

the *exo* carbonyl groups turn into the cavity to form ligands with the metal ion [5,6,10-12]. In addition, *cis/trans* isomerism of amide bonds may occur [2,18], intramolecular hydrogen bonds are broken [1,2,18], and elongated peptide ring backbones become folded. Examples will be presented.

REFERENCES

- [1] I.L. KARLE, *Int. J. Pept. Protein Res.*, **23**, 32-38 (1984).
- [2] I.L. KARLE, J. KARLE, *Proc. Natl. Acad. Sci. USA*, **78**, 681-685 (1981).
- [3] G. KARTHA, K.I. VARUGHESE, S. AIMOTO, *Proc. Natl. Acad. Sci. USA*, **79**, 4519-4523 (1982).
- [4] Y.H. CHIU, L.D. BROWN, W.N. LIPSCOMB, *J. Am. Chem. Soc.*, **99**, 4799-4802 (1977).
- [5] I.L. KARLE, *J. Am. Chem. Soc.*, **96**, 4000-4006 (1974).
- [6] I.L. KARLE, *Biochemistry*, **13**, 2155-2162 (1974).
- [7] M. PINKERTON, L.K. STEINRAUF, P. DAWKINS, *Biochem. Biophys. Res. Commun.*, **35**, 512-518 (1969).
- [8] K. NEUPERT-LAVES, M. DOBLER, *Helv. Chim. Acta*, **58**, 432-442 (1975).
- [9] L.K. STEINRAUF, J.A. HAMILTON, M.N. SABESAN, *J. Am. Chem. Soc.*, **104**, 4085-4091 (1982).
- [10] I.L. KARLE, E.N. DUESLER, *Proc. Natl. Acad. Sci. USA*, **74**, 2602-2606 (1977).
- [11] I.L. KARLE, *J. Am. Chem. Soc.*, **91**, 5152-5157 (1977).
- [12] I.L. KARLE, TH. WIELAND, H. FAULSTICH, H.C.J. OTTENHEYM, *Proc. Natl. Acad. Sci. USA*, **76**, 1532-1536 (1979).
- [13] I.L. KARLE, *J. Am. Chem. Soc.*, **100**, 1286-1289 (1978).
- [14] I.L. KARLE, in A. EBERLE, R. GEIGER, TH. WIELAND (eds.), «Perspectives in Peptide Chemistry», S. Karger, Basel, 1981, pp. 261-271.
- [15] W.L. DUAX, H. HAUPTMAN, C.M. WEEKS, D.A. NORTON, *Science*, **176**, 911 (1972).
- [16] I.L. KARLE, *J. Am. Chem. Soc.*, **97**, 4379-4386 (1975).
- [17] G.D. SMITH, W.L. DUAX, D.A. LANGS, G.T. DE TITTA, J.W. EDMONDS, D.C. ROHRER, C.M. WEEKS, *J. Am. Chem. Soc.*, **97**, 7242-7247 (1975).
- [18] M. CZUGLER, K. SASVÁRI, M. HOLLÓSI, *J. Am. Chem. Soc.*, **104**, 4465-4469 (1982).



PS5.15 — TH

PETER M. MAY
KEVIN MURRAY
DANIEL PEAPER

Department of Applied Chemistry
UWIST
Cardiff
U.K.

THE EFFECT OF SODIUM ION INTERFERENCE ON BIOINORGANIC FORMATION CONSTANTS DETERMINED BY GLASS ELECTRODE POTENTIOMETRY

Recently, a library of computer programs for the determination of metal-ligand formation constants, called ESTA (Equilibrium Simulation for Titration Analysis), has been developed [1]. These programs permit various corrections which are important in the measurement of thermodynamic parameters required by those modelling metal-ion interactions in biological fluids (e.g. blood plasma, intestinal juice and saliva [2]). Changes in ionic activities, liquid junction potentials and ion-selectivity of the electrodes used for potentiometric titrations can be calculated [3].

Such corrections become necessary when the background ionic strength of a titration is not high enough to remain reasonably constant. This is often the case in work of biological relevance, where ionic strengths less than 200 mmol dm⁻³ are commonplace. Moreover, the formation constants of many bioinorganic systems are such that pH measurements need to be made in relatively alkaline solutions where sodium ion interference with the glass electrode response is most pronounced. The object of the present work was to quantify the effect of this interference and to assess the seriousness of neglecting it in a typical study of a metal-ligand interaction with bioinorganic interest.

In the first stage, potential differences arising from the presence of sodium ions in the titration

solutions were characterised in terms of two parameters, K and α . K is the selectivity coefficient in the NICOLSKI equation [4] when $\alpha = 1$. Data were collected experimentally and from the literature [5].

In the second stage, experimental titration data for the binding between zinc(II) and the amino acid, cysteine [6,7] were analysed using the ESTA program. Sodium ion interference was found to introduce a systematic error, rising to several millivolts towards the end of each titration. As a result, the first protonation constant of cysteine ($\log \beta_{101} = 10.01$) was lowered by 0.03 log units by omitting from the numerical analysis the effects of sodium ion in the background electrolyte. Larger differences were found for the metal-ligand formation constants (e.g. $\Delta \log \beta_{210} = 0.06$; $\Delta \log \beta_{330} = 0.1$). Generally, the errors were about ten times larger than the calculated standard deviations for the corresponding formation constants.

It may be concluded that significant systematic errors have affected many bioinorganic formation constants determined in sodium ion background electrolyte solutions. However, with modern glass electrodes, the magnitude of these errors is probably about the same as other systematic effects (such as those arising from errors in the analytical concentrations of the solutions being titrated). Nevertheless, they are sufficiently serious to warrant attention in any precise determination of formation constants for bioinorganic purposes.

REFERENCES

- [1] K. MURRAY, P.M. MAY, «ESTA User's Manual», Department of Applied Chemistry, UWIST, Cardiff, 1984.
- [2] P.M. MAY, R.A. BULMAN, *Prog. Med. Chem.*, **20**, 225 (1983).
- [3] P.M. MAY, K. MURRAY, D.R. WILLIAMS, *Talanta*, **32**(6) (1985), in press.
- [4] B.P. NICOLSKY, *Acta Physiochim. USSR*, **7**, 597 (1937).
- [5] N. LINNET, «pH Measurements in Theory and Practice», Radiometer, Copenhagen, 1970.
- [6] C. FURNIVAL, P.M. MAY, D.R. WILLIAMS, unpublished data.
- [7] G. BERTHON, P.M. MAY, D.R. WILLIAMS, *J. Chem. Soc., Dalton Trans.*, 1433 (1978).



PS5.16 — MO

ADRIANO BENEDETTI

CARLO PRETI

LORENZO TASSI

GIUSEPPE TOSI

Instruments Centre

Department of Chemistry

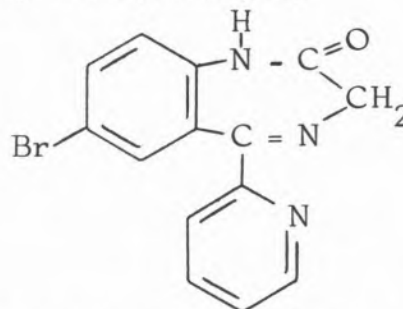
University of Modena

Via G. Campi, 183, 41100 Modena

Italy

SYNTHESIS AND CHARACTERIZATION OF d-BLOCK COMPLEXES WITH BROMAZEPAM AS LIGAND

Working in the field of 1,4-benzodiazepines of biological and pharmacological interest as ligands, we report the complexes of ruthenium(III), osmium(III), rhodium(III), iridium(III), palladium(II) and platinum(II) halides with 7-bromo-1,3-dihydro-5-(2-pyridil)-2H-1,4-benzodiazepin-2-one (bromazepam).



These new derivatives, of the ML_3X_3 and MLX_2 type, have been characterized on the basis of elemental analyses, IR and electronic spectra, multinuclear NMR studies, conductivity measurements, magnetic susceptibility data and thermal analyses. These studies suggest a pseudo-octahedral structure for rhodium and iridium derivatives and a square planar geometry for the palladium and platinum ones. The ligand behaves always as bidentate through the nitrogen in 4-position of the diazepine ring and the nitrogen of the pyridine ring.

Assignments for the metal-ligand and metal-halide bands have been made.

The results will be compared with those obtained with other 1,4-benzodiazepines.