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Organophosphorus Complexones†

M.I.Kabachnik, T.Ya.Medved', N.M.Dyatlova, and M.V.Rudomino

Organophosphorus complexones are a new group of highly effective complex-forming compounds capable of binding metal ions in aqueous media. The principal trends in the development of studies on the synthesis and properties of organophosphorus complexones are discussed and methods for the modification of their structures and their most interesting applications are indicated.
The bibliography includes 130 references.

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I. INTRODUCTION

Progress in many branches of science and engineering is to a large extent associated with the development of the chemistry of coordination compounds with polydentate ligands, among which complexones occupy one of the leading places. The chemistry of complexones opens up virtually unlimited possibilities for the modification of the properties of cations, which creates vast prospects for their extensive application. However, the inadequate assortment of these compounds has limited the range of their applications. Until recently, these ligands were used mainly only in analytical chemistry as titrating and masking agents. Virtually the only available and widely used complexone was ethylenediaminetetra-acetic acid, the possible applications of which are extremely limited[1,2].

The development of modern engineering and of the national economy places new tasks before science. A number of important problems of this kind, such as the cleaning of thermal power engineering equipment, the separation of elements with similar properties, the treatment of plant chlorosis, the elimination of incorporated metals from the organism, the metallation of dielectric materials, and the stabilisation and catalysis of complex systems can be solved successfully by employing complexones. However, the complexone-type ligands used in the solution of these problems must possess in each individual case a set of properties ensuring their optimal applicability. For this reason, it was necessary to create a large assortment of complexones with a wide range of complex-forming properties and in the first place complex-forming agents capable of giving rise to complexes with maximum stability over a wide pH range, from strongly acid to strongly alkaline media, and also selectively acting compounds with a specific set of properties. The first of these problems is solved by combining in the structure of the complexone the highly basic nitrogen atoms with polydentate salt-forming groups. The solution of the second problem involves much greater difficulties, since it is necessary to chelate selectively metal ions with similar physical and chemical properties, dimensions, steric configurations, and, what is most important, similar tendencies towards complex formation. The difficulties are aggravated also by the fact that, by virtue of their polydentate nature and in most cases the flexibility of their steric configuration which permits a multiplicity of conformations with deformation of the bond angles and lengths within certain limits, complexones become very readily adapted to the geometrical requirements of the cations.

A higher selectivity in chelate formation, particularly for polydentate compounds, can be achieved only by synthesising a special reagent taking into account the complete set of properties of the internal ligand contour and the cation and also the postulated structure of the chelate to be formed. The change in the electronic states at the sites responsible for coordination and the rigidity of the system is also important.

The ligand molecule with the specified properties should be synthesised on the basis of the known correlation between the structure of the ligand and its properties, the theory of the action of complexones (by varying the number of their binding sites), the nature of the electron-donating atoms and their immediate environment, the stereochemistry of the molecule as a whole, the number of rings formed and their dimensions, the rigidity of the system, and the distribution of electron density among the sites responsible for coordination.

One of the fundamentally new and promising ways of the specific synthesis of a complexone molecule involves the incorporation in the latter of aminoalkylphosphonic acid groups[2-4]. The specificity of the chelating agent containing a phosphonic acid group is determined primarily by its stereochemistry, which differs from that of the carboxy-group. The phosphonate ion is almost tetrahedral (distorted tetrahedron) with a threefold symmetry axis. The carboxylate ion is planar with a planar symmetry. The valence angles and bond lengths are also different.

π-Bonding between the oxygen and phosphorus atoms is much weaker than between oxygen and carbon atoms in the carboxy-group. The polarisability of the P–O bonds in

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the phosphoryl group is greater than that of the C–O bond in the carboxy-group. For this reason, on the one hand the inductive effect plays a major role in phosphonic acid compounds and on the other the phosphonic acid group is highly nucleophilic. In the presence of the two hydroxy-groups of the phosphonic acid which are potentially capable of coordination, the stereochemistry of such complexones allowed an *a priori* assumption that the higher stability of their chelates is a result of the possible formation of additional rings and led to the expectation that they will be selective with respect to cations with an enhanced coordination capacity and high electrostatic characteristics.

Although the properties of aminoalkylenephosphonic acids were first reported by Schwarzenbach and coworkers as early as 1949,[5] the interesting and extremely specific properties of organophosphorus complexones were not discovered either in that investigation or in later studies by Martell and coworkers[6-9] dealing with the phosphorus analogues of the familiar complexone ethylenediamine-tetra-acetic acid (EDTA). Only comprehensive investigations using potentiometric, polarographic, infrared spectroscopic, NMR, and ESR methods, carried out mainly by Soviet investigators, led to the discovery of the specificity of the interaction of phosphorus-containing complexones with the cations of elements in various Groups of Mendeleev's Table[2-4,10-16].

The present review does not claim to cover completely the literature on organophosphorus complexones, since its aim is to characterise the principal trends of the developments in this field. At the start of studies on

Table 1. Complexones and their abbreviated designations.

Acid	Formula	Abbreviation	Refs.
Ethylenediamine-*NN'*-di-(methylenephosphonic)	$(HO)_2P(O)CH_2NH(CH_2)_2NHCH_2P(O)(OH)_2$	EDDMPO	14, 18, 26
Ethylenediamine-*NN'*-bis-(dimethylmethylene-phosphonic)	$(HO)_2P(O)C(CH_3)_2NH(CH_2)_2NHC(CH_3)_2P(O)(OH)_2$	EDBDMPO	18
Oxybisethylenediamine-*NN'*-bis(dimethylmethylene-phosphonic)	$(HO)_2P(O)C(CH_3)_2NH(CH_2)_2O(CH_2)_2NHC(CH_3)_2P(O)(OH)_2$	OEDBDMPO	19
Thiobisethylenediamine-*NN'*-bis(dimethylmethylene-phosphonic	$[(HO)_2P(O)C(CH_3)_2NH(CH_2)_2]_2S$	TEDBDMPO	20
Diethylenetriamine-*NN'*-bis-(dimethylmethylenephos-phonic)	$[(HO)_2P(O)C(CH_3)_2NH(CH_2)_2]_2NH$	DETBDMPO	19
Pentamethylenediamine-*NN'*-bis(dimethylmethylene-phosphonic)	$(HO)_2P(O)C(CH_3)_2NH(CH_2)_5NHC(CH_3)_2P(O)(OH)_2$	PMDBDMPO	20
N-(2-Hydroxyethyl)ethylene-diamine-*NN'N'*-tri(methylene-phosphonic)	$(HO)_2P(O)CH_2N(CH_2CH_2OH)(CH_2)_2N[CH_2P(O)(OH)_2]_2$	HEEDTMPO	33
Ethylenediamine-*NNN'N'*tetra-methylenephosphonic)	$[(HO)_2P(O)CH_2]_2N(CH)_2N[CH_2P(O)(OH)_2]_2$	EDTMPO	6, 14, 26
Diethylenetriamine-*NNN'-N'N''*-penta(methylenephosphonic)	$[(HO)_2P(O)CH_2]_2N(CH_2)_2N(CH_2P(O)(OH)_2)(CH_2)_2N[CH_2P(O)(OH)_2]_2$	DETPMPO	22
Ethylenediamine-*NN'*-diacetic-*NN'*-di(methylenephosphonic)	$(HO)_2P(O)CH_2N(CH_2COOH)(CH_2)_2N(CH_2P(O)(OH)_2)CH_2COOH$	EDDADMPO	9, 18
Ethylenediamine-*NN'*-di(phenyl-methylenephosphonic)	$(HO)_2P(O)CHNH(CH_2)_2NHCHP(O)(OH)_2$ (C$_6$H$_5$ groups)	EDDPMPO	18
Ethylendiamine-*NN'*-di(phenyl-*methylenephosphonous*)	HO, H, OH, H on P(O)CHNH(CH$_2$)$_2$NHCHP(O) (C$_6$H$_5$ groups)	EDDPMPOS	34
Ethylenediamine-*NN'*-di(*o*-hydroxy-phenylmethylenephosphonic)	$(HO)_2P(O)CHNH(CH_2)_2NHCHP(O)(OH)_2$ (C$_6$H$_4$OH groups)	EDDHPMPO	34
Ethylenediamine-*NN'*-di(*o*-hydroxy-phenylmethylenephosphonous)	HO, H, OH, H on P(O)CHNH(CH$_2$)$_2$NHCHP(O) (C$_6$H$_4$OH groups)	EDDHPMPOS	34
Nitrilotri(methylphosphonic)	$N[CH_2P(O)(OH)_2]_3$	NTP	21
Ethylenediamine-*NNN'N'*-tetra-acetic	$(HOOCH_2C)_2N(CH_2)_2N(CH_2COOH)_2$	EDTA	
Nitrilotriacetic	$N(CH_2COOH)_3$	NTA	
Diethylenetriamine-*NNN'N'N''*-penta-acetic	$(HOOCH_2C)_2N(CH_2)_2N(CH_2COOH)(CH_2)_2N(CH_2COOH)_2$	DTPA	

organophosphorus complexones, polyaminopolyphosphonic acids were difficult to obtain. For this reason, a special series of studies were made to develop convenient methods for the synthesis of compounds of this type.

They were based on the principle of the synthesis of α-aminoalkylphosphonic acids discovered by Kabachnik and Medved' at the beginning of the 1950s, which consists of the simultaneous or consecutive treatment of an amine and an oxo-compound by phosphorus(III) derivatives capable of existing in the form of two tautomers [3,17-22].

In the synthesis of alkylenediaminediphosphonic and alkylenediaminepolyphosphonic acids the amine is the corresponding diamine (usually ethylenediamine) and the oxo-compounds are aldehydes or ketones or the Schiff bases prepared beforehand from the diamine and the oxo-compound.

The phosphorus-containing component can be any derivative of phosphorous, phosphonous, or hypophosphorous acid. Esters, for example dialkyl phosphites or phosphonites, are used in the two-stage synthesis; the ester group is subsequently hydrolysed. In the single-stage synthesis (a modification of the method of Moedritzer and Irani[21]) phosphorous acid is employed. In the synthesis of ethylenediaminedi(alkylenephosphonous) acid we employed hypophosphorous acid as the phosphorus-containing component.

There is now a possibility of obtaining the following principal types of organophosphorus complexones by the above methods which have a wide range of applicability.

(1) Alkylenepolyaminebis[dialkyl(arylalkyl)methylenephosphonic] acids:

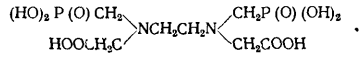
$$(HO)_2P(O)C(R'R'')NH[CH_2-X-CH_2]_nCH_2NHC(R'R'')P(O)(OH)_2$$

R', R''=H, Alk, Ar; $n = 0,1$; X=O, NH, S, CH_2 .

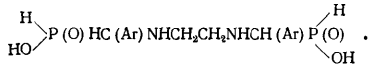
(2) Alkylenepolyaminepoly(alkylenephosphonic) acids, for example:

$$[(HO)_2P(O)CH_2]_2NCH_2CH_2N[CH_2P(O)(OH)_2]_2 .$$

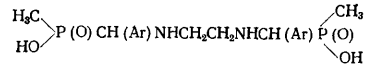
(3) Alkylenediaminediaceticdi(alkylenephosphonic) acids:



(4) Alkylenediaminedi(arylmethylenephosphonous) acids:



(5) Alkylenediaminedi(arylmethylenephosphinic) acids:



As a result it became possible to synthesise and investigate a series of compounds the structure of which includes phosphonic, phosphonous, and phosphinic acid fragments, fully phosphorylated derivatives of polyamines, complexones with heteroatoms and aromatic groups, and complexones containing simultaneously carboxy- and phosphono-groups or phosphono- and hydroxy-groups.

Some of the complexones synthesised and the abbreviations used to designate them are listed in Table 1, which also includes references to their syntheses. The last three acids in Table 1, the widely familiar carboxyl-containing complexones, are included for comparison.

II. DISSOCIATION OF AMINOPHOSPHONIC ACIDS

A betaine-like zwitter-ionic structure is characteristic of both aminocarboxylic acids and their phosphorus analogues but the basicity of the amino-group in aminophosphonic acids is higher than in aminocarboxylic acids (Table 2).

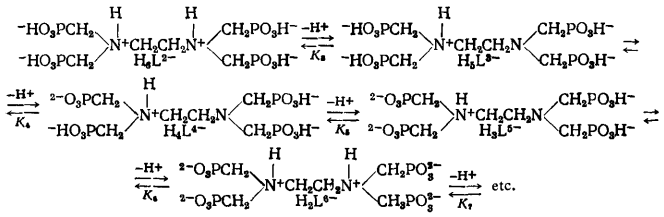
Table 2. Negative logarithms of the dissociation constants of phosphorus-containing complexones.

Designation	pK_1	pK_2	pK_3	pK_4	pK_5	pK_6	pK_7	pK_8	pK_9	pK_{10}
NTA	1.89	2.49	9.73							
NTP	0.3	1.5	4.64	5.88	7.3	12.1				
HMP*	1.7	2.0	5.1	6.45	10.98					
EDTA	2.00	2.76	6.16	10.26						
EDDMPO	4.61	5.72	8.02	10.47						
EDBDMPO	4.95	6.00	8.55	11.68						
OEDBDMPO	5.15	6.40	10.56	11.48						
TEDBDMPO	5.51	6.34	10.38	11.48						
DETBDMPO	5,39	6.55	10.40	11.20						
PMDBDMPO	5.77	6.13	11.0	>11						
HEEDTMPO	1.7	2.81	5.50	6.85	9.10	10.93				
EDTMPO	1.1	1.5	3.02	5.23	6.54	8.08	10.18	12.10		
DETPMPO	—	—	2.8	4.45	5.50	6.38	7.17	8.15	10.10	12.0
EDDADMPO	1.5	2.30	4.65	6.13	8.36	10.34				
EDDPMPO	4.18	5.56	7.44	9.69						
EDDPMPOS	4.32	7.58								
EDDHPMPO	4.37	5.41	6.64	8.77	9.94	11.19				
EDDHPMPOS	4,61	7.57	10.84	11.25						

*Hexamethylphosphoramide (Ed. of Translation).

The study of the deprotonation of polyaminopolyphosphonic acids showed[2-4,23,24] that the PO_3H_2 group dissociates at low pH. With increase of pH, the PO_3H^- groups dissociate and finally in the alkaline region the protons dissociate from the betaine nitrogen atoms. When the complexone molecule contains hydroxyphenyl groups, the phenolic hydroxyls are the last to dissociate at still higher pH than the betaine protons. In such cases stable hydrogen bonds may be formed.

In the course of more far-reaching studies on the mechanism of the acid dissociation of aminopolyphosphonic acids by infrared spectroscopy it was shown[25] that the dissociation of the third, fourth, and fifth protons from ethylenediaminetetra(methylenephosphonic) acid results in the formation of anionic forms in which protonated phosphono-groups are linked to one protonated and one non-protonated nitrogen atom, as shown below:



The presence of a deprotonated nitrogen atom in the anions H_5L^{3-}, H_4L^{4-}, and H_3L^{5-} suggests that metal–nitrogen bonds are more likely to be formed in acid complexes of EDTMPO.

It has been shown, also by infrared spectroscopy, that in the dissociation of ethylenediaminediaceticdi(methylenephosphonic) acid the species with protonated and deprotonated nitrogen atoms may exist in equilibrium. A similar view concerning the order of the dissociation of

protons in ethylenediaminemono(methylenephosphonic) and ethylenediaminedi(methylenephosphonic) acids was expressed by Uhlig and Achilles[28].

Comparison of the dissociation constants of aminophosphonic acids in the group under consideration with those of the analogous aminocarboxylic acids shows that the unusually high and close values of the last two dissociation constants, corresponding to the dissociation of the betaine protons, constitute a significant difference. In diphosphonic acid this is shown particularly clearly with increase of the length of the methylene chain joining the aminoalkylphosphonic acid groups; the difference between the last dissociation constants decreases to a factor of ten and less, which can be accounted for by the decrease of the inductive effect exerted by one amino-group on another.

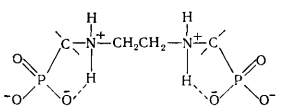
In tri-, tetra-, and penta-phosphonic acids the decrease of the mutual influence of the two positively charged nitrogen atoms is probably associated partly with the high charge of the anion and partly with the electrostatic binding (hydrogen bonding) of the betaine protons.

Table 2 shows that an increase of the number of iminomethylphosphonic acid groups initially increases the last two dissociation constants on passing from ethylenediaminedi(methylenephosphonic) acid to ethylenediaminetetra(methylenephosphonic) acid, but, on passing from the latter acid to diethylenetriaminepenta(methylenephosphonic) acid, the last two constants hardly change. This can be accounted for by an increase of the basicity of the nitrogen atom with the increasing negative charge in the molecule. Then, when the charge becomes large, the introduction of a new group alters it relatively little. A similar phenomenon has been observed in phosphates.

The combination of highly basic betaine nitrogen atoms and polydentate salt-forming groups in alkylenepolyaminepoly(alkylenephosphonic) acids leads to their deprotonation over a wide pH range, which extends the pH range in which complexes exist.

III. COMPLEXES WITH ALKALI METALS

All phosphorus-containing complexones form complexes on interaction with alkali metal cations. Thus ethylenediaminebis(dimethylmethylenephosphonic) acid forms the equimolar complexes



in the region corresponding to the dissociation of the betaine protons, i.e. at pH > 8 (K_{st} = 3.06 for LiX, 2.30 for NaX, < 1 for KX, and 3.37 for CsX). Their stability exceeds that of the corresponding EDTA complexes. We attribute this to the specific features of the effect of the phosphono-group and in particular to the involvement in complex formation of both oxygen atoms in the hydroxy-groups at the phosphorus atom. The participation of phosphono-groups of ethylenediaminebis(dimethylmethylenephosphonic) acid in coordination to alkali metals only at fairly high pH values can probably be explained by the necessity for the dissociation of the hydrogen bonds in the structure (see above) to liberate all the oxygen atoms of the phosphono-groups and also by the necessity to increase the overall negative charge of the molecule.

IV. COMPLEXES WITH ALKALINE EARTH METALS AND BERYLLIUM

Polyalkylenepolyaminepolyphosphonic acid containing not more than two phosphono-groups forms hardly any complexes with alkaline earth metals including calcium. An increase of the number of phosphono-groups and also their combination with carboxy-groups leads to the formation of stable complexes with alkaline earth metals, the logarithms of whose stability constants reach 8–9 (Table 3). Depending on the pH of the medium, complexes protonated to different extents are formed[2-4,12-14,27].

Table 3. Logarithms of the stability constants of the complexes MX.

Cation	EDBDMPO	EDDADMPO	EDTMPO	DETPMPO
Mg^{2+}	<2	8.54	8.63	6.40
Ca^{2+}	<2	9.02	9.33	7.11

The consecutive protonation of the normal complexes as the pH is reduced can be demonstrated for magnesium complexes of nitrilotrimethylphosphonic acid[12,13].

Table 4. Parameters of the infrared and NMR spectra of magnesium complexes of nitrilotri(methylphosphonic) acid.

Complex anion	ν(CH), cm^{-1} as	ν(CH), cm^{-1} s	ν(PO_3), cm^{-1}		δ_H, p.p.m.	$\delta_{^{31}P}$, p.p.m.
MgL^{4-}	2946					
	2877	2841	1099,1068	971	3.20	16.63
$MgHL^{3-}$	3000	2937	1106	973	2,83	7,65
MgH_2L^{2-}	2998	2946	1164,1103	971	2,76	7.20
MgH_3L^{-}	—	—	1167,1084	966	—	—
	2939					
L^{6-}	2845	2790	1083	969	3.45	17.67

The infrared spectrum of the solution of the normal complex $[MgL]^{4-}$ shows an increase in the symmetrical stretching vibration wavenumber ν(C–H) approximately by 50 cm^{-1} compared with the fully deprotonated free ligand. This is associated with the formation of a stable covalent Mg ← N bond. The formation of this bond is also confirmed by the chemical shifts to a high field of the proton doublet in the ^1H NMR spectra and the phosphorus triplet in the ^{31}P NMR spectra relative to the free ligand.

The bond between magnesium and oxygen atoms of the phosphono-groups is largely ionic, which is also indicated by the slight increase of the PO_3^- vibration frequency in the complex compared with the ligand.

When the first proton adds to the complex, the N–H bond is formed, this being accompanied by a characteristic increase of the C–H stretching vibration wavenumbers by 100 cm^{-1}. The second proton adds to an oxygen atom of one of the phosphono-groups, which is reflected by the appearance in the spectrum of the PO_3H^- band with a characteristic wavenumber of 1164 cm^{-1}. The third

proton adds to the second phosphono-group (the intensity of the 1164 cm^{-1} band then increases). All these conclusions are confirmed also by the ^{1}H and ^{31}P NMR spectra.

Table 5. Logarithms of the stability constants of polynuclear ethylenediaminebis(dimethylmethylenephosphonic) acid.

M^{2+}	$BeMH_2L$	$AlMH_2L$	$LaMH_2L$	$CdMH_2L$	M^{2+}	$BeMH_2L$	$AlMH_2L$	$LaMH_2L$	$CdMH_2L$
Mn	8.7	9.8	6.2	6.9	Ni	8.9	10.3	6.3	7.0
Fe	8.8	10.0	6.3	7.0	Cu	13.5	14.8	11.4	11.8
Co	8.9	10.1	6.3	7.0	Zn	10.1	11.3	7.2	7.8

The ability of these compounds to form stable mononuclear and dinuclear complexes with beryllium is particularly noteworthy[28-30]. The study of the mechanism of the complex formation process showed that it involves the interaction of beryllium with the phosphono-groups only; the nitrogen atoms of the iminoalkylphosphonic acid groups are not involved in complex formation. The free coordination sites in the complexes can be occupied by other cations with formation of polynuclear complexes having two coordination centres consisting of two different cations[28-31] (Table 5).

V. COMPLEXES WITH TRANSITION METALS

In the interaction with transition metals the specific features of phosphorus-containing complexones are shown primarily by the formation of stable hydrogen-bonded complexes, which is not characteristic of the carboxyl-containing prototypes. Among the normal complexes, those of copper are particularly stable (Table 6).

Thus the stability constant of the copper complex of ethylenediaminebis(dimethylmethylenephosphonic) acid (EDBDMPO, phosphicine) exceeds that of the corresponding EDTA complex by two powers of ten. The difference between the stabilities of the copper and other transition metal complexes is exceptionally large. Thus the stability of the phosphicine-copper complex exceeds those of the nickel and zinc complexes approximately by nine powers of ten (the stabilities of the corresponding EDTA complexes are similar). It has been established by ESR and electronic spectroscopy[11] that in the ground state of the copper(II) complex of ethylenediaminebis(dimethylmethylenephosphonic) acid the unpaired electron is in the $d_{x^2-y^2}$ orbital (the x and y axes are directed towards the electron-donating ligand atoms) and therefore the complex has the structure of an extended octahedron. The copper atom is linked to the two nitrogen atoms, which are located in the plane containing the unpaired electron and the other coordination sites are occupied by the oxygen atoms of the phosphono-groups. The bonds in the plane of the complex have an amount of covalent character typical for copper complexes.

Stable complexes with phosphorylated derivatives of polyamines are formed by readily hydrolysed elements: iron, aluminium, indium, gallium, titanium, and chromium. The high stability of their protonated complexes, in many cases exceeding the stability of the normal complexes of the corresponding aminopolycarboxylic acids, is remarkable.

The nature of these interactions can be illustrated using as an example the formation of aluminium nitrilotri(methylphosphonate). Aluminium forms two types of complexes with nitrilo(trimethylphosphonic) acid: sparingly soluble polynuclear compounds and soluble monoprotonated and normal compounds. In the region corresponding to the dissociation of the first three protons an insoluble compound is formed and is isolated as the hydrate $Al_3H_3L_2 \cdot 9H_2O$.

Table 6. Logarithms of the stability constants of transition metal complexes.

Complexone	Cu^{2+}	Ni^{2+}	Co^{2+}	Zn^{2+}	Mn^{2+}	Cd^{2+}
NTP	17.75	11.96	14.37	>16.37	10.20	11.55
EDBDMPO	8.83	3.84	3.84	4.31	3.57	
	20.35	11.23	11.19	13.38	8.00	
EDTMPO	11.14	9.12	8.51	9.90	6.99	8.81
	18.95	15.30	15.49	17.05	12.70	13.88
EDDADMPO	9.4	9.49			7.0	
	18.5	15.23	16.03	16.85	13.63	

Note. The numerals in the upper row refer to the $\lg K_{st}$ for the protonated complexes MH_2L and those in the lower row refer to the $\lg K_{st}$ for the normal complexes ML.

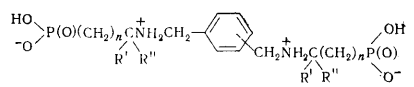
Infrared spectra show that in polynuclear compounds of this kind the bond between aluminium and nitrogen is weakened; evidently in this case the entire coordination capacity of aluminium is saturated by the oxygen atoms of the phosphono-groups. With increase of pH, the polynuclear complex gradually dissolves with formation of the soluble mononuclear complex AlH_2L^{2-} and its subsequent deprotonation and the formation of the stable normal mononuclear complex AlL^{3-}. In the presence of an excess of aluminium in the pH range 5–6 the sparingly soluble dinuclear complex Al_2L is formed and is isolated from solution as the hexahydrate. The study of the ^{1}H NMR spectra of the normal mononuclear complex showed the presence of the Al–N bond. The change of the chemical shifts relative to the fully deprotonated ligand reaches 0.28 p.p.m. The addition of an excess equivalent of alkali (pH 6.86–9.08) does not cause precipitation and no changes take place in the NMR spectra. A further increase of pH (9.1–10.7) leads to the appearance in the spectrum of two pairs of signals; one of these is intense and corresponds to the aluminium complex and the second, weak signal corresponds to the monoprotonated form of the ligand (HL). A further increase of pH leads to an increase of the intensities of the second pair of bands with their subsequent equalisation and is accompanied by the precipitation of aluminium hydroxide from solution.

In all probability the complex AlL^{3-} is present in solution in equilibrium with the monohydroxo-complex $[(AlOH)HL]^{3-}$, which is due to the great tendency of aluminium to form a bond with the water hydroxyl. This hypothesis is confirmed by the presence in the infrared spectrum of the solution of bands indicating the formation of a bond between nitrogen and a proton (N–H). The existence in the complexes of, as it were, a "disproportionated" water molecule is probably generally characteristic of compounds formed by readily hydrolysed cations.

The interaction of phosphorus-containing complexones with iron is unusual. Interpretation of the infrared, NMR, and ESR spectra and also of potentiometric data for iron complexes of carboxyl- and phosphorus-containing analogues leads to the conclusion that at low pH the interaction of the cation with the two groups of ligands proceeds via different mechanisms. Whereas carboxylated amines form very stable water-soluble normal 1 : 1 complexes with Fe^{3+}, phosphorylated amines give rise to protonated polynuclear water-insoluble complexes. Their inner sphere consists entirely of the oxygen atoms of the phosphono-groups. On passing to alkaline media, the stability of the nitrilotriacetic, EDTA, and other complexes with Fe^{3+} falls owing to the weakening of the bonds between the oxygen atoms of the carboxy-groups and the central ion caused by hydrolytic processes. Under these conditions, polynuclear complexes of phosphorylated amines are converted into normal soluble mononuclear and dinuclear complexes with formation of a thermodynamically favourable ring comprising M–N bonds [32].

Analysis of the ESR spectra of iron complexonates established the symmetry of the immediate environment of the central atom in these compounds. The compounds have a spectrum characteristic of Fe^{3+} in the high-spin state $^6A_1$—it consists of a single broad symmetrical line, which indicates hexagonal symmetry of the local environment of the iron ion; the splitting caused by the tetragonal or trigonal components of the crystal field is absent. These results are fully consistent with the determinations of the magnetic susceptibilities of these complexes (μ_{eff} = 5.86 Bohr magnetons, i.e. $s = 5/2$).

Table 7. Logarithms of the stability constants of the protonated complexes of xylylenediaminedialkylenephosphonic acids.



Position in ring	n	lg K_{st} for MH_2L complexes						
		R′	R″	Ni^{2+}	Cu^{2+}	Fe^{3+}	Dy^{3+}	UO_2^{2+}
m-	0	CH_3	CH_3	—	3.92	—	6.48	8.40
p-	0	CH_3	CH_3	—	<3	—	4.78	8.32
p-	1	H	H	—	4.08	—	6.17	9.4(ppt)
		EDBDMPO		3.84	8.33	>10	6.20	8.52

The introduction of a hydroxyl into the structure of the chelating agent increases the stability of the resulting compounds. *N*-(2-Hydroxyethyl)ethylenediaminetri(methylenephosphonic) acid prevents the hydrolysis of iron even when the complexes are boiled at pH > 12. [33]

Extremely stable highly coloured iron(III) and titanium(IV) complexes are formed by ethylenediaminedi-(*o*-hydroxyphenylmethylenephosphonic) and the corresponding phosphonous acids. However, the mechanisms of complex formation are different in the two cases: complexes with simultaneous participation in the coordination of all the electron-donating atoms may be formed with the phosphonous acid, while in the case of the phosphonic acid, where there is a greater number of binding sites, there is apparently competition between the oxygen atoms of the phosphono-group and the phenoxide ion [34,35].

The potential ability of aminoalkylphosphonic acids to increase the number of their binding sites by the inclusion of the oxygen atoms of the phosphono-groups favours the formation of complexes with the lanthanides, which have high coordination numbers and a high affinity for oxygen. Thus the stability of the protonated complexes of ethylenediaminebis(dimethylmethylenephosphonic) acid with the lanthanides is close to that of the corresponding normal ethylenediaminediacetic acid (EDDA) complexes and the stability of the protonated complexes of ethylenediaminediaceticdi(methylenephosphonic) acid exceeds that of the normal EDDA complexes by 6–7 powers of ten. A definite selectivity in the formation of complexes with individual lanthanides is observed.

The formation of complexes with the uranyl ion is interesting: the stability of its protonated complexes with phosphorylated polyamines is very high. The enhanced selectivity in relation to the lanthanides and the uranyl ion is promoted by the increased rigidity of the polymethylene chain joining the nitriloalkylphosphonic acid groups [36]. Thus xylylenediaminebis(dimethylmethylenephosphonic) acids, where the presence of the aromatic ring in the chain between the nitrogen atoms prevents the free rotation of the individual units and fixes the positions of the electron-donating atoms in space, proved to be effective only in relation to the large lanthanide and uranyl cations and to behave as weak complex-forming agents in relation to transition metals, including iron(III) (Table 7).

The difference between the pH ranges where polynuclear insoluble complexes of the above triply charged elements exist permitted the employment of organophosphorus complexones, particularly nitrilotri(methylenephosphonic) acid, as new selective reagents for gravimetric analysis [37].

Aluminium is deposited in the form of the polynuclear complex $Al_3H_3L_2.9H_2O$ from 0.1 *N* hydrochloric acid solutions. In this medium magnesium and alkaline earth metals altogether fail to form complexes. Certain transition metals, such as chromium, copper, and zinc, form less stable soluble complexes, so that their undesirable effect as well as the coprecipitation of transition metals can be eliminated by adding diethylenetriaminepenta-acetic acid as a masking agent (Table 8).

Table 8. Schemes for the possible determinations of metal cations in the presence of a number of elements.

Element determined	Conditions of determination	Elements not interfering with determination	Masking substance
Al	0,1 *M* HCl	Ni,Co,Cu,Zn,Cd,Mn, Cr,Fe,Ca,Mg,Sr,Ba	DTPA
Fe	2 *M* HCl	Ca,Mg,Sr,Ba,Be,Al, Ni,Co,Cu,Zn,Cd,Mn	—

The iron complexonate is stable even in 2 *N* hydrochloric acid, i.e. iron can be determined in the presence of the same elements as in the determination of aluminium. The possibility of determining iron in the presence of aluminium, whose complex decomposes in this medium, is most interesting. The difficulty of separating these metals and also of determining one metal in the presence of the other is generally known.

Our quantitative analytical methods can be successfully used in the analysis of polymetallic systems, in particular

in the analysis of various alloys and steels. Studies on these lines are being continued and the first successful results have already been obtained.

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The specific features of the activities shown by phosphorylated polyamine derivatives, distinguishing them from their carboxy-containing analogues, can be accounted for by the unusual structure of the internal ligand contour, caused by the increase of the number of electron-donating atoms by the inclusion of the oxygen atoms of the phosphono-groups, their high nucleophilicity, and their stereochemistry, which determines the geometry of the complex.

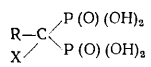
On this basis and experimental results, we postulated three most probable mechanisms for complex formation involving the phosphono-group[4,30,37]. The first mechanism presupposes the formation of a four-membered ring in which the metal ion is coordinated to the two oxygen atoms of the phosphono-group. Under these conditions, the metal can be coordinated in two ways. In the first way the metal ion is coordinated at the midpoint between the two oxygen atoms of each phosphono-group so that the ligand field has an approximately octahedral or tetrahedral coordination, but the oxygen atoms are not located at the vertices of the corresponding polyhedron, forming a new distorted polyhedron in which the coordination number of the metal is higher than usual. This hypothesis does not rule out the possibility of the formation by certain metal ions of complexes whose structure includes four-membered rings where the oxygen atoms of the phosphono-groups lie at the vertices of the polyhedra. Our approximate calculations showed that the strain in the rings with sp^2-hybridised oxygen atoms is insignificant.

The second mechanism presupposes the formation of an eight-membered ring where at least two metal ions are coordinated in turn to the four oxygen atoms of the two phosphono-groups. The complex can then be stabilised by internal hydrogen bonds formed by the coordinated water and the oxygen atoms of the phosphono-groups.

Finally the third type of coordination involves the formation of a network polymer in which the phosphono-group behaves as the tridentate moiety of the ligand. This type of coordination is characteristic, for example, of the insoluble polynuclear beryllium complex of nitrilotri(methylenephosphonic) acid. Three atoms of tetracoordinate beryllium close the ring within one complexone molecule. The remaining oxygen atoms are joined via the metal atoms to other similar molecules.

VI. HYDROXY- AND AMINO-ALKYLIDENEDIPHOSPHONIC ACIDS

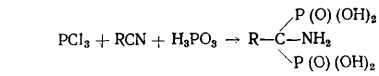
Our conclusion concerning the ability of phosphorylated complexones to form stable protonated complexes, based on the employment in the interaction with cations of only the electron-donating functions of the oxygen atoms in the phosphono-groups, constituted the basis for a detailed study of structurally simpler ligands containing a compact complex-forming group—half-substituted alkylidenediphosphonic acids with a hydroxy- or an amino-group at the carbon atom joined to two phosphono-groups. 1-Hydroxyalkylidenediphosphonic and 1-aminoalkylidenediphosphonic acids are compounds of this kind.



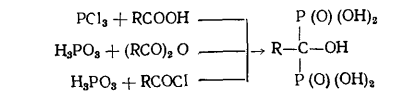
[X = OH or NH_2 and R = alkyl(C_1–C_{11}) or aryl].

Examples of this group of substances have been known for a long time. Thus hydroxyethylidenediphosphonic acid $CH_3C(OH)(PO_3H_2)_2$ has been known since the end of the previous century. During the last decade, many patents dealing with the methods of synthesis of substances of this type were published and various practical applications were suggested for them (see below), but quantitative studies on their complex-forming properties were carried out recently mainly by the present authors.

Aminoalkylidenediphosphonic acids were synthesised by the interaction of phosphorus trihalides with carboxylic acid nitriles in the presence of phosphorous acid[37,38]:

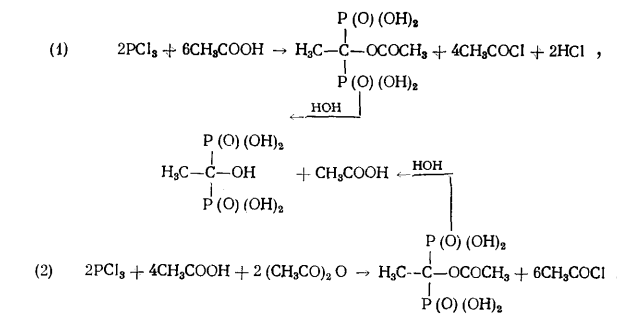


Hydroxyalkylidenediphosphonic acids were obtained by the acylation of phosphorous acid or phosphorus trichloride by carboxylic acids, their anhydrides, or halides[39–43]:



Among the compounds investigated, 1-hydroxyethylidenediphosphonic acid (HEDP) is at present of greatest practical interest. This is due to the ready availability of the starting material and the comparative simplicity of the synthesis, which have made industrial manufacture of this product a realistic proposition.

The reaction of phosphorus trichloride with acetic acid has been used to synthesise HEDP [reaction (1)]:



Together with acetoxyethylidenediphosphonic acid, which is readily hydrolysed to HEDP, acetyl chloride and hydrogen chloride are also produced in this reaction[42,43]. This permitted the joint industrial synthesis of HEDP and acetyl chloride. By the additional introduction of acetic anhydride into the reaction [reaction (2)], the maximum utilisation of the starting material is achieved and corrosive hydrogen chloride is virtually eliminated.

The complex-forming properties of α-substituted alkylidenediphosphonic acids are due to their structures[38,44]. The combination in one molecule of two highly acidic phosphono-groups and also of hydroxy- or amino-groups, which play the role of the basic centre in the molecule, enable these ligands to form stable complexes, not only normal but also protonated, with alkaline earth, transition, and lanthanide elements (Table 9), extending thereby the pH range corresponding to the existence of the complexes from acid to alkaline solutions. A unique property of HEDP is its ability to interact with cations in a strongly acid medium, up to 6 *N* nitric acid.

The steric configuration of their molecules enables α-substituted alkylidenediphosphonic acids to behave as tridentate ligands in coordination with a single cation despite

the presence of five electron-donating atoms and promotes the formation of very stable dinuclear complexes with both alkaline earth and transition metals. HEDP is known to form not only dinuclear but also polynuclear chain complexes with certain cations, in particular with calcium.

With aluminium, iron(III), thorium, and zirconium ions, the relatively low effective number of binding sites in HEDP, which cannot "saturate" the coordination capacity of the complex-forming ion, gives rise to the possibility of the formation of 1 : 2 metal : ligand complexes in the presence of an excess of HEDP, while in the presence of another ligand in the system mixed complexes may be formed. The frequent employment of HEDP in a mixture with other complex-forming agents is due to its ability to form such mixed complexes.

Table 9. Logarithms of the stability constants of alkylidenediphosphonic acid complexes.

	MDP			HEDP				ABDP			
	ML	M_2L	ML_2	ML	MHL	M_2L	ML_2	ML	MHL	M_2L	ML_2
Be^{2+}	—	19.1		16.5	13.4	25.7		16.2	10.4	23.4	
Al^{3+}	14.1		23.0	21.4	15.3	27.2	25.9	18.8	22.5		26.3
Fe^{3+}	19.9		26.6	21.6	16.2	29.1	25.2				
Ln^{3+}	12—13		20—22	18—20	15—16			16—17	11—12		22—24

Comparison of alkylidenediphosphonic acids with organophosphorus ligands containing a nitrogen atom in the alkylene chain linking the two phosphono-groups showed that the complex-forming capacity of alkylidenediphosphonic acids is not inferior, at any rate in the acid region, and in many instances actually superior to that of alkylenepolyamine-di(alkylenephosphonic) acids in which nitrogen is involved in coordination with the metals only after the betaine protons have been titrated.

Together with common properties determined by the presence of phosphono-groups, namely the preferential formation of complexes with cations having small (beryllium and iron) or large (alkaline earth metals) radii, the capacity to form stable complexes at acid pH, the tendency to form dinuclear complexes, etc., alkylidenediphosphonic acids have a number of characteristic features.

Thus alkylidenediphosphonic acids form fairly stable complexes with alkaline earth metals and very stable complexes with beryllium. Comparison of the stabilities of the complexes MHL of hydroxy- and amino-alkylidenediphosphonic acids with methylenediphosphonic acid (MDP) complexes ML, which have the same structure and are formed only via the coordination of the cation to the oxygen atoms of the phosphono-groups, shows that the stability constants of the complexes of substituted alkylidenediphosphonic acids with alkaline earth and certain transition metals differ little from the corresponding constants of the MDP complexes.

The stability constants of the protonated HEDP complexes of multicharged readily hydrolysed cations are higher than the constants of the corresponding normal MDP complexes, which is evidence for additional coordination of the hydroxy-group to these cations (Table 9).

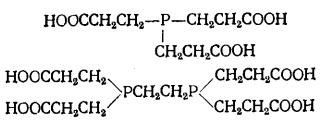
The higher stability of the normal complexes of these cations apparently indicates the involvement of the deprotonated hydroxy-group in complex formation. It is noteworthy that the stability constants of such HEDP complexes are higher than the constants of the corresponding aminobenzylidenediphosphonic acid (ABDP).

The stability of the normal HEDP complexes with iron(III), thorium, and uranium cations is particularly high. Apart from the high coordination capacity, the tendency to form coordinate bonds with oxygen is in this instance of primary importance.

The high capacity of these compounds to combine with metals and the selectivity of their action in relation to beryllium, aluminium, titanium, and thorium combined with their ready availability make them extremely promising ligands.

VII. COMPLEXONES WITH TERVALENT PHOSPHORUS

The specific features of the formation of complexes by organophosphorus complexones make possible the solution of many interesting problems. However, the problem relating to the formation of complexes in an aqueous medium of elements such as silver, mercury, vanadium, and molybdenum could not be solved with the aid of polyamine derivatives. We suggest that complexones in which tervalent phosphorus atoms instead of nitrogen atoms behave as electron-donating species are of interest in this respect[27,45].



The tendency of the above metals to stabilise the bonds with tervalent phosphorus atoms by the formation of an additional d_π bond (apart from the phosphorus–metal coordinate σ-bond), as a result of the transfer of an electron pair from the 4*d* orbitals of the above metals to the unfilled *d* orbitals of phosphorus which have similar energies, leads to the formation of stable complexes with these elements.

We have now investigated complexone analogues derived from phosphines, in which electron-donating phosphorus(III) atoms and acidic phosphono-groups are combined in the same molecule. These constitute a new type of promising ligands.

VIII. APPLICATIONS OF PHOSPHORUS-CONTAINING COMPLEXONES

The knowledge of the main physicochemical characteristics and of the specific features of the behaviour of phosphorus-containing complex-forming ligands suggests many potential applications of these substances in various branches of science and engineering.

Systematic study of the biological properties of alkylenebisnitrilodialkylphosphonic acids has led to the possibility of the employment of substances of this kind for the elimination from the organism of incorporated toxic metals and also has led to the discovery of their influence on the elimination of certain biologically important elements and on the state of metal complexes in the organism.

A biological investigation of organophosphorus complexones carried out at the Institute of Labour Hygiene and Professional Diseases of the Academy of Medical Sciences of the USSR revealed a unique property of this group of substances, namely virtual absence of toxicity.

The ability of alkylenebisnitrilodialkylphosphonic acids to form very stable complexes with copper leads to the elimination of copper from the organism and to the possibility of their use in the treatment of haepatocerebral dystrophy. The formation of stable water-soluble complexes with beryllium suggested that ethylenediaminebis-(dimethylmethylenephosphonic) acid ("phosphicine") can be used as an agent for accelerating the elimination of beryllium from the organism without affecting the calcium metabolism [3,46-48]. Experimental studies demonstrated the usefulness of phosphicine for the acceleration of the elimination of lead from the organism [3]. The efficiency of diethylenetriaminepenta(methylenephosphonic) acids in eliminating uranium has been discovered [49].

HEDP salts, particularly the sodium salt, are able to regulate the calcium content, which suggests their employment in the treatment of the imbalance of the calcium metabolism in the organism and to prevent or reduce the formation of stone, including dental calculus [50-57]. It has been shown that HEDP salts have an inhibiting effect on the deposition of calcium phosphate *in vitro* and *in vivo* in the aorta and in the kidneys of rats [58-60]; they retard osteoporosis [61].

HEDP salts increase the bactericidal activity of phenolic compounds, which suggests their employment in disinfectants, shampoos, mouth washes, tooth pastes, and many other similar products [62-64]. Ditin salts of HEDP have been suggested for the prophylaxis of dental caries [65].

In view of their high capacity for combination with metals, phosphorus-containing complexones may be recommended as effective agents for the dissolution of corrosive deposits and also for the etching of aluminium.

HEDP and its bivalent metal, cobalt, chromium, lead, nickel, and particularly zinc complexes inhibit the corrosion of aluminium, iron, copper, and alloys [66-73]. Metal diphosphonates are not hydrolysed, in contrast to the familiar corrosion inhibitors (polyphosphates) and are stable in the temperature range 20-300°C [71].

The HEDP complex of zinc (sodium or ammonium salt) has been proposed as an inhibitor of the corrosion of a copper surface and as an inhibitor of the corrosion of iron and its alloys [66,70]. It has been noted that the zinc complex is non-toxic [67,73], which makes it superior to the familiar inhibitors, for example chromates.

The employment of HEDP in the composition of alkaline etching solutions for aluminium and its alloys makes it possible to prevent completely the formation of hydrated alumina on the surfaces of the components in etching baths [74,75] and improves the quality of the varnishing of the aluminium surface; it is used as a reagent for the electrochemical deposition of metals [77-79].

The applications of complexones in electroplating led to the development of a highly effective process for the metallation of dielectric materials (which is extremely important for radioelectronics and space engineering) and of a fundamentally new technology for the deposition of metals on the surface of steels without the employment of toxic electrolytes. By varying the process conditions, a wide range of colours of various metallic and non-metallic materials was obtained [75].

Studies dealing with the employment of phosphorus-containing complexones in synthetic detergent and wetting agent compositions have developed particularly extensively in the last decade [80-92]. Hitherto sodium triphosphate has been used as the activating additive to synthetic wetting agents. Its disadvantages include a tendency to hydrolyse with conversion into insoluble orthophosphates, which are deposited on the surfaces of the reservoirs or the articles being treated. On the other hand, wetting agents containing organophosphorus ligands prevent the formation of insoluble deposits [93] and maintain the cleaning capacity of the solutions for a longer time than polyphosphates [94], improve the properties of anionic, non-ionic, and amholytic detergents [85], and in combination with surface-active agents synergise the wetting capacity of detergents [95-97].

Detergents containing HEDP are suitable for washing even in cold water [87].

Complexone salts are used as components of soap [97,98], including toilet soap. The addition of a mixture of HEDP and a polyaminopolycarboxylic acid, for example EDTA, to superfat soaps stabilises them [99] and permits the manufacture of soaps which are effective in hard water [100].

Hydroxyethylidenediphosphonic and nitrilotri(methylphosphonic) acids have been suggested as stabilisers for peroxide compounds; the efficiency of the additive is not lost even in the presence of considerable amounts of polyvalent cations [82,101-104]. The applications of HEDP in cosmetics are described in a number of publications [105,106].

To improve the contrast and colour purity in the treatment of monochrome and colour photographic reversal materials in acid and alkaline solutions, the employment of a tin complex of HEDP has been recommended [107].

The specific features of the action of the new complexones have opened up great possibilities also in the traditional field of the application of complexones, namely in analytical chemistry for effective and in certain instances also selective analytical determinations, which were impossible or difficult when EDTA was used. Alkylenepolyaminedi(alkylmethylenephosphonic) and polyalkylphosphonic acids can be used for the fractional determination of cations in combinations which are difficult to separate (copper-nickel, beryllium-alkaline earth metals, individual pairs of lanthanides, etc.). It has been suggested that ethylenediaminebis(dimethylmethylenephosphonic) acid be used as a highly sensitive titrant in the amperometric determination of beryllium in its alloys with magnesium and aluminium [108]. The quantitative deposition of zirconium by means of this acid in highly acid media can be used to determine zirconium and to separate it from associated elements. Ethylenediaminedi-(*o*-hydroxyphenylmethylenephosphonous) and ethylenediaminedi-(*o*-hydroxyphenylmethylenephosphinic) acids are highly sensitive selective reagents for titanium and tervalent iron [34,35,109]. HEDP has been suggested as a titrant in the complexometric determination of thorium [110].

Nitrilotri(methylphosphonic) acid is used in the determination of beryllium in the presence of alkaline earth and other elements [111].

The application of organophosphorus complexones as masking agents is noteworthy. Thus ethylenediamine-*NN'*-diacetic-*NN'*-di(methylenephosphonic) acid masks beryllium in the hydroxide precipitation reaction, this being the first instance of the masking of beryllium [112]; HEDP can be used as a masking and complex-forming agent for calcium [113-115], aluminium, and titanium [116], and polyvalent and heavy metals [117,118].

The differentiation of the stabilities and solubilities of protonated lanthanide complexes as a function of pH permits the chromatographic separation of yttrium, cerium, and other lanthanides with similar properties using eluent solutions of ethylenediaminebis(dimethylmethylenephosphonic), ethylenediaminetetra(methylenephosphonic), and hydroxyethylidenediphosphonic acids [119,120]. The use of HEDP for the re-extraction of protactinium [121] and also for the elimination of neptunium from plutonium

and the radiometric determination of neptunium in its preparations[122] have been described.

The ability of polyaminopolyphosphonic acids with a large number of binding sites and also of NTP and HEDP to bind alkaline earth metals in complexes permitted the application of these compounds as water softeners[123,124], to prevent the precipitation of calcium carbonate, sulphate, hydroxide, and phosphate in industrial equipment[125,126], and to remove scale formed previously[127].

In view of its ability to bind metal ions, HEDP can be used in the textile industry[128] to eliminate calcium and magnesium ions, which can give rise to undesirable tints on dying and can distort the colour of the fabric.

Phosphorus-containing complexones can be used in the chemical industry to remove admixtures of metal ions from the starting material.

Compounds of this kind can be used effectively in the petroleum and gas extraction industry. Thus it has been recommended that HEDP[129] be added to solutions of inorganic acid used to acidify boreholes and to impart greater fluidity to the liquid being extracted, which makes it possible to maintain in solution calcium, magnesium, and iron salts.

Phosphorus-containing complexones also found applications in agriculture[130]. Apart from the most important elements such as potassium and phosphorus, which are introduced into the soil, in many instances it is necessary to introduce also microelements—manganese, molybdenum, copper, and cobalt. However, when these elements are added to soil in the form of liquid phosphate fertilisers they are precipitated as insoluble complexes. The addition of a complex-forming agent such as HEDP eliminates this defect[55,115]. HEDP esters are used as pesticides in the fight against pests damaging agricultural crops[117]. Thus comprehensive studies of the properties of phosphorus-containing complexones and their salts have led to an unusually wide range of their possible applications, some of which have already been successfully realised in practice.

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Institute of Organic Derivatives
of the Elements,
USSR Academy of Sciences,
Moscow