RUSSIAN CHEMICAL REVIEWS
Uspekhi Khimii

September 1976

Translated from *Uspekhi Khimii*, **45**, 1537-1567 (1976)

U.D.C. 541.49

Methods for the Synthesis of Complexones—Aminopolyacetic Acids

V.G.Yashunskii and O.I.Samoilova

Methods for the synthesis of "true" complex-forming agents containing one or several iminodiacetic acid groups are examined and discussed.
The bibliography includes 203 references.

CONTENTS

I.	Introduction	777
II.	The carboxymethylation reaction	778
III.	The synthesis of complexones from iminodiacetic acid and its esters	784
IV.	Other methods for synthesising complexones	787

I. INTRODUCTION

Among organic complex-forming agents, one of the most important places is occupied by polyaminopolyacetic acids—the so called complexones derived from iminodiacetic acid. Compounds of this series are capable of interacting with almost all metal cations, forming chelate complexes readily soluble in water. By virtue of these properties, complexones have found applications in various branches of science and engineering, agriculture, biology, and medicine.

Complexones are widely used as water softening agents[1], for example, in the leather, textile, and food industries and in photography. Complexometry[2], an analytical procedure based on the use of complexones whereby almost all metals can be determined quantitatively, has been developed extensively and is widely used in analytical chemistry. The employment of complexones for the separation of cations of elements having similar properties (particularly lanthanides) and for obtaining them in a pure form has become very important under laboratory and industrial conditions[3]. Complexones have proved to be extremely valuable in power engineering, primarily in nuclear power engineering as agents for the washing and passivation of the equipment, where they are used as such or in the form of compositions[4,5].

The ability of complexones to bind strongly heavy metal ions is used to inhibit the oxidation processes catalysed by these cations, which has served as a basis for the application of complexones as stabilisers and antioxidants, particularly in the chemical and pharmacological industries[6,7], biology, and preparative organic chemistry. The ability of complexones to form stable water-soluble complexes with metals (particularly those important for plants) led to their use as agents in the fight against chlorosis in certain agricultural crops[8]. Some complexones, for example ethylenediaminetetra-acetic and diethylenetriaminepenta-acetic acids, have found application as medicinal agents accelerating the elimination from the organism of toxic metals, including radioactive metals[9,10].

More than 30 years have elapsed since the first, parent substances of the class of complexones—nitrilotriacetic and ethylenediaminetetra-acetic acids—were obtained. During this period, a large number of similar compounds have been synthesised and investigated, as can be seen from the extensive monograph, review, periodical, and patent literature. Particular attention has been devoted to the study of the complex-forming capacity and practical applications of complexones. The problems of the synthesis and methods for the preparation of polyaminopolyacetic acids are dealt with in a number of reviews [11-14], which are clearly obsolete, and there is a short section in a recently published monograph by Dyatlova et al. [15]

The present review deals with methods for the preparation of only the "true" complexones, i.e. compounds containing one or several iminodiacetic acid groups in the molecule.

There are several ways of synthesising complexones, which can be divided into three groups. The methods of the first group are based on the reactions of various mono- or poly-amines with halogenoacetic acids or formaldehyde and cyanides, which may be combined by the term "carboxymethylation reaction". The second group embraces methods for the preparation of complexones in which the starting material is iminodiacetic acid or its esters. The third group comprises procedures for the preparation of complexones by the modification of the structural analogues or derivatives of iminodiacetic acid as well as other less common procedures.

II. THE CARBOXYMETHYLATION REACTION

This method is most widely used in the synthesis of complexones, since it is based on the employment of fairly readily available amines as the starting materials. The method for the synthesis of complexones by treating amines with halogenoacetate esters followed by hydrolysis of the esters [formed] is closely related.

The "indirect" carboxymethylation reaction—cyanomethylation with simultaneous or subsequent hydrolysis of the nitrile groups—has found fairly extensive applications in the synthesis of complexones.

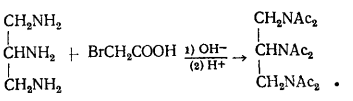
1. Alkylation of Amines by Monohalogenoacetic Acids

The "direct" carboxymethylation reaction is frequently used to prepare complexones under laboratory and industrial conditions. It takes place in accordance with the following mechanism:

$$R{-}NH_2 + HalCH_2COOH \xrightarrow{OH^-} RN(CH_2COO^-)_2 \xrightarrow{H^+} RNAc_2, \qquad (Ac = CH_2COOH)$$

The reaction consists in the treatment of the amine by a halogenoacetic acid in an alkaline medium. At the end of the reaction, the salt formed is converted into the complexone by acidification.

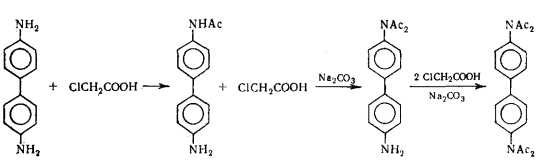
The carboxymethylating agent most frequently employed is the readily available monochloroacetic acid, which reacts with aliphatic and aromatic mono-, di-, and poly-amines, forming complexones in fairly high yields. In some cases, when the reaction with chloroacetic acid does not proceed, or does not proceed satisfactorily, monobromoacetic acid is used. Thus, when 1,2,3-triaminopropane was treated with chloroacetic acid, the corresponding hexa-acetic acid could not be obtained; the complexone (I) was obtained in a low yield by the reaction of the triamine with bromoacetic acid [16]:



(I)

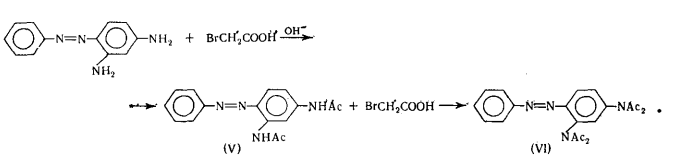
Much higher yields were obtained in the alkylation of 1-phenylethylenediamine and racemic 1,2-diphenylethylenediamine with bromoacetic acid than in the reaction with chloroacetic acid [17]. It follows from the literature data that bromoacetic acid is most frequently used for the carboxymethylation of aromatic amines [18-20]. The use of iodoacetic acid has also been reported [21]. The employment of iodide salts as additives in conjunction with chloroacetic acid, which leads to a more complete and rapid carboxymethylation reaction, has also been described [16,22]. For example, it has been shown [22] that the rate of reaction of aniline with chloroacetic acid increases by approximately 30% in the presence of potassium iodide.

For more complete substitution of the hydrogen atoms of the amino-groups, an excess of halogenoacetic acid, varying in the range 20–100% relative to the stoichiometric amount, is always used. The excess alkylating agent accelerates the reaction, ensures exhaustive carboxymethylation, and "meets the requirement" of the obligatory accompanying side reaction—the hydrolysis of the halogen in the halogenoacetic acid. When a deficiency of halogenoacetic acid is employed, it is possible to isolate products of the incomplete substitution of the amino-groups. Thus when benzidine is heated with one mole of chloroacetic acid in the absence of a condensing agent, benzidinemonoacetic acid (II) is formed [23]. When the reaction is carried out with two moles of the acid in the presence of sodium carbonate, the *NN*-diacetic acid (III) is obtained. On further treatment with chloroacetic acid and Na_2CO_3, the latter yields the tetra-acetic acid (IV):



(II) (III) (IV)

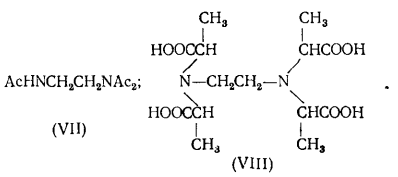
Crysoidinediacetic acid (V) was isolated as an intermediate when crysoidine was treated with bromoacetic acid in molar proportions of 1 : 6. The corresponding tetra-acetic acid (VI) was obtained by its reaction with bromoacetic acid [25]:



(V) (VI)

On carrying out the reaction of ethylenediamine with chloroacetic acid in molar proportions of 1 : 3 at a low temperature, Blackmer and Hamm [24] isolated ethylenediaminetriacetic acid (VII) from the reaction mixture in 36% yield and identified it in the form of the cobalt complex. The attempts to isolate this triacetic acid by other procedures proved unsuccessful [25,26]. When a large excess of the halogenoacetic acid is introduced into the carboxymethylation reaction, the isolation and purification of the final product may be hindered.

Apart from halogenoacetic acids, α-halogenopropionic acids may be used to synthesise complexones. Thus ethylenediaminetetra-(α-propionic) acid (VIII) was isolated in 15% yield after the reduction of ethylenediamine and α-chloropropionic acid[27]:



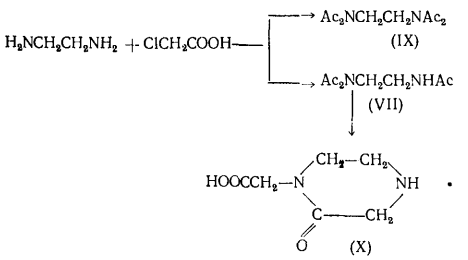
(VII) (VIII)

Together with the tetra-acetic acid (VII), di- and tri-substitution products were isolated from the reaction mixture, which indicates steric hindrance to exhaustive alkylation.

The carboxymethylation reaction is always carried out in the presence of bases in order to neutralise the initial halogenoacetic acid, capable of protonating the amine, and to prevent the protonation of the amino-groups during the reaction as a result of the liberation of the proton during alkylation. The protonated amino-group is incapable of reacting with the electrophilic alkylating agent. The use of a neutralising and condensing agent is particularly important in the carboxymethylation of aliphatic amines, since aromatic amines are protonated with much greater difficulty, being much weaker bases. Solutions of sodium hydroxide are frequently used as the condensing agent in the carboxymethylation of aliphatic and aliphatic-aromatic amines. The reaction is carried out at a constant pH (10–11) maintained by the gradual addition of alkali. The employment of sodium carbonates in the carboxymethylation of ethylenediamine has been described[28].

Since the reactions of aromatic and heteroaromatic amines with halogenoacetic acids are carried out at lower pH values (8–10), alkali metal carbonates[28–30] and even magnesium oxide[31] are frequently used together with the alkali. In a few instances, for example in the carboxymethylation of *p*-phenylenediamine[32], the reaction is carried out in the absence of a condensing agent.

As a rule, the alkylation with a halogenoacetic acid is performed in an aqueous medium, but, when amines readily soluble in water are to be alkylated, a solvent miscible with water is sometimes added, mainly acetone[33] and alcohol[34–36]. Several examples of the carboxymethylation reaction using aqueous suspensions of amines have been described[37,38]. The temperature and duration of the reaction are as a rule related. The carboxymethylation of aliphatic and aliphatic-aromatic amines proceeds fairly rapidly (3–10 h) at 40–95°C. An increase of temperature promotes a more complete substitution of the nitrogen atoms, but side reactions are intensified at the same time. A decrease of temperature requires an appreciable increase of the reaction time and incomplete substitution products are then detected in the reaction mixture together with the fully carboxymethylated amines. Genik-Sas-Berezowsky and Spinner[39] investigated in detail the reaction of ethylenediamine with chloroacetic acid at room temperature. After allowing the reaction system to stand for 8 days, they isolated a complex mixture of products consisting largely of ethylenediaminetetra-acetic acid (IX) and ethylenediaminetriacetic acid (VII); the latter cyclised during the reaction to the lactam (X):

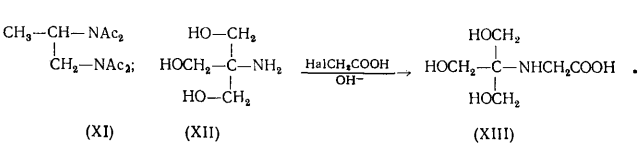


On the other hand, it has been shown[40] that, when racemic propylenediamine is heated with chloroacetic acid, the expected tetra-acetic acid (XI) is formed in an insignificant yield, while the reaction carried out in the course of 6 days at 20°C gives an 82% yield of the complexone (XI).

The carboxymethylation of aromatic amines is usually carried out at a higher temperature (of the order of 80–110°C) in order to increase the reaction rate. The duration of the process does not then exceed 4–10 h.

The main reaction, the alkylation of the amines to synthesise complexones by direct carboxymethylation, is to a greater or lesser extent accompanied by side processes, which may have a significant influence on the yield and purity of the final products. The main secondary and competing reaction is the hydrolysis of the halogenoacetic acid in an alkali medium, which reduces the concentrtion of the alkylating agent. This reaction, occurring simultaneously with the main process, is promoted by an increase of temperature and of alkalinity. Together with the hydrolysis of the halogenoacetic acid, the carboxymethylation reaction may involve other side processes, for example the formation of incomplete carboxymethylation products. Apart from temperature and the insufficiency of the alkylating agent, the degree of formation of these side products may be influenced by the structural characteristics of the amines, preventing their exhaustive methylation at the amino-group.

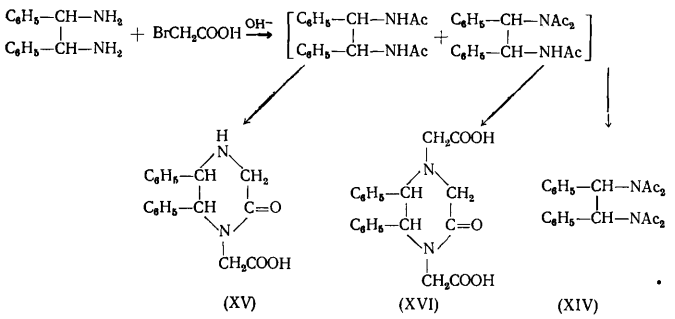
In the carboxymethylation of tri(hydroxymethyl)aminomethane (XII) with chloro- and bromo-acetic acids, it was not possible to introduce two acetic acid residues into the amino-group[41] despite the modification of the reaction conditions; only the monocarboxymethylation product, namely tri(hydroxymethyl)sarcosine (XIII), was always isolated from the reaction mixture:



(XI) (XII) (XIII)

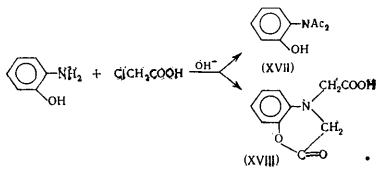
It has been observed[17] that, in contrast to racemic 1,2-diphenylethylenediamine, the meso-analogue reacts with bromoacetic acid with much difficulty, forming only traces of the tetra-acetic acid (XIV). In this case the main reaction products were the lactams (XV) and (XVI),

formed by the cyclisation of the products of the incomplete carboxymethylation of the diamine:



(XV) (XVI) (XIV)

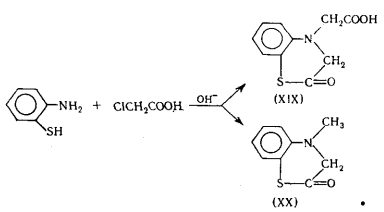
The carboxymethylation reaction may be in many instances complicated by the presence in the molecule of the initial amine of other functional groups or groupings. Thus, when *o*-aminophenol is treated with chloroacetic acid at pH 8–10, the δ-lactone (XVIII) is formed together with *o*-hydroxyphenyliminodiacetic acid (XVII):[42]



(XVII) (XVIII)

The extent of the latter reaction may be reduced by adding potassium iodide to the reaction mixture[22], which makes it possible to perform the process at a lower pH and reduce thereby the reactivity of the phenolic hydroxyl.

The carboxymethylation of *o*-aminothiophenol proceeds in a more complex manner. On treatment with chloroacetic acid (60°C, pH 8–10), the thiolactone (XIX) was isolated from the reaction mixture together with its decarboxylation product (XX):[42]

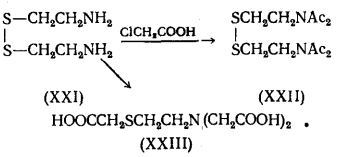


(XIX) (XX)

In the amino-β-naphthol series, it was impossible to obtain the corresponding complexone, since naphthoxy-acids are formed under the conditions of "direct" carboxymethylation.

In order to prevent the possible alkylation of the glycolic hydroxyls in 2,3-dihydroxypropylamine, the latter was carboxymethylated at pH < 9 at room temperature[41].

When di(aminoethyl) disulphide (XXI) was carboxy-methylated under the conditions leading to the formation of complexones from aliphatic diamines, the expected tetra-acetic acids (XXII) were not isolated[44]. The only reaction product was the triacetic acid (XXIII), the formation of which takes place, according to the authors, as a result of the cleavage of the disulphide linkage in the alkaline medium and alkylation of the nitrogen and sulphur atoms:



(XXI) (XXII)

$HOOCCH_2SCH_2CH_2N(CH_2COOH)_2$ (XXIII)

This process could not be prevented even by employing oxidising agents. Only when the reaction was carried out in a neutral medium was the previously described[45] tetra-acetic acid (XXII) obtained, but its yield was low.

The mechanism and kinetics of the carboxymethylation reaction have been studied in relation to the interaction of aqueous ammonia with chloro- and bromo-acetic acids[46]. In the first place, it was observed that the rate of reaction of bromoacetic acid with ammonia at 60°C is 26–40 times faster than with the chloroacetic acid. It was found[46] that the reaction proceeds consecutively via an S_N2 mechanism and its maximum rate is reached at pH 10–11. It has been shown that glycine reacts approximately ten times more vigorously with chloroacetic acid than does ammonia:

$$NH_3 \xrightarrow{HalCH_2COOH} H_2NCH_2COOH \xrightarrow{HalCH_2COOH} HN(CH_2COOH)_2 \xrightarrow{HalCH_2COOH} N(CH_2COOH)_3.$$

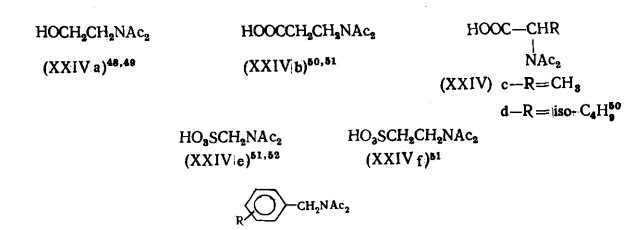
Continuing the investigation of the mechanism of the carboxymethylation reaction, Temkina[22] confirmed the consecutive mechanism of the process in relation to methylamine and aniline. She found that the rate-limiting stage of the reaction is the addition of the first carboxy-methyl group.

The "direct" carboxymethylation reaction is applicable to a wide variety of amino-compounds. The reaction of chloroacetic acid with ammonia proceeds smoothly and leads to the formation of nitrilotriacetic acid (NAc_3). Under the same conditions, hydrazine leads to hydrazine-*NN*-diacetic acid[30]; semicarbazide-*NN*-diacetic acid ($NH_2CONHNAc_2$) is obtained similarly[30].

A series of *N*-alkyl-derivatives of iminodiacetic acid, from the methyl derivatives to the $C_{15}H_{31}$ analogue, have been synthesised by the "direct" carboxymethylation reaction[35,47].

The preparation of certain derivatives of alkylimino-diacetic acid (XXIV, a – f), containing functional groups in the alkyl chain, by the reaction of the corresponding substituted alkylamines with chloro- or bromo-acetic acid, has been described[48–52].

The "direct" carboxymethylation method has been used successfully to synthesise cyclohexyl derivatives (XXV, a and b)[42,53], benzyl derivatives (XXVI, a –g)[50,54–57], and phenylethyl derivatives (XXVII)[50,58,59] of iminodiacetic acid and also to synthesise heterocyclic complexones (XXVIII, a – i)[33,37,60–63] with a single iminodiacetic acid group. These complexones are listed below (together with the appropriate references):



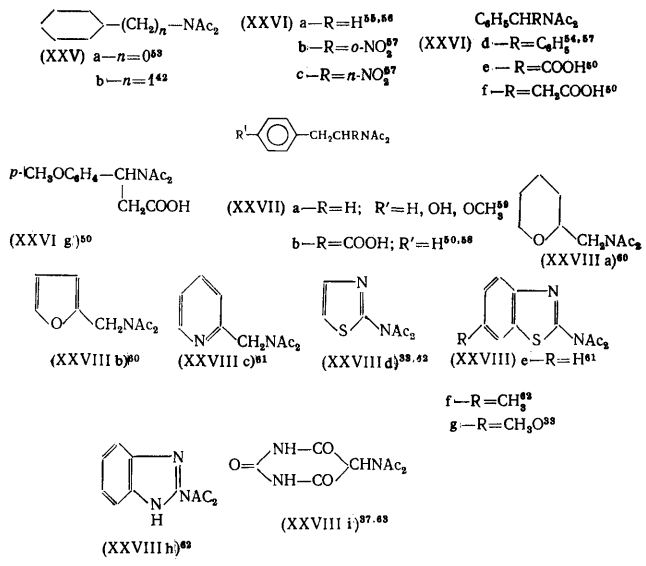
$HOCH_2CH_2NAc_2$ (XXIV a)[48,49]

$HOOCCH_2CH_2NAc_2$ (XXIV b)[50,51]

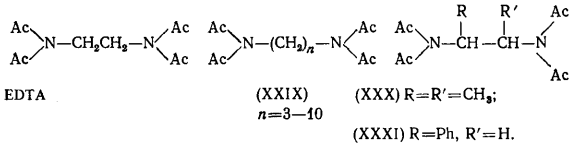
HOOC—CHR | NAc_2 (XXIV) c–R=CH_3 d–R=iso-C_4H_9[50]

$HO_3SCH_2NAc_2$ (XXIV e)[51,52]

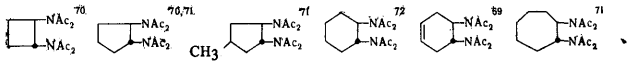
$HO_3SCH_2CH_2NAc_2$ (XXIV f)[51]



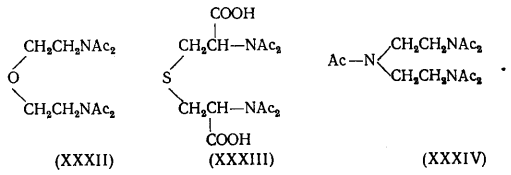
A large number of examples of the synthesis of complexones by the direct carboxymethylation of aliphatic amines have been described in the periodical and patent literature. Ethylenediaminetetra-acetic acid (EDTA)[64,65], its homologues with hydrocarbon chain lengths ranging from 3 to 10 (XXIX)[54,66,67], as well as derivatives with methyl [(XI)[40] and (XXX)[68]] and aryl [(XIV)[17] and (XXXI)[69]] substituents in the ethylene chain:



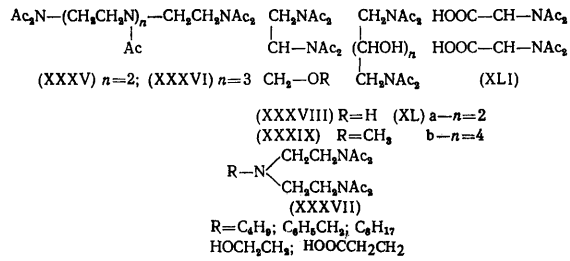
A series of cyclic analogues of EDTA have been obtained by the condensation of alicyclic 1,2-diamines with chloro- and bromo-acetic acids[69-72]:



The direct carboxymethylation method has found extensive applications in the synthesis of analogues of ethylenediaminetetra-acetic acid containing heteroatoms or functional groups in the hydrocarbon chain. In contrast to di(aminoethyl) disulphide (see above), the carboxymethylation of the corresponding ether to (XXXI)[72] and the sulphide with carboxy-groups to (XXXIII)[74] proceeds normally:

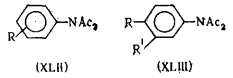


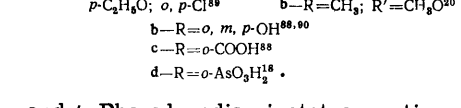
The EDTA analogues with amino-groups in the hydrocarbon chain have attracted much attention in view of their high complex-formation capacity. The direct carboxymethylation method has proved extremely convenient for the synthesis of diethylenetriaminepenta-acetic acid (XXXIV)[74]—one of the most effective complexones, which has found applications in engineering, medicine, and agriculture[5]. Its higher homologues triethylenetetraaminehexa-acetic acid (XXXV) and tetraethylenepentaaminehepta-acetic acid (XXXVI) have been synthesised by the same method[75]. *N*-Substituted diethylenetriaminetetraacetic acids (XXXVII) have been obtained in fairly high yields from the corresponding diamines and chloroacetic acid[76-79]:



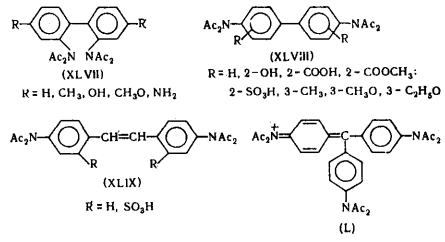
The carboxymethylation of di- and tri-amines containing hydroxy-groups in the hydrocarbon chain takes place smoothly. 2,3-Diamino-1-hydroxypropanetetra-acetic acid (XXXVIII) and 2,3-diamino-1-methoxypropanetetra-acetic acid (XXXIX)[80], racemic 1,4-diamino-2,3-dihydroxybutanetetra-acetic acid and its *meso*-form (XLa)[81-83], D-*manno*-1,6-diamino-1,6-dideoxy-2,3,4,5-tetrahydroxyhexanetetra-acetic acid (XLb)[84,85], and *N*-hydroxyethyldiethylenetriaminetetra-acetic acid (XXXVII, R = $HOCH_2CH_2$)[86] have been obtained by the same method. Side reactions involving the hydroxy-groups were never observed under these conditions. The formation of the EDTA analogue (XLI) containing carboxy-groups at the carbon atoms in the chain has been described[87] and 1,2,3-triaminopropanehexa-acetic acid, mentioned above, has been synthesised by the same method.

A large number of examples of the preparation of aryliminodiacetic acids with various substituents in the benzene ring [compounds (XLII) and (XLIII)] have been described[18,20,42,88-90]. The complexones with the appropriate references are indicated below:

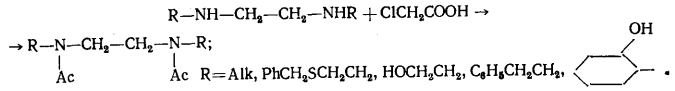




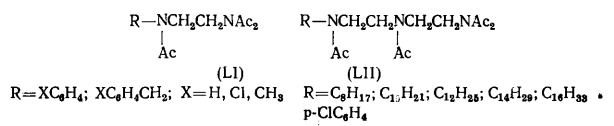
o-, *m*-, and *p*-Phenylenediaminetetra-acetic acids (XLIV)[91], (XLV, a and b)[23,92,93], and (XLVI, a and b)[21,22,94], a series of diaminobiphenyltetra-acetic acids (XLVII)[34] and (XLVIII)[25,95] and diaminostilbenetetra-acetic acids (XLIX)[38,96], as well as a complexone of the triphenylmethane series (L)[97] have been synthesised by the same method:



The carboxymethylation reaction has been used to prepare analogues of ethylenediamine-*NN'*-diacetic acid with various substituents at the nitrogen atom[58,98-100]:

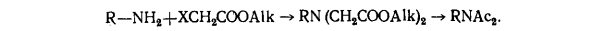


The simultaneous carboxymethylation and arylalkylation or arylation of ethylenediamine, resulting in the formation of EDTA analogues of type (LI), has been described[101]:



Similar compounds have been synthesised also from diethylenetriamine, for example (LII)[102,103].

In many cases halogenocarboxylate esters are used instead of the acids themselves. This makes it possible to carry out the reaction in a non-aqueous medium in the absence of alkalis. The iminodiacetate esters thus obtained are converted into the corresponding complexones by hydrolysis:



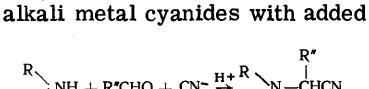
The reaction is carried out as a rule with ethyl monobromoacetate in the absence of a solvent or in alcohol in the presence of potassium carbonate[48]. The esters formed can be purified by distillation. This fact and also the mild reaction conditions make this method very convenient for the synthesis of aliphatic complexones in those cases where an aqueous alkaline medium must be avoided.

2. The Cyanomethylation Reaction

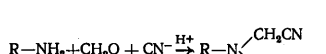
Another method for the carboxymethylation of amines is based on the cyanomethylation reaction. Several versions of this method are used in the synthesis of complexones.

1. Cyanomethylation in an acid medium with formation of the corresponding iminodiacetonitriles and their subsequent conversion into the acids.
2. Cyanomethylation in an alkaline medium with simultaneous hydrolysis of the nitrile groups.
3. Cyanomethylation with the aid of glycolonitrile followed by hydrolysis of the nitrile formed.

Cyanomethylation in an acid medium. This reaction has been known for a long time as the "Strecker reaction"[104] and is widely used in the synthesis of a large variety of aminoacetonitriles[105]. It is based on the reaction of primary or secondary aliphatic amines with aldehydes and hydrocyanic acid. The latter may be replaced by alkali metal cyanides with added acid:



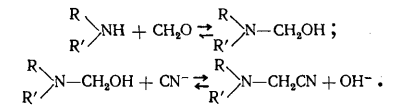
Complexones are synthesised by a specific example of this reaction—the reaction of primary mono-, di-, and poly-amines with formaldehyde and hydrocyanic acid (or its salts in an acid medium) with substitution of both hydrogen atoms in the amino-group by cyanomethyl residues:



The reaction is usually carried out in an aqueous medium at 0–20°C for several hours at pH 1–6.5. Since the use of liquid hydrocyanic acid is relatively inconvenient, sodium or potassium cyanides are usually employed and the added acids are hydrochloric, sulphuric, phosphoric, acetic, or formic acids[106].

The aminonitriles formed in the reaction may be isolated from the reaction mixture and hydrolysed. When water-soluble nitriles are obtained, they are converted into acids without isolation. The hydrolysis of iminodiacetonitriles proceeds most smoothly on heating with alkali or barium hydroxides. Inorganic acids are used for this purpose less frequently.

According to current ideas, the cyanomethylation of amines proceeds via a stage involving the formation of hydroxymethyl derivatives:

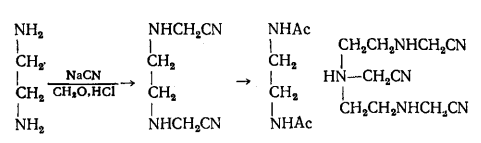


Di(cyanomethyl) derivatives are probably formed in a similar manner.

The introduction of a single cyanomethyl residue into both aliphatic and aromatic primary amines proceeds readily and smoothly. However, the substitution of a second hydrogen atom by the cyanomethyl group is much more difficult, owing to the sharp reduction of the basicity of the monocyanomethylated amino-group[107].

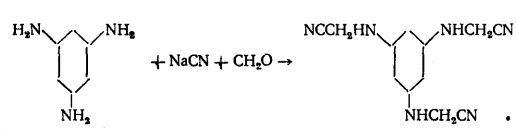
The cyanomethylation reaction is therefore most widely used in the synthesis of aliphatic complexones. However, in this case too the reaction may be stopped at the first substitution stage. The resulting monocyanomethylamines are converted after hydrolysis into complexone analogues—glycine derivatives. In this respect the cyanomethylation reaction has an advantage over direct carboxymethylation, which cannot as a rule yield amine monosubstitution products.

When ethylenediamine is treated with two moles of sodium cyanide and formaldehyde in hydrochloric acid, ethylenediamine-*NN'*-di(acetonitrile) (LIII) is obtained in a high yield and after hydrolysis gives rise to ethylenediamine-*NN'*-diacetic acid (LIV), which is the starting material for the synthesis of complexones[39,108-110]:



The *NN'N"*-tricyanomethyl derivative (LV) has been synthesised by treating diethylenetriamine with three moles of hydrocyanic acid and formaldehyde[110].

Having treated *cis*, *cis*-1,3,5-triaminocyclohexylamine with sodium cyanide in alcoholic hydrochloric acid, Zompa and Shindler[111] obtained the corresponding tri(aminoacetonitrile) (LVI):

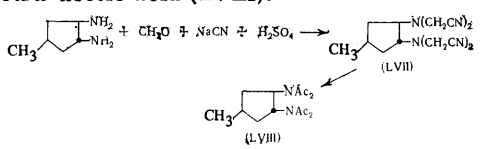


A series of iminodi(acetonitrile) derivatives with aliphatic[45,48] and aliphatic-aromatic[111] substituents have been obtained by the cyanomethylation reaction in an acid

medium. Several examples of the synthesis by this method of cyanomethylated di-, and poly-amines, which were converted by hydrolysis into complexones of the type of ethylenediaminetetra-acetic and diethylenetriaminepenta-acetic acids [112-114], including tetra-acetic acids containing a hydroxy-group [compound (XXXVIII)] [80] or heteroatoms [(compound (LVII)] in the chain joining the two imino-diacetic acid groups have been described [45]:

$$Ac_2NCH_2CH_2—X—CH_2CH_2—NAc_2$$
$$X=CH_3N;\ S—CH_2CH_2—S;\ —N(CH_3)—CH_2CH_2—N(CH_3)—$$

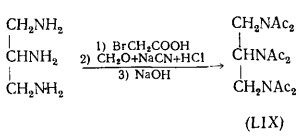
"Acid" cyanomethylation is used in those cases where the synthesis of aliphatic complexones by "direct" carboxymethylation involves difficulties. Thus, when *trans*-1,2-diamino-3-methylcyclopentane was treated with chloroacetic acid, the corresponding tetra-acetic acid could not be isolated [71]. The cyanomethylation of this diamine gave a 32% yield of the tetranitrile (LVII), which was then hydrolysed to *trans*-1,2-diamino-3-methylcyclo-pentanetetra-acetic acid (LVIII):



(LVII)

(LVIII)

It was already mentioned above that, when 1,2,3-triaminopropane is treated with bromoacetic acid, the corresponding hexa-acetic acid (LIX) is formed in a low yield [16]; the authors succeeded in synthesising this complexone in 84% yield by treating the reaction mixture (after carboxymethylation) with formaldehyde and sodium cyanide in an acid medium and subsequent hydrolysis:

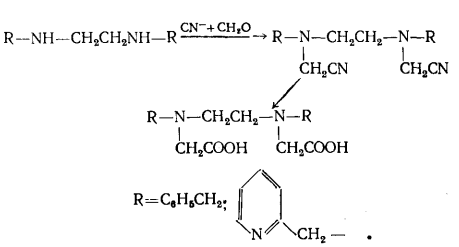


(LIX)

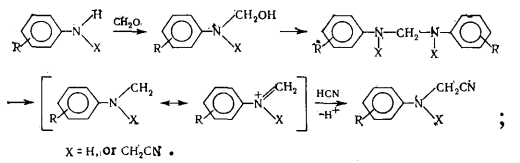
The cyanomethylation reaction in an acid medium has been used to synthesise complexones and their analogues from aliphatic secondary amines. Schwarzenbach et al. [48] synthesised cyanomethyliminodiacetic acid by treating iminodiacetic acid with formaldehyde and sodium hydroxide in hydrochloric acid:

$$HN(CH_2COOH)_2 + NaCN + CH_2O + HCl \rightarrow NCCH_2NAc_2.$$

The synthesis of *NN'*-di(carboxymethyl) derivatives of ethylenediamine by cyanomethylation in an acid medium has been described [115]:



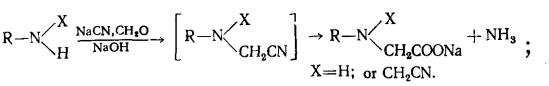
Satisfactory results were obtained in the cyanomethylation of ammonia in an acid medium; this results in the formation of a high yield of tri(cyanomethyl)amine, which is converted into nitrilotriacetic acid by hydrolysis with alkali [116-120]. Being weaker bases, aromatic amines enter into the cyanomethylation reaction with greater difficulty than aliphatic and aliphatic-aromatic amines. The introduction of the second cyanomethyl residue requires the use of glacial acetic acid as the solvent and formaldehyde must be replaced by paraformaldehyde [121,122]. However, this method is suitable only for aniline derivatives without electronegative substituents. Derivatives containing such substituents must be di(cyanomethylated) in the presence of a catalyst—zinc chloride [121]. It is suggested [122] that the cyanomethylation of aromatic amines proceeds in accordance with the following mechanism:



X = H, or CH_2CN.

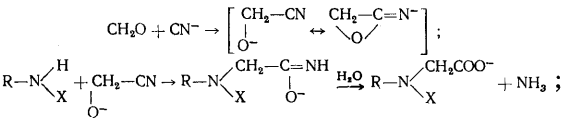
Under the above conditions, arylaminodiacetonitriles can be obtained in 60-90% yield.

Cyanomethylation in an alkaline medium. The cyanomethylation of amines can be carried out by heating in an alkaline medium [123-130]. Under these conditions, the acetonitriles formed are hydrolysed to the corresponding acids with evolution of ammonia:



X=H; or CH_2CN.

If the ammonia is not removed from the reaction mixture, it is cyanomethylated with formation of nitrilo-triacetonitrile and then nitrilotriacetic acid [126,131]. In order to avoid this side reaction, a method was developed in which the cyanomethylating components are introduced periodically with subsequent repeated distillation of ammonia at a reduced pressure during the reaction [124,130,132]. It has been suggested that the cyanomethyl derivatives are not formed in an alkalkine medium, the initial products of the reaction of the cyanide and formaldehyde being glycolo-nitrile or its salts, the subsequent interaction of which with the amine immediately leads to the formation of the iminodiacetate salt [124-126]:



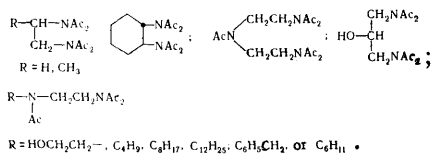
X=H, or CH_2CN X=H; or CH_2COO^-.

It is suggested that the alkalinity of the medium is necessary for the formation of the glycolonitrile alkoxide ion, which catalyses the cyanomethylation reaction [133].

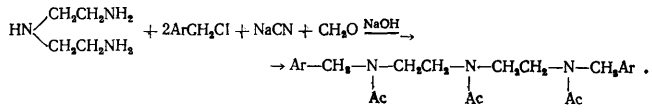
The yield of polyaminopolycarboxylic acids obtained by this procedure is nearly quantitative when ammonia is rapidly eliminated and the cyanomethylating agents are introduced slowly [134]. As in acid cyanomethylation, in this case it is also possible to carry out the process in a single stage, i.e. one carboxymethyl group may be introduced at each nitrogen atom. It has been found [108,109] that the optimum conditions for this process obtain when the pH of the reaction medium is maintained at approximately 9. Cyanomethylation in an alkaline medium proved to be a convenient procedure for the synthesis of ethylene-diamine-*NN*-diacetic acid (LIV), mentioned above [108,109,135]. Its analogues and derivatives can be synthesised similarly [101,108,109,124].

Although the synthesis by the alkaline cyanomethylation method of complexones with a single iminodiacetic acid

group, for example nitrilotriacetic acid [131], butyl- and cyclohexyl-iminodiacetic acids [130], and ethyl- and hydroxyethyl-iminodiacetic acids [127], has been described, in the main this method is used to synthesise polyamino-polycarboxylic acids [109,124,130,132,136]. Complexones obtained by this method are indicated below:

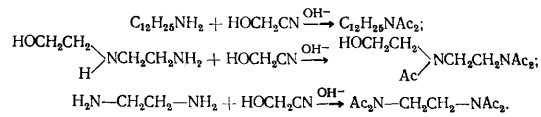


As for direct carboxymethylation, the use of alkaline cyanomethylation simultaneously with arylalkylation of polyamines for the synthesis of complexones with aryl substituents has been described [102,137], for example:



Satisfactory results were obtained when alkaline cyanomethylation was used in the synthesis of arylimino-diacetic acids: *o*-carboxyphenyliminodiacetic acid [127] and certain naphthalene complexones [22,43,76,90,138] have been synthesised in fairly high yields.

A very interesting modification of the cyanomethylation reaction involves treating amines with glycolonitrile [139,140]. The reaction is carried out at pH 11–12 in an aqueous medium heated to 90°C. It has been shown for dodecylamine, ethylenediamine, and hydroxyethylethylenediamine as examples that the corresponding complexones are obtained in nearly quantitative yields under these conditions [139]:



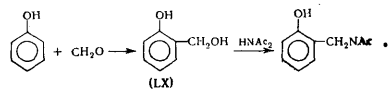
III. THE SYNTHESIS OF COMPLEXONES FROM IMINODIACETIC ACID AND ITS ESTERS

This group of methods combines two procedures for the synthesis of complexones: 1. The reaction of iminodiacetic acid with phenols and formaldehyde (the Mannich reaction). 2. The condensation of iminodiacetic acid and its esters with halogeno-derivatives.

The Mannich Reaction

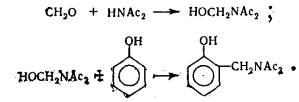
The reaction of iminodiacetic acid with phenols and formaldehyde is a special case of the Mannich reaction [141]. It is usually carried out in acetic acid (pH 2–3) at 5–10°C [87,142,143], but it can also be performed in an alkaline medium at pH ≤ 10. [87,144] The reactants are usually introduced into the reaction in equimolar amounts [87].

It has been suggested [22] that the first stage of this reaction, carried out in an aqueous medium, is the formation of the phenolic alcohol (LX), which then interacts with iminodiacetic acid, the process being accompanied by the elimination of water:



(LX)

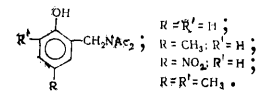
However, there is no direct evidence for this mechanism and one cannot therefore rule out the possibility that the process can also proceed via a different mechanism:



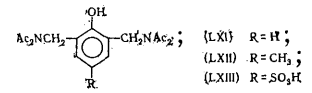
The problem of the mechanism of the Mannich reaction still continues to be controversial; views have been expressed in the literature concerning the above two mechanisms of this reaction [145,146].

The formation of complexones in both acid and alkaline media is accompanied by side reactions leading to the formation of various admixtures and side products, caused mainly by the oxidation of phenols and the interaction of the latter with formaldehyde, leading to the formation of phenol-formaldehyde oligomers and polymers, methylene-bisphenol compounds, phenolic poly(hydroxymethyl) derivatives, etc.

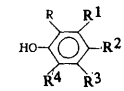
Not only phenol itself [145], but also its methyl and other derivatives [87,142,144,147–149] react with iminodiacetic acid, the methyleneiminodiacetic acid group always entering the *ortho*-position with respect to the hydroxy-group:



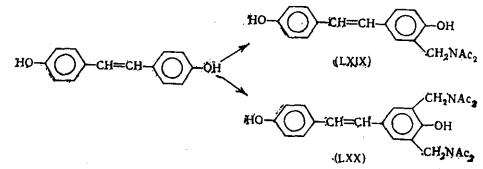
Interesting studies on the application of the Mannich reaction in the synthesis of complexones have been carried out by Temkina and coworkers [76,140,142,143,150–152]. They showed that phenol and *p*-cresol can form di(methyliminodiacetic) acid derivatives (LXI) and (LXII) [142,148]. The analogous compound (LXIII) has been obtained from *p*-hydroxybenzenesulphonic acid [153–156]:



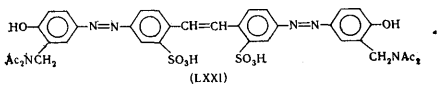
The same workers succeeded in introducing dihydric phenols and even phloroglucinol into the Mannich reaction with iminodiacetic acid [150–152]. It has been shown (Table 1) that the complexones formed under these conditions have the following structure [compounds (LXIV)–(LXVIII)]:



More complex phenolic compounds also undergo the Mannich reaction. Interesting results have been obtained for the reaction of iminodiacetic acid and formaldehyde with dihydroxystilbene [157]. For equimolar reactant ratios, the product is the monosubstituted derivative (LXIX); a second methyleneiminodiacetic acid group enters the same ring compounds (LXX):



The substitution in stilbenediazo-derivatives involves both benzene rings, containing a phenolic hydroxyl, with formation of a symmetric product (LXXI) [158]:



(LXXI)

Table 1.

Compound	R	R^1	R^2	R^3	R^4
(LXIV)	$CH_2N(CH_2COOH)_2$	H	OH	H	H
(LXV)	$CH_2N(CH_2COOH)_2$	H	OH	$CH_2N(CH_2COOH)_2$	H
(LXVI)	OH	$CH_2N(CH_2COONa)(CH_2COOH)$	H	H	H
(LXVII)	$CH_2N(CH_2COOH)_2$	OH	H	H	H
(LXVIII)	OH	$CH_2N(CH_2COOH)_2$	OH	H	H

Complexones have been synthesised by the Mannich reaction from indophenol and its derivatives (LXXII) and (LXXXIII) [159-166] (Table 2):

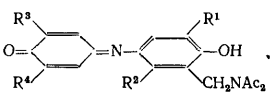
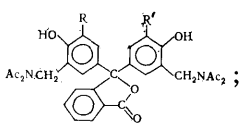


Table 2.

Compound	R^1	R^2	R^3	R^4	Compound	R^1	R^2	R^3	R^4
(LXXII)	H	H	Cl	Cl	(LXXVIII)	C_2H_5	CH_3	Cl	Cl
(LXXIII)	H	H	Br	Br	(LXXIX)	C_2H_5	CH_3	Br	Br
(LXXIV)	CH_3	H	Cl	Cl	(LXXX)	OCH_3	H	Cl	Cl
(LXXV)	CH_3	H	Br	Br	(LXXXI)	OCH_3	H	Br	Br
(LXXVI)	CH_3	CH_3	Cl	Cl	(LXXXII)	H	CH_3	Cl	Cl
(LXXVII)	CH_3	CH_3	Br	Br	(LXXXIII)	H	CH_3	Br	Br

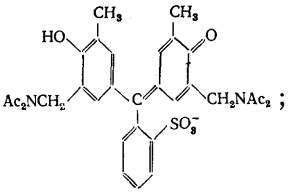
The methods for the introduction of methyleneiminodiacetic acid groups in the synthesis of complexones from phthalein indicators have acquired particular importance. More than 50 compounds of this kind, forming coloured complexes with different metals, have been synthesised by this procedure. Because of this, some of them are used as metalloindicators [1, 167].

The first complexone of this type was 3,3-di-(*NN*-dicarboxymethylaminomethyl)-*o*-cresolphthalein (LXXXIV), synthesised by Schwarzenbach and coworkers, which has been called "phthalein complexone" [144]:

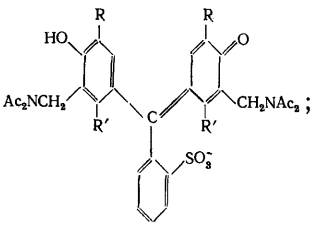


(LXXXIV) R=CH_3; R′=H;
(LXXXV) R=R′=H;
(LXXXVI) R=$(CH_3)_2CH$; R′=CH_3.

The method for the synthesis of metalloindicators was developed further by Korbl and coworkers [159,160,162,165,168]. They synthesised the phthalein complexone analogues (LXXXV) and (LXXXVI) [168] as well as methyleneiminodiacetic acid derivatives of sulphophthalein (LXXXVII) [169], (LXXXVIII), and (LXXXIX) [159,160,162,165]:

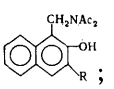


(LXXXVII)



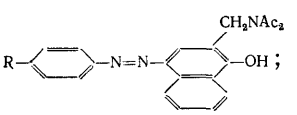
(LXXXVIII) R=CH_3; R′=H;
(LXXXIX) R=$(CH_3)_2CH$; R′=CH_3.

The aminomethylation reaction can also be used to obtain complexones from condensed phenols. β-Naphthol reacts smoothly with iminodiacetic acid and formaldehyde, forming an α-substituted derivative of methyleneiminodiacetic acid (XCa) [147, 152]. (3-Carboxy-2-hydroxy-1-naphthyl)methylenediacetic acid (XCb) has been synthesised in a high yield [170]:



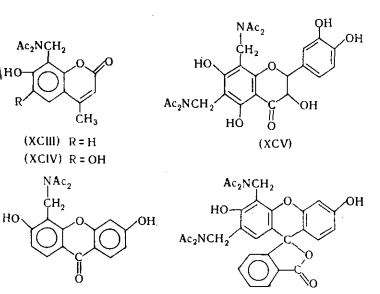
(XC) a - R = H; b - R = COOH.

Complexones based on napthalene analogues [compounds (XCI) and (XCII)] have been synthesised similarly to indophenol derivatives [171]:



(XCI) R=NO_2;
(XCII) R=SO_3H.

More complex condensed phenols containing a hydrogen atom in the *o*-position also react with iminodiacetic acid and formaldehyde. The synthesis by this method of fluorescent indicators—iminodiacetic acid derivatives of coumarone [compounds (XCIII) and (XCIV)] [172-174], flavone (XCV) [175], and xanthone (XCVI) [172] has been described:



(XCIII) R=H
(XCIV) R=OH
(XCV)
(XCVI)
(XCVII)

The complexone (XCVII) has been synthesised from fluorescein [176]. Initially a symmetrical structure was attributed to this compound [176-178], but subsequently it

was established that both methyleneiminodiacetic acid groups are in the same benzene ring[153,155].

NN-Di(carboxymethylaminomethyl)anthraquinone derivatives (XCVIII)–(CII) [179] have also been obtained with the aid of the Mannich reaction (Table 3):

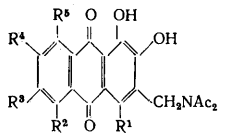
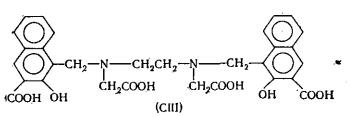


Table 3.

Compound	R^1	R^3	R^5	R^4	R^5
(XCVIII)	H	H	H	H	H
(XCIX)	H	OH	H	H	H
(C)	H	H	OH	H	H
(CI)	H	H	H	OH	H
(CII)	H	OH	H	H	OH

An attempt has been made, with 2-hydroxy-3-naphthoic acid as an example, to use ethylenediamine-*NN'*-diacetic acid as the amino-component in the Mannich reaction[170], but the expected complexone (CIII) was obtained in a yield not exceeding 20%, despite the employment of copper salts as the catalyst:



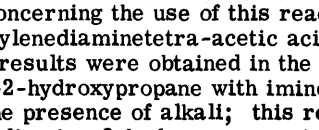
(CIII)

The main reaction product was the corresponding diarylmethane. The complexone (CIII) was obtained in a higher yield by the condensation of chloromethyl-2-hydroxy-3-naphthoic acid with ethylenediamine-*NN'*-diacetic acid[170].

The Reaction of Iminodiacetic Acid and Its Esters with Halogeno-Derivatives

The reaction of iminodiacetic acid with halogeno-derivatives is carried out in an aqueous medium at pH 8.5–9 and a temperature of 40–100°C. Alkali or carbonates may be used as condensing agents. There are potent data[180] concerning the use of this reaction for the synthesis of ethylenediaminetetra-acetic acid.

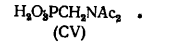
Satisfactory results were obtained in the condensation of 1,3-dichloro-2-hydroxypropane with iminodiacetic acid (80°C, 5 h) in the presence of alkali; this resulted in the isolation of 1,3-diamino-2-hydroxypropanetetra-acetic acid (CIV) in 52% yield.[181] It was not possible to obtain the tetra-acetic acid by this procedure from *d*- and 1,6-dichloro-1,6-dideoxymannitol[85]:



(CIV)

The synthesis of the tetra-acetic acid (CIV) by treating 2-chloromethyloxiran with iminodiacetic acid has been described recently[182]. Certain analogues of compound (CIV) have been synthesised by this method[182,183].

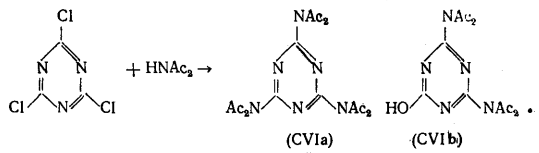
When iminodiacetic acid was treated with chloromethylphosphonic acid (20°C, pH 10–11, 8 days), the complexone (CV) was synthesised[184]:



(CV)

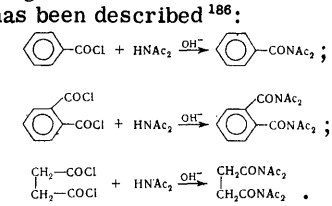
The application of this method to the synthesis of iminodiacetic acid derivatives of triazine proved successful. Thus the corresponding hexa-acetic acid (CVIa) was synthesised by the reaction of cyanuryl chloride with iminodiacetic acid in the presence of an aqueous solution of sodium hydroxide[185].

The tetra-acetic acid (CVIb) was synthesised similarly from 4,6-dichloro-2-hydroxytriazine[185]:

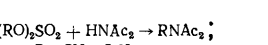


(CVIa) (CVIb)

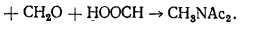
The condensation of the chlorides of benzoic, succinic, and phthalic acids with iminodiacetic acid in an alkaline medium, resulting in the formation of the corresponding complexones, has been described[186]:



Alkyl sulphates have been used frequently in place of halogeno-derivatives for the alkylation of iminodiacetic acid[187]:

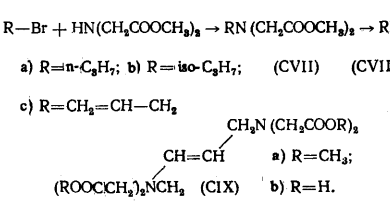


The methylation of iminodiacetic acid by the Hess method has also been described[45]:



When halogeno-compounds are allowed to react with iminodiacetic acid, there is a difficulty involving the elimination of the initial iminodiacetic acid from the final product. To avoid this, the halogeno-derivatives may be condensed with iminodiacetate esters with subsequent hydrolysis of the ester group in an alkaline medium.

The conditions governing the synthesis of *N*-alkyliminodiacetate esters have been investigated in detail in relation to the reactions of propyl, isopropyl, and allyl bromides with dimethyl iminodiacetate[188]. It has been found that best results are obtained when alcohols isopropyl alcohol and ethylene glycol) are used as solvents and the condensing agent is the iminodiacetate ester itself. Iminodiacetate esters (CVII) are obtained most readily by this method and with a high yield from alkyl or arylalkyl derivatives with a mobile (allyl or benzyl) halogen: dimethyl allyliminodiacetate (CVIIc) was obtained in a yield of about 80%; the yield of tetramethyl *trans*-1,4-diaminobut-2-enetetra-acetate (CIXa) was somewhat lower:



(CVII) (CVIII)

(CIX)

The acids (CVIII) and (CIXb) were obtained smoothly from the esters.

Shtacher and Taub [189] described the synthesis by this method of a whole series of aliphatic-aromatic derivatives of iminodiacetic acid (CX). The authors hydrolysed the resulting diesters with sodium hydroxide or lithium hydroxide (in the case of readily soluble acids):

$$\underset{\text{(CX)}}{R{-}NAc_2}$$

$R = C_6H_5CH_2$; p-$FC_6H_4CH_2$; p-$IC_6H_4CH_2$; 3-OH-4-$BrC_6H_3CH_2$;

$C_6H_5CH_2CH_2$; p-$FC_6H_4COCH_2$; p-$BrC_6H_4COCH_2$; m-$BrC_6H_4COCH_2$;

$C_6H_5OCH_2CH_2$; p-$FC_6H_4OCH_2CH_2$ p-$BrC_6H_4OCH_2CH_2$;

p-$BrC_6H_4NHCOCH_2$; p-$FC_6H_4NHCOCH_2$.

Several alkyl derivatives of iminodiacetic acid with substituents in the hydrocarbon chain have been synthesised by the condensation of halogeno-derivatives with iminodiacetates [48]. Thus dimethyl cyanomethyliminodiacetate (CXI) was obtained in a high yield by the reaction of chloroacetonitrile with dimethyl iminodiacetate without solvent at room temperature. By hydrolysis with zinc perchlorate, it was converted via the zinc salt into cyanomethyliminodiacetic acid (LIX) [48]:

$$NCCH_2Cl + HN(CH_2COOCH_3)_2 \rightarrow NCCH_2N(CH_2COOCH_3)_2 \rightarrow$$
$$\rightarrow \left[NCCH_2N\begin{matrix}CH_2COO^-\\CH_2COO^-\end{matrix}\right]Zn^{2+} \rightarrow \underset{\text{(CXI)}}{NCCH_2NAc_2}.$$

The reaction with chloroacetamide was carried out under the same conditions but with heating to 100°C.

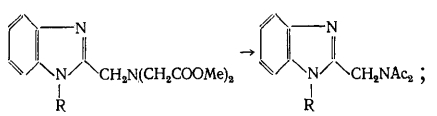
Diethyl 2-nitroethyliminodiacetate (CXII) was synthesised in a quantitative yield by the reaction of 2-chloronitroethane with diethyl iminodiacetate in ethyl acetate at 0°C. However, it could not be hydrolysed, since it proved to be extremely unstable:

$$\underset{\text{(CXII)}}{O_2NCH_2CH_2N(CH_2COOC_2H_5)_2}.$$

Dimethyl acetonyliminodiacetate (CXIII) was synthesised under the same conditions, but with heating (60–70°C, 4 h), from monobromoacetone and dimethyl iminodiacetate. Without isolation, it was converted into the corresponding iminodiacetic acid (CXVI) in 70% yield [190]:

$$CH_3COCH_2Br + HN(CH_2COOMe)_2 \rightarrow \underset{\text{(CXIII)}}{CH_3COCH_2N(CH_2COOMe)_2}$$
$$\downarrow \text{1) Ba(OH)}_2\text{ 2) H}_2\text{SO}_4$$
$$\underset{\text{(CXIV)}}{CH_3COCH_2NAc_2}.$$

The application of this method to the synthesis of heterocyclic derivatives of iminodiacetic acid has been described: 2-chloromethylbenzimidazole and its 1-methyl derivative react with methyl iminodiacetate to give the corresponding diesters (CXV), which are converted by hydrolysis into the complexones (CXVI); the overall yield is about 50% [191]:



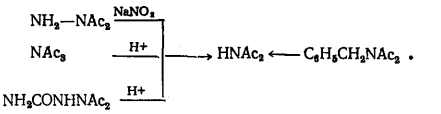
(CXV) (CXVI)

R=H, CH_3.

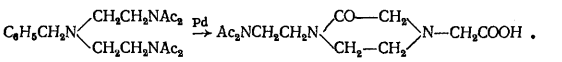
IV. OTHER METHODS FOR SYNTHESISING COMPLEXONES

There exist several specific methods for the synthesis of complexones. They include, for example, reactions whereby the molecules of iminodiacetic acid derivatives are modified. Thus the most convenient method for the synthesis of iminodiacetic acid, which is used in industry, involves the cleavage of hydrazine-*NN*-diacetic acid under the influence of sodium nitrite [30, 192].

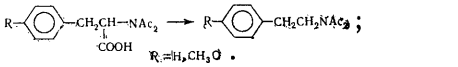
The synthesis of iminodiacetic acid by the acid cleavage of nitrilotriacetic [193, 194] and semicarbazide-*NN*-diacetic [30] acids and by the catalytic debenzylation of benzyliminodiacetic acid [55] has been described:



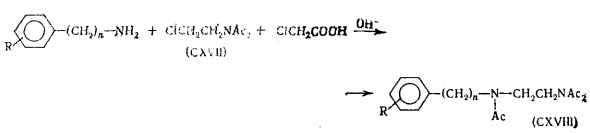
Debenzylation has also been used to synthesise diethylenetriaminetetra-acetic acid, which was isolated as the lactam [137]:



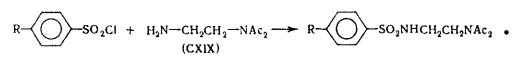
The use of the decarboxylation reaction for the modification of complexones has been described. Thus phenylethyliminodiacetic acid was obtained from phenylalanine [50] and its p-methoxy-derivative was synthesised [195]:



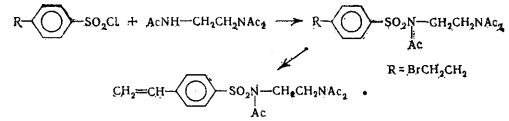
There are several examples of the synthesis of complexones using β-substituted ethyliminodiacetic acids. Thus the interaction of β-chloroethyliminodiacetic acid (CXVII) with arylalkylamines and with chloroacetic acid led to the synthesis of complexones of type (CXVIII). [101] β-Mercaptoethylaminodiacetic acid was synthesised by treating the diacetic acid (CXVII) with sodium hydrogen sulphide [196]:



β-Aminoethyliminodiacetic acid (CXIX) was obtained from *N*-acetamidoethyl-*NN*-iminodiacetic acid [197] and was used to synthesise complexones with the sulphonamide group [compounds (CXX)] [39]:

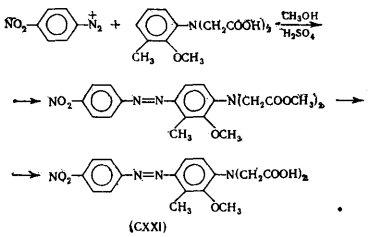


Similar reactions have been carried out with ethylenediaminetriacetic acid [39]; the compounds with a bromoethyl substituent thus obtained were converted into vinyl derivatives:



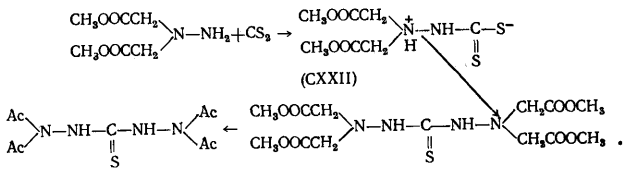
The complexone (CXXI) was synthesised by coupling the p-nitrophenyldiazonium cation to 2-methoxy-3-methylphenyliminodiacetic acid [23] in methanol in the presence of

sulphuric acid with subsequent hydrolysis of the resulting ester:



(CXXI)

By treating dimethyl hydrazine-*NN*-diacetate with carbon disulphide, Podgornaya[198] obtained a dithiocarbazic acid derivative (CXXII), which yielded thiocarbohydrazide-tetra-acetic acid (CXXIII) after dimerisation in alcohol and hydrolysis:



(CXXII)

CXXIII

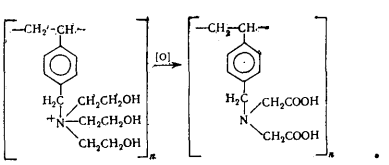
In addition, several examples of the synthesis of complexones by the conversion of *N*-di(hydroxyethyl) groups into aminodiacetic acid groups have been described.

The oxidation is carried out in the presence of catalysts (for example, cadmium or its oxide)[199] or under the influence of alkali at 200–260°C.[200] Nitrilotriacetic acid, ethylenediaminetetra-acetic acid, and its analogues have been obtained by this method[200,201]:

$$N(CH_2CH_2OH)_3 \xrightarrow{[O]} N(CH_2COOH)_3;$$

$$(HOCH_2CH_2)_2NCH_2CH_2N(CH_2CH_2OH)_2 \xrightarrow{[O]} Ac_2NCH_2CH_2NAc_2 .$$

The method has been used to synthesise polymeric complexones of the type of benzyliminodiacetic acid[202]:



Finally, a method has been described for the synthesis of complexones on the basis of the reaction of amines with aminoacids, particularly with glycine[203]:

$$H_2NCH_2CH_2NH_2 + NH_2CH_2COOH \rightarrow Ac_2NCH_2CH_2NAc_2 + NH_3 .$$

The reaction is carried out in an aqueous alkaline medium in the absence of air with elimination of the ammonia formed. However, this interesting reaction has only limited applicability.

Consideration of the existing methods for the synthesis of aminopolycarboxylic acids permits the conclusion that the simplest and universal procedure is the carboxy-methylation reaction with mono- and poly-amines as the starting materials. Under laboratory conditions, the direct carboxymethylation method is mainly used, i.e. condensation with halogenoacetic acids. In industry, the procedure based on the cyanomethylation of amines in an alkaline medium competes with the above method, being more economical.

However, the carboxymethylation reaction is in many cases unsuitable for the synthesis of complexones with functional groups, since the latter may undergo transformations under the conditions of these processes, which involve heating with aqueous solutions of alkalis or inorganic acids. Furthermore, the method may suffer from limitations due to the low availability of the initial amines. Other methods of synthesis, based on the employment of halogeno-, hydroxy-, and other derivatives as starting materials instead of amines, may be more successful under these conditions.

REFERENCES

1. R. Přibil, "Complexony v Chemické Analyse" (Translated into Russian), Inostr. Lit., Moscow, 1960.
2. G. Schwarzenbach and H. Flaschka, "Complexometric Titrations" (Translated into Russian), Izd. Khimiya, Moscow, 1970.
3. Symposium, "Redkozemel'nye Elementy" (The Lanthanide Elements), Izd. Nauka, Moscow, 1963.
4. A. A. Kot, "Vodopodgotovka i Vodnyi Rezhim AES" (The Preparation of Water and the Water Regime in Atomic Power Stations), Atomizdat, Moscow, 1964.
5. T. Kh. Margulov (Editor), "Vodnyi Rezhim Teplovykh Elektrostantsii" (The Water Regime in Thermal Power Stations), Izd. Energiya, Moscow, 1965.
6. V. G. Yashunskii, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 10, 679 (1965).
7. V. G. Yashunskii, Med. Prom. SSSR, No. 4, 29 (1961).
8. Symposium, "Kompleksony kak Sredstvo Protiv Izvestkovogo Khloroza Rastenii" (Complexones as Agents against Lime-Induced Plant Chlorosis), Izd. Naukova Dumka, Kiev, 1965.
9. V. S. Balabukha, L. M. Razbitnaya, N. O. Razumovskii, and L. I. Tikhonova, "Problema Vyvedeniya iz Organizma Dolgozhivushchikh Radioaktivnykh Izotopov" (The Problem of the Elimination of Long-Lived Radioactive Isotopes from the Organism), Atomizdat, Moscow, 1962.
10. M. D. Meshkovskii, "Lekarstvennye Sredstva" (Medicinal Substances), Izd. Meditsina, Moscow, 1972, Part II, pp. 235–237.
11. J. K. Aiken, Chem. Ind. (London), 1334 (1956).
12. J. Willems, Belg. Chem. Ind., 23, 1105 (1958).
13. J. Biermans and P. Henrard, Ind. chim., 39, 6 (1952).
14. Houben-Weyl, "Methoden der Organischen Chemie" 1958, Vol. 4, 1112, p. 404.
15. N. M. Dyatlova, V. Ya. Temkina, and I. D. Kolpakova, "Kompleksony" (Complexones), Izd. Khimiya, Moscow, 1970.
16. M. Miyazaki, Y. Moriguchi, and K. Ueno, Bull. Chem. Soc. Japan, 41, 838 (1968).
17. R. Okaku, K. Toyoda, Y. Moriguchi, and K. Ueno, Bull. Chem. Soc. Japan, 40, 2326 (1967).
18. R. P. Lastovskii, I. D. Kolpakova, and L. I. Kozhelenko, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 65 (1962).
19. R. P. Lastovskii, I. D. Kolpakova, and L. I. Kozhelenko, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 73 (1962).

20. R. P. Lastovskii, I. D. Kolpakova, L. V. Krinitskaya, T. I. Ivanova, and L. D. Zav'yalova, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 12, 79, 89 (1965).
21. R. B. Rodriguez and A. Mederos, Anales real Soc. espaň. Fis. Quim., 64, 983 (1968).
22. V. Ya. Tëmkina, Doctoral Thesis, GEOKhI, USSR Academy of Sciences, Moscow, 1968.
23. R. P. Lastovskii, I. D. Kolpakova, L. V. Krinitskaya, T. I. Ivanova, and L. D. Zav'yalova, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 12, 125 (1965).
24. G. L. Blackmer and R. E. Hamm, J. Amer. Chem. Soc., 91, 2400 (1969).
25. K. A. Schroeder and R. H. Hamm, Inorg. Chem., 3, 391 (1964); 6, 139 (1967).
26. D. L. Venezky and W. B. Moniz, Anal. Chem., 41, 11 (1969).
27. C. A. Goetz and F. J. Debbrodz, J. Sci. Iowa State, Coll., 33, 267 (1959); Chem. Abs., 53, 12 166 (1959).
28. D. J. Reeds and W. J. Stephen, J. Chem. Soc., 5101 (1961).
29. A. Reissert, Ber., 47, 672 (1914).
30. J. Beiley and N. Road, J. Amer. Chem. Soc., 36, 1747 (1914).
31. German P. 383 180 (1923).
32. S. Ulig and D. Herrmann, Z. anorg. Chem., 359, No. 3, 135, 158 (1968).
33. V. G. Yashunskii and V. V. Sidorenko, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 80 (1962).
34. G. F. Kirkbright and W. J. Stephen, J. Chem. Soc., 5101 (1961).
35. A. Stein, H. P. Gregor, and P. H. Spoerri, J. Amer. Chem. Soc., 77, 191 (1955).
36. A. R. Frost and A. E. Martell, J. Amer. Chem. Soc., 72, 3743 (1950).
37. H. Irving and L. Z. da Silva, J. Chem. Soc., 448 (1963).
38. G. F. Kirkbright, D. J. Reeds, and W. J. Stephen, Anal. Chim. Acta, 27, 558 (1962).
39. R. M. Genik-Sas-Berezowsky and I. H. Spinner, Canad. J. Chem., 48, 163 (1970).
40. P. P. Duyer and F. L. Garvan, J. Amer. Chem. Soc., 81, 2955 (1959).
41. O. I. Samoilova and V. G. Yashunskii, Zhur. Org. Khim., 8, 991 (1972).
42. H. Irving and L. Z. da Silva, J. Chem. Soc., 3308 (1963).
43. G. F. Yaroshenko, V. Ya. Tëmkina, and R. P. Lastovskii, Zhur. Org. Khim., 4, 2187 (1968).
44. O. I. Samoilova, O. Yu. Lavrova, N. M. Dyatlova, and V. G. Yashunskii, Zhur. Obshch. Khim., 32, 3372 (1962).
45. G. Schwarzenbach, H. Senn, and G. Anderegg, Helv. Chim. Acta, 40, 1886 (1957).
46. Y. Ogata and A. Kawasaki, J. Org. Chem., 33, 1107 (1968).
47. R. Hering, W. Kruger, and G. Kuhn, Z. Chem., 2, 374 (1962).
48. G. Schwarzenbach, G. Anderegg, W. Schneider, and H. Senn, Helv. Chim. Acta, 38, 1147 (1955).
49. R. P. Lastovskii, V. Ya. Tëmkina, and E. I. Mironova, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 3, 40 (1961).
50. N. F. Kazarinova, N. I. Latosh, and I. Ya. Postovskii, Izv. Sibir. Otd. Akad. Nauk SSSR, No. 2, 60 (1960).
51. G. Schwarzenbach, H. Ackermann, and P. Ruckstuhl, Helv. Chim. Acta, 32, 1175 (1949).
52. Swiss P. 275 435 (1951); Chem. Abs., 47, 144 (1953).
53. R. P. Lastovskii, I. D. Kolpakova, and N. I. Ivanova, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 60 (1962).
54. R. P. Lastovskii, Yu. I. Vainshtein, N. M. Dyatlova, I. D. Kolpakova, and V. Ya. Tëmkina, Zhur. Anal. Khim., 10, 128 (1955).
55. B. H. Chase and A. M. Downes, J. Chem. Soc., 3874 (1953).
56. R. P. Lastovskii, I. D. Kolpakova, and T. I. Ivanova, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 62 (1962).
57. T. Ando, Bull. Chem. Soc. Japan, 35, 1395 (1962).
58. B. P. 718 849 (1954); Chem. Zentr., 9391 (1955).
59. I. D. Kiselëva, T. I. Tikhonova, L. I. Ivanova, and V. G. Yashunskii, Zhur. Obshch. Khim., 41, 2599 (1971).
60. H. Irving and L. Z. da Silva, J. Chem. Soc., 1144 (1963).
61. H. Irving and L. Z. da Silva, J. Chem. Soc., 945 (1963).
62. P. Biddle, E. S. Lane, and J. L. Willans, J. Chem. Soc., 2369 (1960).
63. G. Schwarzenbach, E. Kampitsch, and R. Steiner, Helv. Chim. Acta., 29, 364 (1946).
64. US P. 2 103 505 (1936); Chem. Abs., 31, 17 184 (1937).
65. USSR P. 151 326; Byul. Izobret., No. 21 (1962).
66. G. Schwarzenbach and H. Ackermann, Helv. Chim. Acta, 31, 1029 (1948).
67. USSR P. 215 944 (1967); Byul. Izobret., No. 14, 21 (1968).
68. T. Majer and E. Dvorakova, Chem. Zvesti, 17, 402 (1963).
69. V. G. Yashunskii, V. F. Vasil'eva, L. I. Tikhonova, and M. N. Shchukina, Zhur. Obshch. Khim., 29, 2709 (1959).
70. V. G. Yashunskii, Zhur. Obshch. Khim., 28, 1056 (1958).
71. R. Belcher, W. Hoyle, and T. S. West, J. Chem. Soc., 667 (1961).
72. V. G. Yashunskii, D. D. Smolin, and V. G. Ermolaeva, Zhur. Obshch. Khim., 30, 12, 3917 (1960).
73. H. Kroll and M. Gordon, Ann. New York Acad. Sci., 83, 341 (1960); Chem. Abs., 55, 2476 (1961).
74. N. M. Shchukina, V. G. Yashunskii, and O. I. Samoilova, USSR P. 144 479; Byul. Izobret., No. 3 (1962).
75. V. G. Yashunskii and O. I. Samoilova, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 8, 360 (1963).
76. V. G. Yashunskii, V. F. Vasil'eva, N. M. Dyatlova, and O. Yu. Lavrova, Zhur. Obshch. Khim., 36, 674, 1724 (1966).
77. USSR P. 165 703; Byul. Izobret., No. 20 (1964).
78. USSR P. 172 821; Byul. Izobret., No. 14 (1965).
79. USSR P. 172 753; Byul. Izobret., No. 14 (1965).
80. O. I. Samoilova and V. G. Yashunskii, USSR P. 229 533; Byul. Izobret., No. 33 (1968).

81. O. I. Samoilova and V. G. Yashunskii, USSR P.178 365; Byul. Izobret., No. 3 (1966).
82. N. M. Dyatlova, I. A. Seliverstova, O. I. Samoilova, and V. G. Yashunskii, Dokl. Akad. Nauk SSSR, 172, 94 (1967).
83. I. A. Seliverstova, O. I. Samoilova, N. M. Dyatlova, and V. G. Yashunskii, Zhur. Obshch. Khim., 37, 2643 (1967).
84. V. G. Yashunskii and O. I. Samoilova, USSR P.213 013; Byul. Izobret., No. 10 (1968).
85. O. I. Samoilova, I. A. Seliverstova, N. M. Dyatlova, and V. G. Yashunskii, Zhur. Obshch. Khim., 43, 365 (1973).
86. L. M. Timakova, V. Ya. Tëmkina, G. F. Yaroshenko, and R. P. Lastovskii, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 26, 226 (1974).
87. G. Schwarzenbach, G. Anderegg, and R. Sallmann, Helv. Chim. Acta, 35, 1785 (1952).
88. R. P. Lastovskii, V. Ya. Tëmkina, G. F. Varoshenko, and I. P. Fadeeva, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 12, 93 (1965).
89. V. P. Khilya and G. A. Lezenko, Zhur. Org. Khim., 6, 2048 (1970).
90. R. P. Lastovskii, V. Ya. Tëmkina, and L. I. Samylova, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 67, 68, 70 (1962).
91. K. Otozai and I. Kato, Bunseki Kagaku, 8, 259 (1959); Chem. Abs., 56, 3379 (1962).
92. R. P. Lastovskii, I. D. Kolpakova, and T. I. Ivanova, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 72 (1962).
93. E. Blasius and G. Olbrich, Z. Anal. Chem., 151, 81 (1956).
94. J. R. Cox and B. D. Smith, J. Org. Chem., 29, 488 (1964).
95. G. F. Kirkbright and W. J. Stephen, Anal. Chim. Acta, 28, 327 (1963).
96. R. P. Lastovskii, V. V. Sidorenko, I. V. Lapshina, and T. P. Konoplëva, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 12, 103 (1965).
97. R. P. Lastovskii, Yu. I. Vainshtein, N. M. Dyatlova, and V. Ya. Tëmkina, Zhur. Anal. Khim., 11, 405 (1956).
98. S. S. Skorokhodov and A. A. Vanshtert, Vysokomol. Soed., 2, 1405 (1960).
99. US P. 2 599 807 (1952); Chem. Abs., 47, 4360 (1953).
100. J. V. Princiotto, M. Rubin, G. C. Shashaby, and E. J. Zapobcki, J. Clin. Invest., 43, 825 (1964).
101. US P. 2 624 757–8 (1953); Chem. Zentr., 10 330 (1955).
102. US P. 2 624 756, 2 624 759 (1953); Chem. Zentr., 10 330, 10 331 (1955).
103. T. C. Lacobelli, M. Palmera, F. Maracci, and A. Margani, Ann. Chim. (Italy), 60, 674 (1970).
104. A. Strecker, Annalen, 75, 27 (1850).
105. "Organic Synthesis" (Translated into Russian), Inostr. Lit., Moscow, 1949, Vol. I, p. 20.
106. BRD P. 1 177 646 (1964); Chem. Abs., 61, 14 538 E (1967).
107. A. Marker, Helv. Chim. Acta, 37, 166 (1954).
108. US P. 2 558 923 (1951); Chem. Abs., 46, 10 331 (1952).
109. US P. 2 387 735 (1945); Chem. Abs., 40, 1171 (1946).
110. German P. 638 071; Fdl., 23, 157 (1938).
111. L. J. Zompa and J. M. Shindler, J. Chem. Soc., D, 65 (1971).
112. US P. 2 845 457 (1958); Chem. Abs., 53, 1146 (1959).
113. US P. 2 855 428 (1958); Chem. Abs., 53, 6084 (1959).
114. US P. 2 945 881 (1960); Chem. Abs., 54, 22 369 (1960).
115. R. G. Lacoste, G. V. Christoffers, and A. E. Martell, J. Amer. Chem. Soc., 87, 2385 (1965).
116. US P. 3 061 628 (1962); Chem. Abs., 58, 7836 (1964).
117. French P. 1 368 588 (1964); Chem. Abs., 62, 1571 (1968).
118. French P. 1 368 589 (1964); Chem. Abs., 62, 7642 (1968).
119. US P. 3 183 262 (1965); Chem. Abs., 63, 4165 (1969).
120. G. Schwarzenbach, E. Kampitsch, and R. Steiner, Helv. Chim. Acta, 28, 828 (1945).
121. K. Dimroth and V. Pintschovins, Annalen, 639, 102 (1961).
122. K. Dimroth and H. G. Aurich, Ber., 98, 3902 (1965).
123. US P. 2 259 167 (1942); Chem. Abs., 36, 494 (1942).
124. R. Smith, J. Bullock, F. Bersworth, and A. Martell, J. Org. Chem., 14, 355 (1949).
125. A. Martell and F. Bersworth, J. Org. Chem., 15, 46 (1950).
126. L. Ziemlak, J. Bullock, F. Bersworth, and A. Martell, J. Org. Chem., 15, 255 (1950).
127. US P. 2 387 735 (1945); Chem. Abs., 40, 1171 (1946).
128. B. P. 600 629 (1947); Chem. Abs., 42, 7324 (1948).
129. B. P. 686 748 (1952); Chem. Abs., 47, 4898 (1953).
130. US P. 2 407 645 (1946); Chem. Abs., 41, 776 (1947).
131. B. P. 661 146 (1952); Chem. Abs., 46, 5795 (1958).
132. A. Bruno, S. Chaberek, and A. Martell, J. Amer. Chem. Soc., 78, 2723 (1956).
133. O. M. Lerner and I. Kh. Fel'dman, Zhur. Prikl. Khim., 36, 1347 (1963).
134. US P. 2 461 519 (1949); Chem. Abs., 43, 3449 (1949).
135. R. P. Lastovskii, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 18, 223 (1969).
136. B. P. 727 483 (1955); Chem. Abs., 49, 12 022 (1955).
137. V. F. Vasil'eva, O. Yu. Lavrova, N. M. Dyatlova, and V. G. Yashunskii, Zhur. Vses. Khim. Obshch., 14, 461 (1969).
138. V. Ya. Tëmkina, N. V. Tsirul'nikova, G. F. Yaroshenko, and M. N. Rusina, Zhur. Obshch. Khim., 41, 1334 (1971).
139. US P. 2 860 164 (1958); Chem. Abs., 53, 7994 (1959).
140. US P. 3 153 668 (1964); Chem. Abs., 62, 448 (1968).
141. H. Hellmann and G. Opitz, "N-Aminoalkylirung", Verlag Chemie, Weinhein, 1960.
142. V. Ya. Tëmkina, N. V. Tsirul'nikova, and R. P. Lastovskii, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 18, 122 (1969).
143. N. N. Basargin and M. I. Starostina, USSR P.17 554; Byul. Izobret., No. 20 (1965).
144. G. Anderegg, H. Flaschka, R. Sallmann, and G. Schwarzenbach, Helv. Chim. Acta, 37, 113 (1954).
145. I. H. Burckhalter, I. N. Wells, and W. J. Mayer, Tetrahedron Letters, 1353 (1964).

146. H. Hellmann and G. Opitz, Angew. Chem., 68, 265 (1956).
147. G. Schwarzenbach, G. Anderegg, and R. Sallmann, Helv. Chim. Acta, 35, 1794 (1952).
148. V. Ya. Tëmkina, N. M. Dyatlova, M. N. Rusina, N. V. Tsirul'nikova, B. V. Zhadanov, and R. P. Lastovskii, Dokl. Akad. Nauk SSSR, 180, 88 (1968).
149. H. Diehe and I. Eilingboe, Anal. Chem., 28, 882 (1956).
150. N. V. Tsirul'nikova, N. A. Kostromina, B. V. Zhadanov, and V. Ya. Tëmkina, Zhur. Org. Khim., 7, 327 (1971).
151. N. V. Tsirul'nikova, V. Ya. Tëmkina, N. M. Dyatlova, M. N. Rusina, B. V. Zhadanov, and R. P. Lastovskii, Zhur. Anal. Khim., 25, 839 (1970).
152. N. V. Tsirul'nikova, V. Ya. Tëmkina, G. F. Yaroshenko, and R. P. Lastovskii, Khim. Prom., 22, 502 (1971).
153. D. F. Hoelz-Wallach and T. L. Stack, Anal. Chem., 35, 1035 (1963).
154. D. F. Hoelz-Wallach, D. Surgenor, I. Soderberg, and E. Delano, Anal. Chem., 31, 456 (1959).
155. S. U. Kreingol'd and I. A. Bozhevol'nov, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 25, 358 (1963).
156. R. P. Lastovskii, V. V. Sidorenko, T. P. Konoplëva, and N. N. Lapshina, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 12, 34 (1965).
157. V. Ya. Tëmkina and R. P. Lastovskii, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 18, 86 (1968).
158. V. Ya. Tëmkina, R. P. Lastovskii, and N. M. Dyatlova, "Sbornik Nauchno-Tekhnicheskoi Informatsii" (Collected Scientific and Technical Information), Izd. IREA, 1963, Nos. 3–4, p. 27.
159. B. Rehak and I. Korbl, Coll. Czech. Chem. Comm., 25, 797 (1960).
160. I. Korbl and B. Kakac, Coll. Czech. Chem. Comm., 23, 889 (1958).
161. G. S. Tereshin, L. R. Rubinshtein, and I. V. Tananaev, Zhur. Anal. Khim., 20, 1082 (1965).
162. I. Korbl and R. Pribil, A. Emr. Coll. Czech. Chem. Comm., 22, 961 (1957).
163. I. Korbl and R. Pribil, Chem. Anal., 45, 102 (1956).
164. I. Korbl and R. Pribil, Coll. Czech. Chem. Comm., 23, 873 (1958).
165. I. Korbl and R. Pribil, Chem. Ind. (London), 233 (1957).
166. S. Srivastava and A. Mukherji, Anal. Chim. Acta, 30, 495 (1964).
167. I. Dragushin, Zhur. Anal. Khim., 16, 611 (1961).
168. I. Korbl and R. Pribil, Coll. Czech. Chem. Comm., 23, 1213 (1958).
169. O. Olson and D. Margerum, Anal. Chem., 34, 1299 (1962).
170. V. Ya. Tëmkina, M. N. Rusina, G. F. Yaroshenko, M. Z. Branzburg, L. M. Timakova, and N. M. Dyatlova, Zhur. Obshch. Khim., 45, 1564 (1975).
171. B. Badesinsky, Coll. Czech. Chem. Comm., 22, 1579 (1957).
172. I. Eggers, Talanta, 4, 382 (1960).
173. D. Wilkins, Talanta, 4, 182 (1960).
174. D. Harvey, Anal. Chem., 39, No. 3, 12 (1967).
175. R. P. Lastovskii and V. V. Sidorenko, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 76 (1962).
176. H. Diche and I. Killingboe, Anal. Chem., 28, 882 (1956).
177. B. Tucher, Analyst, 82, 284 (1957).
178. I. Korbl and F. Yydra, Coll. Czech. Chem. Comm., 23, 622 (1958).
179. R. Belcher, T. West, and M. Leonard, J. Chem. Soc., 2390 (1958).
180. US P. 2 419 157; Chem. Abs., 41, 4804 (1947).
181. O. I. Samoilova and V. G. Yashunskii, USSR P. 213 015 (1966); Byul. Izobret., No. 10 (1968).
182. French P. 2 192 554.
183. BRD Appl. 2 241 134, 1975; Ref. Zhur. Khim., 13N60P (1975).
184. G. Schwarzenbach, H. Ackermann, and S. Ruckstuhi, Helv. Chim. Acta, 32, 1175 (1949).
185. R. P. Lastovskii, I. D. Kolpakova, and N. M. Dyatlova, Zhur. Anal. Khim., 15, 419 (1960).
186. A. I. Cherkesov and N. K. Astakhova, Symposium, "Novye Issledovaniya po Analiticheskomu Primeneniyu Organicheskikh Reagentov" (New Studies on the Analytical Applications of Organic Reagents), Izd. Saratov, 1967, pp. 82–83; Ref. Zhur. Khim., 14G7 (1968).
187. I. V. Dubsky, Ber., 49, 1037 (1916); 52, 221 (1919).
188. V. M. Plakhotnik, A. B. Aprokhorov, O. I. Samoilova, L. I. Takhonova, and V. G. Yashunskii, Zhur. Obshch. Khim., 44, 600 (1974).
189. G. Shtacher and W. Taub, J. Medicin. Pharmaceut. Chem., 9, 197 (1966).
190. A. Takeshi, Bull. Chem. Soc. Japan, 36, 1593 (1963).
191. H. Irving and O. Weber, J. Chem. Soc., 2296 (1959).
192. R. P. Lastovskii, V. Ya. Tëmkina, and I. P. Fadeeva, "Metody Polucheniya Khimicheskikh Reaktivov i Preparatov" (Methods for the Synthesis of Chemical Reagents and Preparations), Trudy IREA, 6, 59 (1962).
193. W. Heintz, Annalen, 149, 88 (1869).
194. G. Schwarzenbach and E. Kampitsch, Helv. Chim. Acta, 28, 1135 (1945).
195. S. Kanao, J. Pharm. Soc. Japan, 66, 6 (1946).
196. French P. 1 474 733.
197. S. P. Ivashchenko, V. Ya. Tëmkina, N. V. Tsirul'nikova, B. V. Zhadanov, and R. P. Lastovskii, Zhur. Org. Khim., 10, 2312 (1974).
198. I. V. Podgornaya, Candidate's Thesis, Institute of Chemistry, The Urals Branch of the USSR Academy of Sciences, Sverdlovsk, 1963.
199. B. P. 601 817 (1948); Chem. Abs., 42, 7325 (1948).
200. US P. 2 384 816–7 (1945); Chem. Abs., 40, 353 (1946).
201. US P. 3 833 650.
202. E. B. Trostyanskaya, I. P. Losev, and G. Z. Nefëdova, Zhur. Vses. Khim. Obshch., 5, 108 (1960).
203. US P. 2 387 976; Chem. Abs., 40, 2736 (1946).