and is known to exist in solid mixed ligand complexes [6].

Aromatic-ring stacking is another very subtle possibility for an influence and equilibrium (1) may even be shifted to its right side, *i.e.* for the logarithm of the corresponding equilibrium constant, $\Delta \log K_M$

$$M(A) + M(B) \rightleftharpoons M(A)(B) + M \quad (1)$$

$$\Delta \log K_M = \log K^{M(A)}_{M(A)(B)} - \log K^{M}_{M(B)} = \log K^{M(B)}_{M(B)(A)} - \log K^{M}_{M(A)} \quad (2)$$

(eqn. 2) [1], positive values are observed. For example, for the Mg^{2+} or Ca^{2+}/1,10-phenanthroline (Phen)/adenosine 5'-triphosphate (ATP^{4-}) system $\Delta \log K_M \simeq 0.5$ due to the intramolecular stacking between the purine moiety of ATP^{4-} and the aromatic-ring system of Phen (studied by potentiometric pH-titrations, UV-difference spectrophotometry and ^{1}H-NMR shift measurements) [7]. This leads to an intramolecular equilibrium (3) between an 'open' and 'closed' isomer of the ternary com-

$$M(A)(B)_{open} \rightleftharpoons M(A)(B)_{closed} \quad (3)$$

plex, M(A)(B). About 90% of $Ca(Phen)(ATP)^{2-}$ exist in the 'closed' form [4], while for M(tryptophanate)$(ATP)^{3-}$ where $M^{2+} = Mn^{2+}$, Cu^{2+} or Zn^{2+} the corresponding percentages are 55, 41 and 76 [4].

Hydrophobic interactions are observed between the isopropyl residue of leucinate (Leu) and Phen; *e.g.* of $Zn(Phen)(Leu)^+$ exist about 30% in the 'closed' form [8]. Estimations for M(phenylalaninate)(norvalinate) complexes, where $M^{2+} = Co^{2+}$, Ni^{2+} or Cu^{2+}, give 21, 5 and 11%, respectively, for the isomer with an intramolecular hydrophobic interaction [4, 8].

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Protonation and Complexation Equilibria of Macromolecular Bioligands in Aqueous and Mixed Solvent Solutions. The Solvent Effect

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Coordination chemical equilibria of macromolecular polyfunctional ligands in solution are extremely sensitive to changes in the composition of the solvent. The conformation of such molecules is usually solvent dependent and their conformational changes may result in the alteration of the H-bridge formation reactions in the system. These are reflected by the protonation and complexation equilibria [1, 2].

The characterization of the functional groups taking part in such processes by equilibrium constants is made, however, difficult by the overlap of several analogous (*e.g.* protonation) equilibria in the system, resulting *e.g.* in the formation of protonation isomers (species of equal ligand: bound proton ratios but of different structure).

For the characterization of the single functional groups in overlapping protonation or complexation equilibria a new evaluation method [3] was elaborated leading to the determination of 'group constants'.

Protonation equilibria of several macromolecular polypeptides (*e.g.* corticotropin fragments, angiotenzine analogs and the basic tripsin inhibitor Kunitz Base) were studied in aqueous and mixed solvent solutions and the new evaluation method was used for the determination of the equilibrium constants. The silver and zinc complex formation of these peptides has been also studied.

The effect of the solvent on the equilibria in solution will be discussed in the lecture.

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