CHELATING EXTRACTANTS OF IMPROVED SELECTIVITY

Progress Report
for Period September 1, 1976-October 31, 1977

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ABSTRACT

During the current contract period, new means of characterizing metal chelating reagent selectivity have been developed and incorporated into a theoretical factor analysis of the chelate stability constants of 24 metal ions with 14 ligands of the EDTA family. The factor analysis will be extended to extracting ligand families. A computer-controlled automated metal chelate stability constant apparatus has been assembled and successfully tested. A high performance liquid chromatograph has been set up and preliminary examination of comparison of reversed phase chromatographic separation of metal ions with their solvent extraction behavior begun.

PROGRESS REPORT

During the current contract period, the research carried out generally followed the course indicated in the original proposal and complied within the contract requirements. As outlined in the original proposal work was to be undertaken in (a) pattern recognition study of chelating extractant selectivity and (b) experimental evaluation of selected extractants using conventional and chromatographic approaches.

Inasmuch as aqueous solution equilibria, particularly the metal chelate stability constants, dominate the overall extraction constants and further, because quality data for lanthanide (and other pertinent) ions were available for the largest number of ligands within the EDTA

family, it was decided that our pattern recognition study would be initiated with such data from the compilation of critically evaluated data of Smith and Martell (1). From the theoretical factor analysis, four independent factors were found sufficient to reproduce the data to within experimental uncertainty. We defined a new parameter, the susceptibility, which estimates the possibility of varying reagent selectivity of given groups of metal ions. With factor analysis we were able to isolate those structural features, particularly steric factors, which bear significantly on the susceptibility. The results have been submitted to Analytical Chemistry for publication (2) and a copy is here appended. Having demonstrated the usefulness of this approach we plan to explore and intercompare various chelate families in a similar fashion.

One of the serious problems that must be resolved in order to fully exploit the pattern recognition approach to improved extractant design is the absence of sufficient reliable data in the literature. Despite the appearance of almost exhaustive coverage of chelate stabilities in the literature, e.g. the great collection of Stability Constants (3), there are extremely disabling absences with many reagents represented by measurements of one or two metals, if at all. The laboratory component of this research has been designed to incorporate the determination of critically needed stabilities particularly those involving the lanthanide ions and with sterically hindered ligands. An automated potentiometric stability constant apparatus based on the use of a Mettler digital burette and controlled by a DataGeneral Nova 2/10

minicomputer equipped with a Xebec dual flexible disc drive has been assembled and software developed. The entire system has been successfully tested with the lanthanide chelates of 8-quinolinol and we are planning to measure the sterically hindered 2-methyl-8-quinolinol next.

We have obtained a Spectra Physics HPLC Gradient Elution system equipped with a Schoeffl variable wavelength detector with which we are carrying out a feasibility study of the separation via reversed phase chromatography of metal ions using LIX 65 (a high molecular weight extractant with the chelating grouping of an α -hydroxyoxime available from General Mills) or KELEX 100 (a high molecular weight extractant available from Ashland Co. that is a 7-alkenyl-8-quinolinol. Preliminary results indicate that we shall be able to use this approach as a convenient way to obtain important extraction parameters as well as a means for trace metal analysis.

The principal investigator has spent 10% of his time during the academic year and one summer month on this research.

Literature Cited

1. A. E. Martell and R. M. Smith, "Critical Stability Constants," Vol. 1, Plenum Press, New York (1974).
2. D. L. Duewer and H. Freiser, "Relating Molecular Structure to Metal Chelate Stability and Reagent Selectivity: Abstract Factor Analysis of the Chelate Formation Equilibria for some Diaminetetraacetic Acids," submitted to Analytical Chemistry (copy appended).
3. L. G. Sillén and A. E. Martell, "Stability Constants," 2nd Ed., Special Public. No. 17, Chemical Society (London) (1964) and Supplement No. 1, Special Public. No. 25 (1971).

Relating Molecular Structure to

Metal Chelate Stability and Reagent Selectivity:

Abstract Factor Analysis of the Chelate Formation Equilibria for
some Diaminetetraacetic Acids

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Introduction

The search for the molecular structural bases of the behavior of metal chelating agents has been of major interest to analytical and inorganic coordination chemists since the introduction of organic analytical reagents. Among the earliest and most productive of the investigators is Fritz Feigl whose monumental contributions (1) to analytical reagent design is all the more remarkable for its independence of contemporary theory. In the last thirty years, structure-behavior studies have focussed on the use of equilibrium formation constants of proton and metal ion complexes as criteria. The long range analytical objectives of such investigations are to develop a sufficiently complete and detailed understanding of the structural factors affecting chelate stability that would provide effective guidelines for the design of reagents of improved selectivity.

In a landmark study that set the approach for the many others that followed, Calvin and Wilson (2) used the potentiometrically determined formation constants of copper(II) chelates of substituted β -diketones and salicylaldehydes to point out the fundamental relationship of the proton affinity and metal chelating ability of a ligand. Significant departures from the linear free energy relationship between the two were attributed to other structural factors as steric hindrance and chelate ring "resonance". Since then a vast amount of metal complex stability data has been determined in the continued search for structure-behavior relationships. The compilation of Commission V. 6 of I.U.P.A.C.'s Analytical Division, Stability Constants (3) is an impressive and useful collection of formation constants and other equilibrium data on metal

complexes of both organic and inorganic ligands. It records the results of innumerable studies which have been largely limited to interpretations based on a relatively small data population. Typically the studies involve the comparison of a parent or model ligand with substituted analogs. Nevertheless, from these studies have arisen interesting and useful generalizations concerning factors affecting stability of metal chelates such as the proton affinity and electronic structure of the bonding atoms of the ligand, the number and size of chelate rings, and other steric factors (4, 5, 6). Insofar as reagent selectivity, as measured by the differences in stability constants of the chelates of various metal ions, is concerned, it was recognized early on (7, 8, 9) that a natural stability sequence exists among the metal ions. This sequence is related to the ionization potentials of gaseous metal ions and is rather independent of the nature of the ligand although subject to partial sequence alteration with ligands possessing special features, particularly those involving steric hindrance (10) and nature of the bonding atoms (11).

All of these studies have been limited not only to using only a small fraction of the data now available but to developing expressions which revealed qualitative trends rather than quantitative relationships. While data which deviated by as little as 0.5 in the log stability constant from the predicted value was used to infer the active influence of a new factor not incorporated in the expression under study, the paucity of the data employed in its derivation as well as the (usually reasonable) assumption that inter-laboratory reproducibility of the stability constant values would not permit it, no serious statistical analysis of the validity or quantitative reliability of the various expressions was undertaken.

Two factors make a careful analysis of stability constant data timely and significant. Although the definition of reliability of available stability constant data has been improving greatly over the last fifteen years, the compilations of Martell and Smith (12, 13, 14) of critically evaluated constants represent a real breakthrough. Further, only recently have suitable statistical methods for the analysis of this data become available to, and accepted by, the chemical community. The methodology of abstract factor analysis or principal component analysis is uniquely suited for both the determination of the number of independent correlations exhibited in a body of data and for aiding their interpretation. (Several excellent reviews of this methodology as applied to chemical problems have appeared recently (15, 16), hence it will not be here discussed in any detail.) By this means it should be possible to critically examine far larger data bases and to derive more generally applicable and quantitatively reliable explanatory and predictive relationships as well as to evaluate the data with respect to its intrinsic experimental uncertainty.

We have selected the family of ligands related to EDTA as a first test of the usefulness of our statistical approach because of the widespread utility and interest in the chelates of this group as well as for the availability of well-characterized, reliable stability constant data. It is expected that this study will provide a suitable guide for further examination of problems of analytical reagent design.

Description of the Data Base

The proton and metal ion formation constant data used in this study were obtained from Martell and Smith, Vol. 1 (12), a compilation of critical values of constants for essentially all amino acid chelating agents known prior to 1974. Ligands capable of forming 1:1 metal complexes and having the general formula:

where x and y may be either H or a substituent group and n varies from 2 to 8, were considered. The twenty-four ligands listed in Table I have data for a sufficient number of ions to be of some utility in our study. Only the first fourteen of these ligands, however, have complete enough data for the primary analyses. These fourteen ligands constitute the training set ligands. The remaining twelve ligands, used in some phases of the evaluation of analyses performed on the training set data, constitute the evaluation set data (17).

Formation constants for the ions Mg^{+2} , Ca^{+2} , Sr^{+2} , Ba^{+2} , La^{+3} , Ce^{+3} , Pr^{+3} , Nd^{+3} , Sm^{+3} , Eu^{+3} , Gd^{+3} , Tb^{+3} , Dy^{+3} , Ho^{+3} , Er^{+3} , Tm^{+3} , Yb^{+3} , Lu^{+3} , Mn^{+2} , Co^{+2} , Cu^{+2} , Zn^{+2} , Cd^{+2} , and Pb^{+2} comprise the body of the chelate stability data used. No other ions, unfortunately, have evaluated constants with a sufficient number of the above ligands to be included in the training set. The data for complexes evaluated at 20°C and 0.1 μ have been used where available. The mean and standard deviation for ligands and ions in the training set are given in Table II.

Experimental uncertainties have been assigned by the authors to each formation constant used. Where given, the range of "acceptable" values listed in (12) has been used as an estimate of the uncertainty. Where the range was not given, an uncertainty of 0.1 was assigned if the data were reported to two significant places in the mantissa, 0.2 if only one significant place and 0.5 if only the characteristic was available. An additional uncertainty of 0.05 was assigned for every 5°C and 0.1 μ deviation from the "normal" 20°C and 0.1 μ . These values were chosen on the basis of the authors' experience and are intended only as reasonable estimates. The average uncertainty assigned to each ligand and ion in the training set is given in Table II.

Three formation constants (Tb^{+3} , Ho^{+3} , Tm^{+3} with ligand #14) have not been experimentally determined. As the lanthanides are regularly periodic, it proved possible to adequately "fill in" these three values and retain this ligand in the training set. A step-wise least squares fit was made to each missing value, using only the experimentally determined constants of the remaining training set ligands. The statistical estimate of error was doubled and used as the uncertainty estimate for each of these values: for all three ions, the assigned uncertainty is 0.5.

It should be noted that the least square approach minimizes the impact of the missing values for variance and/or correlation analysis, being based on a minimum variance error criterion, but that no new information can be generated in this manner. As will be shown later in the paper, the ions of the first transition series are rather unique compared to the alkaline earths and/or the lanthanides. For this reason it proved impossible to reliably estimate the missing or inadequate values for Mn, Co, Cu and Zn of ligand #17.

Measures of Chelate Stability and Ligand Selectivity

A more straightforward approach to the analysis of the structural bases of stability would be possible if ΔH° and ΔS° data were available so that factors affecting bond strengths and entropic contributions to overall stability (ΔF°) could be separately assessed. Unfortunately, such data are still rather sparse so that $\log \beta_{i,l}$, the logarithm of the formation constant of the 1:1 complex of metal ion i with ligand l , is our inevitable choice as a measure of stability. Furthermore, $\log \beta$ is a practical index of chelate stability.

The selectivity of a ligand towards a pair of ions is given by the difference between their respective stabilities: $S_{l(i,j)} = \log \beta_{i,l} - \log \beta_{j,l}$. This difference, ignoring pH and other effects, indicates how practical a separation of the two ions is with the particular ligand. This concept can be extended to measure the expected difference in stability of a given pair of ions for a family of similar ligands by taking the average of the individual ligands' selectivity:

$$\bar{S}_{i,j} = \frac{\sum_{l=1}^n S_{l(i,j)}}{n}$$

where n = number of ligands. The greater the average selectivity, the more likely that a ligand similar to those studied will be useful in the separation of the two ions.

The extent to which the selectivity between two ions can be modified by changes in ligand structure is of more interest than the simple average selectivity, however. This susceptibility of the ligand family to changes in selectivity can be estimated from the standard deviation of the selectivities:

$$\sigma_{i,j} = \left[\sum_{k=1}^n (S_{k,(i,j)} - \bar{S}_{i,j})^2 / (n-1) \right]^{1/2}$$

The greater the susceptibility the more hopeful the design of a ligand from within the family studied which could provide superior separation for the two ions. Certainly, if a ligand family shows both low average selectivity and low susceptibility for a given pair of ions then there is little hope for using ligands of that family for their separation.

Note that susceptibility is dependent upon there being more than one factor responsible for the complex stability. If, for all ions, there was but one type of interaction with the ligands of a given family then any change in the ligand structure would affect all complexes proportionately. The magnitude of the stability could certainly be changed, but the selectivity would remain essentially unchanged.

The selectivity/susceptibility matrix, Fig. 1, provides a concise summary of these two values for the ligands studied for all 24 ions. (Some of the lanthanide data have been excluded from the figure for graphic clarity.) The vertical bar represents the average selectivity, $\bar{S}_{i,j}$, and the horizontal bar the susceptibility, $\sigma_{i,j}$. Both values have been normalized to their respective maximum values. Note that the scale for the selectivity is more than an order of magnitude greater than that of the susceptibility: the structural modifications represented by the DTA ligands studied do not radically vary in their response to the various ions considered.

It is, however, readily apparent that there are regular differences in the behavior of the ligands towards the different ions. The $S_{i,j}$

between the alkaline earths and the lanthanides are large and increase in a regular manner across the lanthanide series; the $\sigma_{i,j}$, however, remain modest and remarkably constant. In contrast, the $S_{i,j}$ between (Co, Cu and Zn) and the lanthanides are rather small while the $\sigma_{i,j}$ are quite large; further, the $\sigma_{i,j}$ between these three transition ions and the alkaline earths are noticeably smaller than for the lanthanides.

The pairs of ions for which $S_{i,j}$ is very small are those for which good analytical differentiation is difficult. For this reason, such pairs having appreciable $\sigma_{i,j}$ values are of special interest because this indicates that the particular ligand family offers the possibility of design of improved ligands. In principle, the "natural order" of ion selection can be reversed in such cases, which is of obvious general analytical utility.

We have found that the selectivity/susceptibility matrix makes the identification of such potentially interesting and useful situations very much simpler. The intercomparison of such matrices for different families of ligands should be of great value in proper reagent selection.

Methods of Mathematical Analysis

For the purposes of this paper, "abstract factor analysis" may be considered as a method for obtaining the best least-square-error definition orthogonal variables for the linear description of the data (18). This is accomplished via the eigenanalysis of a dispersion matrix formed from the data matrix. The eigenvalues, λ_k , obtained from this analysis characterize the number and importance of the linear factors exhibited in the data. The eigenvectors, $\vec{v}_k$, may be used to isolate and aid in the interpretation of the abstract factors.

We have chosen to formulate the data matrix of stability constants as ions by ligands; that is, in the terminology of pattern recognition, the ions are "objects" and the ligands are "measurements" (17). This formulation is indicated for this data by having more ions than ligands: the statistics of the analysis are better defined with such an arrangement. The data arrangement has the happy result, moreover, of allowing the analysis to be stabilized towards a probable source of analytical uncertainty.

In our analysis, we first autoscale the data to normalize the measurement means to zero and the variances to unity:

$$x'_{ij} = (x_{ij} - \bar{x}_j)/r_j$$

$$\bar{x}_j = \sum_{i=1}^m x_{ij}/m$$

$$r_j = [\sum_{i=1}^m (x_{ij} - \bar{x}_j)^2]^{1/2}$$

m = number of objects (ions)

$x_{ij} = \log \beta_{ion, ligand}$

This normalization has been shown to provide a dispersion matrix (the Pearson correlation matrix) less sensitive to random uncertainty and to give more easily interpreted factors than do nonnormalized or just mean or variance normalized data (19). With this data, the mean normalization tends to isolate in the removed mean any constant displacement in a particular ligand's stability values. This type of uncertainty is expected for several reasons, perhaps the most important being that the critical evaluation involved some modification of the data for internal consistency (20). Also, any uncertainty in the proton association constants used in the calculations will be propagated throughout a given laboratory's data. Since many of the constants have been determined via competition studies using one or more reference ions, uncertainty in one constant can be propagated throughout much of the rest of the data of that ligand. If the data matrix were arranged as ligands by ions, autoscaling would not isolate such ligand characteristic uncertainty into the measurement means.

Several procedures have been used to determine the number of orthogonal factors, p , necessary to adequately describe the data. Those we have found useful in this study will be briefly described in a later section.

The eigenvectors, $\vec{v}_k$, of the dispersion matrix define an orthonormal set of axes covering the same space as did the normalized data. The length of each axis is given by the associated eigenvalue, the

vector having been normalized such that $\sum_{j=1}^m v_{kj}^2 = 1.0$. The direction of the vector relative to the normalized measurements is given by the coefficients, v_{kj} : coefficient v_{kj} is the k -th cofactor of ligand j , denoting the contribution of the j -th ligand to the description of the variance spanned by factor k .

The normalized data may be projected onto the eigenvector axes, giving the ion cofactors. The k -th cofactor of ion i , f_{ik} , is given by:

$$f_{ik} = \sum_{j=1}^n (x'_{ij})(v_{kj})$$

n = number of measurements (ligands)

This cofactor denotes the contribution of the i -th ion to the description of the variance spanned by factor k . Since the eigenvector axes are orthonormal, the sum over all ions of each cofactor is zero and the variance is equal to the eigenvalue associated with the factor:

$$\sum_{i=1}^m f_{ik} = 0$$

$$\sum_{i=1}^m f_{ik}^2 = \lambda_k$$

The product of the ion and ligand cofactors provides the least-square-error description of the data:

$$x'_{ij} = p_{F_{ij}} = \sum_{k=1}^p (f_{ik})(v_{kj})$$

p = number of factors used in given data model

If all possible factors are used, i.e. if p is equal to n , then $x'_{ij} = P_{F_{ij}}$ for all data.

Two evaluators from traditional least-squares fitting methodology are very convenient for comparing the various factor-models to the original data: the Pearson correlation-to-property (CORR) and the standard estimate of error (SEE). The CORR is a measure of the strength and direction of the linear relation between the original and the calculated data. It is defined:

$$\text{CORR} = \frac{\sum_{i=1}^m \sum_{j=1}^n (x'_{ij})(P_{F_{ij}})}{[(r_x)(r_F)]^{1/2}}$$

$$r_x^2 = \frac{\sum_{i=1}^m \sum_{j=1}^n (x'_{ij} - \bar{x}_j)^2}{n}$$

$$r_F^2 = \frac{\sum_{i=1}^m \sum_{j=1}^n (P_{F_{ij}} - \bar{P}_{F_j})^2}{\sum_{k=1}^p \lambda_k}$$

Since the autoscaled and original data are related through a linear transform, this value is identical to that if the original data were compared directly. The SEE is the estimate of the standard deviation expected for the calculated data. Its value for the normalized data is given by:

$$\text{SEE}' = \left[\frac{\sum_{i=1}^m \sum_{j=1}^n (x'_{ij} - P_{F_{ij}})^2}{(mn - p - 1)} \right]^{1/2}$$

A Monte Carlo method for using the data uncertainty estimates in the evaluation of the analyses has proven useful in this study. This method is described in detail in (19). Since we have estimates for the uncertainty associated with the stability of each complex, it is possible

to randomly perturb each datum of the original data matrix within its own uncertainty distribution. Several of these uncertainty-perturbed (or UP-) data matrices can be analyzed and the results intercompared and compared with those of the original data. Such a comparison allows the limits of meaningful analysis to be estimated. We have used this method both in determining the number of factors and in the physical interpretation of the abstract factors. All UP-data derived results in this paper are based upon the analysis of ten such matrices.

The Number of Factors

Examination of the eigenvectors and the statistics from the various factor-models reveals that there is but one primary factor with this data (Table III). This primary factor accounts for 99% of the normalized variance and reconstructs the original data with a correlation of 0.996. The SEE of 0.38 indicates data uncertainty greater than that assigned to the original data ($RMS = 0.18$), however. Furthermore, the maximum difference between the original data and the one-factor reconstruction is an unacceptable 2.64. Hence, while the one-factor model accounts for most of the data variance, it is not in itself a completely adequate description. This agrees with the observation made from the selectivity/susceptibility matrix that, although their magnitude is small, there are significant differences in ligand behavior.

It is not immediately obvious from the data in Table III just how many factors are needed to describe the data, although the number is certainly less than eight. The SEE of the uncertainty becomes smaller than the average uncertainty assigned to the data at factor 4, but the maximum difference observed becomes less only at factor 7. Comparison of the eigenvalues from the original data with those from the UP-data analyses indicates that the data uncertainty begins to dominate the analysis at factor 5 (Fig. 2a). The cross-correlation of the original data ion cofactors with the corresponding cofactors from the UP-data (19) is revealing: factor 2 is very insensitive to the assigned uncertainty, factors 3 and 4 are more sensitive (and approximately equally so), while factor 5 is marginal (Fig. 2b).

The recently introduced "Indicator Function" (IND) (20) gives results which agree well with the above conclusions (Fig. 2c). This function is defined:

$$IND = RE/(n - p)^2$$

$$RE = \left[\sum_{j=p+1}^n \lambda_j / (m(n - p)) \right]^{1/2}$$

The initial minimum is reached at factor 5, however the broad minimum from factor 4 through 8 again suggests that factor 5 is marginal.

It is of interest to compare the "Real Error", which has been shown to approximate the intrinsic data uncertainty with much chemical data (21), with the SEE values. As can be seen in Fig. 2d, the values are quite similar and identical in trend. The "Real Error" is consistently slightly larger, perhaps reflecting the assumption that all uncertainty is equally distributed about each datum. With the data considered in this study, certain ligands and ions are significantly less reliably determined than others (Table II). Using either the "Real Error" or the SEE values, and assuming either four or five factors, the intrinsic data uncertainty is approximately 0.1 log units. This is somewhat less than, but in good agreement with, the 0.18 RMS uncertainty assigned by the authors.

We therefore conclude that four factors are required to satisfactorily account for this data, with some suggestion of a fifth factor at or near the limits of the data uncertainty. The four-factor data model adequately reproduces the data, giving a CORR of 0.9996, a SEE of 0.11 and a maximum difference of 0.48. This model for the data implies that

the intrinsic data uncertainty is slightly less than that assigned to the data by the authors. The maximum difference occurs with a complex that has a relatively high assigned uncertainty and may well reflect experimental, as well as data-model difficulties.

Discussion of Results

The ion and ligand cofactors for the first five factors are pictorially presented in Fig. 3. The ligand cofactors are arranged in decreasing magnitude and labeled with a structure-emphasizing symbol (see Table I) to facilitate interpretation. The ion cofactors are arranged in an arbitrary sequence which we have found convenient. The one standard deviation error bars associated with each cofactor, derived from the UP-data analyses, are included to indicate the limits of meaningful interpretation. The contribution of each factor in the total reconstruction of the original data is calculated by the following relation:

$$\log \beta_{i,l} = (r_l)(f_{i,k})(v_{k,l})$$

The first factor accounts for much the greatest fraction of the data variance and, as such, may be considered the "average stability" (and "average selectivity") factor. Within graphical resolution the ligand cofactors for this factor are constant. This immediately suggests that, to a good first approximation, the only difference between the EDTA-like ligands considered is their average stability and that the selectivity for all ligands is about the same. The ion cofactors are concomitantly almost exactly parallel to the average ion stability:

$$\log \beta_i = \sum_{l=1} \log \beta_{i,l} / n = a + b(F_{i,1})$$

The least-squares fit of this function gives a CORR of 1.000, a SEE of 0.006 and a maximum difference of 0.015 log unit.

To this first approximation, then, a very simple model for the data is suggested:

$$\log \beta_{1,l} = C_F + b(C_l) + c(C_i)$$

where C_l and C_i are constants characteristic of the particular ligand and ion, respectively. The obvious constants to use are the average ion stability, defined above, and the average ligand stability:

$$\overline{\log \beta_l} = \frac{m}{\sum_{i=1}^m} \log \beta_{1,l} / m$$

The results of the least-squares fit of this function are given in Table IV: the similarity of the CORR, SEE, and maximum difference values to those from the one-factor data reconstruction is very evident.

In a predictive sense, however, the use of $\overline{\log \beta_l}$ as C_l is very unsatisfactory: all ion complexes must be experimentally obtained in order to calculate it. It is more practical to use the stability of a single ion for each ligand as C_l . As all ligands in the set considered have data for the alkaline earth complexes, one (or all) of these ions appear to be the most appropriate to use as C_l . The least squares fit statistics using $\log \beta_{Sr,l}$ are given in Table IV. Since it would be desirable to include complexes of ions other than those twenty-four we have considered in the data model, we have also tested the least squares fit using the EDTA (C_2) complexes as C_i along with $\log \beta_{Sr,l}$ as C_l (Table IV). The use of these single ion and single ligand values do not much degrade the data model. The "expected stability" for any complex may be predicted if only one ion has been measured for a given ligand.

To test this model with data other than that of the training set ligands, the forty-three complexes of the two-central-carbon ($n = 2$) ligands and the forty-one complexes of the $n > 3$ ligands were separately evaluated. With the $n = 2$ ligands, using the $\log\beta_{i,C_2}$ and $\log\beta_{Sr,l}$ parameters, an excellent fit was achieved: CORR of 0.997, SEE of 0.38, and maximum difference of 0.9. This is comparable, and in fact slightly better than, the training set statistics. The $n > 3$ ligands do not provide as satisfactory a fit: CORR of 0.933, SEE of 1.71, and maximum difference of -3.75. It is apparent that the model only applies well to the $n = 2$ ligands. The longer central ring required with these ligands apparently significantly alters the mechanics of chelate formation (21).

It would be desirable to predict the C_l and C_i parameters on a more fundamental basis. In particular, it would be desirable to adequately predict C_l without the necessity of synthesizing the ligand! Recent progress in "practical" conformation and quantum descriptions perhaps offer an interesting possibility for such description (22,23).

A linear relationship between the proton association constants and the metal stabilities has often been observed (2) and postulated for EDTA-like ligands (24):

$$\log\beta_{i,l_1} = \log\beta_{i,l_2} + (pK_{H_{l1}} - pK_{H_{l2}})$$

where pK_{H_l} is the appropriate combination of pK values, generally assumed for the EDTA family to be $pK_4 - pK_3$. The best least-squares fit between either $\log\beta_i$ or $\log\beta_{Sr,l}$ and the four pK values possible

with these ligands gives a CORR of only 0.79, a SEE of 1.35 and a maximum difference of -3.14. The pK_2 and pK_1 values are superfluous in this relationship, and the "best" pK_H function is essentially $pK_H = pK_4 - pK_3$. It has long been observed that the normal relationship between the proton and the complex association constants may not hold where steric changes dominate the complex (4). These pK values represent the proton affinities of the two N atoms. The value of n , the number of central carbon atoms will obviously affect the strength of the H-bonding between the two nitrogens and, therefore, the values of both pK_3 , which should decrease with increasing H-bond strength, and pK_4 which should increase under these circumstances. The influence of H-bonding on these pK values does not apply to metal complexes and therefore complicates the normal relationship. The significance of the value of the difference in pK_4 and pK_3 is that this may serve to reduce the effect of H bonding on the pK values and thereby give a more direct correlation with $\log \beta$ values.

It may be significant that with the series of ligands from $n = 2$ to 8, an excellent fit between $(pK_4 - pK_3)$ and $\log \beta_{Sr, \ell}$ may be made: CORR of 0.997, SEE of 0.26, and maximum difference of 0.36. It is not unreasonable that, as the central ring becomes longer, there is an increasing tendency for the two ends of the ligand to act independently and H-bonding between the two nitrogens to decrease.

There is a strong correlation between C_i and z/r (formal charge/ionic radius) for many of the ions considered in this study (Fig. 4), as is expected from the results of many past studies. The relationship

between $\overline{\log\beta_i}$ and z/r is remarkably strong for the heavier alkaline earths and the lanthanides and is very similar for the two groups. It is interesting to note that, while $\log\beta_{Mg}$ does not follow the remainder of the alkaline earths for the ligands used in the training set, it does follow the linear trend from ligands C_4 to C_8 .

Apparently the three first row transition metals included in the study also show a strong relationship to z/r , but it is a much different relationship than with the electropositive ions. It proved impossible to adequately predict C_i for all 24 ions using z/r alone or in linear combination with other proposed parameters: ionization potentials, enthalpy and entropy of the aqueous ion, metal-oxygen bond energy, effective nuclear charge/ r , and crystal field terms. It seems reasonable that such terms should largely account for the observed $\overline{\log\beta_i}$, but on an individual or individual group basis rather than as equal contributions to all ions. Fortunately, the $\overline{\log\beta_i}$ determined here or the $\log\beta_{i,C_2}$ appear quite adequate for use in ligand design within this family of ligands.

The four remaining factors, accounting for less than 1% of the total variance, describe all the susceptibility exhibited in the ligands studied. Factor 2 accounts for over half the variance not spanned by the "expected stability" primary factor. As has already been noted, and may be readily seen from the error bars of Fig. 3, the factor 2 is quite stable with respect to the assigned data uncertainty, the factors 3 and 4 are less so and factor 5 is essentially buried in the data uncertainty.

It is apparent from the ion cofactors of factor 2 that this factor primarily describes the susceptibility shown towards Co^{+2} , Zn^{+2} and especially Cu^{+2} in respect to the selectivity towards all other ions. As may be seen in Figure 1, the largest susceptibilities encountered involve these three ions. The average susceptibility for pairs of ions not involving these three is less than half that for those pairs which do: 0.41 compared to 0.83 log units. The ligand cofactors for factor 2 show a clear trend, qualitatively corresponding to a decrease in bulk steric hindrance near the bonding nitrogens for both the x- and y-substitution sites. While ligand #14 (C_3) appears to dominate this factor, virtually the identical pattern in both ion and ligand cofactors is obtained if this ligand is not included in the analysis. The increased size of the central ring with this ligand apparently has much the same, but augmented, effect as high steric hindrance near the amine donors.

Thus, ligands having steric hindrance to complex formation (primarily the C_3 and the meso and DL) are overestimated by the one-factor model, i.e. their Co^{+2} , Cu^{+2} and Zn^{+2} (and to a lesser extent to Mg^{+2} and Cd^{+2}) complexes are more stable than is predicted by the model. They are somewhat less stable than predicted towards Ba^{+2} and both ends of the lanthanide series, with little effect for the remaining ions. The reverse is true for the ligands which are not highly hindered. Apparently with the flexible structure of the EDTA family of ligands, Co^{+2} , Cu^{+2} , and Zn^{+2} are not as susceptible to steric influences as are the more electropositive ions. We do not expect this to be the case with more rigid ligand systems.

The dip in the factor 2 lanthanide cofactors is not an artifact of the eigenanalysis: the same pattern is observed for the susceptibilities of the lanthanide ions with Mg^{+2} , Co^{+2} , Cu^{+2} , Zn^{+2} , and Cd^{+2} . This may reflect an "optimum size" for the ions, reached near Gd^{+3} . Ions which are too large (La^{+3}) or too small (Lu^{+3}) are relatively less able to overcome the adverse steric influence of the hindered ligands and thus show greater susceptibility, resulting in more difference in stability between the hindered and unhindered ligand complexes. Although the magnitude of this effect is small, about 0.1 to 0.2 log units from La^{+3} and Lu^{+3} to Gd^{+3} , it is significant relative to the other susceptibilities shown with this data.

The trends shown in factors 3 and 4 are rather more poorly defined than those of factor 2. The most striking pattern in the ion cofactors is the general increase in lanthanide cofactor magnitude across the series. Both factors show a well defined "gadolinium break" and both indicate that the first and second half-shell lanthanides are much more distinct from the other half-shell than they are amongst themselves. This general behavior has often been observed. Factors 3 and 4 are also about equally descriptive of the Mn^{+2} and Cd^{+2} data, although for these ions the two factors are in opposition.

The trend shown by the ligand cofactors of factor 3 seems to be related to the substitution-site of the ligands, however the factor is dominated by the meso ligand. The error-bars for the remaining ligand cofactors indicate that any further interpretation of this factor need be made with caution. This factor was not identifiable on analysis made excluding the meso-ligand data.

The trend shown by the ligand cofactors of factor 4 is somewhat more clearly defined, being related to extensive "DL" steric effect at the y-substitution sites. It is notable that the DL and meso

ligand cofactors are in opposition for this factor, having been very similar with the previous three. It would be desirable to compare the cis-cyclohexaneDTAA data in relation to this factor, as the trans-cyclohexaneDTAA and DL ligand cofactors are of similar magnitude. Only the first three alkaline earth ions have been evaluated for the cis ligand, however: no meaningful comparison of small selectivity trend is possible. The available data does indicate, however, a striking similarity in stabilities between the cis- and the meso-ligands.

The ion cofactors for factor 5 indicate that this factor is primarily concerned with the description of Mg^{+2} , Mn^{+2} and, in an opposite sense, Cd^{+2} and Pb^{+2} . Its ligand cofactors indicate a general opposition between the x- and the y-site substitution. No detailed interpretation for this factor should be made, however, since it is of marginal significance.

If the ion cofactor trend of factor 2 can be validly interpolated to other first-row transition ions, the "expected stability" model can be extended for these ions with the training set ligands. The only ions for which this is possible are Fe^{+2} and Ni^{+2} since only for these ions are the "neighboring" $f_{i,2}$ values available: here, $f_{Mn,2}$, $f_{Co,2}$ and $f_{Cu,2}$. The one- and two-factor reproduction of the data for Fe^{+2} , Co^{+2} and Ni^{+2} are given in Table IV. Note that the $v_{2,l}$ terms must be modified for the two-factor model: the first order model is centered

at C_2 and not at the average, or zero, of the 14 ligands. The appropriate ligand cofactor term is thus $v_{2,2} - v_{2,C_2}$.

It is evident that the data for Co^{+2} is reproduced very well with the two-factor model, the Fe^{+2} data is predicted less well and the Ni^{+2} data is predicted rather inadequately. Since all Fe^{+2} data are predicted to be less stable than is experimentally observed, it appears that the simple interpolation between $f_{Mn,2}$ and $f_{Co,2}$ underestimates the importance of the 2nd factor in the description of the Fe^{+2} data. That is, Fe^{+2} is much more like Co^{+2} in its response to the various ligands than it is to Mn^{+2} . This is consistent with the ion cofactor trend of factor 2, and is confirmed by the significantly better fit using $f_{Co,2}$ as the $f_{Fe,2}$ value (Table IV). The Ni^{+2} data is well predicted for the ligand most affected by factor 2, C_3 , hence we conclude that the interpolation of $f_{Ni,2}$ is approximately correct. The Ni^{+2} complexes of ligand #13 (cyclo) is predicted to be more stable with the one-factor model than it is. This is contrary to the pattern shown by the other transition ions with this ligand and results in the two-factor model increasing the prediction discrepancy. This difference between the model prediction and experiment may indicate either a significant deviation from the model behavior with this ligand or that experimental problems were encountered with this ion. The Ni^{+2} data has significantly greater assigned uncertainty than do the other ions considered in this study.

Conclusions

We have shown that the values of all available critically evaluated formation constants of the EDTA ligand family can be predicted by a simple model derived from abstract factor analysis. Using only four factors (out of a possible fourteen) the data can be reproduced to within experimental uncertainty.

To a good first approximation the stabilities can be described by the equation

$$\log \beta_{1,l} = C_F + C_i + C_l$$

where C_F is characteristic of the ligand family, C_i of the ion, and C_l of the ligand. Examination of C_l has shown that the traditional linear relationship of the pK values of the ligand to the stabilities is not a reliable index for the EDTA family. The value of C_i is strongly related to the ionic potential (z/r) of most of the electropositive ions but the same relationship does not extend over the rest of the metal ions.

As a consequence of this relationship, the selectivities are approximately constant. Nevertheless, the variation in selectivity is significantly above uncertainty in the data. These variations, which we have systematized in a parameter termed susceptibility, have been isolated and described by the factor analysis. The greater the susceptibility the greater the differences between a pair of metal ions in respect to the interactions possible within a ligand family. The unique contribution of factor analysis lies in the isolation of those structural features which bear significantly on the susceptibility, a parameter which estimates the possibility of varying reagent selectivity

of given groups of metal ions. In this study three different trends contributing to the total susceptibility are revealed in the factor analysis. As an illustration, factors 3 and 4 indicate the importance of highly hindered, γ - γ' substituted ligands such as meso and cyclo for lanthanide susceptibility. This suggests that search for new ligands in this family for improved lanthanide separations should focus on changes which bring about increased steric restrictions between the nitrogen atoms.

It would also seem reasonable to suppose that modification of lanthanide group selectivity is largely a function of steric hindrance in other ligand families.

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Table I. Ligands

Name	Symbol	Number of Metal Ions	x	y	y'	z
1. Ethylenedinitrilotetraacetic acid	C ₂	24	-	-	-	-
2. dl-(Methylethylene)dinitrilotetraacetic acid	y-CH ₃	24	-	-CH ₃	-	-
3. dl-(Ethylethylene)dinitrilotetraacetic acid	y-CH ₂ CH ₃	24	-	-CH ₂ CH ₃	-	-
4. dl-(2-Propylethylene)dinitrilotetraacetic acid	y-CH(CH ₃) ₂	24	-	-CH(CH ₃) ₂	-	-
5. dl-(2-Methylpropylethylene)dinitrilotetraacetic acid	y-CH ₂ CH(CH ₃) ₂	24	-	-CH ₂ CH(CH ₃) ₂	-	-
6. dl-(1,2-Dimethylethylene)dinitrilotetraacetic acid	DL	24	-	-CH ₃	-CH ₃	-
7. meso-(1,2-Dimethylethylene)dinitrilotetraacetic acid	meso	24	-	-CH ₃	-CH ₃	-
8. dl-(Phenylethylene)dinitrilotetraacetic acid	y-φ	24	-	-C ₆ H ₅	-	-
9. dl-Ethylenedinitrilo-N,N'-di(2-propanoic)-N,N'-diacetic acid	x-CH ₃	24	-CH ₃	-	-	-
10. dl-Ethylenedinitrilo-N,N'-di(2-butanoic)-N,N'-diacetic acid	x-CH ₂ CH ₃	24	-CH ₂ CH ₃	-	-	-
11. dl-Ethylenedinitrilo-N,N'-di(2-pentanoic)-N,N'-diacetic acid	x-CH ₂ CH ₂ CH ₃	24	-CH ₂ CH ₂ CH ₃	-	-	-
12. dl-Ethylenedinitrilo-N,N'-bis-(2)-(3-methyl-butanoic)-N,N'-diacetic acid	x-CH(CH ₃) ₂	24	-CH(CH ₃) ₂	-	-	-
3. trans-1,2-Cyclohexylenedinitrilotetraacetic acid	cyclo	24	-		-	-
4. Trimethylenedinitrilotetraacetic acid	C ₃	21	-	-	-	-CH ₂ -

Name		Number of Metal Ions	x	y		y'	z
15. dl-(Propylethylene)dinitrilotetraacetic acid	γ -CH ₂ CH ₂ CH ₃	5	-	-	-CH ₂ CH ₂ CH ₃	-	-
16. dl-(1,2-Diphenylethylene)dinitrilotetraacetic acid	DL-0	6	-	-	-C ₆ H ₅	-C ₆ H ₅	-
17. trans-1,2-Cyclopentylenedinitrilotetraacetic acid	trans-cyclopentyl	20	-	-		-	-
18. cis-1,2-Cyclohexylenedinitrilotetraacetic acid	cis-cyclohexyl	3	-	-		-	-
19. trans-4,5-benzocyclohexanediaminetetraacetic acid	trans-benzocyclo	3	-	-		-	-
20. Tetramethylenedinitrilotetraacetic acid	C ₄	11	-	-	-	-	-(CH ₂) ₂ -
21. Pentamethylenedinitrilotetraacetic acid	C ₅	10	-	-	-	-	-(CH ₂) ₃ -
22. Hexamethylenedinitrilotetraacetic acid	C ₆	10	-	-	-	-	-(CH ₂) ₄ -
23. Octamethylenedinitrilotetraacetic acid	C ₈	10	-	-	-	-	-(CH ₂) ₆ -
24. 1,2-Phenylenedinitrilotetraacetic acid	phenyl	4	-	-		-	-

Table II. Logarithmic Stability Constant Statistics

Ligand values, summed over all ions				Ion values, summed over all ligands			
Ligand	$\bar{x}$	s	$\bar{u}^a$	Ion	$\bar{x}$	s	$\bar{u}^a$
1. C ₂	16.03	3.52	0.13	1. Mg ⁺²	8.99	1.76	0.09
2. y-CH ₃	16.91	3.48	0.12	2. Ca ⁺²	10.41	2.01	0.10
3. y-CH ₂ CH ₃	17.30	3.62	0.16	3. Sr ⁺²	8.33	1.93	0.09
4. y-CH(CH ₃) ₂	17.26	3.58	0.17	4. Ba ⁺²	7.14	1.83	0.11
5. y-CH ₂ CH(CH ₃) ₂	17.23	3.54	0.17	5. La ⁺³	15.01	1.95	0.17
6. DL	17.60	3.50	0.12	6. Ce ⁺³	15.61	1.90	0.16
7. Meso	15.52	3.59	0.16	7. Pr ⁺³	15.96	1.91	0.16
8. y-Ø	16.28	3.36	0.16	8. Nd ⁺³	16.25	1.93	0.15
9. x-CH ₃	15.53	3.65	0.16	9. Sm ⁺³	16.83	1.85	0.16
10. x-CH ₂ CH ₃	15.01	3.82	0.15	10. Eu ⁺³	17.09	1.81	0.18
11. x-CH ₂ CH ₂ CH ₃	15.08	3.77	0.15	11. Gd ⁺³	17.20	1.78	0.17
12. x-CH(CH ₃) ₂	11.98	3.70	0.12	12. Tb ⁺³	17.74	1.75	0.19
13. Cyclo	18.30	3.74	0.17	13. Dy ⁺³	18.13	1.79	0.14
14. C ₃	<u>12.60</u>	<u>3.66</u>	<u>0.19</u>	14. Ho ⁺³	18.37	1.81	0.19
	15.90	3.61	0.15	15. Er ⁺³	18.67	1.91	0.21
				16. Tm ⁺³	19.01	1.92	0.24
				17. Yb ⁺³	19.28	1.93	0.24
				18. Lu ⁺³	19.45	1.98	0.21
				19. Mn ⁺²	14.12	2.21	0.14
				20. Co ⁺²	16.97	1.56	0.16
				21. Cu ⁺²	19.64	1.51	0.14
				22. Zn ⁺²	16.97	1.66	0.12
				23. Cd ⁺²	16.69	2.02	0.16
				24. Pb ⁺²	<u>17.80</u>	<u>1.97</u>	<u>0.22</u>
					15.90	1.86	0.15

a. Average assigned uncertainty

Table III. Eigenvalues and Data-reproduction Statistics

No. Factors (p)	λ_p	$100 \frac{\sum_{i=1}^n (\lambda_i - \lambda_p)}{\sum_{i=1}^n \lambda_i}$	CORR ^a	SEE ^a	Maximum Difference		
					Diff.	Complex ^b	Uncert.
1	13.86	98.99	0.9959	0.36	2.64	Cu:C ₃	0.10
2	0.089	99.62	0.9985	0.22	1.03	Mn:Cyclo	0.10
3	0.022	99.78	0.9991	0.17	0.86	Mn:Cyclo	0.10
4	0.018	99.91	0.9996	0.11	0.48	Pb:x-CH(CH ₃) ₂	0.20
5	0.006	99.96	0.9998	0.08	0.55	Pb:x-CH(CH ₃) ₂	0.20
6	0.003	99.97	0.9999	0.06	-0.23	Ba:x-CH ₃	0.10
7	0.002	99.99	0.9999	0.04	0.15	Mg:DL	0.06
8	0.001	99.99	1.000	0.03	-0.10	Yb:C ₂	0.30

a. Definitions given in text

b. Ligand symbols are given in Table I

Table IV. One-factor Data Models.

$$\log \beta_{i,l} = C_F + b(C_i) + c(C_l)$$

Variable	$\bar{x}$	s	Coefficient	CORR	Fit Statistics	
C_F			-15.90 ± 0.021		CORR	0.996
b $\log \beta_i$	15.90	3.52	1.000 ± 0.006	0.890	SEE	0.38
c $\log \beta_l$	15.90	1.76	1.000 ± 0.012	0.446	Max	2.59
C_F			-7.81 ± 0.025		CORR	0.993
b $\log \beta_i$	15.90	3.52	1.000 ± 0.007	0.890	SEE	0.47
c $\log \beta_{Sr,l}$	8.33	1.86	0.937 ± 0.014	0.440	Max	2.14
C_F			16.28 ± 0.028		CORR	0.991
b $\log \beta_{i,C_2}$	16.03	3.45	1.016 ± 0.008	0.885	SEE	0.53
c $\log \beta_l$	15.90	1.76	1.000 ± 0.016	0.446	Max	3.51
C_F			-8.19 ± 0.032		CORR	0.989
b $\log \beta_{i,C_2}$	16.03	3.45	1.016 ± 0.009	0.885	SEE	0.59
c $\log \beta_{Sr,l}$	8.33	1.86	0.937 ± 0.017	0.440	Max	3.07

Table V. One- and Two-factor Models for Fe^{+2} , Co^{+2} , and Ni^{+2}

Ligand	$v'_{2,\text{lig}}$	$\log\beta_{\text{Fe}^{+2},\ell}$				$\log\beta_{\text{Co}^{+2},\ell}$			$\log\beta_{\text{Ni}^{+2},\ell}$		
		Expt.	Model ^a ₁	Model ^b ₂	Model ^c ₃	Expt.	Model ^a ₁	Model ^b ₂	Expt.	Model ^a ₁	Model ^b ₂
1 C ₂	-0.322	14.32±0.10	14.30	14.30	14.30	16.31±0.10	16.31	16.31	18.62±0.10	18.67	18.67
2 γ -CH ₃	-0.232	15.5 ±0.30	15.18	15.28	15.38	17.3 ±0.30	17.20	17.41	19.6 ±0.30	19.55	19.78
6 DL	0.189	17.1 ±0.20	15.87	16.44	17.04	18.9 ±0.20	17.89	19.06	22.4 ±1.00	20.24	21.58
7 Meso	0.257	15.2 ±0.20	13.79	14.45	15.15	17.1 ±0.20	15.81	17.18	20.2 ±1.00	18.16	19.71
8 γ -Ø	-0.151	-	14.55	14.73	14.93	16.91±0.10	16.57	16.95	19.2 ±1.00	18.92	19.35
9 α -CH ₃	-0.215	14.18±0.10	13.80	13.92	14.06	16.2 ±0.20	15.82	16.08	-	18.17	18.46
13 Cyclo	0.057	19.0 ±0.20	16.57	17.02	17.50	19.62±0.10	18.59	19.52	20.3 ±0.20	20.93	22.00
14 C ₃	0.781	13.42±0.10	10.87	12.15	13.52	15.55±0.10	12.89	15.54	18.18±0.10	15.24	18.26
Least-squares Fit Stats: CORR			0.86	0.94	0.98		0.86	0.99		0.67	0.84
SEE			2.01	1.49	0.87		1.49	0.13		2.12	1.14
Max.Dif.			2.55	1.98	1.50		2.66	-0.17		2.94	-1.70

a) One-factor model: ${}^1\log\beta_{i,\ell} = -16.28 + \overline{\log\beta_{\ell}} + (1.016)(\log\beta_{i,\text{C}_2})$

b) Two-factor model: ${}^2\log\beta_{i,\ell} = {}^1\log\beta_{i,\ell} + (24-1)^{1/2}(\sigma_{\ell})(v_{2,\ell} - v_{2,\text{C}_2})(f_{i,2})$

$$f_{\text{Fe},2} = (f_{\text{Mn},2} + f_{\text{Co},2})/2 = 0.066; f_{\text{Co},2} = 0.137; f_{\text{Ni},2} = (f_{\text{Co},2} + f_{\text{Cu},2})/2 = 0.156$$

c) Two-factor model same as above except that $f_{\text{Fe},2} = 0.137$

Figure Captions

Figure 1. Selectivity/Susceptibility Matrix

The average selectivity, $\bar{S}_{i,j}$, is represented by the vertical bar; full scale is equal to 12.5 log units. The susceptibility, $\sigma_{i,j}$, is represented by the horizontal bar; full scale is equal to 1.2 log units.

Figure 2. Criteria for Determining the Number of Factors

- Eigenvalues, λ , for the true- ($\diamond$) and UP-data (+) analyses.
- Cross-correlation between true- and UP-data factors.
- Malinowski Indicator Function for true-data analysis.
- Malinowski's Real Error (+) and the Standard Estimate of Error ($\diamond$)

Figure 3. Ligand and Ion Cofactors from UP-data analyses

Ligand cofactors are arranged in order of true-data coefficient, the shorthand symbols denoting which ligands the ligand cofactors correspond to are given in Table I. Horizontal bar marks average of UP-data values, vertical bar denotes $\pm$ std. dev.

Figure 4. Correlation of Ion Average Stability with z/r

Fe^{+2} and Ni^{+2} $\log \beta$ values extrapolated from available data. Ionic radii used from: Advanced Inorganic Chem., F. A. Cotton and G. Wilkinson (1972).

Fig. 1

Mg	→	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Ca	→		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sr	-	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Ba	→	+	→		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
La	+	+	+	+		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
Gd	+	+	+	+	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
Tb	+	+	+	+	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
Lu	+	+	+	+	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
Mn	+	+	+	+	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Co	+	+	+	+	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Cu	+	+	+	+	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Zn	+	+	+	+	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Cd	+	+	+	+	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Pb	+	+	+	+	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	
Mg	Ca	Sr	Ba	La	Ce	Pr	Nd	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	Mn	Co	Cu	Zn	Cd	Pb

Fig. 2

Fig. 4