

## Studies on the synthesis, characterisation and antimicrobial activity of new Co(II), Ni(II) and Zn(II) complexes of Schiff base derived from ninhydrin and glycine

N. S. R. R. M. M. Koteswara Rao and M. G. Ram Reddy

Department of Chemistry, Osmania University, Hyderabad 500 007, India

Received October 18, 1989

**Summary.** For the first time, Co(II), Ni(II) and Zn(II) complexes have been synthesized involving an intermediate Schiff base, indane-1,3-dione-2-imine-*N*-acetic acid the condensed product of ninhydrin and glycine. These coloured complexes were characterised by elemental analysis, molar conductivity, thermogravimetric analyses/differential thermal analysis, infrared, magnetic susceptibility, NMR and electronic spectral studies. Mechanisms for their formation have been proposed. The experimental studies reveal that the complexes possess octahedral stereochemistry whereas the Schiff base behaves as a monobasic tridentate ligand. A molecular structure for the metal complexes is also proposed. A comparative study of the antimicrobial activity of ninhydrin and the corresponding metal complexes against *Escherichia coli*, *Proteus mirabilis*, *Staphylococcus aureus* and *Streptococcus faecalis* has been undertaken and the results are discussed.

**Key words:** Metal complexes – Tridentate Schiff base indane-1,3-dione-2-imine-*N*-acetic acid – Antimicrobial activity

### Introduction

Ninhydrin exhibits bacteriostatic, virucidal, fungistatic, antigen-antibody-reactive, inhibitive and diabetogenic properties (Yuki et al. 1966; Izard 1960; Tiffany et al. 1957; Kondo et al. 1954; Tayean and Faure 1953). The physiological activity of organic compounds has been observed to undergo a significant enhancement on addition of metals (Chrissey et al. 1988; Sorenson 1980). In particular, Schiff bases and their metal complexes have attracted a great deal of attention in biochemistry because of their vast applications as anticancer, antituber-

cular, anticonvulsant, insecticidal, antibacterial, antifungal, antiviral, antibiotic, anti-inflammatory agents and plant growth regulators (Shrivastava et al. 1986; Tondon 1986; Rao and Ganorkar 1981; Cyba 1968).

The qualitative and quantitative determination of amino acids, peptides and proteins is of major and growing importance in many areas of biochemical investigation. The most sensitive characteristic reaction in such determination is that between the amino acids and ninhydrin (triketo-hydrindene hydrate or 2,2-dihydroxy-1,3-indandione). The chemistry of this reaction has been extensively studied (MacFadyen 1950) and reviewed (McCaldin 1960). A number of workers established the mechanism by which ninhydrin reacts with amino acids producing a characteristic purple-coloured Schiff base, the Ruhemann's purple (diketo-hydrindylene diketo-hydrindamine) (Zlatkis et al. 1973; Mordecai 1975). The reaction kinetics and the pH dependence of the reaction were studied both in aqueous and mixed-solvent systems, viz. methyl cellosolve/water and dimethylsulphoxide/water (Lamothe and McCormick 1972; Friedman and Sigel 1966). In the chromatographic studies of ninhydrin/amino acid reactions, the transition metal ions were found to stabilize the bluish-violet pigment, Ruhemann's purple (Kawerau and Wieland 1951). It is observed that the interaction between ninhydrin and glycine in aqueous methyl cellosolve medium produced coloured solids in the presence of transition metal ions instead of the expected Ruhemann's purple. This has led to the present investigation, the synthesis and characterisation of new complexes of metals in the 3d group using ninhydrin and various amino acids. In this communication we report the findings on Co(II), Ni(II) and Zn(II) chelates of the Schiff base, indane-1,3-dione-2-imine-*N*-acetic acid (IDIAA), formed by the condensation of ninhydrin with glycine. In view of the physiological activities of ninhydrin and Schiff base complexes, a comparative study on the antimicrobial activity of ninhydrin and these metal complexes has been undertaken against *Escherichia coli*, *Proteus mirabilis*, *Staphylococcus aureus* and *Streptococcus faecalis* and the results are also presented.

## Materials and methods

**Materials.** Glycine (Reanal, Hungary), ninhydrin (Sigma), methyl cellosolve (E. Merck) and all other chemicals used were AnalaR grade.

**Analyses.** Infrared spectra were recorded on Perkin-Elmer 983 and Shimadzu-435 spectrophotometers using the KBr wafer technique in the range 4000–400  $\text{cm}^{-1}$ . Electronic spectra of the complexes in the range 200–1500 nm were recorded in dimethylsulphoxide on a Shimadzu UV-Vis recording spectrophotometer UV-240 (Graphicord) equipped with Shimadzu graphic printer PR-1 and Varian Cary 17D spectrophotometers. NMR spectra were obtained in  $\text{CDCl}_3$  at a concentration of 1–0.01 mM on a Varian EM-390 NMR spectrometer, using tetramethylsilane as the internal standard. Conductivity measurements were carried out using a Digital direct reading conductivity meter. Thermogravimetric analysis (TGA) and differential thermal analysis (DTA) were recorded on a Lintus type 2041-DTA/TGA simultaneous unit. The experiments were conducted at a heating rate of 10° C/min. Magnetic susceptibilities of the complexes were measured at room temperature on a PAR EG & G Princeton Applied Research vibrating sample magnetometer model 155. Nitrogen estimation was carried out by the microvolumetric method using a micro-Kjeldahl apparatus; C and H contents were estimated by micro-analytical methods. The metals were analysed on a Perkin-Elmer 1280 atomic absorption spectrophotometer.

**Preparation of complexes.** The complexes were prepared following a general procedure. An aqueous solution of M(II) nitrate [M(II) = Co(II), Ni(II) or Zn(II)] (0.01 mol) was added to a solution of ninhydrin (0.02 mol) in 50% (by vol.) aqueous methyl cellosolve (100 ml). The mixture was refluxed for 2 h. To the hot contents, an aqueous solution of glycine (0.02 mol) was added and refluxing was continued for another 2 h. Then the solution was concentrated under reduced pressure to half its volume and kept over night. The coloured solid that separated out was filtered, repeatedly washed with water and finally with aqueous ethanol. The compounds were dried *in vacuo*. Due to the photosensitive character of the refluxing mixture, all the operations during the preparation of the complexes were carried out in apparatus coated with black enamel paint.

**Measurement of antimicrobial activity.** Ninhydrin and metal complexes were dissolved in dimethylsulphoxide at 1 mg/ml concentration. The composition of the penassay agar medium was 6 g peptone (Difco), 1.5 g beef extract (Hi media), 1.5 g yeast extract (Oxoid), 1.0 g D-glucose, 1.5 g NaCl, 1.32 g  $\text{KH}_2\text{PO}_4$ , 3.68 g  $\text{K}_2\text{HPO}_4$ , 2% agar, 1 l distilled water; final pH 7.2. After 18 h, the exponentially growing cultures of the four bacteria in penassay broth at 37° C were diluted in further sterile broth. From each of these diluted cultures, 1 ml was added to 100 ml sterilized and cooled penassay agar media to give a final bacterial count of  $2 \times 10^6$  cells/ml. The plates were allowed to set at room temperature and later dried at 37° C for 2 h. Paper discs (6 mm, punched from Whatmann no. 41 paper) were ultraviolet sterilized and were used for the assay. Discs were soaked in different concentrations of the test solutions and placed on the inoculated agar media at regular intervals of 6–7 cm. Care was taken to ensure that excess solution was not on the discs. All samples were taken in triplicate. The plates were incubated at 37° C in an inverted fashion. The inhibition zones were measured after 24 h.

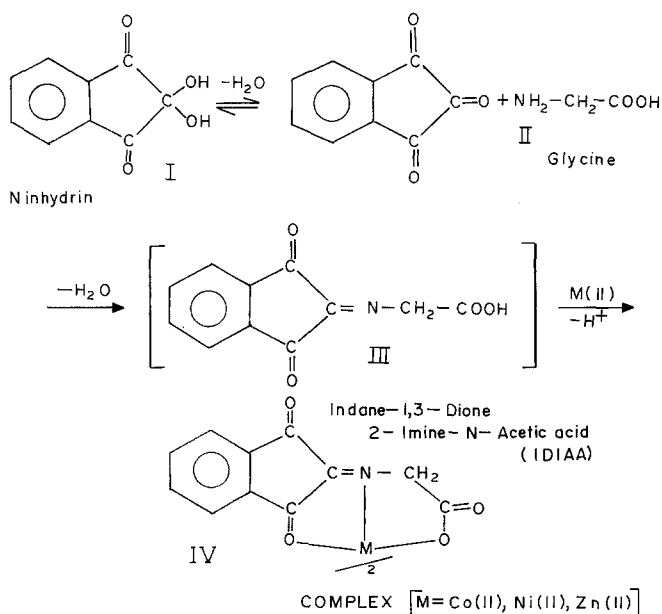
## Results and discussion

Glycine yields a bluish-violet Schiff base, Ruhemann's purple, with ninhydrin. The reaction involves the condensation of ninhydrin and glycine followed by decar-

boxylation. Hydrolysis of the intermediate gives a 2-amino-1,3-diketone, which undergoes further condensation with another molecule of ninhydrin, resulting in Ruhemann's purple (Zlatkis et al. 1973). The present investigation indicates that in the presence of metal ions [M(II) = Co(II), Ni(II) and Zn(II)] the reaction appears to stop just after the condensation of ninhydrin and glycine forming an intermediate Schiff base, indane-1,3-dione-2-imine-*N*-acetic acid (IDIAA). This condensed product after deprotonation results in the formation of an anion, indane-1,3-dione-2-imine-*N*-acetate (IDIA), which acts as a potential tridentate metal-binding ONO donor producing stable five-membered metal chelates (Scheme I). The presence of M(II) ions in the system most probably favours the condensation of ninhydrin and glycine by enhancing the polarisation of carbonyl groups, thereby promoting the nucleophilic attack resulting in the production of IDIAA (Holm et al. 1966) which in turn binds the metal ion after deprotonation. The neighbouring —COOH with a replaceable hydrogen increases the basicity of the azomethine group in IDIAA (Smith 1970) thus favouring the formation of a stable metal chelate.

The products obtained in the presence of Co(II), Ni(II) and Zn(II) ions are characterised as IDIA metal complexes on the basis of elemental analysis, molar conductance, TGA, DTA, spectral and magnetic data.

All the complexes are coloured, stable towards air and moisture, decompose at high temperatures and are partially soluble in methanol, ethanol and chloroform and completely soluble in dimethylsulphoxide. The analytical data (Table 1) of the complexes indicate the metal/ligand ratio at 1:2. Molar conductance values of the complexes in 1 mM dimethylsulphoxide were found to be in the range of 0.1–0.4  $\text{M ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$ , suggesting their nonelectrolytic character.



**Scheme I.** Reaction of glycine with ninhydrin in the presence of metal(II) ions

**Table 1.** Analytical data of IDIA metal complexes

Complex	Molecular formula	Colour	Decomp. temp. (°C)	Found (calc) (%)			
				Carbon	Hydrogen	Nitrogen	Metal
Co(II) IDIA	Co(C <sub>11</sub> H <sub>6</sub> O <sub>4</sub> N) <sub>2</sub>	Dark green	> 320	53.65 (53.77)	2.45 (2.45)	5.72 (5.70)	12.08 (12.02)
Ni(II) IDIA	Ni(C <sub>11</sub> H <sub>6</sub> O <sub>4</sub> N) <sub>2</sub>	Green	> 360	53.96 (53.80)	2.44 (2.45)	5.76 (5.70)	11.74 (11.96)
Zn(II) IDIA	Zn(C <sub>11</sub> H <sub>6</sub> O <sub>4</sub> N) <sub>2</sub>	Brown	> 320	52.97 (53.08)	2.45 (2.41)	5.76 (5.63)	12.82 (13.15)

Thermogravimetric measurements showed that the metal complexes do not contain either crystalline water or coordinated water as no endotherm was observed in DTA curves in the range of 95–325°C (Sharma et al. 1986; Baker et al. 1985) and they are quite stable thermally. Decomposition of the complexes took place at relatively high temperatures in the range 340–440°C.

The infrared spectral data for the new metal complexes of IDIA, glycine, ninhydrin and Ruhemann's purple are presented in Table 2 with their assignments. The infrared spectrum of ninhydrin exhibits  $\nu_{\text{OH}}$  at 3300–3200 cm<sup>-1</sup> and the  $\nu_{\text{C=O}}$  at 1753 cm<sup>-1</sup> and 1712 cm<sup>-1</sup> respectively. Glycine shows  $\nu_{\text{NH}_2}$  at 3200–2800 cm<sup>-1</sup> and  $\nu_{\text{COO(asp)}}$  at 1600 cm<sup>-1</sup>. The complexes indicate a band in the range of 1630–1610 cm<sup>-1</sup> assigned to  $\nu_{\text{COO(asp)}}$ . A positive shift of 10–30 cm<sup>-1</sup> is observed in the antisymmetric stretching frequencies of the carboxylate group of IDIAA and follows Nakamoto's order (Nakamoto et al. 1963; antisymmetric stretching frequencies increase while symmetric stretching frequencies decrease due to coordination); this indicates that the deprotonation of IDIAA and subsequent coordination occurs through the carboxylate group (Bellamy 1975; Baranwaal et al. 1984). The infrared frequencies for the carbonyl groups in ninhydrin are shifted from 1753 cm<sup>-1</sup> and 1712 cm<sup>-1</sup> to 1720–1710 cm<sup>-1</sup> and 1705–1700 cm<sup>-1</sup>. The negative shift of about 30–40 cm<sup>-1</sup> indicates the involvement of one of the two carbonyl groups of ninhydrin in coordination with the metal ion in the form of IDIA. The infrared frequencies corresponding to the N—H of glycine and —OH of ninhydrin are absent in the spectra of the

complexes. Instead, a new strong and sharp peak characteristic of  $\nu_{\text{C=N}}$  has been observed at 1510–1500 cm<sup>-1</sup>, suggesting the formation of an azomethine group due to condensation of glycine and ninhydrin (Colthup and Daly 1964; Jana and Sahoo 1984; Shrivastava et al. 1986; Sharma et al. 1987). The usual frequency at which  $\nu_{\text{C=N}}$  appears is about 1670–1600 cm<sup>-1</sup> (Dhakarey and Saxena 1987; Yao 1964). Its negative shift by about 100 cm<sup>-1</sup> is a clear indication of the participation of azomethine nitrogen in coordination (Singh and Mishra 1986; Mahto 1981). This fact is further confirmed by the absence of such a peak in the individual spectrum of either glycine or ninhydrin. The non-ligand bands appearing in 750–600-cm<sup>-1</sup> region of spectra of complexes may be assigned to  $\nu_{\text{(M—N)}}$  and  $\nu_{\text{(M—O)}}$  modes respectively (Nakamoto 1970; Vekatarman et al. 1986). It could therefore be concluded that IDIAA behaves as a tridentate ONO donor involving a carbonyl oxygen, a carboxyl oxygen and an azomethine nitrogen in coordination.

The <sup>1</sup>H-NMR spectra of the metal complexes show two prominent resonance signals: Co(II),  $\delta$  6.9, 1.48; Ni(II),  $\delta$  7.0, 1.6, Zn(II),  $\delta$  7.1, 2.1, respectively. Signals around  $\delta$  7.0 are due to aromatic protons and those occurring between  $\delta$  1.48–2.1 are of methylene protons (Mann et al. 1974). Free glycine as a zwitterion was expected to give signals at  $\delta$  7.6 (NH<sub>3</sub><sup>+</sup>) and  $\delta$  4.2 (CH<sub>2</sub>) (Bovey and Tiers 1959). The peak due to the charged amino group at  $\delta$  7.6 is absent in the present complexes. But the signal for CH<sub>2</sub> protons has been shifted from  $\delta$  4.2 to  $\delta$  1.48–2.1 which can be attributed to the coordination. Further, the absence of any signal around  $\delta$

**Table 2.** Infrared spectral characteristics of IDIA metal complexes

Compound	$\nu_{\text{NH}_2}$	$\nu_{\text{CH}_2}$	$\nu_{\text{OH}}$	$\nu_{\text{C=O}}$	$\nu_{\text{COO}}$	$\nu_{\text{C=N}}$	$\nu_{\text{C=C}}$	$\nu_{\text{M—N/M—O}}$
Glycine	3200–2800 b	1420 s			1600 m			
Ninhydrin			3300–3200 b	1753 s 1712 m			1590 s	
Ruhemann's purple	3200–3000 b			1700 m	1600 m		1585 m	
Co(II) IDIA		1420 m		1710 s 1705 m	1610 s	1500 vs	1585 s	700 m, 740 m, 760 m
Ni(II) IDIA		1440 m		1720 s 1705 m	1630 s	1510 vs	1590 s	650 m, 700 m, 730 m, 750 m
Zn(II) IDIA		1420 m		1710 s 1700 m	1610 s	1500 vs	1590 s	660 m, 700 m, 740 m, 760 m

vs = very strong; s = strong; m = medium; b = broad

**Table 3.** Magnetic and electronic spectral data

Compound	$\mu_{\text{eff.}}$ (BM)	Band positions ( $\text{cm}^{-1}$ )	Assignment	$D_q$ ( $\text{cm}^{-1}$ )	$\nu_2/\nu_1$	$B'$	$\beta$
Co(II) IDIA	4.3	7787, 16700, 20000 (multiple band), 31250 (CT)	$4T_{1g} \rightarrow 4T_{2g}$ $4T_{1g} \rightarrow 4A_{2g}$ $4T_{1g} \rightarrow 4T_{1g}$ (P)	891.2	2.1446	889	0.7938
Ni(II) IDIA	2.8	11993; 20620; 24690; 16660	$3A_{2g} \rightarrow 3T_{2g}$ $3A_{2g} \rightarrow 3T_{1g}$ (F) $3A_{2g} \rightarrow 3T_{1g}$ (P) $3A_{2g} \rightarrow 1T_{1g}$	1199.3	1.7193	622	0.5759
Zn(II) IDIA	Diamagnetic						

$D_q$  is a measure of crystal field splitting energy

12.0, characteristic of  $-\text{COOH}$  protons, supports the deprotonation; the presence of signals only due to aromatic and methylene protons confirms the involvement of IDIA in chelation.

The magnetic moment values, the electronic spectral data and corresponding assignments of the complexes are presented in Table 3. The Co(II) and Ni(II) complexes are paramagnetic with magnetic moments at room temperature of 4.3 and 2.8 BM respectively ( $1 \text{ BM} = 9.2732 \text{ J T}^{-1}$ ). These values show the presence of three unpaired electrons in Co(II) ( $d^7$ ) and two unpaired electrons in Ni(II) ( $d^8$ ). These magnetic moments are consistent with octahedral geometry which is further supported by electronic spectral data.

The Co(II) complex exhibits three absorptions at 7787, 16700 and 20000  $\text{cm}^{-1}$  (multiple band) which are assigned to the three spin-allowed transitions in octahedral stereochemistry. In addition there is a band observed at 31250  $\text{cm}^{-1}$  assignable to a charge-transfer transition. Similarly, three bands observed for an Ni(II) complex at 11993, 20620 and 24690  $\text{cm}^{-1}$  fall in the three distinct regions (Lever 1984) which are characteristic of octahedral geometry. A low-intensity band is also observed at 16660  $\text{cm}^{-1}$  which is assigned to a spin-forbidden transition. Table 3 also presents  $D_q$ ,  $\nu_2/\nu_1$ , Racah inter-electron repulsion parameter ( $B'$ ) and nephelauxetic parameter ( $\beta$ ) for the complexes (Gupta et al. 1982). The calculations show appreciable metal-ligand interaction resulting in a large electron delocalisation and good covalent character of the me-

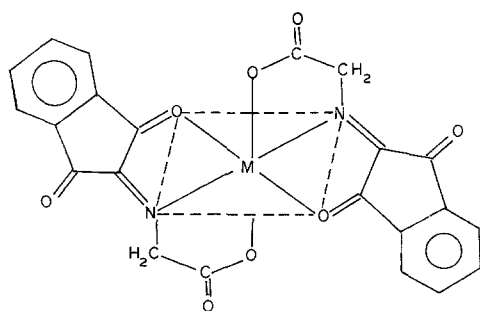
tal-ligand bonds. The covalent character increases from Co(II) to Ni(II) complex.

On the basis of the elemental analysis, conductivity, infrared and electronic spectra and magnetic moments data, octahedral geometry is proposed for the Co(II) and Ni(II) complexes. The Zn(II) complex is diamagnetic and has no absorption in the range 200–1500 nm. Due to the  $d^{10}$  configuration, the Zn(II) complex is not expected to have any paramagnetic moment nor show any absorption in the visible region. On the basis of metal-ligand stoichiometry, conductance and other data, the Zn(II) complex is also assumed to have octahedral geometry. The proposed structure is given in Fig. 1.

#### Antimicrobial activity of ninhydrin and its metal chelates

The following bacterial cultures were tested for their susceptibility to ninhydrin and the metal chelates by the disc diffusion method (Grove and Randall 1955; Kavanagh 1972) in penassay agar media: *Escherichia coli*, *Proteus mirabilis*, *Staphylococcus aureus* (Oxford strain) and *Streptococcus faecalis*. The results obtained are shown in Table 4.

Free ninhydrin is highly active against *E. coli* and *S. aureus* and moderately active against *P. mirabilis* and *S. faecalis*. The marked activity of free ninhydrin has been attributed to the keto groups present in the molecule (Sproessig and Muecke 1963). The activity of ninhydrin is totally lost in the metal-bound state of the complexes of Co(II), Ni(II) and Zn(II) with IDIA. The ineffectiv-



**Fig. 1.** The proposed structure of the M(II) Schiff base complex derived from ninhydrin and glycine

**Table 4.** Antimicrobial activity

Bacterial cultures	Ninhydrin	Co(II) IDIA	Ni(II) IDIA	Zn(II) IDIA
<i>E. coli</i>	+++	—	—	—
<i>P. mirabilis</i>	++	—	—	—
<i>S. aureus</i>	+++	—	—	—
<i>S. faecalis</i>	++	—	—	—

Symbols: + + +, highly sensitive; + +, moderately sensitive; —, insensitive

ity of the complexes may be due to the binding of the carbonyl group with metal ion in coordination and also its involvement in azomethine formation. Hence it may be concluded that the metal ions are functioning as quenching agents of the antimicrobial activity of ninhydrin in the presence of glycine. In view of lack of bioactivity of metal complexes, quantitative studies involving tube dilution methods were not carried out.

**Acknowledgements.** Thanks are due to Prof. T. Navaneeth Rao (Vice-Chancellor, Osmania University) for his keen interest and constant encouragement. One of the authors (N S R R M M K R) is grateful to the University Grants Commission for the award of teacher fellowship under the Faculty Improvement Programme.

## References

- Baker LCW, Mukherjee HG, Shyamali de (1985) Synthesis and characterisation of tritellurato-cobaltate(III) complex. *J Indian Chem Soc* 58:569-571
- Baranwaal BP, Parashar GK, Mehrotra RC (1984) Synthesis and physico-chemical studies of some binuclear mixed carboxylates of copper(II). *J Indian Chem Soc* 61:923-925
- Bellamy LJ (1975) The infrared spectra of complex molecules. Chapman and Hall, London
- Bovey FA, Tiers GVD (1959) Proton NMR spectroscopy V. Studies of amino acids and peptides in trifluoroacetic acid. *J Am Chem Soc* 81:2870-2878
- Chrissey LA, Sharidi Bonjar GH, Hecht SM (1988) DNA strand scission by (–)-epicatechin and procyanidin B<sub>2</sub>. *J Am Chem Soc* 110:644-646
- Colthup NB, Daly LH (1964) Introduction to infrared and Raman spectroscopy. Academic Press, New York
- Cyba HA (1968) US Patent 3398170
- Dhakarey R, Saxena G (1987) Synthesis, spectral and magnetic studies of Ni(II) complexes with Schiff bases of heterocyclic aldehydes. *J Indian Chem Soc* 64:685-686
- Friedman M, Sigel CW (1966) A kinetic study of the ninhydrin reaction. *Biochemistry* 5:478-484
- Grove DC, Randall WA (1955) Assay methods of antibiotics. Medical Encyclopedia Inc, New York
- Gupta HK, Mourya P, Dey AK (1982) Mannich bases as potential polydentate ligands: 2,5-bis(benzylaminomethyl) hydroquinone complexes. *J Indian Chem Soc* 59:216-218
- Holm RH, Everett GM Jr, Chakravorty A (1966) Metal complexes of Schiff's bases and  $\beta$ -keto amines. *Prog Inorg Chem* 7:104
- Izard C (1960) Utilization of ninhydrin as an adjuvant of serological reaction in gel: application to the viruses of plants. *Compt Rend* 250:3906-3908
- Jana AK, Sahoo B (1984) Tetranuclear metal complexes of copper(II) with *m*-bis(1,3,5-trioxohexyl)benzene and *m*-bis(1,3,5-trioxo-5-phenylpentyl)benzene and corresponding macrocyclic Schiff base complexes formed with *O*-phenylenediamine. *J Indian Chem Soc* 61:936-939
- Kavanagh F (1972) Analytical microbiology 2nd edn. Academic Press, New York, pp 1-86
- Kawerau E, Wieland T (1951) Conservation of amino acid chromatograms. *Nature* 168:77-78
- Kondo K, Chiba W, Kawai F (1954) The mechanism of inhibition by ene-diol compounds, aminobenzene derivatives and ketone compounds. *Bull Res Inst Food Sci* 13:53-59
- Lamothe PJ, McCormick PG (1972) Influence of acidity on the reaction of ninhydrin with amino acids. *Anal Chem* 44:821-825
- Lever ABP (1984) Inorganic electronic spectroscopy, 2nd edn. Elsevier, Amsterdam, pp 507
- MacFadyen DA (1950) On the mechanism of the reaction of ninhydrin with  $\alpha$ -amino acids. *J Biol Chem* 186:1-12
- Mahto CB (1981) Studies on the complexes of 3-hydroxy-2-naphthaldehyde thiosemicarbazone with some divalent and trivalent metal ions. *J Indian Chem Soc* 58:935-936
- Mann CK, Vickers TJ, Gulick WM (1974) Instrumental analysis. Harper and Row, New York pp 537-543
- McCaldin DJ (1960) The chemistry of ninhydrin. *Chem Rev* 60:39-51
- Mordecai BR (1975) The chemistry of vicinal polyketones. *Chem Rev* 75:177-202
- Nakamoto K (1970) Infrared spectra of inorganic and coordination compounds. Wiley Interscience, New York, pp 247-251
- Nakamoto K, Morimoto Y, Martell AE (1963) Infrared spectra of aqueous solutions I. Metal chelate compounds of amino acids. *J Am Chem Soc* 83:4528-4536
- Rao DS, Ganorkar MC (1981) Synthesis of some transition metal chelates of furfurylidene and 5-nitrofurfurylidene benzoylhydrazones as potential fungicides. *J Ind Chem Soc* 58:217-219
- Sharma IB, Batra S, Balla S, Gupta RK (1986) Thermal decomposition of  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ . *J Ind Chem Soc* 63:520-523
- Sharma RK, Sharma CP, Sharma A (1987) Synthesis and spectroscopic investigations on bisdithio-carbamato complexes of di-*p*-*tert*-butyl-phenyl tin(IV). *J Ind Chem Soc* 64:205-208
- Shrivastava VS, Bhasin LP, Saxena GC (1986) Spectral and magnetic and antibacterial studies of some newly synthesized Mn(II), Co(II), Ni(II) and Cu(II) complexes. *J Ind Chem Soc* 63:865-868
- Singh B, Misra H (1986) Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and dioxouranium(II) complexes of thiophene-2-aldehyde-4-phenyl thiosemicarbazone. *J Ind Chem Soc* 63:1069-1070
- Smith JW (1970) Basic and Complexing properties. In: Patai S (ed) The chemistry of the carbon-nitrogen double bond. Interscience, New York, pp 239-240
- Sorenson RJJ (1980) US Patent 4-221785
- Sproessig M, Muecke H (1963) Inactivation of viruses by  $\alpha$ -dicarbonyl compounds. *Acta Virol* 7:472-474
- Tayean F, Faure F (1953) Ninhydrin and the antigen-antibody reaction. *Bull Soc Chem Biol* 35:1193-1199
- Tiffany BD, Wright JB, Moffett RB, Heinzelman RV, Strube RE, Aspergren BD, Lincoln EH, White JL (1957) Antiviral compounds. I. Aliphatic glyoxals,  $\alpha$ -hydroxy-aldehydes and related compounds. *J Am Chem Soc* 79:1682-1687
- Tondon JP (1986) Synthesis of some novel boron Schiff base and allied derivatives. *J Ind Chem Soc* 63:451-459
- Venkataraman VR, Kather MS, Mansoor I, Nagarajan S (1986) Nickel(II) and copper(II) complexes with 2',4'-dihydroxy-5'-(4-methoxy)cinnamoyl-4-methoxy chalcone. *J Ind Chem Soc* 63:925-926
- Yao HC (1964) Azohydrazone conversion II. The coupling of diazonium ion with  $\beta$ -diketone. *J Org Chem* 29:2959-2963
- Yuki H, Sano F, Takama S, Suzuki S (1966) Antiviral agents I. Relation between chemical reactivity of sulfhydryl reagents and their inactivating activity of adenovirus 5. *Chem Pharm Bull (Tokyo)* 14:139-146
- Zlatkis A, Breitmaier E, Jung G (1973) A concise introduction to organic chemistry. McGraw Hill, New York