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THE STRUCTURE OF COMPLEXONES AND THEIR COMPLEX-FORMING POWER

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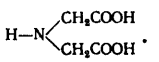
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I. INTRODUCTION

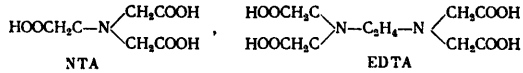
The increasing importance of complex compounds in different fields of theoretical research and, particularly, in practical applications, has led to the rapid developement of the chemistry of multidentate reagents. The complexones form some of the most interesting and promising compounds of this type [1-7].

The term complexone is usually applied to compounds that contain at least one iminodiacetate group $-N(CH_2COOH)_2$, linked to various aliphatic or aromatic substituents by residues of acetic or alkyliminodiacetic acid. At present a series of complexones are also known which are derivatives of iminodipropionic acid, and also aminomethyl--phosphonic and -sulphonic acids [8-17].

The simplest representative of this class of compounds is iminodiacetic acid:



Nitrilotriacetic acid (NTA), ethylenediaminetetraacetic acid (EDTA), and other polyethylenepolyaminepolyacetic acids may be regarded as its structural analogues:



NTA EDTA



where $n = 0, 1, 2...$

These compounds were first mentioned in 1936 when NTA, EDTA, and their salts were patented by I. G. Farbenindustrie and put on the world market under the names Trilon A† and Trilon B‡ as compounds suitable for water

† At present also marketed under the names: Complexone I, Chelaton I, and Titriplex I [these refer to NTA (Ed. of Translation)].

‡ At present also marketed under the names: Complexone III, Chelaton III, Sequestrene, Versene, Irgalon, Titriplex III, Nervanid [most of these refer to the dihydrate of the disodium salt of EDTA, EDTA itself being known as Complexone II, etc. (Ed. of Translation)].

softening. The subsequent work of Schwarzenbach[3,4,18-20] on the determination of the physicochemical constants of the complexones, and on the kinetics and mechanism of their reactions with cations, opened great possibilities for the use of these compounds and provided fruitful ground for the creation of a whole series of new complexones. At the present time there are more than 200 complexones.

These multidentate chelating agents, which created unlimited possibilities for modification of the properties of the central atom and ligands by the formation of highly stable water-soluble complexes, found wide use in many branches of science and technology; this is shown by the tremendous number of publications and patents that have appeared in both Soviet and non-Russian literature.

The introduction of complexones into analytical chemistry opened great possibilities in volumetric[2-7,18-24], gravimetric[2-7,18,19,25-30], colorimetric[2,3,6,7,18,19,31-37], polarographic[2,3,6,7,18,19,38-42], amperometric[6,7,18,19,43,44], and other methods of analysis[6,7,18-20,45-50]. By the use of these compounds the simplest methods of determining cations occurring in difficult combinations without preliminary separation could be developed.

In order to show more clearly the importance of complexones in analysis, it is sufficient to note that at the present time over 60 elements of Mendeleev's Table (practically all the cations and many anions) can be determined by direct or indirect methods with the aid of complexones. These compounds indeed form the nucleus of modern volumetric analysis, which means of analytical chemistry as a whole. The complexones are no less important in the purification and preparation of various elements and compounds. One of the most difficult tasks, the separation of the rare-earth elements, has now been solved by the use of complexones[51-62].

The complexones are of great importance in biology and medicine. These compounds are quite effective in removing toxic metals from the body, including radioactive isotopes and their fission products[63-67]. They are also used for removing radioactive compounds from various contaminated surfaces[68-74]. By the use of complexones and complexonates in some branches of agriculture, the metal content of the soil can be regulated and chlorosis of plants can be prevented[75-78]. Moreover complexones have been widely used in the textile, leather, food, and paper industries, in the production of metals, varnishes, paints, and rubbers, and in the purification of petroleum, wax, fats, etc.[8,9,49]

The number of papers on the use of complexones is very large. Most of them have been summarised and presented as monographs and reviews[2-8].

Problems connected with the study of the effect of the structure of these multidentate chelating agents on their complexing properties, and also on the kinetics and mechanism of their interaction, are dealt with practically only in the original literature. In this connection we consider it expedient to devote the present article to these important questions with a preliminary examination of the fundamental principles of chelate formation.

II. PROPERTIES OF COMPLEXONES AND PRINCIPLES OF CHELATE FORMATION

Complexones are multidentate chelate-forming reagents. The term "chelate" was proposed by Morgan[79] to denote those cyclic structures that are formed as a result of the union of a cation with two or more donor groups belonging to one molecule of complexing agent. The same is derived from the Greek word "χιλη" which denotes a claw (from which another name for these compounds "clawlike" is derived). This type of ring formation can, of course, only be formed by polyfunctional reagents which can replace more than one position in the coordination sphere of the metal[80-85]. In this connection we distinguish bi-, ter-, quadri-, and multi-dentate complexing agents; these can form one, two, three, and more chelate rings with the metal ion.

Iminodiacetic acid is an example of a terdentate, NTA of a quadridentate, and EDTA of a sexidentate complex-forming agent.

The normal complexes are formed as a result of the interaction of a cation with the completely dissociated anion of the complexone, or in the extreme case, when only betaine hydrogen is present in it. For example, EDTA (denoted below by H_4Y) forms a complex by the reaction

$$M_{aq}^{n+} + Y^{4-} \rightleftarrows MY^{n-4} + aq.$$

In an acid medium a weakly basic hydrogen complex may be formed, and in an alkaline medium a hydroxo-complex. In solution the formation of compounds of this kind proceeds in the following manner. When the complexone is introduced into the solution conditions are created for competition between water molecules of the hydration shell of the cation and molecules introduced into the solution by the chelating agent. The necessary conditions for displacing water from the aquo-complex are: a higher donor power of the ligand groups bonding with the metal; a suitable pH value of the solution; and a sufficiently convenient structure of the chelating agent, for otherwise steric hindrance makes coordination impossible.

The competing complexing agent (Y), satisfying these requirements is, under suitable conditions, capable of displacing water from the coordination sphere of the aquo-complex (M_{aq}) with the formation of a new complex (MY). The stability of the complexes formed in solution may be denoted by the equilibrium constant (the formation or stability constant):

$$K = \frac{a_{MY}}{a_M a_Y},$$

where a is the activity of compounds taking part in the reaction (the charge is omitted in the formula).

The inverse quantity, the instability constant, is often used[2,3,4,78-85,86]. This quantitative characteristic, indicating the magnitude of the displacement of equilibrium in the direction of complex formation, is derived from the law of mass action, without taking account of successive replacement of the coordination positions in the aquo-complex and the possibility of the formation of several intermediate complexes. At constant ionic strength, concentration ("apparent") stability constants of the complex may be successfully used; these are derived from the equation

$$K_{MY} = \frac{[MY]}{[M][Y]}.$$

These constants show the ratio between the concentrations of ion bound in the complex and the free ion of the metal for every given concentration of the complexing agent.

High thermodynamic stability is an outstanding property of chelate compounds. This is mainly due to the spatially favourable arrangement of complexing groups, leading to the possibility of using in the complex all donor atoms of the ligand, both oxygen and nitrogen, with fairly large polarisability [3,87-90].

EDTA is an ideal example of compounds of this type. This complexone is a universal sexidentate reagent, capable of fully saturating the coordination capacity of most cations, thereby creating the optimal variant of an intra--complex compound with the maximal number of five--membered rings and comparatively little spatial stress.

However, it should be mentioned that there are cases when not all groups of the ligand capable of coordination take part in the formation of rings of a given chelate; as a result less stable compounds are formed. This may be explained by too large a strain on the rings with maximal use of chelate groups capable of coordination, or by the large volume of the coordinating groups, often preventing the achievement of the maximal coordination number of the ions. Phenomena of this kind are undoubtedly connected with the geometrical structure of the internal ligand contour of the chelating agent, and also with the nature of the donor atoms and the central metal ion. Cases are known in which multidentate reagents do not occupy all possible coordination positions in the internal sphere of the complex [3,91-93]. This is mainly observed with small cations and also with some metal ions that form complex compounds with a planar structure. Moreover, the presence in the solution of other donor atoms firmly bound to the cation also leads to a number of cases of incomplete substitution of its coordinating positions by the chelating agent.

The chelate compounds are usually more stable than their non-chelate analogues. In the general case, the equilibrium constant of the substitution reaction

$$ML_n + mY \rightleftarrows MY_m + nL, \qquad (1)$$

where n, the number of unidentate ligands replaced by m related multidentate ligands (occupying the same number of coordination positions), is greater than unity. Schwarzenbach called this increased stability that arises through the formation of a ring the "chelate" effect [94,95]. This effect is so general that isolated cases of a negative value of $\log K$ of substitution may be explained either by the complete absence of chelate rings or by a hypothesis about their strain.

Most authors [86,96-100] connect the chelate effect with a greater increase in entropy in reactions in which chelate compounds are formed than in reactions connected with the addition of some simple ligands. Many attempts have been made to determine the entropy change for this effect. Calvin and Bailes proposed that the positive entropy change for the equilibrium substitution, Reaction (1), is mainly due to a gain in translational entropy; however, the effect is observed much less frequently than would be expected from this hypothesis [101]. Martell noted that the value of ΔS for a number of complexonates increases with increasing number of donor atoms and with decreasing radius of the cation [96]. He also found that the dependence of ΔS on the number of coordinating acetate groups is linear. Schwarzenbach proposed that the entropy contribution to the chelate effect is related to ring closure and in the main does not depend on the nature of the metal ion or on the bonding atom of the ligand [94]; the greatest chelate effect is observed in the formation of the smallest ring free from strain, which usually consists of five members in a saturated ring and of six members in an unsaturated ring. Adamson [102] considers that the chelate effect is more apparent than real; it is to a large degree a packing effect, which appears as configurational entropy. However, it should be noted that since the chelate effect is expressed by the difference between the logarithms of the stability constants of the chelate complex and the complex with simple ligands of the same type, there is a correlation between factors affecting the stability of the complexes formed and a ring effect. In this connection, the unequal changes of these two constants with a change in the concentration of the complexing agent for a different number of ligands should be taken into account. The value of the stability constant of a simple complex by n ligands (L) given by the equation

$$K_{ML_n} = \frac{[ML_n]}{[M][L]^n},$$

changes with change in concentration of the complexing agent much faster than in the case of chelate formation, expressed by the equation:

$$K_{MY} = \frac{[MY]}{[M][Y]};$$

therefore the standard state of the reacting compounds is usually taken as a 1 M solution of the completely hydrated ions or molecules.

Another important characteristic of the complexing reaction is the kinetics of the process [2,3,85]. Although practically the same quantities (charge, size, and stereochemical configuration, electronegativity, polarisability of the central metal ion and ligands) enter into the factors affecting the rate of reaction and the stability of the complexes formed, it has been stated in the literature [85] that these two quantities are not correlated, that is, the stability of the complexes does not characterise their kinetic behaviour in formation or substitution reactions. A low rate of displacement does not inevitably mean a high stabilisation of the bond. A few studies in the complexone field have shown that the whole process of interaction of the metal with complexones is subject to the same kinetic laws; the exchange proceeds both by a second-order reaction (direct exchange between metal and complex) and by a first-order reaction (dissociation of various protonated complexes) [103-105].

Protonation of the ligand reduces the electron density at the metal bond and increases the rate of dissociation of this bond. For example, HCd(EDTA) dissociates 20 times faster than Cd(EDTA), that is, aquation appears to be catalysed by acids. The formation of complexes of the external shell type Fe(EDTA) is practically instantaneous; the formation of complexes of the internal shell type, in which there is at least one electron on each d-shell — for example, Cr(EDTA) and Co(EDTA) — proceeds incomparably slower [103]. Therefore, in compounds of this type the formation and decomposition of the complexes are essential kinetic factors equivalent to the effect of electronic structure. The formation of complexes with cyclohex-1,2-ylenebis(iminodiacetic acid) is somewhat slower [2,3,106], which is probably connected with rigid fixation at a definite distance and the corresponding directional alignment of the complexing groups.

A considerably larger number of investigations have been devoted to the substitution reactions of complexes, in which the central metal ion or a ligand is exchanged. Many complexes enter into exchanges with free metal ions with measurable velocity; very often the exchange proceeds in several stages, sometimes with partial opening of the

chelate ring and the formation of new metal–ligand bonds; in all cases the mechanism of the exchange reaction and the constants for the rate of formation of complexes depend on pH[3,85]. Cation-exchange reactions of most complexonates of NTA and EDTA[103] are practically instantaneous, but the reactions of complexonates of cyclohex-1,2-ylenebis(iminodiacetic acid) are much slower (10 to 100 times). Thus, establishment of the equilibrium

$$FeY^- + Th^{4+} \rightleftarrows ThY + Fe^{3+}$$

takes several days[106] but displacement of nickel from cyclohex-1,2-ylenebis(iminodiacetate) by other cations in general does not reach equilibrium in a measurable time. Of particular interest are the rates of oxidation-reduction processes, and in particular between two oxidation states of the same element in the complex. These reactions are practically instantaneous. Thus, the rate of the exchange reaction $[Co(EDTA)]^{2-}$–$[Co(EDTA)]^-$ is 4×10^{-7} mole^{-1} s^{-1} and that for the reaction $[Fe(EDTA)]^{2-}$–$[Fe(EDTA)]^-$ exceeds 1×10^{-3} mole^{-1} s^{-1}.

Summarising, one should note that this side of the question of complex formation, which is important in practice and interesting from a theoretical standpoint, has been studied insufficiently; it is therefore not always possible to compare results obtained and to give basic interpretations of observed facts.

III. THE EFFECT OF THE STRUCTURE OF COMPLEXONES ON THEIR COMPLEXING POWER

The question of the relation between the structure of chelating compounds and their reactivity is a very important and topical one from both the practical and the theoretical viewpoints. A knowledge of the fundamental physical constants and the variety of factors that affect complex formation, forms a definite scientific base, which has already made the use of complexones possible not only in a number of problems in analytical chemistry, but also in finding new fields of application for these compounds. This knowledge has been used to solve some most important problems in the national economy and has given rise to promising possibilities of further development.

The theoretical side of the problem is also of undoubted importance; complexones are multidentate reagents[99] that form stable complex compounds with practically all cations and, for this reason, if some degree of selectivity is to be conferred on them, a special structure of the molecule is necessary, account being taken of electronic structure, nature of the coordinating atoms, and the stereochemistry of the complexes. All studies connected with the elucidation of the principles of change in the complexing action of complexones are very valuable contributions to the setting up of a theory of organic reagents. Furthermore, these principles make possible theoretical predictions, which in a number of cases permit the synthesis of new complexones with predetermined properties.

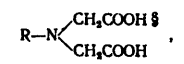
Modifications of the complexone molecule have been carried out in the following main directions:

(1) introduction into the complexone molecule of various substituents not taking part in complex formation but affecting the basicity of the coordinating nitrogen of the iminodiacetate grouping; (2) increasing the denticity of the chelating agent by introducing into the complexone molecule heteroatoms and iminoacetate and characteristic analytical groupings that tend to form complexes with certain elements; (3) changing the geometry of the internal ligand contour.

The following Sections of this review will be devoted to this aspect of the problem.

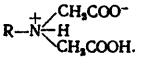
1. The Effect of the Basicity of the Nitrogen of the Iminodiacetate Group

One of the main factors affecting the complexing power of complexones is the basicity of the nitrogen atom of the iminodiacetate groups. This effect has been well studied on derivatives of iminodiacetic acid, which is the simplest structural model of complexones. At the present time a considerable number of compounds with the general formula:



have been synthesised, where R represents various aliphatic, aromatic, or alicyclic substituents containing functional and non-functional groups[107-118]. Data on the complexing properties of these compounds are collected in Table 1.

The first three vertical columns of Table 1 contain values of the acid dissociation constants of the complexones. In accordance with the views of Schwarzenbach, the betaine structure is ascribed to all these acids[18,108-115]:



The betaine structure of these compounds also explains the high value of the negative logarithm of the dissociation constant for the first hydrogen atom, the mobility of which depends on the basicity of the nitrogen atom linked to it. The basicity of the nitrogen atom in turn changes with the inductive effect of substituents R linked to nitrogen. When hydrogen in the iminodiacetic acid group is replaced by the CH_3 group, the basic properties of the nitrogen are increased as a result of the positive inductive effect of the CH_3 group. If one, or particularly two, phenyl groups are introduced into the methyl group the basicity of the nitrogen decreases somewhat due to the comparatively strong electron-acceptor properties of these groups. In the case of aniline, the electron pair of the nitrogen is displaced towards the benzene nucleus, which leads to a still greater weakening of the basic properties of the nitrogen.

A definite relation between the mobility of the betaine proton and the coordinating power of the nitrogen atom would therefore be expected. In fact, for complexones containing alkyl, alkylaryl, and alicyclic radicals a simple linear relationship is observed between the basicity of the nitrogen, as expressed by the acid dissociation constant of the last proton, and its coordinating power (Fig. 1).

As Fig. 1 shows, the introduction of alkyl and alkylaryl radicals increases the complexing power of the complexones, and, on the contrary, when the phenyl radical is a direct neighbour, the complexing power of the iminodiacetic acid group is lowered.

§ In future the iminodiacetate group $-N\langle^{CH_2COOH}_{CH_2COOH}$ will be denoted by the symbol $-N\langle$.

TABLE 1. Negative logarithms of dissociation constants and stability constants of complexes of iminodiacetic acid and its derivatives.

Complexone	Formula	pK dissociation			pK_{MY}												References
		pK_1	pK_2	pK_3	Mg^{++}	Ca^{++}	Sr^{++}	Ba^{++}	Mn^{++}	Fe^{++}	Co^{++}	Ni^{++}	Cu^{++}	Zn^{++}	Cd^{++}	Pb^{++}	Hg^{++}	
Iminodiacetic acid	$HN(CH_2COOH)_2$	9.12	2.54	—	3.86	3.41	—	1.67	—	—	6.9	8.2	10.3	7.0	5.4	—	—	111,114,116
Methyliminodiacetic acid	$CH_3N(CH_2COOH)_2$	9.65	2.12		3.44	3.75	2.85	2.59	5.40	6.65	7.62	8.73	11.09	7.65	6.77	8.02	5.47	110,114,115
N(3,3-Dimethylbutyl)-iminodiacetic acid	$CH_3-C(CH_3)_2-CH_2-CH_2-N(CH_2COOH)_2$	10.24	2.4		3.60	3.68	2.70	2.41	5.55	—	7.78	8.70	11.49	7.92	7.12	8.16	5.91	114
2-Hydroxyethyliminodiacetic acid	$HO-CH_2-CH_2-N(CH_2COOH)_2$	8.72	2.2		3.44	4.63	3.77	3.42	5.55	6.78	7.90	9.28	11.86	8.33	7.52	9.41	5.48	114
2-Mercaptoethyliminodiacetic acid	$HS-CH_2-CH_2-N(CH_2COOH)_2$	10.79	8.17	2.14	3.32	4.88	3.62	3.55	9.32	11.72	14.67	13.75	—	15.92	16.72	17.03	16.16	114
2-Methoxyethyliminodiacetic acid	$CH_3O-CH_2-CH_2-N(CH_2COOH)_2$	8.96	2.2		4.31	4.53	3.84	3.56	5.53	6.81	7.96	9.39	12.24	8.43	7.53	9.49	5.94	114
2-Methylthioethyliminodiacetic acid	$CH_3S-CH_2-CH_2-N(CH_2COOH)_2$	8.91	2.1		3.02	3.34	2.71	2.62	5.10	7.12	8.51	10.0	12.63	8.28	7.89	9.12	8.01	114
2-Aminoethyliminodiacetic acid	$H_2N-CH_2-CH_2-N(CH_2COOH)_2$	11.05	5.58		4.58	4.63	3.55	3.19	7.71	9.81	11.78	13.73	15.90	11.93	10.58	12.22	9.75	114
Nitrilotriacetic acid	$HOOC-CH_2-N(CH_2COOH)_2$	9.73	2.49	1.89	5.41	6.41	4.98	4.82	7.44	8.83	10.38	11.53	12.96	10.67	9.83	11.39	—	108,112,113
Nitrilotriacetic acid monoamide	$H_2N-C(=O)-CH_2-N(CH_2COOH)_2$	6.60	2.30		2.47	3.96	3.03	2.88	4.93	—	6.91	8.02	9.68	7.30	7.08	8.40	3.82	114
Nitrilotriacetic acid mononitrile	$N\equiv C-CH_2-N(CH_2COOH)_2$	4.34	3.06		1.86	2.75	2.15	1.98	3.50	—	5.38	6.20	7.45	5.80	4.43	—	2.40	114
2-(Trimethylammonio)-ethyliminodiacetic acid	$(CH_3)_3N^+-CH_2-CH_2-N(CH_2COOH)_2$	5.45	2.32		1.42	1.88	1.22	1.34	2.87	—	5.51	6.00	7.73	5.34	4.62	5.40	2.77	114
N-[2-(2-Ethoxycarbonylamine(ethyl)]iminodiacetic acid	$C_2H_5O-C(=O)-NH-CH_2-CH_2-N(CH_2COOH)_2$	8.57	2.20		2.68	2.99	2.14	2.00	4.60	—	6.71	7.94	10.50	6.86	5.86	7.25	4.50	114
2,2′,3″-Nitrilodiaceticpropionic acid	$HOOC-CH_2-CH_2-N(CH_2COOH)_2$	9.66	—		5.28	5.04	3.87	3.40	—	—	—	—	—	—	—	—	—	114
Taurine-*N*-diacetic acid	$^-O_3S-CH_2-CH_2-N(CH_2COOH)_2$	8.16	2.28	1.90	3.48	4.15	3.26	3.01	—	—	—	—	—	—	—	—	—	110
N-Phosphonomethyliminodiacetic acid	$^-HO_3P-CH_2-N(CH_2COOH)_2$	10.76	5.57	2,25 2.00	6.28	7.18	5.59	5.35	—	—	—	—	—	—	—	—	—	107,110
N-2-Phosphoethyliminodiacetic acid	$^-HO_3P-CH_2-CH_2-N(CH_2COOH)_2$	6.54 10.46	27.45 7.00	2.0 2.74	6.38	5.44	4.10	3.64	—	—	—	—	—	—	—	—	—	107,110
Phenyliminodiacetic acid	$C_6H_5-N(CH_2COOH)_2$	5.18 4.96	2.40 2.51		1.15	1.5	—	—	1.58	2.01	2.90	3.53	6.57	3.22	2.16	3.49	—	107,109,117
o-Sulphophenyliminodiacetic acid	$HO_3S-C_6H_4-N(CH_2COOH)_2$	6.29	3.10	1,0	2.68	4.57	3.50	3.48	—	—	—	—	—	—	—	—	—	109
m-Sulphophenyliminodiacetic acid	$HO_3S-C_6H_4-N(CH_2COOH)_2$	4.78	2.36	1	1.26	1.26	—	—	—	—	—	—	—	—	—	—	—	109
p-Sulphophenyliminodiacetic acid	$HO_3S-C_6H_4-N(CH_2COOH)_2$	4.54	2.31	1	1.15	0.95	—	—	—	—	—	—	—	—	—	—	—	109
o-Carboxyphenyliminodiacetic acid	$HOOC-C_6H_4-N(CH_2COOH)_2$	7.75	2.98	2,35	3.91	5.06	3.91	3.57	—	—	—	—	—	—	—	—	—	109,118
m-Carboxyphenyliminodiacetic acid	$HOOC-C_6H_4-N(CH_2COOH)_2$	5.10	4.06	2.40	1.38	1.46	1.0	1.0	—	—	—	—	—	—	—	—	—	109
p-Carboxyphenyliminodiacetic acid	$HOOC-C_6H_4-N(CH_2COOH)_2$	5.20	4.28	2.31	1.30	1.30	1.0	1.0	—	—	—	—	—	—	—	—	—	109

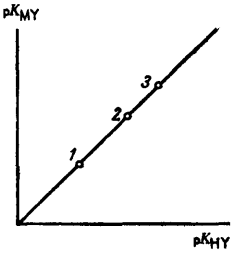


Fig. 1. Dependence of the coordinating power of the nitrogen on its basicity, expressed as an acid dissociation constant of the last betaine proton:
1) benzyliminodiacetic acid; 2) cyclohexyliminodiacetic acid; 3) methyliminodiacetic acid.

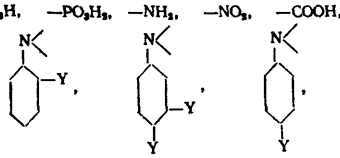
More complex relationships are observed when various functional substituents are introduced into the hydrocarbon radical of iminodiacetic acid.

Schwarzenbach [110-114] studied derivatives of iminodiacetic acid and anilinediacetic acid with the general formulae:

$X-CH_2-N(CH_2COOH)_2$, $X-CH_2-CH_2-N(CH_2COOH)_2$,

where X = $-SO_3H$, $-PO_3H_2$, $-NH_2$, $-NO_2$, $-COOH$, $-OH$.

and



where Y = $-SO_3H$, $-COOH$.

The introduction of similar substituents on iminodiacetic and phenyliminodiacetic acid has a twofold effect on the complexing power of the compounds. On the one hand, the basicity of the imino-nitrogen changes because of the electrostatic effect of the substituents; on the other hand, the complexing power of the compounds changes because of the tendency of some of the substituents introduced to form additional rings. The latter factor mainly affects α-derivatives of alkylaminodiacetic acid and *ortho*-derivatives of phenyliminodiacetic acid [109]. For ligands of this kind, containing several types of group capable of coordinating, the linear dependence between the basicity of the nitrogen and coordinating power only holds approximately; the dependence holds only for a number of ligands of similar structure that form the same number of chelate rings of the same size and having the same π bonding tendency. If there is no steric hindrance, then the change in free energy (enthalpy) shifts in parallel with the values of pK for HY^- (in water). A greater or lesser deviation from linear dependence between pK(MY) and pK(HY^-) is probably due to enthalpy or entropy effects, or to both.

A comparison of various oxygen-containing donors indicates that the stability of the bond practically always increases with increasing basicity of nitrogen, although the relation is not always linear.

2. The Effect of Functional-Analytical Groupings and Heteroatoms on the Complexing Power of Complexones

The question of the selectivity of the chelating agent for a given cation is of great interest. One way in which this selectivity can be achieved is by the introduction into the complexing molecule of characteristic functional groupings with a definite specificity; this often leads to the required analytical effect. The presence of these groupings in the complexone, without changing the main reaction mechanism, often promotes a clearer development of the analytical effect, and is favourably reflected in the character of the final product.

The introduction into the complexone molecule of hetero-atoms — sulphur, nitrogen, oxygen — capable of coordinating with a metal to form a new ring, has a similar action. The nature of the donor atom plays the main part in increasing the selectivity.

The effect of the introduction of various groupings on the complexing power of the complexone in the aliphatic series has been studied in detail on derivatives of iminodiacetic acid with the general formula $X-CH_2-N<$ [110,114,115,117,118]. Different substituents have different effects on the complexing power.

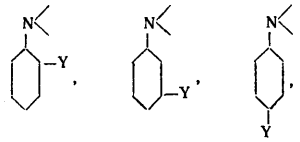
The nitrogen, oxygen, sulphur, and phosphorus atoms of aliphatically bound groups, $-OH$, $-OCH_3$, $-SH$, $-SCH_3$, $-PO_3H$, $-SO_3H$, $-NH_2$, form a coordinate bond with metals and this considerably increases the stability of the complexes. The maximal effect is observed when the substituent is in the α-position to the nitrogen of the iminodiacetate group. In the case of the β-position the stabilising effect is much weaker. The complexone acquires a definite selectivity depending on the grouping introduced and the nature of the donor atom. Many workers have noted a specificity for iron in complexones containing hydroxyethyl groups [120-126]; this has been utilised in a number of practical problems.

Complexones containing a mercapto-group sulphur atom and an amino-group show a great tendency to form complexes with heavy metals [114]. Sulphur in *NNS*-mercaptoethylaminotriacetic acid shows the same activity [127]. The presence in this compound of an additional complex-forming group makes it more selective than iminodiacetic acid. It has been shown that this complexone is selective with regard to the rare-earth elements; it forms complexes with only four cations out of 14. Moreover, complexes of different stability with the cations of copper and lead, cadmium and zinc, and cobalt, nickel, and zinc may be used for the separation of these metals.

The group of ethyl carbamate, the nitrile group, the positively charged amino-group, and the trimethylammonium group show practically no tendency to coordination; their effect on the stability of complexes is only connected with the change in the basicity of the coordinating nitrogen.

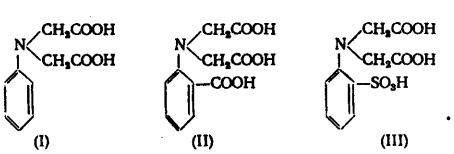
Uramildiacetic acid [perhydro-2,4,6-trioxopyrimidine--5-iminodiacetic acid (Ed. of Translation)], which forms stable complexes, is of considerable interest. The great basicity of the nitrogen atom, and evidently, the presence of a barbituric acid residue greatly increases the stability of complexes formed with uramildiacetic acid [128]. The stability of the complexes increases in the order Ba, Sr, Ca, Mg. The remaining derivatives of the alkyliminodiacetic acids shown in Table 1 are not now widely used and are mainly of theoretical interest.

Schwarzenbach studied the effect of the introduction of substituents into complexones of the aromatic series, using derivatives of anilinediacetic acid [109]:

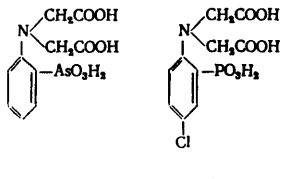


where Y = $-SO_3H$, $-COOH$. The introduction of carboxylic and sulpho-groups *ortho*, *para*, and *meta* to the iminodiacetate grouping has different effects, on the complexing power of the complexone.

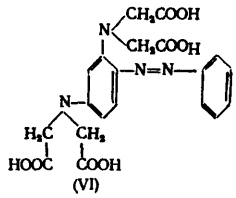
Substituents in the *meta*-, and *para*-positions have no material effect on the basicity of the iminodiacetate group nitrogen and the stability of the complexes formed. Substituents in the *ortho*-position greatly increase the complexing power; the effect of the substituent on the complexing power is in the same order as in the aliphatic series, that is, $-COOH > -SO_3H$. We have continued investigations in this direction, studying the effect of the introduction of arsonic, phosphonic, and azo-groups *ortho* to the iminodiacetate group of the benzene ring, on complexing power; as is well known, these groups comprise the analytical groupings of many valuable reagents. With this object 2-arsonophenyliminodiacetic acid (IV) [129], 4-chloro-2-phosphorophenyliminodiacetic acid (V), and chrysoidinetetraacetic acid [azobenzene-2,4-bis(iminodiacetic acid) (Ed. of Translation)] (VI) [130] have been synthesised and investigated. The complexing properties of these compounds were compared with the properties of phenyliminodiacetic (I), 2-carboxyphenyliminodiacetic (II), and 2-sulphophenyliminodiacetic (III) acids



(I) (II) (III)



(IV) (V)



(VI)

The stability of the complexes formed were recorded on the basis of the displacement of the half-wave potential $\Delta E_{1/2}$ = = $E_{1/2}$ (I, II, III, ...) - $E_{1/2}$ (without complexone) (Table 2).

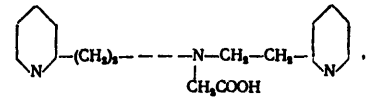
The results obtained showed that the introduction of these groupings increases the complexing properties of phenyliminodiacetic acid, makes the complexone more specific and thus more interesting from a practical point of view. Thus, 2-arsonophenyliminodiacetic acid forms stable complexes with lead and cobalt. This enables lead to be determined polarographically in the presence of copper and bismuth, and cobalt to be determined complexometrically. The presence of the phosphonic acid group enables cations to be determined when present together (Cu, Pb, Cd, As, Zn, Mo) in an acid medium.

The combination in the chrysoidinetetraacetic acid complexone molecule of azo- and iminodiacetate groupings increases the specificity of this compound compared with *m*-phenylenebis(iminodiacetic acid). The presence of a polarographically active azo-group in this complexone enables arsenic, manganese, and aluminium to be determined polarographically and amperometrically.

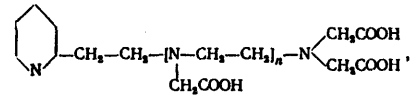
The effect of the groupings enumerated above in the *ortho*-position in phenyliminodiacetic acid is determined both by the electrostatic influence of the substituent and by its direct participation in the formation of the complex.

Following the success achieved in the field of analytical reagents, we made other attempts to increase the specificity of complexones by the introduction of special analytical grouping into the skeleton of polyaminecarboxylic acids.

The introduction of pyridine and quinoline nuclei with their marked tendency to bind transition metals (especially Co and Ni) and also some heavy metals (U, V, Pb, Zn, etc.) in stable complexes led to the creation of new complexones selective for heavy metals[9]. Thus, for Co and Ni the complexone

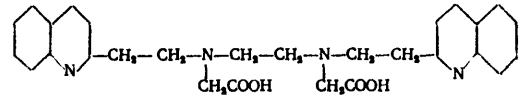


and for Pb, V, Zn, and U the complexone



where n = 1–3, have been proposed.

In a number of compounds the pyridine ring was replaced by the quinoline ring:



These examples, as well as some others, bridge the gap between special reagents for cations and complexones, and to a certain extent enable the theoretical prerequisites developed in the field of organic reagents to be applied to the effect of the structure of the complexones on their specificity.

The complexing power of a complexone is affected to at least an equal degree by the inclusion of the heteroatoms oxygen, sulphur, and nitrogen in the hydrocarbon chain of its molecule.

The part played by the heteroatom in complexones of the aliphatic series has been studied on compounds of the general formula [131]:

$$(HOOC{-}CH_2)_2{=}N{-}(CH_2)_n{-}X{-}(CH_2)_n{-}N{=}(CH_2COOH)_2,$$

where for $n=2$, X = —O—, —S—, —S′—S—, —N(CH$_3$)—;

for $n=3$–4, X = —O—.

$$(HOOC{-}CH_2)_2{=}N{-}(CH_2)_3{-}X{-}(CH_2)_3{-}X{-}(CH_2)_3{-}N{=}(CH_2COOH)_2,$$

where X = —O—, —S—, —N(CH$_3$)—.

TABLE 2. Half-wave potentials of cations in the absence and presence of (I), (II), (III), (IV), (V), and (VI), measured relative to the saturated calomel electrode.

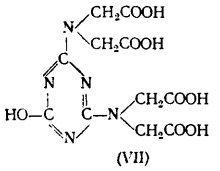
Cations	pH 2.5							pH 9.3						
	$E_{1/2}$ without complexone	$E_{1/2}$ with complexone						$E_{1/2}$ without complexone	$E_{1/2}$ with complexone					
		(I)	(II)	(III)	(IV)	(V)	(VI)		(I)	(II)	(III)	(IV)	(V)	(VI)
Pb^{2+}	—0.38	—0.42	—0.47	—0.44	—0.52	—0.42	—0.58	—0.18	—0.36	—0.49	—0.44	—1.0	—	0.9
Cu^{2+}	+0.02	—0.04	—0.28	—0.2	vanishes	—0.02	—0.02	—0.29 —0.54	—0.54	—0.4	—0.31	—0.68	—0.30	—0.29
Ca^{2+}	—0.60	—0.61	—0.65	—0.66	—0.70	—0.61	—0.74	—0.66	—0.68	—0.69	—0.69	—0.8	—0.92	—0.69
As^{III}	—0.80	—1.05	—1.13	—1.10	—0.27 vanishes	—0.90	vanishes	—	—	—	—	—1.05	—1.72	—1.71
Zn^{2+}	—1.01	—1.09	—1.08	—1.08	—1.24	—1.07	—1.12	—1.14	—1.28	—1.28	—1.20	—1.20	—	—1.02
Ni^{2+}	—0.96	—1.04	—1.08	—	—1.24	vanishes	—1.00	—0.91	—0.88	—1.06	—1.06	vanishes	—1.14	—0.98
Co^{2+}	—1.12	—1.32	—	—1.22	—1.22	vanishes	—1.15	—1.01	—	—1.24	—1.22	vanishes	—1.66	—1.10
Mn^{2+}	—	—1.01	—	—	—0.43	vanishes	vanishes	—1.58	—0.1	—1.66	—1.64	—	—	—1.54
Mo^{VI}	—0.44	—0.64	—0.44	—0.78	—0.41 vanishes	—0.52	—0.7	—	—	—	—	—	—	—
Ti^{IV}	—0.65 —0.97	—0.68 —1.01	—0.69 —1.01	—0.70 —1.10	—0.68 vanishes	—0.47 —	—0.48	—0.48	—	—	—	—	—0.50	—0.48

It has been shown that the introduction into the complexone molecule of the heteroatoms N, O, S, which tend to coordinate with metals, leads to an increase in the complexing power of these complexones. Participation in complex formation of the additional N, O, or S atoms confers some specificity on the complexone molecules in relation to certain metal cations [16,132]. Thus, for the alkaline earth cations the relative order of stability is O > N > S; for the transition elements with almost completely filled *d* orbitals the order of stability is N > S > O. With the rare-earth elements the complexing power increases in the order S < N < O.

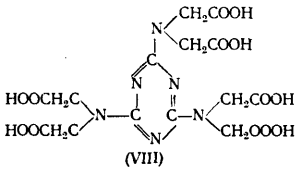
Van Uitert and Fernelius attempted to explain phenomena of this kind by considering the effective electronegativities of hybrid bonds of the ligand and the metal ion [133].

The studies of Izalt, Fernelius, and Block in this field agree with the ligand field theory [134]. Thus, cations especially sensitive to ligand field stabilisation form the most stable compounds with donor atoms that cause large ligand field splitting and conversely.

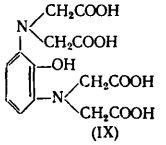
The effect of a heteroatom is also shown in cyclic compounds. This was studied on complexones of the triazine series [135,136] and on derivatives of benzthiazole and aminothiazole [137]. The properties of 2-hydroxy-1,3,5-triazin--4,6-diylbis(iminodiacetic acid) (VII), and 1,3,5-triazin--2,4,6-triyltris(iminodiacetic acid) (VIII), containing the 1,3,5-triazine ring are compared in Table 3 with the properties of *m*-phenylenebis(iminodiacetic acid) (IX). The instability constants of the complexes of (VII) and (VIII) are in all cases greater than the constant for compound (IX); moreover (VIII) has a tendency to form more stable complexes than (VII).



(VII)

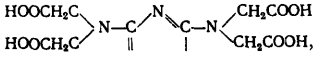


(VIII)



(IX)

A characteristic of (VII) and (VIII) is the presence of the same grouping



which is capable of forming complexes with metal cations.

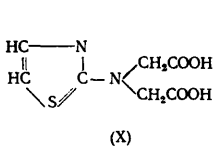
TABLE 3. Logarithms of stability constants of cations with complexones at pH 2.5.

Cations	(VII)	(VIII)	(IX)
Pb^{2+}	4.75	5.08	3.73
Cu^{2+}	3.78	4.07	3.36
As^{3+}	5.08	6.10	5.01
Zn^{2+}	6.70	7.10	3.40
La^{III}	5.08	5.56	3.05
Ti^{IV}	3.89	4.22	—

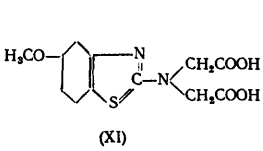
It is natural to suppose that the nitrogen of the triazine ring participates in complex formation. It is this that leads to an increase in the complexing power of (VII) and (VIII) compared with (IX).

The increase in the complexing power of (VIII) compared with (VII) may be ascribed to symmetry in the molecule (three iminodiacetic acid groups), leading to easier formation of complexes, sometimes with a large number of rings.

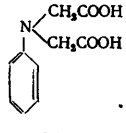
The complexing properties of 1,3-thiazol-2-yliminodiacetic acid (X) and 5-methoxybenzothiazol-2-yliminodiacetic acid (XI), containing two heteroatoms, nitrogen and sulphur, were studied [137] by the polarographic method of displacement of half-wave potentials; these compounds showed a reduction in analytical activity against a series of cations in comparison with a complexone containing an aromatic ring (phenyliminodiacetic acid) (XII):



(X)



(XI)



(XII)

Table 4 shows that (XII) forms weak complexes with nearly all the cations mentioned, while (X) and (XI) behave differently.

In the acid range, pH 2.5–4.4, these complexones form complexes only with Cu, Mo, As, Pb, and Co; in the alkaline range they form complexes with Co, Sb, Pb, Zn, and As, which indicates that they have some specificity. The reduction in analytical activity is probably due to the spatial proximity of the heterocyclic sulphur and nitrogen atoms, which considerably reduces the basic properties of the iminodiacetate nitrogen. The introduction of functional groups and heteroatoms into the complexone molecule is one way of obtaining complexones with a selective action.

3. The Effect of Replacing Carboxymethyl Groups on the Nitrogen Atom by Other Groupings

Apart from complexones with a changed composition of radicals on the iminodiacetate group, a number of compounds have been described in which acetic acid residues on the nitrogen atom are replaced by other groups [138-140].

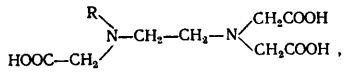
TABLE 4. Half-wave potentials of cations in the presence of (X) and (XI) in comparison with (XII).

Cations	pH 2.7				pH 9.4			
	$E_{1/2}$ without complexone	$E_{1/2}$ with (X)	$E_{1/2}$ with (XI)	$E_{1/2}$ with (XII)	$E_{1/2}$ without complexone	$E_{1/2}$ with (X)	$E_{1/2}$ with (XI)	$E_{1/2}$ with (XII)
Pb^{2+}	−0.38	−0.42	−0.42	−0.42	—	−0.72	—	−0.36
Cu^{2+}	+0.02	−0.02	−0.1	−0.04	−0.29 −0.54	—	−0.3 −0.6	−0.54
Bi^{3+}	−0.00	−0.01	−0.09	−0.10	—	—	—	−0.43
Cd^{2+}	−0.60	−0.60	−0.60	−0.61	−0.66	−0.68	−0.66	−0.68
Tl^{+}	−0.46	−0.46	−0.46	−0.43	−0.48	−0.48	−0.48	−0.50
As^{3+}	−0.80	−1.12	−0.88	−1.05	−1.71	−1.70	−1.31	not repr.
Sb^{3+}	−0.19	−0.88	−0.19	−0.2	—	−1.02	−0.82	−0.67
Zn^{2+}	−1.06	−1.06	−1.04	−1.09	−1.14	−1.20	−1.26	−1.28
Ni^{2+}	−0.96	−1.16	−1.04	−1.04	−0.91	−0.94	−1.10	−0.88
Co^{2+}	−1.12	—	−1.20	−1.32	−1.10	−1.18	−1.20	—
Mn^{2+}	—	—	—	−0.01	−1.58	−1.54	−1.58	−0.10
Mo^{VI}	−0.44	−0.54	−0.54	−0.64	—	—	—	−0.38

Complexones in which the carboxyl groups are completely or partially replaced by residues of sulphonic, arsonic, or phosphonic acids or by hydroxyalkyl groups are of definite interest. Experimental results in papers by Schwarzenbach [110], Kabachnik [17,141,142], and others on complexones with phosphonic groupings and comparison of their properties with those of the corresponding aminocarboxylic and aminosulphonic acids indicate that the greatest effect is obtained when two types of complexing groups are present on the nitrogen of the complexone. As our investigations showed, with some cations *NN'*-bisphosphonomethylethylenebis(aminoacetic acid) forms more stable complexes than the corresponding analogues containing only carboxymethyl or phosphonomethyl groups [141].

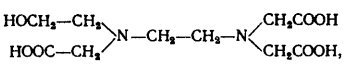
A certain selectivity in compounds of this type should be noted. It was shown by Kabachnik and his coworkers [141,142] that, apart from diethylenetriaminepentaacetic acid, the most powerful complexing agents for rare-earth ions are methylphosphonic acid and *NN'*-bisphosphonomethylethylenebis(aminoacetic acid); these complexing agents are recommended for removing the rare-earth elements from the body. Manecke and Gergs have pointed out the selectivity of ethylenediamine-*NN'*-bisethylarsonic acid for copper [143].

Bruno and coworkers [138] have studied *N*-substituted *NN'N'*-ethylenediaminetriacetic acids of the type:

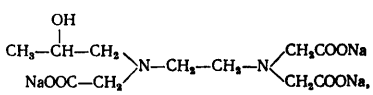


where R = n-butyl, n-octyl, n-dodecyl, cyclohexyl, or benzyl. Replacement of the carboxymethyl group by these radicals leads to the changes in the properties of EDTA shown in Table 5.

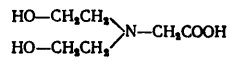
With copper the *N*-benzyl derivative gives a less stable complex than EDTA and a more stable one than the *N*-butyl and *N*-octyl derivatives. *N*-Cyclohexylethylenediaminetriacetic acid forms the weakest complex with copper, and *NN'*-dicyclohexylethylenebis(aminoacetic acid) does not form such complexes at all. With calcium these acids behave as weak complexing agents. However, the *N*-benzyl derivative forms the most stable complexes. Replacement of the $-CH_2COOH$ group in the complexone molecule by hydroxyalkyl groups gave compounds capable of complexing iron in a moderately alkaline medium [9,144]. *N*-(2-Hydroxyethyl)ethylenediaminetriacetic acid:



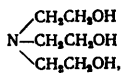
the trisodium salt of *N*-(2-hydroxypropyl)ethylenediaminetriacetic acid:



and *NN*-di-(2-hydroxyethyl)aminoacetic acid:



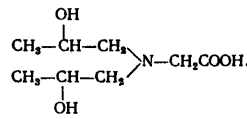
are examples of compounds of this type. The last compound has a characteristic tendency to form a complex with the Fe^{3+} ion, in the same way as the structurally similar triethanolamine:



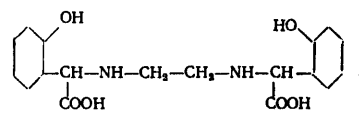
which, as is well known, is a very powerful complexing agent for the Fe^{3+} ion.

It should be noted that the alkaline earth ions do not form complexes with dihydroxyethylglycine; this compound cannot therefore be used alone for removing the hardness from water and it is generally employed as a mixture with EDTA.

It has been shown that, in contrast to *NN*-di-(2-hydroxyethyl)aminoacetic acid, *NN*-di-(2-hydroxypropyl)aminoacetic acid does not form stable complexes with iron:



This is probably due to steric factors when the hydroxyethyl groups in the complexone molecule are replaced by hydroxypropyl groups. Ethylenebis[amino-(*o*-hydroxyphenyl)acetic acid] is the most specific complexone for tervalent iron; this compound contains the hydroxyphenyl grouping which is characteristic for complex formation with Fe^{3+}:



The instability constant of this complex with iron is 10^{-35}, that is, one of the smallest ever measured for complexes in aqueous solution.

Data on the stability of complexes with some metal ions are given in Table 6.

Thus, the introduction into the complexone molecule skeleton of groupings containing hydroxyalkyl or hydroxyaryl groups led, as would be expected, to the formation of complexones specific for the Fe^{3+} ion [139-145].

TABLE 5. Complexing power of *N*-substituted ethylenediaminetetraacetic acids.

R	Dissociation constants of acids			pK	
	pK_1	pK_2	pK_3	Cu^{2+}	Co^{2+}
Butyl	1.8	6.64	10.04	12.7	1.6
Cyclohexyl	1.6	6.47	10.15	11.5	1.7
Octyl	1.9	6.53	9.76	12.5	—
Benzyl	1.9	5.10	9.84	16.8	6.7
Dodecyl	2.0	6.56	9.77	—	—

TABLE 6. Stability constants of ethylenebis-[amino-(*o*-hydroxyphenyl)acetic acid] with some metals.

Metal ion	pK_{MH_2Z}	pK_{MHZ}	pK_{MZ}
Cu^{2+}	15	20	24
Ni^{2+}	11.4	15.6	19.7
Zn^{2+}	9.3	12.9	16.9
Cd^{2+}	7.8	10.1	13.1
Mg^{2+}	2.9	5.2	8.0
Ca^{2+}	1.7	4.8	7.2
Fe^{3+}	—	—	35

4. The Effect of Increasing Denticity When Additional Iminoacetic Acid Groups Are Introduced into the Complexone Molecule

The effect of increasing the denticity without changing the fundamental structure of the complexone has been studied on analogously constructed polyethylenepolyaminepolycarboxylic acids [146-149]: diethylenetriaminepentaacetic acid (DTPA), triethylenetetraaminehexaacetic acid (TTHA), and tetraethylenepentaaminehexaacetic acid (TPHA).

A study of their complexing properties, determination of dissociation and stability constants of their complexes with a number of metals (Table 7) and also comparison of the results obtained with corresponding values for NTA and EDTA have shown that the stability of the complexes for practically all cations increases from nitrilotriacetates to diethylenetriaminepentaacetates (DTPA) and then falls with triethylenetetraaminehexaacetates (TTHA) and tetraethylenepentaaminehexaacetates (TPHA) (Figs. 2, 3, 4).

However, it should be noted that a change in the denticity has a different effect on the instability constants of complexes of different metals.

Potentially, the octo-, deca-, and dodeca-dentate character of these polyethylenepolyaminepolyacetic acids, differing by steric accessibility of the coordinating groups, can ensure full saturation of the coordination capacity of such elements as thorium, aluminium, molybdenum, and the rare-earth elements with a coordination number of 8. The number of rings linked with one metal cation then increases

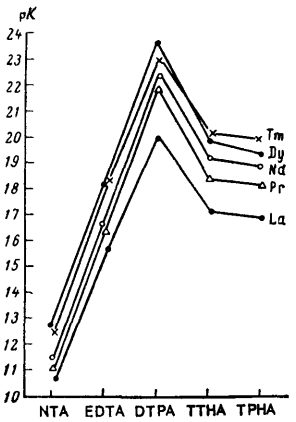


Fig. 2. Dependence of the stability of complexes of the rare-earth elements (pK) on the denticity of the complexone.

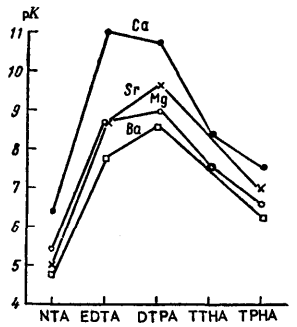


Fig. 3. Dependence of the stability of Ca, Mg, Ba, and Sr complexes on the denticity of the complexone.

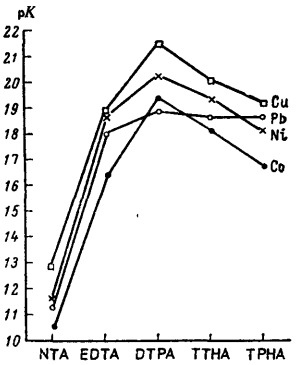


Fig. 4. Dependence of the stability of Ni, Co, Cu, and Pb complexes on the denticity of the complexone.

to 7, and in addition the stability of the complexes formed increases in comparison with that of the ethylenediaminetetraacetates. The comparatively small reduction in the stability of the complexes in the series DTPA, TTHA, and TPHA is probably connected with the change in basicity of the coordinating nitrogen atoms of the iminodiacetate groupings and the possibility of the formation of associated complexes.

For Mg, Ca, Sr, Ba with TTHA and TPHA the formation of complexes of the type M_2Y is characteristic; this accounts for the observed fall in stability and the position of the constants between the corresponding values of

TABLE 7. Logarithms of stability constants of complexes of some metals with polyethylenepolyaminepolyacetic acids [146-149].

Complexone	pK dissociation						pK_{MY}						
	pK_1	pK_2	pK_3	pK_4	pK_5	pK_6	Ca	Mg	Zn	Cu	Mn	Fe^{2+}	Fe^{3+}
Diethylenetriaminepentaacetic acid	1.79	2.56	4.42	8.76	10.42	—	10.71	9.03	18.55	21.53	15.60	15.97	27.50
Triethylenetetraminehexaacetic acid	—	2.64	4.08	6.26	9.67	10.82	8.40	7.62	17.4*	20.1	14.62	15.32	26.20
Tetraethylenepentaminehexaacetic acid	—	2.73	3.82	5.56	8.88	9.95	7.51	6.61	17.80	19.20	14.0	13.6	26.4

nitrilotriacetates and ethylenediaminetetraacetates. For such elements as Co, Ni, Cu, Zn, and Pb, the formation of associated complexes of the 3 : 2 type is also characteristic: this probably gives rise to five rings on each complexing cation. The equality in the stability of these complexes with the corresponding ethylenediaminetetraacetates therefore becomes clear. This kind of increase in denticity of complexing agents without change in structure and without disturbance of the optimal symmetry of chelating groups is thus effective for voluminous cations with high coordination capacity. This may be explained by the possibility of forming additional rings; the optimum variant in the structure of a multidentate complexone is still DTPA. Further increase in the denticity by introducing additional acetate groups into the complexone molecule, does not, as a rule, lead to significant stabilisation of the complexes, but rather to increased selectivity. However, because of the very rapid formation and the high stability of complexes of multivalent cations, these complexones could be successfully used in analytical chemistry to mask interfering impurities and for the determination of a number of cations by physicochemical methods.

5. The Effect of Steric Factors on the Stability of the Complexes Formed

Analysis of the structure of chelate rings is of great importance in evaluating the effect of the structure of organic chelating agents on their complexing properties and on increased selectivity in the determination of elements. Alkaline earth and rare-earth elements with constant valency and varying atomic volume are ideal systems for this kind of investigation. The effect on complex formation of such stereochemical factors as ligand isomerism, conformation, distance between the main complexing groups, and the arrangement of the chelate rings may be examined in complexones containing two iminodiacetate groups, such as ethylenediaminetetraacetic acid, cyclohex-1,2-ylenebis(iminodiacetic acid), and cyclopent-1,2-ylenebis(iminodiacetic acid).

The most typical representatives of this group of compounds are EDTA and cyclohex-1,2-ylenebis(iminodiacetic acid) (CHDTA). These compounds with a definite stereochemical configuration differ from one another in the distances between the atoms of nitrogen and their arrangement in relation to the framework of the molecule [150-153]. A study of the chelates of these compounds in the solid state by infrared spectroscopy and thermal analysis permitted elucidation of the nature of the bonds and a precise establishment of coordination numbers for different metals. The ionic bond with carboxyl groups is characteristic of alkaline earth, doubly-charged and some triply-charged cations; the covalent bond is characteristic of transition metals of higher valency and lead.

In most cases these compounds behave as sexi- or quinque-dentate chelating agents, and only in the case of palladium and platinum as bi- and quadri-dentate agents. The presence of two residues of iminodiacetic acid and the close arrangement of the nitrogen atoms ensure a high complexing power in these compounds [11-14,95,143-145].

It follows from Table 8 that *trans*-cyclohex-1,2-ylene- and *trans*-cyclopent-1,2-ylene-bis(iminodiacetic acids) are stronger complexing agents for alkaline earth metals than the corresponding *cis*-analogues and EDTA. However, it should be noted that the stability of the complexes does not increase proportionally with the decrease in the distance between the nitrogen atoms in the ligand molecule. The change in the stability constants of the complexes takes place in the following order: *trans*-CHDTA > *trans*-CPDTA > > *cis*-CHDTA, while the distance between the complexing $-N(CH_2COOH)_2$ groupings decreases in a different order: *cis*-CHDTA ≤ *trans*-CHDTA ≤ *trans*-CPDTA. The reduced stability of alkaline earth metal chelates with *cis*-CHDTA is due to steric hindrance in the chelating reaction:

TABLE 8. Logarithms of the stability constants (pK) of complexes of the alkaline earth elements with ethylenediaminetetraacetic acid and cyclohex-1,2-ylene- and cyclopent-1,2-ylene-bis(iminodiacetic acid) [150-153].

Complexone	Distance between complexing groups, Å	pK_1	pK_2	pK_3	pK_4	pK_{MY}			
						Mg	Ca	Sr	Ba
Ethylenediaminetetraacetic acid	—	2.67	2.79	6.16	10.26	8.69	10.59	8.63	7.76
cis-Cyclohex-1,2-ylenebis(iminodiacetic acid)	2.0	2.44	3.50	5.21	10.70	8.32	9.45	7.33	8.00
trans-Cyclohex-1,2-ylenebis(iminodiacetic acid)	2.2	2.43	3.52	6.12	11.76	10.32	12.50	10.69	—
trans-Cyclopent-1,2-ylenebis(iminodiacetic acid)	2.6	2.40	3.30	7.56	10.80	9.05	11.08	9.49	7.7

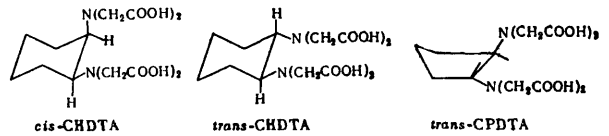


Fig. 5. Models of cyclohex-1,2-ylenebis(iminodiacetic acid) and cyclopent-1,2-ylenebis(iminodiacetic acid).

As the models show (Fig. 5) the *trans*-forms of CHDTA and CPDTA have the maximal number of equatorial substituents. With such an arrangement of ligand groups, the metal–chelate rings are in the same plane as the alicyclic radicals, which leads to a favourable geometrical structure for the molecule. In *cis*-CHDTA the axial hydrogen atoms of the cyclohexane ring prevent free rotation of the carboxymethyl groups, and the plane of the chelate ring is at an acute angle to the plane of the hydrocarbon ring. The steric hindrance produced by this kind of structure of chelating agent in *cis*-compounds and the lack of coplanarity due to it lead to great strain in the complexes formed and to a reduction in their stability.

It is interesting to note that complexes formed by *trans*-CPDTA are more stable than the corresponding compounds with EDTA in spite of the fact that the distance between the iminodiacetate groups in the active form of EDTA is less than the corresponding distance in *trans*-CPDTA. The reduced stability of complexes of EDTA compared with those of CPDTA is connected with the necessity of expending additional energy for converting form (I) into form (II) (Fig. 6), which is capable of forming chelates with metal ions. Moreover, the five condensed chelate rings when EDTA is used as a sexidentate agent form a greatly warped octahedron around the central metal atom with great deformation in the $-N(CH_2)_2N-$ chelate ring plane, in which there are two –N–CO–O– rings at angles deviating greatly

from the normal values [154]. All this produces additional strain in the cyclic structure and also leads to a reduction in the expected stability of the complexes with EDTA. In *trans*-CPDTA the nitrogen atoms are spatially fixed by the cyclopentane ring, which excludes the necessity of expending energy in rotation, and the structure is less strained:

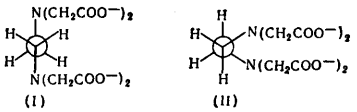


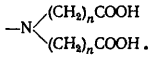
Fig. 6. Models of the two forms of EDTA.

Thus, in these compounds the predominating factor affecting the stability of compounds formed is the mutual arrangement of the ligand groups in the contour of the chelating agent, capable of forming complex structures with more or less strain. However, it should be noted that there are a number of compounds where the decisive part is played by the distance between the complexing groups.

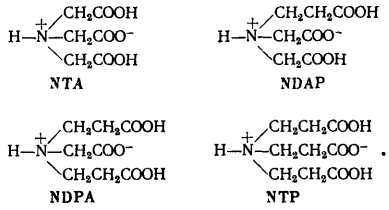
When the distance between the nitrogen atoms is significantly increased, their mutual interaction is weakened and a decrease is observed in the complexing power of the complexone; this is clearly shown by the homologues of EDTA: tri-, tetra-, penta-, etc. polymethylenediaminetetraacetic acids [155-160] (Table 9).

Data on stability constants show that when $n = 2$, with EDTA, the stabilisation produced by the formation of a ring is at a maximum. When the length of the chain of methylene groups (the quantity n) increases, the stability due to ring formation disappears and is even replaced by a weak destabilisation effect. This may be explained in the following way: rings with more than seven members are not formed, and when complexones containing four, five, and more hydrocarbon atoms interact with metal ions, the di(carboxymethyl)amino-groups act independently, forming complexes of the composition M_2Y. Analogous results were obtained by Schwarzenbach and Ackermann [111] in studying the isomeric cyclohexylenebis(iminodiacetates). The 1,3- and 1,4-derivatives form significantly less stable complexes than 1,2-CHDTA and show a tendency to coordinate with two metal cations and not to form a closed ring. All these results again emphasise the special stability of five-membered rings. However, it should be noted that an increase in the length of the polymethylene bridge in homologues of EDTA ($n = 6$ or 8) promotes the development of specificity in the complex; this specificity is expressed, for example, in increased stability of the complexes with silver and mercury. This is explained by a linear arrangement of valencies in these cations. As the ring increases in size its strain decreases, probably because of bending of the *sp* orbitals of the metal ion.

The distance between the carboxyl group and the nitrogen atom also has a considerable effect on the complexing power of the complexone:



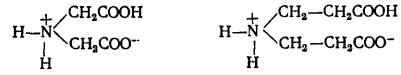
A study of this phenomenon [122] was carried out on a number of derivatives and homologues of iminodiacetic acid and ethylenediaminetetraacetic acid. The following series was investigated: nitrilotriacetic acid (NTA), nitrilodiaceticpropionic acid (NDAP), nitriloaceticdipropionic acid (NDPA), and nitrilotripropionic acid (NTP) (Table 10):



The value of the dissociation constant pK_3, and therefore the basicity of the nitrogen, decreases in the order NTA > NDAP = NDPA > NTP.

The stability of the complexes of most metals decreases in the same order as the basicity of the nitrogen atom: NTA > NDAP > NDPA > NTP; the replacement of one or two acetate groups by propionate groups only slightly reduces the stability. A possible explanation is that the propionate group in NDAP and NDPA forms six-membered rings with Cu, Ni, Co, and Zn which are more suitably arranged in space than the five-membered ring in the case of NTA and set up less strain over the whole molecule of complex.

Iminodiacetic acid and iminodipropionic acid:



are similar in structure to the four acids considered [116]. The value of the stability constant of iminodipropionic acid complexes is two orders less than the value of the constant for iminodiacetic acid complexes.

TABLE 9. Logarithms of the stability constants of complexes of the alkaline earth metals with polymethylenediaminetetraacetic acids [109,131,155-160].

Complexone	pK of dissociation				pK_{MY}				
	pK_1	pK_2	pK_3	pK_4	Mg	Ca	Sr	Ba	Na
Ethylenediaminetetraacetic acid	10.26	6.16	2.67	—	8.69	10.59	8.63	7.76	1.66
Trimethylenediaminetetraacetic acid	10.27	7.90	2.67	2.00	6.66	7.12	5.18	4.24	—
Tetramethylenediaminetetraacetic acid	10.45	9.07	2.66	1.90	3.44	5.05	2.80	2.40	—
Pentamethylenediaminetetraacetic acid	10.48	9.50	2.7	2.2	3.63	4.62	2.72	2.38	—

TABLE 10. Logarithms of the stability constants of metals with NTA, NDAP, NDPA, and NTP. [108-113,122]

Complexone	pK of dissociation			pK_{MY}				
	pK_1	pK_2	pK_3	Co	Ni	Cu	Zn	Cd
Nitrilotriacetic acid	1.89	2.49	9.73	10.38	11.53	12.96	11.67	9.83
Nitrilodiaceticpropionic acid	2.10	3.69	9.66	7.9	9.0	11.6	7.9	5.6
Nitriloaceticdipropionic acid	3.25	3.98	9.67	7.9	9.1	11.9	8.0	5.6
Nitrilotripropionic acid	3.67	4.24	9.30	4.8	5.8	9.1	5.3	3.4

A number of derivatives of ethylenediaminediacetic acid (EDDA) in which the acetate groups were replaced by propionate groups were investigated with the object of studying the effect of the distance of nitrogen from the carboxyl group on the complexing power of the complexone.

Comparison of the complexing power of ethylenediaminepolycarboxylic acids with various doubly-charged cations showed that the replacement of one acetate group of EDTA by a propionate group lowers the pK_{Me} by approximately 3–4 units. This effect is much greater with tetrapropionic acids. Symmetrical replacement of two propionate groups in these compounds by acetate groups increases the pK_{Me} in general by 6–7 units. It is clear from the examples given that acetate groups form more stable chelate structures than propionate groups and therefore in this case increasing the distance of the carboxyl group from the nitrogen atom leads to a decrease in the stability of the complexone complexes with most cations. However, it should be noted that there is some selectivity with regard to copper, which may be explained by the planar structure of the complex formed.

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It follows from the foregoing that the synthesis of complexing agents with the maximum possible affinity for metal ions and the development of selective reagents differing as much as possible from one another and having specific complex properties are important problems in coordination chemistry.

After the synthesis and application of such complexes as ethylenediaminetetraacetic acid and cyclohex-1,2-ylenebis(iminodiacetic acid), the first problem could be considered to be practically solved, but the second is still far from solution.

Ethylenediaminetetraacetic acid appears to be an ideal structural example of a multidentate reagent in its effectiveness in coordinating metal ions. Attempts to make some kind of change in the structure of EDTA which would be expected to increase its complexing power appreciably have, in the main, not given good results; in some cases they showed an effect with only certain groups of elements. Replacement of some acetic acid residues by propionic acid, or of the ethylene bridge joining the two nitrogen atoms by trimethylene, that is, increasing some of the five-membered chelate rings in the EDTA complexes to six-membered rings, reduces the stability of the complexes, although it would seem that this modification of the EDTA molecule should lead to a considerable reduction in the strain which is observed in condensed chelate rings of a complex, particularly in the $-N-(CH_2)_2-N$ plane, and also to stabilisation of the complexes. The behaviour of the oxygen atom of the phosphonic acid group as a ligand atom in ethylenediamine- and 1,2-diaminecyclohexane-tetraacetic acid was also studied. It was found that complexes of completely phosphorylated analogues are more selective, but in many instances less stable than the corresponding carboxyl compounds. This appears to be connected with insufficient use of the complexing atoms of the ligand carrying two negative charges, because of the great expenditure of energy when charged particles approach at the time of coordination. Complexes of beryllium, germanium, and copper, which are highly stable, are exceptions.

Closing of the alicyclic ring in CHDTA, which reduced the free rotation of the amino-group in the ligand and formed an additional ring in the structure, led to an increase in the stability of practically all chelates by 2–3 pK units. Combination in the complexone of two types of grouping on the nitrogen — *NN'*-bisphosphonomethylethylenebis(aminoacetic acid) — increased the stability only of the complexes with certain cations.

In going from EDTA to DTPA, with its greater denticity, there is an increase in affinity for highly charged (3+, 4+) metal ions, while the stability of the complexes with Ca and Mg remains practically unchanged. Further increase in the denticity by introduction of additional iminoacetate groups (TTHA and TPHA) into the molecule leads to stabilisation of complexes formed with cations with the maximal coordination number (rare-earth elements, Th). The special structure of the complex molecule achieved by the introduction of heteroatoms and functional groups, by changing the distance between the iminodiacetate groups, and also between nitrogen and the carboxyl groups, by replacement of the carboxymethyl group by hydroxyethyl and phosphonomethyl groups, or by increasing the electron density of the whole system and destroying the electron density of individual links, as has been shown above, leads to the development of selective complexing agents, but not always to an increase in stability of the complexes formed.

The examples given above thus confirm that in most cases modification of the EDTA molecule leads to some specific activity and only sometimes to a slight increase in the stability of the complexes formed. In this connection, it is desirable that further work on the synthesis and application of complexones should deal with selectivisation linked to both a deeper study of compounds already described in the literature and to the development of complexones and complexing indicators with a specific action.

High selectivity in chelate formation, especially in the case of multidentate reagents is achieved rarely in practice and then only with comparative difficulty. However, the great amount of material in the literature on this subject enables syntheses of complexones with definite properties to be postulated.

According to Schwarzenbach, suitable selectivity of the complex can only be achieved by a special structure of the multidentate ion, account being taken of the maximal geometrical relationship of the internal ligand contour and of the cation. However, such a relationship, besides increasing the stability of chelates with a group of related ions, will hardly increase the selectivity because of the tendency of the ligand to take up a number of conformations and to become deformed to adapt itself to the requirements of other ions. Moreover, the geometric conditions of complex formation for one metal and a given chelate ligand may be close to the conditions for a number of other cations and the same ligand; as a result, the stability of complexes with elements of closely related physical and chemical properties is simply increased. Another way of achieving selectivity is much more promising; this consists in the development of multidentate reagents with the minimum permissible geometric correspondence for a given cation and complete lack of correspondence to the requirements of all other cations [161-163]. This type of variant may be brought about by increasing the rigidity of the system, by limiting free rotation of individual links by steric hindrance, and, finally, by the creation of unusual geometric arrangements of donor atoms with disturbed electron density, achieved by including a weak electron-donor group in the multidentate chelate system. This leads to spatial distortion of the ligand field and to selective action in the reagent. In the creation of model compounds of this type, account must be taken of the

geometric structure of the reagent and chelate molecules, the magnitude of the valency angles and interatomic distances, the change in these parameters under the influence of substituents and other factors, the limits of these changes, the primary coordination of the metal atom, possible distortion of this coordination, the nature of the chemical bond, steric factors, and intramolecular and intermolecular interactions. Besides, in the synthesis of complexones with selectively acting groups, it is desirable to take account of the mobility of the second ligand with regard to the size of the metal ion, so that the distance between the combining atoms corresponds to this volume; this kind of calculation of steric stabilisation increases the selective effect and the stability of the complex. From this point of view complexones would be of great interest if they were capable of reacting with elements of small atomic radius (Be, B, Ti, Ge, Nb, Ta, V, Cr) and high charge, with the rare-earth elements, and also with As, Sb, Sn, Mo, and with anions. Since Be, B, Ti, Ge, and other ions virtually do not coordinate with nitrogen, and the carboxyl groups of the complexones are apparently too voluminous for small cations, complexes of the polyphosphonic or polyarsonic acid type with partial replacement of the acetate groups by amino- and sulpho-groups, and also polyphenols of the pyrocatechol type, or derivatives of 1,8-dihydroxynaphthalene, would be interesting.

For elements that form thio-salts, that is, Sb, As, Sn, Mo, W, and for some platinum metals definite success would be expected from complexones containing mercapto--group sulphur as ligands, which coordinate selectively with these elements. In our opinion, further investigations into the synthesis and detailed study of complexones containing the heteroatoms O, N, S, Se, P, and As appear promising. Investigation of the complexing power of these compounds over a wide pH range, and also in organic solvents, will permit elucidation of the function of these elements in complexones. Moreover, the different nature of the coordinating ligands will increase the stability of these compounds. The preparation of complexones containing arsino- or phosphino-diacetic acids is of undoubted practical and theoretical interest. Since As and P have stronger donor properties than nitrogen, because of the formation of double bonds with metals containing *d* electrons that do not participate in hybrid bond formation, the new complexones will probably form stable complexes with metals of Groups VIII and IB of the Periodic System.

In conclusion, we shall note that the development of complexes capable of binding anions is of great importance. According to Schwarzenbach[4], for this purpose, instead of the nucleophilic atoms, N, O, and S, it would be necessary to introduce electrophilic groups into the molecule; these groups should be capable of coordinating with negatively charged ions. The mercury atom is an electrophilic atom which might be fixed on the framework of the molecule. These compounds would bind halide and other ions.

Studies in the field of the kinetics and mechanism of interaction of complex molecules consisting of different complexing agents and cations would be of undoubted theoretical and practical interest. These complicated systems could potentially form bimetallic and mixed complexes with fundamentally new properties. Moreover, the elucidation of the relative effects of different factors on the kinetics and mechanism of interaction will permit the deliberate direction of reactions and create the necessary conditions for the determination and separation of different cations.

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THE "COAL–METHANE" NATURAL EQUILIBRIUM SYSTEM AND METHODS FOR STUDYING IT

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1. METHANE–COAL DEPOSITS

Deposits of ordinary coal and lignite constitute a gas-producing region of the Earth's crust which is unique and of great practical importance.

The principal components of the gases of coal seams are carbon dioxide, nitrogen, and methane. The appearance of carbon dioxide in coal seams is linked with the oxidation of the coal by oxygen, the metamorphism of the rocks, the migration of the products of the activity of living creatures in the soil layer, and the migration of atmospheric carbon dioxide. The nitrogen has only an atmospheric origin, and the methane is a product of the metamorphism of coal.

The gas phase is not in a quiescent state in the depths of the coalfields: the gases from the metamorphism of coal and rocks move upwards the terrestrial surface, and the gases of atmospheric origin and from biochemical processes move in the opposite direction. The existence of