Session on Thermodynamic Aspects of the Interaction between Metal Ions and Ligands of Biological Interest

---

M1

Thermodynamic Aspects of Solvophobic Forces in Simple and Mixed Complex Formation of Metal Ions with Biofunctional Ligands

ENRICO RIZZARELLI

Istituto Dipartimentale di Chimica e Chimica Industriale, Università di Catania, viale A. Doria 8, 95125 Catania, Italy

Solvophobic [1] or hydrophobic [2, 3] interactions are known to occur in biomolecules and to contribute to the formation of distinct structural conformations, which provide the specificity and the reversibility required in most biological processes [4]. These forces occur between two aliphatic or alicyclic groups, between two aromatic groups and between aliphatic and aromatic groups.

As regards metal complexes of low molecular weight, the presence of this interaction has been invoked to explain i) the biological activity of some coordination compounds [5, 6]; ii) the stability enhancement of some ternary complexes [7]; and iii) other distinct features in their reactivity [8] and their thermodynamic properties [9]. The appearance of this so-called 'secondary' bond has usually been inferred from potentiometric titrations, UV-difference spectra and NMR shift measurements.

Recently, we have shown that the calorimetric technique is a very powerful tool to bring to light the solvophobic interactions in some ATP metal complexes [9]. In particular, the effect of these forces resulted in a more favourable enthalpic and in a less favourable entropic contribution for $[M(ATP)(trp)]^{3-}$ with respect to $[M(ATP)(ala)]^{3-}$ species. As for zinc(II) complexes, the difference was more pronounced in comparison with what was found for copper(II). The formation of $[Zn(ATP)(trp)]^{3-}$ was about 10 Kcal mol^{-1} more exothermic and 30 e.u. lower with respect to $[Zn(ATP)(ala)]^{3-}$. Bearing in mind that in the latter complex stacking interaction is not possible, this difference has been assumed as an index of the presence of solvophobic interaction. Such a favourable trend in ΔH° values has been found for other mixed complexes of zinc(II) with ATP and some biofunctional ligands [10]. Furthermore, on the basis of the thermodynamic properties, the study of the mixed complexes of 2,2′-bipyridyl and mono- or di-alkyl substituted malonate ligands with copper(II) and zinc(II), has shown that the occurring of solvophobic forces is dependent on the geometrical coordination requirement of metal ions. Finally, the role of these interactions in the thermodynamic stereoselectivity of some dipeptide complexation has also been assessed. For example, the formation of $[Cu(L,L\text{-}leu,leuH_{-1})]$ complex is more enthalpically and less entropically favoured with respect to $[Cu(L,D\text{-}leu,leuH_{-1})]$ species. This behaviour is due to favourable orientation of side chains which gives rise to a solvophobic interaction in the 'pure' with respect to the 'mixed' derivative.

1 O. Sinanoglu, *Int. J. Quantum Chem., 18,* 381 (1980).
2 W. Kauzmann, *Adv. Protein Chem., 14,* 34 (1959).
3 A. Ben-Naim, 'Hydrophobic Interactions', Plenum Press, New York, 1980.
4 E. Frieden, *J. Chem. Educ., 52,* 754 (1975).
5 J. K. Barton and S. J. Lippard, in 'Nucleic Acid Metal Ion Interactions', T. G. Spiro ed., Wiley, New York, 1980, p. 31–113.
6 K. S. Rajan, J. M. Davis, R. W. Colburn and F. H. Jarke, *J. Neurochem., 19,* 1099 (1972).
7 C. F. Naumann and H. Sigel, *J. Am. Chem. Soc., 96,* 2750 (1974).
8 Y. Numata, H. Okawa and S. Kida, *Chem. Lett.,* 293 (1979).
9 G. Arena, R. Calì, V. Cucinotta, S. Musumeci, E. Rizzarelli and S. Sammartano, *J. Chem. Soc., Dalton Trans.,* 000 (1983).
10 *idem, ibidem,* submitted for publication.

M2

Thermodynamic Evaluation of Chelate and Cooperativity Effects

A. BRAIBANTI*, F. DALLAVALLE, G. MORI and
M. PASQUALI

Institute of Pharmaceutical Chemistry, Physical Chemistry Section and Institute of General Chemistry, University of Parma, Italy

The chelate effect occurs in the binding of a ligand, containing two or more donor atoms, with a metal ion [1] or a macromolecule [2]. The chelate effect causes an increase in the stability of the complexes with respect to those formed with the same number of donor atoms belonging to separate liganding molecules. The evaluation of the chelate effect has been done up to now by calculating the constant $K_{chel} = K_{ML}/\beta_{MA_2}$, where M = metal or macromolecule, A = monodentate ligand, L = bidentate chelating ligand, K_{ML} = formation constant of the chelate ML, β_{MA_2} = cumulative formation constant of the complex MA_2. L (homotropic chelate) has two donor atoms equal to that of A.