswari, D. Sriram, E. De Clercq, C. Pannecouge and M. Witurouw, *Chemotherapy*, **45**, 192 (1999).
9. S.A. Imam and R.S. Varma, *Experientia*, **31**, 1287 (1975).
10. S.E. Sarcion, P. Audin, I. Delabre, C. Gabrion, A.F. Petavy and J. Paris, *J. Pharm. Sci.*, **82**, 605 (1993).
11. S.K. Sridhar, S.N. Pandeya, J.P. Stables and A. Ramesh, *Eur. J. Pharm. Sci.*, **16**, 129 (2002).
12. W.G. Hanna and M.M. Moawad, *Transition Met. Chem.*, **26**, 644 (2001).
13. A.D. Zuberbühler and T.A. Kaden, *Talanta*, **29**, 201 (1982).
14. E. Sezer, B. Ustamehmetolu and A.S. Saraç, *Int. J. Polym. Anal. Charact.*, **5**, 1 (1999).
15. L. Saccani, *Gazz. Chim. Ital.*, **83**, 899 (1953).
16. G.S. Singh and S. Prakash, *Indian J. Heterocycl. Chem.*, **7**, 145 (1995).
17. A.M.A. Hassan, *Transition Met. Chem.*, **15**, 283 (1990).
18. I.L. Dorokhtei, I.I. Seifullina and S.V. Zubkov, *Russ. J. Coord. Chem.*, **29**, 714 (2003).
19. T.H. Rakha, K.M. Ibrahim and M.I. Khalfa, *Thermochim. Acta*, **144**, 53 (1989).
20. W.J. Geary, *Coord. Rev.*, **7**, 81 (1971).
21. N. Sari and P. Gürkan, *Transition Met. Chem.*, **28**, 687 (2003).

(*Received*: 28 May 2005; *Accepted*: 22 December 2005) AJC-4552

THE PRACTICE OF MODERN HPLC,

DECEMBER 1–2, 2005

RESEARCH TRIANGLE PARK, NC

Contact:
LC Resources, Inc.
2930 Camino Diablo #110
Walnut Creek, CA 94596-9748
Tel: (800)(379-5221, Fax: (925)(977)9375
Website: http://www.LCResources.com