Stability Constant of Complex

Ram Lakhan Meena

Assistant Professor in Chemistry, Govt. College Karauli, Rajasthan, India

ABSTRACT: In coordination chemistry, a **stability constant** (also called **formation constant** or **binding constant**) is an equilibrium constant for the formation of a **complex** in solution. It is a measure of the strength of the interaction between the reagents that come together to form the complex. There are two main kinds of complex: compounds formed by the interaction of a metal ion with a ligand and supramolecular complexes, such as host–guest complexes and complexes of anions. The stability constant(s) provide(s) the information required to calculate the concentration(s) of the complex(es) in solution. There are many areas of application in chemistry, biology and medicine.

**KEYWORDS**: stability, constant, complex, equilibrium, binding, metal, ligand, chemistry, biology, medicine

I.INTRODUCTION

Jannik Bjerrum (son of Niels Bjerrum) developed the first general method for the determination of stability constants of metal-ammine complexes in 1941.[1] The reasons why this occurred at such a late date, nearly 50 years after Alfred Werner had proposed the correct structures for coordination complexes, have been summarised by Beck and Nagypál.[2] The key to Bjerrum's method was the use of the then recently developed glass electrode and pH meter to determine the concentration of hydrogen ions in solution. Bjerrum recognised that the formation of a metal complex with a ligand was a kind of acid–base equilibrium: there is competition for the ligand, L, between the metal ion, M^{n+}, and the hydrogen ion, H^+. This means that there are two simultaneous equilibria that have to be considered. In what follows electrical charges are omitted for the sake of generality. The following twenty years saw a veritable explosion in the number of stability constants that were determined. Relationships, such as the Irving-Williams series were discovered. The calculations were done by hand using the so-called graphical methods. The mathematics underlying the methods used in this period are summarised by Rossotti and Rossotti.[3] The next key development was the use of a computer program, LETAGROP[4][5] to do the calculations. This permitted the examination of systems too complicated to be evaluated by means of hand-calculations. Subsequently, computer programs capable of handling complex equilibria in general, such as SCOGS[6] and MINIQUAD[7] were developed so that today the determination of stability constants has almost become a "routine" operation. Values of thousands of stability constants can be found in two commercial databases.[8][9]

The thermodynamics of metal ion complex formation provides much significant information.[13] In particular it is useful in distinguishing between enthalpic and entropic effects. Enthalpic effects depend on bond strengths and entropic effects have to do with changes in the order/disorder of the solution as a whole. The chelate effect, below, is best explained in terms of thermodynamics. To avoid the complications involved in using activities, stability constants are determined, where possible, in a medium consisting of a solution of a background electrolyte at high ionic strength, that is, under conditions in which Γ can be assumed to be always constant.[15] For example, the medium might be a solution of 0.1 mol dm^{-3} sodium nitrate or 3 mol dm^{-3} sodium perchlorate. When Γ is constant it may be ignored and the general expression in theory, above, is obtained.

All published stability constant values refer to the specific ionic medium used in their determination and different values are obtained with different conditions, as illustrated for the complex CuL (L = glycinate). Furthermore, stability constant values depend on the specific electrolyte used as the value of Γ is different for different electrolytes, even at the same ionic strength. There does not need to be any chemical interaction between the species in equilibrium and the background electrolyte, but such interactions might occur in particular cases. For example, phosphates form weak complexes with alkali metals, so, when determining stability constants involving phosphates, such as ATP, the background electrolyte used will be, for example, a tetralkylammonium salt. Another example involves iron(III) which forms weak complexes with halide and other anions, but not with perchlorate ions.
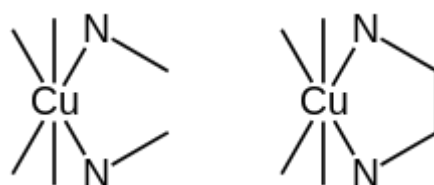
When published constants refer to an ionic strength other than the one required for a particular application, they may be adjusted by means of specific ion theory (SIT) and other theories.[17]
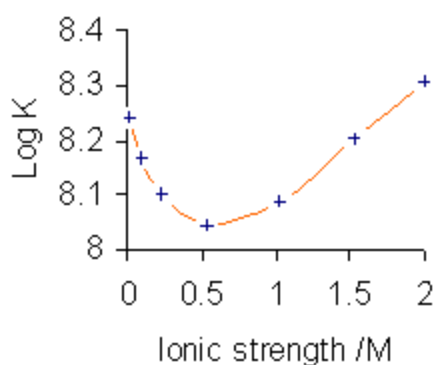
Dependence of the stability constant for formation of $[Cu(glycinate)]^+$ on ionic strength $(NaClO_4)$[16]

In the first reaction the bidentate ligand ethylene diamine forms a chelate complex with the copper ion. Chelation results in the formation of a five-membered ring. In the second reaction the bidentate ligand is replaced by two monodentate methylamine ligands of approximately the same donor power, meaning that the enthalpy of formation of Cu–N bonds is approximately the same in the two reactions. Under conditions of equal copper concentrations and when then concentration of methylamine is twice the concentration of ethylenediamine, the concentration of the bidentate complex will be greater than the concentration of the complex with 2 monodentate ligands. The effect increases with the number of chelate rings so the concentration of the EDTA complex, which has six chelate rings, is much higher than a corresponding complex with two monodentate nitrogen donor ligands and four monodentate carboxylate ligands. Thus, the phenomenon of the chelate effect is a firmly established empirical fact: under comparable conditions, the concentration of a chelate complex will be higher than the concentration of an analogous complex with monodentate ligands.

The thermodynamic approach to explaining the chelate effect considers the equilibrium constant for the reaction: the larger the equilibrium constant, the higher the concentration of the complex.

Cu^{2+} complexes with methylamine (left) end ethylene diamine (right)

In the first reaction the bidentate ligand ethylene diamine forms a chelate complex with the copper ion. Chelation results in the formation of a five-membered ring. In the second reaction the bidentate ligand is replaced by two monodentate methylamine ligands of approximately the same donor power, meaning that the enthalpy of formation of Cu–N bonds is approximately the same in the two reactions. Under conditions of equal copper concentrations and when then concentration of methylamine is twice the concentration of ethylenediamine, the concentration of the bidentate complex will be greater than the concentration of the complex with 2 monodentate ligands. The effect increases with the number of chelate rings so the concentration of the EDTA complex, which has six chelate rings, is much higher than a corresponding complex with two monodentate nitrogen donor ligands and four monodentate carboxylate ligands. Thus, the phenomenon of the chelate effect is a firmly established empirical fact: under comparable conditions, the concentration of a chelate complex will be higher than the concentration of an analogous complex with monodentate ligands.

The thermodynamic approach to explaining the chelate effect considers the equilibrium constant for the reaction: the larger the equilibrium constant, the higher the concentration of the complex.
When the analytical concentration of methylamine is twice that of ethylenediamine and the concentration ijf copper is the same in both reactions, the concentration $[Cu(en)]^{2+}$ is much higher than the concentration $[Cu(MeNH_2)_2]^{2+}$ because $\beta_{11} \gg \beta_{12}$.

The difference between the two stability constants is mainly due to the difference in the standard entropy change, $\Delta S^{\ominus}$. In the reaction with the chelating ligand there are two particles on the left and one on the right, whereas in equation with the monodentate ligand there are three particles on the left and one on the right. This means that less entropy of disorder is lost when the chelate complex is formed than when the complex with monodentate ligands is formed. This is one of the factors contributing to the entropy difference. Other factors include solvation changes and ring formation.

II.DISCUSSION

Some experimental data to illustrate the effect are shown in the following table.[19]

Equilibrium	log β	$\Delta G^{\ominus}$ /kJ mol^{-1}	$\Delta H^{\ominus}$ /kJ mol^{-1}	$-T\Delta S^{\ominus}$ /kJ mol^{-1}
$Cd^{2+} + 4\ MeNH_2 \rightleftharpoons Cd(MeNH_2)_4^{2+}$	6.55	−37.4	−57.3	19.9
$Cd^{2+} + 2\ en \rightleftharpoons Cd(en)_2^{2+}$	10.62	−60.67	−56.48	−4.19

These data show that the standard enthalpy changes are indeed approximately equal for the two reactions and that the main reason why the chelate complex is so much more stable is that the standard entropy term is much less unfavourable, indeed, it is favourable in this instance. In general it is difficult to account precisely for thermodynamic values in terms of changes in solution at the molecular level, but it is clear that the chelate effect is predominantly an effect of entropy. Other explanations, including that of Schwarzenbach,[20] are discussed in Greenwood and Earnshaw.[19]

The chelate effect increases as the number of chelate rings increases. For example, the complex $[Ni(dien)_2)]^{2+}$ is more stable than the complex $[Ni(en)_3)]^{2+}$; both complexes are octahedral with six nitrogen atoms around the nickel ion, but dien (diethylenetriamine, 1,4,7-triazaheptane) is a tridentate ligand and en is bidentate. The number of chelate rings is one less than the number of donor atoms in the ligand. EDTA (ethylenediaminetetracetic acid) has six donor atoms so it forms very strong complexes with five chelate rings. Ligands such as DTPA, which have eight donor atoms are used to form complexes with large metal ions such as lanthanide or actinide ions which usually form 8- or 9-coordinate complexes. 5-membered and 6-membered chelate rings give the most stable complexes. 4-membered rings are subject to internal strain because of the small inter-bond angle is the ring. The chelate effect is also reduced with 7- and 8-membered rings, because the larger rings are less rigid, so less entropy is lost in forming them.

Diethylenetriamine

An EDTA complex
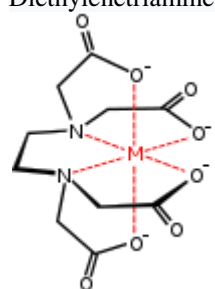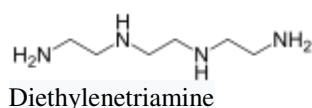
Removal of a proton from an aliphatic –OH group is difficult to achieve in aqueous solution because the energy required for this process is rather large. Thus, ionization of aliphatic –OH groups occurs in aqueous solution only in special circumstances. One such circumstance is found with compounds containing the H_2N–C–C–OH substructure. For example, compounds containing the 2-aminoethanol substructure can form metal–chelate complexes with the deprotonated form, H_2N–C–C–O$^-$. The chelate effect supplies the extra energy needed to break the O–H bond.
An important example occurs with the molecule tris. This molecule should be used with caution as a buffering agent as it will form chelate complexes with ions such as Fe^{3+} and Cu^{2+}.
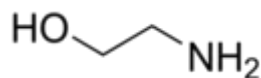
2-aminoethanol
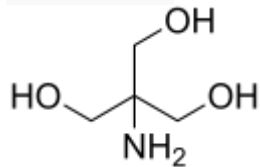
Tris

It was found that the stability of the complex of copper(II) with the macrocyclic ligand cyclam (1,4,8,11-tetraazacyclotetradecane) was much greater than expected in comparison to the stability of the complex with the corresponding open-chain amine.[21] This phenomenon was named the **macrocyclic effect** and it was also interpreted as an entropy effect. However, later studies suggested that both enthalpy and entropy factors were involved.[22]

An important difference between macrocyclic ligands and open-chain (chelating) ligands is that they have selectivity for metal ions, based on the size of the cavity into which the metal ion is inserted when a complex is formed. For example, the crown ether 18-crown-6 forms much stronger complexes with the potassium ion, K^+ than with the smaller sodium ion, Na^+.[23]

In hemoglobin an iron(II) ion is complexed by a macrocyclic porphyrin ring. The article hemoglobin incorrectly states that oxyhemoglogin contains iron(III). It is now known that the iron(II) in hemoglobin is a low-spin complex, whereas in oxyhemoglobin it is a high-spin complex. The low-spin Fe^{2+} ion fits snugly into the cavity of the porphyrin ring, but high-spin iron(II) is significantly larger and the iron atom is forced out of the plane of the macrocyclic ligand.[24] This effect contributes the ability of hemoglobin to bind oxygen reversibly under biological conditions. In Vitamin B12 a cobalt(II) ion is held in a corrin ring. Chlorophyll is a macrocyclic complex of magnesium(II).
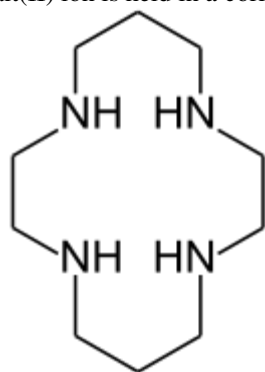
Cyclam
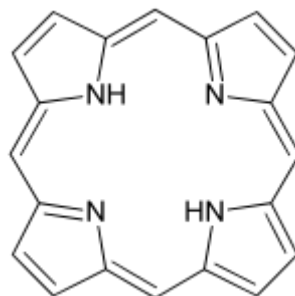
Porphine, the simplest porphyrin.

III.RESULTS

Ahrland, Chatt and Davies proposed that metal ions could be described as class A if they formed stronger complexes with ligands whose donor atoms are nitrogen, oxygen or fluorine than with ligands whose donor atoms are phosphorus, sulfur or chlorine and class B if the reverse is true.[26] For example, Ni^{2+} forms stronger complexes with amines than with phosphines, but Pd^{2+} forms stronger complexes with phosphines than with amines. Later,

Pearson proposed the theory of hard and soft acids and bases (HSAB theory).[27] In this classification, class A metals are hard acids and class B metals are soft acids. Some ions, such as copper(I), are classed as borderline. Hard acids form stronger complexes with hard bases than with soft bases. In general terms hard–hard interactions are predominantly electrostatic in nature whereas soft–soft interactions are predominantly covalent in nature. The HSAB theory, though useful, is only semi-quantitative.[28]

The hardness of a metal ion increases with oxidation state. An example of this effect is given by the fact that Fe^{2+} tends to form stronger complexes with N-donor ligands than with O-donor ligands, but the opposite is true for Fe^{3+}.
The Irving–Williams series refers to high-spin, octahedral, divalent metal ion of the first transition series. It places the stabilities of complexes in the order

$$Mn < Fe < Co < Ni < Cu > Zn$$
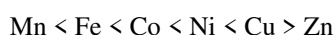
This order was found to hold for a wide variety of ligands.[29] There are three strands to the explanation of the series.

1. The ionic radius is expected to decrease regularly for Mn^{2+} to Zn^{2+}. This would be the normal periodic trend and would account for the general increase in stability.
2. The crystal field stabilisation energy (CFSE) increases from zero for manganese(II) to a maximum at nickel(II). This makes the complexes increasingly stable. CFSE returns to zero for zinc(II).
3. Although the CFSE for copper(II) is less than for nickel(II), octahedral copper(II) complexes are subject to the Jahn–Teller effect which results in a complex having extra stability.

Another example of the effect of ionic radius the steady increase in stability of complexes with a given ligand along the series of trivalent lanthanide ions, an effect of the well-known lanthanide contraction.

Stability constant values are exploited in a wide variety of applications. Chelation therapy is used in the treatment of various metal-related illnesses, such as iron overload in β-thalassemia sufferers who have been given blood transfusions. The ideal ligand binds to the target metal ion and not to others, but this degree of selectivity is very hard to achieve. The synthetic drug deferiprone achieves selectivity by having two oxygen donor atoms so that it binds to Fe^{3+} in preference to any of the other divalent ions that are present in the human body, such as Mg^{2+}, Ca^{2+} and Zn^{2+}. Treatment of poisoning by ions such as Pb^{2+} and Cd^{2+} is much more difficult since these are both divalent ions and selectivity is harder to accomplish.[30] Excess copper in Wilson's disease can be removed y penicillamine or Triethylene tetramine (TETA). DTPA has been approved by the U.S. Food and Drug Administration for treatment of plutonium poisoning.

DTPA is also used as a complexing agent for gadolinium in MRI contrast enhancement. The requirement in this case is that the complex be very strong, as Gd^{3+} is very toxic. The large stability constant of the octadentate ligand ensures that the concentration of free Gd^{3+} is almost negligible, certainly well below toxicity threshold.[31] In addition the ligand occupies only 8 of the 9 coordination sites on the gadolinium ion. The ninth site is occupied by a water molecule which exchanges rapidly with the fluid surrounding it and it is this mechanism that makes the paramagnetic complex into a contrast reagent.

EDTA forms such strong complexes with most divalent cations that it finds many uses. For example, it is often present in washing powder to act as a water softener by sequestering calcium and magnesium ions.
The selectivity of macrocyclic ligands can be used as a basis for the construction of an ion selective electrode. For example, potassium selective electrodes are available that make use of the naturally occurring macrocyclic antibiotic valinomycin.

An ion-exchange resin such as chelex 100, which contains chelating ligands bound to a polymer, can be used in water softeners and in chromatographic separation techniques. In solvent extraction the formation of electrically-neutral complexes allows cations to be extracted into organic solvents. For example, in nuclear fuel reprocessing uranium(VI) and plutonium(VI) are extracted into kerosene as the complexes $[MO_2(TBP)_2(NO_3)_2]$ (TBP = tri-n-butyl phosphate). In phase-transfer catalysis, a substance which is insoluble in an organic solvent can be made soluble by addition of a suitable ligand. For example, potassium permanganate oxidations can be achieved by adding a catalytic quantity of a crown ether and a small amount of organic solvent to the aqueous reaction mixture, so that the oxidation reaction occurs in the organic phase.

In all these examples, the ligand is chosen on the basis of the stability constants of the complexes formed. For example, TBP is used in nuclear fuel reprocessing because (among other reasons) it forms a complex strong enough for solvent

extraction to take place, but weak enough that the complex can be destroyed by nitric acid to recover the uranyl cation as nitrato complexes, such as $[UO_2(NO_3)_4]^{2-}$ back in the aqueous phase.

IV.CONCLUSIONS

Supramolecular complexes are held together by hydrogen bonding, hydrophobic forces, van der Waals forces, π-π interactions, and electrostatic effects, all of which can be described as noncovalent bonding. Applications include molecular recognition, host–guest chemistry and anion sensors.A typical application in molecular recognition involved the determination of formation constants for complexes formed between a tripodal substituted urea molecule and various saccharides.[32] The study was carried out using a non-aqueous solvent and NMR chemical shift measurements. The object was to examine the selectivity with respect to the saccharides.An example of the use of supramolecular complexes in the development of chemosensors is provided by the use of transition-metal ensembles to sense for ATP.[33]Anion complexation can be achieved by encapsulating the anion in a suitable cage. Selectivity can be engineered by designing the shape of the cage. For example, dicarboxylate anions could be encapsulated in the ellipsoidal cavity in a large macrocyclic structure containing two metal ions.[34]The method developed by Bjerrum is still the main method in use today, though the precision of the measurements has greatly increased. Most commonly, a solution containing the metal ion and the ligand in a medium of high ionic strength is first acidified to the point where the ligand is fully protonated. This solution is then titrated, often by means of a computer-controlled auto-titrator, with a solution of CO_2-free base. The concentration, or activity, of the hydrogen ion is monitored by means of a glass electrode. The data set used for the calculation has three components: a statement defining the nature of the chemical species that will be present, called the model of the system, details concerning the concentrations of the reagents used in the titration, and finally the experimental measurements in the form of titre and pH (or emf) pairs.

Other ion-selective electrodes (ISE) may be used. For example, a fluoride electrode may be used with the determination of stability complexes of fluoro-complexes of a metal ion.It is not always possible to use an ISE. If that is the case, the titration can be monitored by other types of measurement. Ultraviolet–visible spectroscopy, fluorescence spectroscopy and NMR spectroscopy are the most commonly used alternatives. Current practice is to take absorbance or fluorescence measurements at a range of wavelengths and to fit these data simultaneously. Various NMR chemical shifts can also be fitted together.The chemical model will include values of the protonation constants of the ligand, which will have been determined in separate experiments, a value for log K_w and estimates of the unknown stability constants of the complexes formed. These estimates are necessary because the calculation uses a non-linear least-squares algorithm. The estimates are usually obtained by reference to a chemically similar system. The stability constant databases[8][9] can be very useful in finding published stability constant values for related complexes.In some simple cases the calculations can be done in a spreadsheet.[35] Otherwise, the calculations are performed with the aid of a general-purpose computer programs. The most frequently used programs are:

- Potentiometric and/or spectrophotometric data: PSEQUAD[36]
- Potentiometric data: HYPERQUAD,[37] BEST,[38] ReactLab pH PRO
- Spectrophotometric data: HypSpec, SQUAD,[39] SPECFIT,[40][41] ReactLab EQUILIBRIA.[42]
- NMR data HypNMR,[43] WINEQNMR2 Archived 2019-07-14 at the Wayback Machine[44]

In biochemistry, formation constants of adducts may be obtained from Isothermal titration calorimetry (ITC) measurements. This technique yields both the stability constant and the standard enthalpy change for the equilibrium.[45] It is mostly limited, by availability of software, to complexes of 1:1 stoichiometry.

REFERENCES

1. Bjerrum, J. (1941). Metal-ammine formation in aqueous solution. Copenhagen: Haase.
2. ^ Beck, M. T.; Nagypál, I. (1990). "Chapter 1". Chemistry of Complex Equilibria. Horwood. ISBN 0-85312-143-5.
3. ^ Rossotti, F. J. C.; Rossotti, H. (1961). The Determination of Stability Constants. McGraw–Hill.
4. ^ Dyrssen, D.; Ingri, N.; Sillen, L. G. (1961). "Pit-mapping - A general approach to Computer refinement of stability constants". Acta Chem. Scand. **15**: 694–696. doi:10.3891/acta.chem.scand.15-0694.
5. ^ Ingri, N.; Sillen, L. G. (1964). "High-speed computers as a supplement to graphical methods, IV. An ALGOL version of LETAGROP-VRID". Arkiv för Kemi. **23**: 97–121.
6. ^ Sayce, I. G. (1968). "Computer calculations of equilibrium constantsof species present in mixtures of metal ions and complexing reagents". Talanta. **15** (12): 1397–1421. doi:10.1016/0039-9140(68)80200-0. PMID 18960446.
7. ^ Sabatini, A.; Vacca, A.; Gans, P. (1974). "MINIQUAD - A general computer program for the computation of Stability constants". Talanta. **21** (1): 53–77. doi:10.1016/0039-9140(74)80063-9. PMID 18961420.
8. ^ IUPAC SC-Database A comprehensive database of published data on equilibrium constants of metal complexes and ligands

9. ^ NIST Standard Reference Database 46 NIST Critically Selected Stability Constants of Metal Complexes: Version 8.0 (This database has been discontinued.)

10. ^ Pearson, R. G. (1997). Chemical Hardness: Applications from Molecules to Solids. Springer-VCH. ISBN 3-527-29482-1.

11. ^ Drago, R. S.; Wong, N.; Bilgrien, C.; Vogel, C. (1987). "E and C parameters from Hammett substituent constants and use of E and C to understand cobalt–carbon bond energies". Inorg. Chem. **26** (1): 9–14. doi:10.1021/ic00248a003.

12. ^ Gutmann, V. (1978). The Donor–Acceptor Approach to Molecular Interactions. Springer. ISBN 0-306-31064-3.

13. ^ Rossotti, F. J. C. (1960). "The thermodynamics of metal ion complex formation in solution". In Lewis, J.; R. G., Wilkins (eds.). Modern coordination chemistry. New York: Interscience.

14. ^ Beck, M. T.; Nagypál, I. (1990). Chemistry of Complex Equilibria. Horwood. ISBN 0-85312-143-5. sections 3.5.1.2, 6.6.1 and 6.6.2

15. ^ Rossotti, F. J. C.; Rossotti, H. (1961). "Chapter 2: Activity and Concentration Quotients". The Determination of Stability Constants. McGraw–Hill.

16. ^ Gergely, A.; Nagypál, I.; E., Farkas (1974). "A réz(II)-aminosav törzskomplexek vizes oldatában lejátszodó protoncsere-reakciók kinetikájának NMR-vizsgálata" [NMR study of the proton exchange process in aqueous solutions of copper(II)-aminoacid parent complexes]. Magyar Kémiai Folyóirat. **80**: 545–549.

17. ^ "Project: Ionic Strength Corrections for Stability Constants". IUPAC. Archived from the original on 2008-10-29. Retrieved 2008-11-23.

18. ^ Atkins, P. W.; De Paula, J. (2006). "Section 7.4: The Response of Equilibria to Temperature". Physical Chemistry. Oxford University Press. ISBN 0-19-870072-5.

19. ^ Greenwood, Norman N.; Earnshaw, Alan (1997). Chemistry of the Elements (2nd ed.). Butterworth-Heinemann. ISBN 978-0-08-037941-8. p. 910

20. ^ Schwarzenbach, G. (1952). "Der Chelateffekt" [The Chelate Effect]. Helv. Chim. Acta. **35** (7): 2344–2359. doi:10.1002/hlca.19520350721.

21. ^ Cabinness, D. K.; Margerum, D. W. (1969). "Macrocyclic effect on the stability of copper(II) tetramine complexes". J. Am. Chem. Soc. **91** (23): 6540–6541. doi:10.1021/ja01051a091.

22. ^ Lindoy, L. F. (1990). "Chapter 6: Thermodynamic considerations". The Chemistry of Macrocyclic Ligand Complexes. Cambridge University Press. ISBN 0-521-40985-3.

23. ^ Pedersen, C. J. (1967). "Cyclic polyethers and their complexes with metal salts". J. Am. Chem. Soc. **89** (26): 7017–7036. doi:10.1021/ja01002a035.

24. ^ Greenwood, Norman N.; Earnshaw, Alan (1997). Chemistry of the Elements (2nd ed.). Butterworth-Heinemann. ISBN 978-0-08-037941-8. p. 1100, Figure 25.7

25. ^ Lundeen, M.; Hugus, Z. Z. (1992). "A calorimetric study of some metal ion complexing equilibria". Thermochim. Acta. **196** (1): 93–103. doi:10.1016/0040-6031(92)85009-K.

26. ^ Ahrland, S.; Chatt, J.; Davies, N. R. (1958). "The relative affinities of ligand atoms for acceptor molecules and ions". Quart. Rev. **12** (3): 265–276. doi:10.1039/QR9581200265.

27. ^ Pearson, R. G. (1963). "Hard and Soft Acids and Bases". J. Am. Chem. Soc. **85** (22): 3533–3539. doi:10.1021/ja00905a001.

28. ^ Beck, M. T.; Nagypál, I. (1990). Chemistry of Complex Equilibria. Horwood. p. 354. ISBN 0-85312-143-5.

29. ^ Irving, H. M. N. H.; Williams, R. J. P. (1953). "The stability of transition-metal complexes". J. Chem. Soc.: 3192–3210. doi:10.1039/JR9530003192.

30. ^ Arena, G.; Contino, A.; Longo, E.; Sciotto, D.; Spoto, G. (2001). "Selective complexation of soft Pb^{2+} and Hg^{2+} by a novel allyl functionalized thioamide calix[4]arene in 1,3-alternate conformation: a UV-visible and H-1 NMR spectroscopic investigation". J. Chem. Soc., Perkin Trans. **2** (12): 2287–2291. doi:10.1039/b107025h.

31. ^ Runge, V. M.; Scott, S. (1998). Contrast-enhanced Clinical Magnetic Resonance Imaging. University Press of Kentucky. ISBN 0-8131-1944-8.

32. ^ Vacca, A.; Nativi, C.; Cacciarini, M.; Pergoli, R.; Roelens, S. (2004). "A New Tripodal Receptor for Molecular Recognition of Monosaccharides. A Paradigm for Assessing Glycoside Binding Affinities and Selectivities by ^{1}H NMR Spectroscopy". J. Am. Chem. Soc. **126** (50): 16456–16465. doi:10.1021/ja045813s. PMID 15600348.

33. ^ Marcotte, N.; Taglietti, A. (2003). "Transition-metal-based chemosensing ensembles: ATP sensing in physiological conditions". Supramol. Chem. **15** (7): 617–717. doi:10.1080/10610270310001605205. S2CID 96018200.

34. ^ Boiocchi, M.; Bonizzoni, M.; Fabbrizzi, L.; Piovani, G.; Taglietti, A. (2004). "A dimetallic cage with a long ellipsoidal cavity for the fluorescent detection of dicarboxylate anions in water". Angew. Chem. Int. Ed. **43** (29): 3847–3852. doi:10.1002/anie.200460036. PMID 15258953.

35. ^ Billo, E. J. (1997). "Chapter 22". Excel for Chemists: A comprehensive guide (2nd ed.). Wiley-VCH. ISBN 0-471-18896-4.

36. **^** Zekany, L.; Nagypál, I. (1985). "Chapter 8: PSEQUAD: A comprehensive program for the evaluation of potentiometric and/or spectrophotometric equilibrium data using analytical derivatives". In Leggett (ed.). Computational methods for the determination of formation constants. Plenum. ISBN 0-306-41957-2.

37. **^** Gans, P.; Sabatini, A.; Vacca, A. (1996). "Investigation of equilibria in solution. Determination of equilibrium constants with the HYPERQUAD suite of programs". Talanta. **43** (10): 1739–1753. doi:10.1016/0039-9140(96)01958-3. PMID 18966661.

38. **^** Martell, A. E.; Motekaitis, R. J. (1992). The determination and use of stability constants. Wiley-VCH.

39. **^** Leggett, D. (1985). "Chapter 6: SQUAD: Stability quotients from absorbance data". In Leggett (ed.). Computational methods for the determination of formation constants. Plenum. ISBN 0-306-41957-2.

40. **^** Gampp, M.; Maeder, M.; Mayer, C. J.; Zuberbühler, A. D. (1985). "Calculation of equilibrium constants from multiwavelength spectroscopic data—I : Mathematical considerations". Talanta. **32** (2): 95–101. doi:10.1016/0039-9140(85)80035-7. PMID 18963802.

41. **^** Gampp, M.; Maeder, M.; Mayer, C. J.; Zuberbühler, A. D. (1985). "Calculation of equilibrium constants from multiwavelength spectroscopic data—II1: Specfit: two user-friendly programs in basic and standard fortran 77". Talanta. **32** (4): 251–264. doi:10.1016/0039-9140(85)80077-1. PMID 18963840.

42. **^** Jplus Consulting Pty Ltd

43. **^** Frassineti, C.; Alderighi, L.; Gans, P.; Sabatini, A.; Vacca, A.; Ghelli, S. (2003). "Determination of protonation constants of some fluorinated polyamines by means of ^{13}C NMR data processed by the new computer program HypNMR2000. Protonation sequence in polyamines". Anal. Bioanal. Chem. **376** (7): 1041–1052. doi:10.1007/s00216-003-2020-0. PMID 12845401. S2CID 14533024.

44. **^** Hynes, M. J. (1993). "EQNMR: A computer program for the calculation of stability constants from nuclear magnetic resonance chemical shift data". J. Chem. Soc., Dalton Trans. (2): 311–312. doi:10.1039/DT9930000311.

45. **^** O'Brien, R.; Ladbury, J. E.; Chowdry, B. Z. (2000). "Chapter 10". In Harding, S. E.; Chowdry, B. Z. (eds.). Protein-Ligand interactions: hydrodynamics and calorimetry. Oxford University Press. ISBN 0-19-963749-0.