In this conformation the N7 atoms are far away from the phosphate group, and the metal ion can bind either to the phosphate or to the base, but not simultaneously to both [4].

Strong interactions were observed between Ni^{2+} ions and the polynucleotide poly(A) [4]. Quantitative data were obtained by using murexide as an indicator for the concentration of free metal ions. The difference from the total metal concentration gives the amount of Ni^{2+} bound to poly(A). This technique is applicable for free Ni^{2+} concentrations 10^{-5}–10^{-3} *M*. At the upper limit, 1 Ni^{2+} is bound per 4.4 mononucleotide units (ionic strength 0.1 *M*). A Scatchard plot yields a straight line, *i.e.* the process can formally be described as the binding of Ni^{2+} to one class of independent binding sites at poly(A). Slope and intercept of the plot yield a value of 0.26 for the number of binding sites per monomer (*i.e.* 4 monomers form one binding site), and a stability constant $K = 8.2 \times 10^3 M^{-1}$ for the binding of Ni^{2+} to these binding sites. In kinetic studies of this system two reaction effects were detected. The kinetic data can be rationalized in terms of a mechanism which involves a second-order (outer-sphere) association process followed by 3 first-order steps (inner-sphere binding, probably to two phosphates and one base [6]). The high overall stability constant is mainly due to strong outer-sphere association (high charge density at poly(A)).

1 R. S. Taylor and H. Diebler, *Bioinorg. Chem., 6*, 247 (1976).
2 A. Peguy and H. Diebler, *J. Phys. Chem., 81*, 1355 (1977).
3 A. Nagasawa and H. Diebler, *J. Phys. Chem., 85*, 3523 (1981).
4 M. J. Hynes and H. Diebler, *Biophys. Chem., 16*, 79 (1982).
5 H. Sigel, K. Becker and D. B. McCormick, *Biochim. Biophys. Acta, 148*, 655 (1967).
6 A. Yamada, K. Akasada and H. Hatano, *Biopolymers, 15*, 1315 (1976).

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Factors Influencing the Affinities between Metal Ions and Donor Atoms in Ligands of Biological Interest

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The biochemistry of a metal in a certain oxidation state is very much determined by its affinity for various ligands. Not only the absolute strengths of the metal–ligand interactions are important, however, but also the relative affinities between ligands of various properties and types.

Two classes of metal ion acceptors have been discerned, characterized by different ligand affinity sequences. These classes termed (a), or hard, and (b), of soft, show the sequences [1–4]:

(a)	(b)
$F \gg Cl > Br > I$	$F \ll Cl < Br < I$
$O \gg S > Se > Te$	$O \ll S < Se \simeq Te$
$N \gg P > As > Sb > Bi$	$N \ll P > As > Sb > Bi$

Ligands preferring hard, or soft, acceptors are also termed hard, or soft, respectively.

The soft acceptors are situated in a roughly triangular area of the periodic system, with the apex of the triangle at copper and the base extending approximately from osmium to bismuth. For a certain element, however, the character depends very much upon the oxidation state. Also, the border-line is not sharp. Thus, copper(I) is typically soft while copper(II) is a border-line case. Though the transition is gradual, the difference in properties between the same oxidation state of neighbour metals across the border-line is considerable. Thus, while mercury(II) is typically soft, and cadmium(II) mildly so, zinc(II) generally behaves as a fairly hard acceptor.

The classification of the metal acceptors was done from stability measurements in aqueous solutions. The stabilities measured evidently depend upon the dielectric and solvating properties of the medium used, however. A high dielectric constant will decrease the strength of all ionic interactions. A further decrease of the stabilities of the complexes will result if both the metal ion and the ligand are strongly solvated; the solvation processes generally compete strongly with the complex formation [5, 6].

If the solvation of the ligands does not present any special features, the change of solvation from one medium to another will be much the same for all ligands in the group. The stabilities of the complexes might thus change considerably, but with much the same factor for all ligands; the relative order will stay the same. If, on the other hand, the ligands of a group are differently preferred by different solvents, changes in the affinity sequence do occur [5].

In the case of the halide ions, the ability to form hydrogen bonds decreases sharply along the series, being very strong for F^- and hardly perceptible for I^-. In the same sequence, the preference for protic solvents where such bonds can be formed sharply decreases. Several examples are known where this factor brings about switches in the affinity sequence.

As mentioned, zinc(II) generally behaves as a hard acceptor, with the affinity sequence $F^- \gg Cl^- > Br^- > I$, as illustrated by the stability constants K_1 measured for the reactions $Zn^{2+} + X^- \rightleftharpoons ZnX^+$ in aqueous solution, Table I. Built into the enzyme carbonic anhydrase, zinc(II) displays the opposite affinity sequence, however, Table I. The reason is certainly that in the enzyme, the coordination site of zinc(II) is situated in a hydrophobic crevice. In order to enter, the ligands have to undergo an extensive

TABLE I. Stabilities of Halide Complexes of Zn^{2+} and of Zn(II) in Carbonic Anhydrase (CA).

Ligand	K_1	
	Zn^{2+} [5, 7][a]	Zn CA [8][b]
F^-	6	5
Cl^-	0.6	25
Br^-	0.3	80
I^-	0.03	630

[a] Aqueous solution, ionic strength I = 1 *M*, 20 °C (F^-); I = 3 *M*, 25 °C (Cl^-, Br^-, I^-). [b] Aqueous solution containing 10% acetonitrile, I = 0.009 *M*, 25 °C.

dehydration. The resulting stability of the complex will depend crucially upon how easily this dehydration can take place. In this respect, the ions are evidently more handicapped the stronger they are hydrogen bonded. Hence a (b)-sequence evolves instead of the (a)-sequence found in ordinary aqueous medium.

The halides act as ligands only as monoatomic halide ions. All other donors, except S^{2-} in strongly alkaline solutions, occur as parts of more or less complicated polyatomic ligands. The donor properties will therefore depend not only upon the donor atom but also upon its atomic environment. In Table II, the influence of various groups attached to S and Se is demonstrated. Strongly electron withdrawing groups, such as the aromatic system of the benzene ring, weaken the donor properties very markedly. The effect is further enhanced by electronegative substituents in the benzene ring, such as SO_3^- or, even more, NO_2. For silver, Se is inherently a better donor than S, the values of K differing throughout by a little less than a power of ten.

The result of another systematic variation of the groups attached to the donor atom is presented in Fig. 1. Here silver complexes formed by phosphine ligands containing three aliphatic, or three aromatic, groups are compared, both in water and in dimethylsulfoxide (DMSO). The complex formation curves indicate that in both solvents the complexes formed by the aromatic phosphines are the much weaker ones. In water, the curve of a phosphine (Dsp) containing two aromatic and one aliphatic group has also been determined. It takes its expected place between the other two. To make the phosphines soluble in water, various hydrophilic groups have to be introduced; this may account for the cross-over in the upper part of the curves referring to aqueous solution. In DMSO, where no such modifications are necessary, the curves are indeed very conform.

TABLE II. Stabilities (stepwise constants K_j/M^{-1}) of Silver Sulfide and Selenide Complexes in Aqueous Solution, at 25 °C [9–11]. Influence of the atomic environment of the donor atom, and of the chelate effect.[a]

Ligand	X = S		X = Se	
	K_1	K_2	K_1	K_2
$p\text{-}EtXC_6H_4SO_3^-$	415	48		
$p\text{-}PhXC_6H_4SO_3^-$	47	22	430	180
$X(C_6H_4SO_3^-\text{-}p)_2$[b]	25	8		
$PhXCH_2COO^-$	590	123	4220	300
$p\text{-}NO_2C_6H_4XCH_2COO^-$	72		660	214
$\text{-}(CH_2XCH_2COO^-)_2$[b]	89000			
$o\text{-}C_6H_4(XCH_2COO^-)_2$[b]	9300			

[a] I = 0.1 *M*, or, for ligands marked [b], 0.2 *M*.

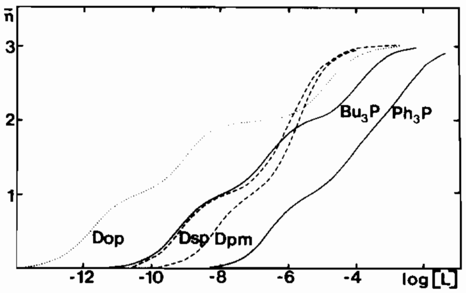

Fig. 1. Complex formation function of silver phosphine systems in water and DMSO, at 25 °C (Dop 22 °C). The curves give the ligand number n̄, *i.e.* the average number of ligands L coordinated per Ag^+, as a function of log[L]. Solid lines refer to the unsubstituted tributyl- and triphenylphosphines measured in DMSO (I = 0.1 *M*). Dashed and dotted lines refer to substituted phosphines measured in water, *viz.* Dop = $Et_2P(CH_2)_2OH$ (I = 1 *M*), Dsp = $Ph_2P(CH_2)_3SO_3^-$ (I = 1 *M*), Dpm = $m\text{-}Ph_2PC_6H_4SO_3^-$ (I = 0.1 *M*).

Polyatomic ligands may contain more than one donor atom. If rings of suitable size can be formed, these donors act in concert. The resulting chelates are much more stable than the complexes containing the same number of donor atoms present in the corresponding monodentate ligands. Examples are given in Table II, where the values of K_1 of the disulfides are much larger than the values of the product K_1K_2 of the corresponding monosulfides. Whether a chelate formation involving the sulfide and carboxylate groups takes place is on the other hand doubtful; the stabilities of the complexes formed by $EtSC_6H_4SO_3^-$ and $PhSCH_2COO^-$ do not differ very much.

A very favourable chelate arrangement may even compensate for a not very strong metal–donor atom interaction. Thus, magnesium(II) is a hard acceptor, generally showing little affinity for nitrogen, a markedly softer donor than oxygen. In chlorophyll, however, the porphine arrangement of four suitably situated nitrogens offers such a favourable possibility for chelate formation that a very stable magnesium complex nevertheless results, a fact clearly recognized quite early [13].

1 S. Ahrland, J. Chatt and N. R. Davies, *Quart. Rev. Chem. Soc., 12*, 265 (1958).
2 R. G. Pearson, *J. Amer. Chem. Soc., 85*, 3533 (1963).
3 S. Ahrland, *Struct. Bonding, 1*, 207 (1966).
4 R. G. Pearson (Ed.), 'Hard and Soft Acids and Bases' (in the series: Benchmark Papers in Inorganic Chemistry); Dowden, Hutchinson and Ross, Stroudsburg, Pa., 1973.
5 S. Ahrland, *Pure Appl. Chem., 51*, 2019 (1979).
6 S. Ahrland, *Pure Appl. Chem., 54*, 1451 (1982).
7 S. Ahrland and K. Rosengren, *Acta Chem. Scand., 10*, 727 (1956).
8 S. Lindskog, *Struct. Bonding, 8*, 153 (1970).
9 S. Ahrland, J. Chatt, N. R. Davies and A. A. Williams, *J. Chem. Soc.*, 264 (1958).
10 D. Barnes, P. G. Laye and L. D. Pettit, *J. Chem. Soc. A*, 2073 (1969).
11 G. J. Ford, L. D. Pettit and C. Sherrington, *J. Inorg. Nucl. Chem., 33*, 4119 (1971).
12 S. Ahrland, E. Avsar and T. Berg, *J. Organomet. Chem., 181*, 17 (1979).
13 R. Willstätter, 'Aus meinem Leben', Verlag Chemie, Weinheim, Bergstrasse, 1949, p. 177.