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Metal-Chelation and Biological Activity

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Importance of chelation of multidentate donors with biologically important metal ions has been emphasized in this work. As metal ions involve practically in phases of biological activity, hence this work throws light on useful information for elucidating the various types of mechanism in biological systems. Thus chelate compounds of the general formula $(ML)_2L^1$ where M = Na, K, Mg and Ca; L = deprotonated organic acids like lactate and oxalate ions L′= *o*-carboxyl-bis-benzene-azo-resorcinol and o-nitro-bis-benzene-azo-resorcinol have been synthesised and studied to develop innovative strategies for preparing improved and better complexes in the light of chelate hypothesis.

Key Words: Metal, Chelation, Biological activity.

INTRODUCTION

Sodium and potassium coordination compounds have been known for more than fifty years[1] and ion pairs have been studied extensively in non-aqueous solution. The outstanding characteristic of alkali metal complexes in solution is their weakness, but they are important because of the common occurrence of alkali metal ions at high concentration, *e.g.*, in biological systems, in sea water, in constant ionic media or when added in a reagent.

It it well known[2] that the heterocyclic compounds containing potential donor atoms N, O and S exhibit antibacterial activity due to the presence of multifunctional (heterofunctional) groups; when such ligands are complexed with the metal ions they have enhanced activity[3–7].

It is also known that sodium and calcium are more important for animal kingdom, while potassium and magnesium are more important for plant kingdom. Thus the present work is devoted to the synthesis and characterisation of the metal chelates by the interaction of multifunctional donor compounds like *o*-carboxyl-bis-benzene azo-resorcinol, (COOH—BAR) *o*-nitro-bis-benzene azo-resorcinol (NO_2—BAR) and sodium, potassium, magnesium and calcium salts of organic acids, *e.g.*, lactic acid and oxalic acid and to the study of the biological activity of metal chelates. The synthesised metal chelates have the general formula $(ML)_2$—COOH—BAR and $(ML)_2$—NO_2—BAR (M = Na, K, Mg and Ca; L = deprotonated organic acid like lactate and oxalate ions.

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RESULTS AND DISCUSSION

Under dry condition the chelates are stable when stored in a desiccator. The chelates of COOH—BAR and NO_2—BAR are all red, deep red or deep brown coloured. The potassium chelates are relatively more thermally stable than their corresponding sodium analogues while magnessium chelates have been found more stable compared to their corresponding calcium analogues. When heated, they undergo decomposition at a temperature higher than the melting point of COOH—BAR and NO_2—BAR. The chelates break on simple heating to form the salts and donor molecules COOH—BAR and NO_2—BAR and as such throw light on the fact that the bonding in these chelates is not much strong. The colour and decomposition temperatures of the compounds are given in Table-1.

The presence of —COOH groups and —OH groups in the *o*, *o'* position to the (—N=N—) groups suggests the possibility of strong intramolecular hydrogen bonding in the ligand COOH—BAR which therefore forms stabler chelate as the metals are chelated in cyclic form. We actually get the solid chelates with the sodium, potassium, magnesium and calcium salts of lactate and oxalate in 95% ethanolic medium, but the presence of —NO_2 group in the NO_2—BAR reduces somewhat the chelating ability of the donor molecule due to its electron withdrawing nature. As a result we get the chelates of sodium and potassium salts of lactic acid in the solution phase while with magnesium and calcium salts of oxalic acid we get the chelate in the solid form.

The —OH stretch at 3050 cm^{-1} (br) of the COOH—BAR is missing in the chelates. The asymmetric stretch of the COO^- group shows up at 1710 cm^{-1} in the COOH—BAR. This shifts down to 1630–1620 cm^{-1}. The —N=N— frequency in the ligand occurs at 1580 cm^{-1}. In the chelates it appears in the 1570–1560 cm^{-1} region.

Thus we conclude that metals are complexed by these heterofunctional groups (—OH, —COO^-, —N=N—) of the COOH—BAR.

In the NO_2—BAR chelates, the —OH stretching frequency occurs at *ca.* 2600 cm^{-1}. Both the antisymmetric and symmetric NO_2 stretch frequencies are lower in the chelate compared to NO_2—BAR. The —N=N— band shows at 1555 cm^{-1} as a small hump and is shifted to about 1540 cm^{-1} in the chelates.

The key IR bands of COOH—BAR, NO_2—BAR and their metal chelates for heterofunctional groups (—OH, —COO^-, —N=N, —NO_2) have been summarised in Table-1.

Biological activity is mainly structually specific *i.e.*, dependent upon factors such as the presence or absence of certain groups, intra-molecular distances, the shape of molecule and the interaction of the chelates with a cellular receptor. The structure reactivity relationship confirms the assumption that the active principle of the drugs has the characteristic groups complementary to the structures of the receptors, *e.g.*, in penicillins and cephalosporins the active part is OCN grouping of the β-lactam thiazolidine ring[2]. In streptomycin molecule, it is the N-methyl-L-glucosamine unit which takes part in chelation with the metal ion through the nitrogen and the oxygen atoms[8,9]. Oxytetracycline molecules chelate with the metal ions through the —COCHC(OH)— grouping using both the oxygen atoms.[10]

TABLE-1
KEY IR BANDS (cm^{-1}) OF THE COMPOUNDS

Compound (Colour)	Decomp. temp. (°C)	ν(OH)	$\nu_{asym}(COO)$	ν(—N=N—)
COOH—BAR=L^{I} (Deep red)	320	3050 br	1710 s	1580 m
$(NaL_1)_2L^{I}$ (brown)	335	—	1650 s	1560 m
$(KL_1)_2L^{I}$ (deep brown)	345	—	1630 s	1550 m
$(MgL_2)_2L^{I}$ (deep brown)	350	—	1615 s	1535 m
$(CaL_2)_2L^{I}$ (red)	330.	—	1620 s	1540. m
	Decomp. temp. (°C)	ν(OH)	$\nu_{asym}(NO_2)$	ν(—N=N—)
NO_2—BAR=L^{II} (deep red)	280	2600 br	1575 s	1555 m
$(NaL_1)_2L^{II}$ (brown)	295	—	1560 s	1540 m
$(KL_1)_2L^{II}$ (deep brown)	300	—	1550 s	1530 m
$(MgL_2)_2L^{II}$ (deep brown)	310	—	1540 s	1520 m
$(CaL_2)_2L^{II}$ (reddish)	292	—	1545 s	1525 m

COOH—BAR(L^{I}) = *o*-Carboxyl bis-benzene azo-resorcinol L_1 =Lactate ion
NO_2—BAR(L^{II}) = *o*-nitro-bis-benzene azo-resorcinol L_2 =Oxalate ion

Since lactic acid is the main constituent of sour milk, It occurs in blood and muscles of human beings where it is produced by the decomposition of glycogen; hence this work throws light on the biological activity as the chelates are weak and decompose in the biological system to compensate the losses of sodium lactate in it. Similarly ammonium oxalate is present in urine and calcium oxalate in many other plants such as grapes and tomatoes. The excess of oxalate ions causes some disorderliness in the biological systems; hence this work may throw light to reduce/compensate the oxalate ion/calcium ion in the systems.

EXPERIMENTAL

The ligands COOH—BAR, NO_2—BAR were prepared by standard methods[12]. Their melting points are 320 and 280°C respectively. All the alkali, alkaline earth metal salts used were prepared in 95% ethanol. The chelates were prepared by the following general method. To the hot absolute ethanolic solution of COOH—BAR and NO_2—BAR, Na and K salts of lactic acid and Mg and Ca salts of oxalic acid were added in 1 : 2 molar ratio. The whole mixture in solution

was refluxed over hot plate using magnetic stirrer for about 1 h. The solution on keeping yielded crystalline solid chelate in the case of oxalate chelates while in some lactate chelates of Na and K we could not isolate the chelate in the solid form. The solid chelates were filtered, washed with absolute alcohol and dried in an oven at 80°C.

REFERENCES

1. D. Midgley, *Chemical Soc. Reviews*, **4**, 549 (1975).
2. Purushottam B. Chakrawarti, *J. Indian Chem. Soc.*, **78**, 273 (2001).
3. A. Tiwary, H.N. Sharma and P.B. Chakrawarti, *Indian J. Chem.*, **19A**, 83 (1980).
4. P.B. Chakrawarti, B. Shrivastava and B. L. Vijayvargiya, *J. Indian Chem., Soc.*, **70**, 158 (1993).
5. P.B. Chakrawarti, M. Chakrawarti and P. Maini, *Proc. Nat. Acad. Sci. India* (A) (in press).
6. F.P. Dwyer, in: Metal Chelates in F.P. Dwyer and D.P. Mellor (Eds.), *Biological Systems*, Academic Press, New York (1964).
7. L. Mishra and V.K. Singh, *J. Agric. Biol. Chem. (Jpn.)*, **55**, 1883 (1991).
8. J.K. Agrawal, H. Harmalkar and R. Vijayvargiya, *Microchem. J.*, **21**, 202 (1978); *J. Indian Chem. Soc.*, **52**, 190, 576 (1975).
9. P.B. Chakrawarti and A. Shinde, *Proc. Nat. Acad. Sci. India*, **62A**, 563 (1992); P. Singh and M.S. Kachhawa, *Vijanan Parishad Anusandhan Patrika*, **32**, 123 (1989).
10. ———, *J. Indian Chem. Soc.*, **70**, 240 (1993).
11. Beilstein-Prager-Jacobson, *Org. Chemic*, Band XVI, System No-2065–2358.

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