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New Trends in the Hydration of Nitriles

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The advances in the hydration of nitrile ligands in complexes with various central ions, in the employment of complexes as homogeneous catalysts of the hydration of nitriles, and in the addition of water to the nitrile group in the presence of manganese(IV) oxide and other metal oxides as well as catalysts containing metallic copper and other metals are examined. The conditions in the synthesis of amides, the influence of the structure of the starting materials on the mode of reaction and on the side reactions accompanying hydration, the reaction mechanisms, and the practical value of individual pathways leading to the conversion of nitriles into amides are discussed.
The bibliography includes 123 references.

CONTENTS

I. Introduction 900
II. Hydration with formation of coordinated amides 900
III. Homogeneous-catalytic hydration 903
IV. Heterogeneous-catalytic hydration 904

I. INTRODUCTION

The hydration of nitriles is frequently used to prepare the corresponding carboxylic acid amides. The classical hydration procedures are based on the interaction of nitriles with water and hydrogen chloride, sulphuric acid, or other inorganic acids and also on the reaction of nitriles with hydrogen peroxide in aqueous alkali. These and certain other methods have been considered in detail in a monograph[1] covering the literature mainly up to 1970 and have still not lost their importance. However, during the past 10–12 years a number of fundamentally new procedures for the conversion of nitriles into amides have been proposed and have developed rapidly. Thus, advances have been made in the hydration of coordinated nitriles, homogeneous-catalytic hydration using catalysts, mainly complexes, has been achieved and is being improved, and particularly significant results have been obtained in liquid-phase heterogeneous-catalytic hydration of nitriles in the presence of certain metal oxides or metals, which made it possible, in particular, to organise the large-scale manufacture of acrylamide by the hydration of acrylonitrile in the presence of catalysts containing metallic copper.[2]

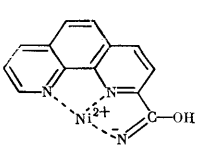
This review deals with the present state of these problems mainly on the basis of the literature up to 1982.

II. HYDRATION WITH FORMATION OF COORDINATED AMIDES

The chemistry of complexes containing nitrile molecules in the inner sphere has attracted much attention.[3] In these complexes the nitriles are as a rule n-coordinated to the central ion but π-complexes are also formed in some cases. The coordination of nitriles results in a sharp increase of their electrophilic reactivity.[3]

The hydration of coordinated nitriles leading to the formation of coordinated amides was first investigated in relation to pyridine derivatives containing the cyano-group in the 2-position, evidently because the amides formed, behaving as bidentate ligands, give rise to relatively stable complexes with many ions, including bivalent cobalt, nickel, copper, and zinc ions; on the other hand, the complexes of these ions with monodentate amide ligands are extremely unstable.

The hydration of 2-cyano-1,10-phenanthroline is greatly accelerated by copper(II) as well as nickel(II) and zinc ions even at room temperature.[4] 1,10-Phenanthroline-2-carboxamide can be isolated quantitatively from the reaction products by treatment with the disodium salt of ethylenediaminetetra-acetic acid. The kinetics and mechanism of the hydration reaction in the presence of salts have been studied and it has been shown that it is of first order with respect to the metal ion complex with the substrate and with respect to hydroxide ions. The second-order rate constant for the reaction catalysed by Ni^{2+} is ~10^7 times greater than for the hydration in the same basic medium but in the absence of metal ions. This acceleration is caused by the appreciable alteration of the entropy of activation (from -50 J mol^{-1} K^{-1} in the absence of nickel to $+59$ J mol^{-1} K^{-1} in its presence). According to the mechanism proposed, the nitrile and Ni^{2+} form a complex in which the CN group is located close to the metal ion but is not coordinated to it; this group is attacked by the OH^- ion with formation of a complex in which Ni^{2+} now interacts with three nitrogen atoms:



The positive entropy of activation is probably associated with the fact that a coordinated water molecule is displaced from the initial nickel complex on formation of the transition state and appreciable desolvation of the nucleophile takes place. The above mechanism is preferred over the alternative mechanism according to which the nitrile group is subjected to the nucleophilic attack by the hydroxo-group coordinated to the central ion and not by a free OH^- ion.[4,5] It is noteworthy that the subsequent hydrolysis of the 1,10-phenanthroline-2-carboxamide formed is also accelerated in the presence of copper(II), nickel(II), and zinc salts but to a much lesser extent than the hydration of the nitrile.[4]

2-Cyanopyridine, coordinated to copper(II) or nickel(II), is rapidly hydrated to pyridine-2-carboxamide on heating in aqueous solutions, the carboxamide remaining bound to the metal ion the form of a chelate compound.[6] The hydration of

2-cyano-8-hydroxyquinoline complexes of nickel(II), cobalt(II), and copper(II) proceeds analogously. In terms of its kinetic features, the reaction differs little from the hydration of coordinated 2-cyano-1,10-phenanthroline examined above. Here too the sharp increase of rate on passing from the free to the coordinated nitrile is associated with the increase of the activation entropy—from −113 to −4 J mol^{-1} K^{-1} in the nickel complex and to −13 J mol^{-1} K^{-1} in the cobalt complex (while the enthalpy of activation remains unaltered).[7,8]

The nitrile group of the *o*-cyanobenzyl ligand coordinated as a bidentate species to platinum(II) [9] and palladium(II) [10] in complexes of the type

$$\left[L_2Pd\begin{matrix}CH_2C_6H_4CN\\ NCC_6H_4CH_2\end{matrix}PdL_2\right]^{2+}(BF_4^-)_2\ ,$$

where L_2 = $2PPh_3$, 1,2-bis(phenylphosphino)ethylene, or 1,2-bis(phenylphosphino)ethane, is hydrated at 50 °C in solution in aqueous acetone. It is believed[9] that the reaction begins with the nucleophilic substitution of the coordinated cyano-group by water, after which the water coordinated to the central ion interacts intramolecularly with the ligand containing the cyano-group and occupying the *cis*-position. The *o*-toluidide and complexes of the type PtL_2Cl_2 have been obtained by treating the dimeric carboxamide-complexes with hydrochloric acid.

Cobalt(III) forms with amides much more stable complexes than the bivalent metals examined above. Even complexes with amides without groups capable of forming an additional coordinate bond with the central ion are distinguished by an appreciable stability; different nitrile complexes based on cobalt(III) are therefore conveient objects for a detailed study of hydration. The reaction was first achieved[11] with pentamminecobalt complexes containing benzonitrile and 3- and 4-hydroxybenzonitriles as ligands:

$$[Co(NH_3)_5NCR]^{3+} + OH^- \rightarrow [Co(NH_3)_5NHCR]^{2+}\ .$$

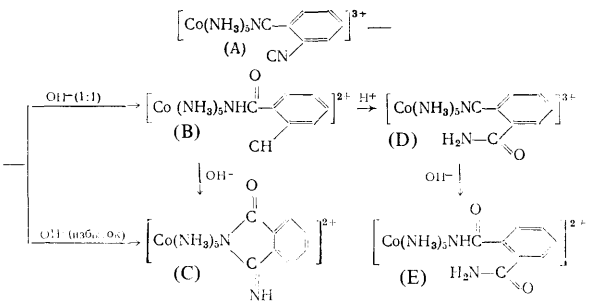
In an acid medium these complexes are reversibly protonated:

$$[Co(NH_3)_5NHCR]^{2+} + H^+ \rightleftarrows [Co(NH_3)_5NH_2CR]^{3+}\ .$$

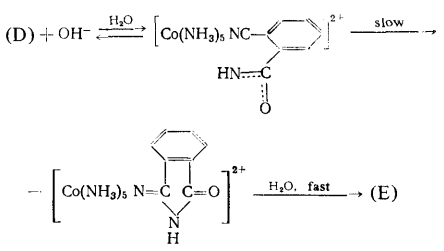
The reaction proceeds analogously also when pentamminecobalt complexes of 3-cyano-, 4-cyano-, 4-acetyl-, 3-formyl-, and 4-formyl-benzonitriles and even 2-, 3-, and 4-cyanopyridines are used.[12,13] The kinetics of the hydration reaction are described by a second order equation—of first order with respect to the complexes and of first order with respect to hydroxide ions. (In the hydration of coordinated formylbenzonitriles the hydration kinetics are complicated by the reversible reaction involving the addition of OH^- ions to the carbonyl group, which takes place simultaneously.[12]) The *n*-coordination of benzonitriles to Co^{3+} makes it possible to increase the rate constants for their hydration by a factor of 10^6–10^7. The rate constants then increase also with increase of the electron-accepting capacity of the substituents in the benzonitrile. The activation parameters for the hydration of coordinated benzonitriles are as follows:[11,12] $\Delta H^{\neq}$ = 51.5–69.1 kJ mol^{-1} and $\Delta S^{\neq}$ = −31–+21 J mol^{-1} K^{-1}. These values of $\Delta S^{\neq}$ are much greater than the $\Delta S^{\neq}$ for the hydration of non-coordinated benzonitriles.

The nitrile group is hydrated under mild conditions and with low yields also in the pentamminecobalt(III) complexes of acetonitrile[14] and acrylonitrile.[15]

The neighbouring functional groups can exert a significant influence on the hydration of the nitrile coordinated to a transition metal. In particular, interesting results have been obtained in the hydration of 1,2-dicyanobenzene coordinated to cobalt(III).[16] The pentamminecobalt complex of the dinitrile (A) reacts with a stoichiometric amount of a base to form the cyanobenzamide complex (B), which cyclises in the presence of an excess of the base to the 3-imino-1-oxoisoindoline complex (C). Coordination, which sharply accelerates the reaction (A) + OH^- – (B), has very little influence on the rate of cyclisation. In an acid medium the complex (B) undergoes an intramolecular rearrangement with formation of the complex (D), in which the nitrile group is coordinated to the cobalt atom, while the amide group is free. In the presence of a base, this nitrile complex is hydrated to the phthalamide complex (E). The rate constant for the last reaction is 10^3 times greater than the rate constant for the reaction (A) + OH^- → (B).



Detailed study of the kinetics of the hydration of coordinated dicyanobenzenes and 2-cyanobenzamide made it possible to refine the mechanism of the catalysis of the hydration of the nitrile group under the influence of the neighbouring carboxamide group in the complex (D).[17] Since the rate of hydration of 1,2-dicyanobenzene is only ~3 times greater than the rate of hydration of 1,3- and 1,4-dicyanobenzenes, it was concluded that the *o*-nitrile group influences the reactivity of the coordinated CN group in the complex (A) solely by virtue of its electron-accepting capacity. On the other hand, the appreciable increase of the rate of reaction in the complex (D) under the influence of the less electron-accepting *o*-carboxamide group shows that the latter influences the hydration via another mechanism. The entropy of activation for hydration in the complex (A) (+4 J mol^{-1} K^{-1}) is of the same order of magnitude as for other complexes of the nitriles in the inner sphere (−31–+21 J mol^{-1} K^{-1}), while the activation entropy for hydration in the complex (D) is unusually high (+184 J mol^{-1} K^{-1}). On the basis of these data and bearing in mind that the hydration of the CN group and the complex (D) is catalysed specifically by OH^- ions, a reaction mechanism has been proposed according to which the amide group is initially deprotonated and this is followed by the inner-sphere nucleophilic attack on the CN group with formation of an isoindole heterocycle, which hydrolyses to compound (E):



According to Balahura and Purcell,[17] the high value of $\Delta S^{\neq}$ is due to the desolvation of both the OH^- ion and the carboxamide anion together with the partial neutralisation of the

charge on cyclisation. Thus the high rate of hydration of the CN group in the complex (D) can be explained by the combination of the effects of coordination and catalysis by the o-carboxamide group.

The coordination of nitriles leads not only to an increase of the electrophilic reactivity of the CN group but also to an appreciable increase of the mobility of the α-hydrogen atoms of the nitrile ligand. Under the conditions of the hydration of coordinated acetonitrile is an alkaline medium, this is expressed by the simultaneous exchange of the protons of the methyl group.[14] The coordination of malononitrile, cyanoacetic acid, and its ethyl ester to pentamminecobalt(III) leads to such a sharp increase of the acidity of these compounds that in aqueous alkaline solutions equilibrium is rapidly established between the initial complexes and complexes containing the deprotonated methylene group. In these systems the initial complexes are hydrated through both OH^- ions and water while in the coordinated carbanions an electron is displaced with formation of the cobalt(II) ion and the corresponding free radical:[15,18]

$$[Co(NH_3)_5(NCCH_2CN)]^{3+} \begin{cases} \xrightarrow{OH^-} [Co(NH_3)_5(NHCCH_2CN)]^{2+}, \\ \xrightarrow{H_2O} [Co(NH_3)_5(NHCCH_2CN)]^{2+} + H^+, \\ \xrightarrow[-H_2O]{OH^-} [Co(NH_3)_5(NCC^-HCN)]^{2+} \rightarrow Co^{2+} + 5NH_3 + NC\dot{C}HCN. \end{cases}$$

The free radicals formed as a result of the reaction of the ligands in a non-aqueous medium initiate the polymerisation of acrylic monomers and styrene.[15]

The hydration of nitriles bound as ligands to the central ion in the pentammine complexes of platinum group metals has been described in a number of studies.[19–21] In weakly alkaline solutions the reaction proceeds at a high rate, which is proportional to the concentrations of both the complex and OH^- ions. The pentammineruthenium(III) complexes of acetonitrile and benzonitrile are hydrolysed ~10^8 times faster than the free nitriles and ~10^2 times faster than the pentamminerhodium(II) complexes of the same nitriles. In the corresponding ruthenium(II) complex of acetonitrile the reaction is ~10^6 times slower than in the ruthenium(III) complex. The high reactivity of the ruthenium(III) complex can be explained by the fact that the ruthenium(III) ion, which is a powerful π-electron acceptor, stabilises the negative charge formed on the ligand as a result of attack by the hydroxide anion on the carbon atom of the nitrile group. The comparatively low reactivity of the ruthenium(II) complex is associated with the fact that in this instance the central ion is a weak π-electron acceptor. It has been found that in hydration in a weakly alkaline medium (pH 8–9) the complex $[Ru(NH_3)_5NCPh]^{3+}$ undergoes a side reaction to a slight extent, namely the disproportionation to the ruthenium(II) and ruthenium(IV) complexes.[20] According to Diamond and co-workers,[22,23] ethyl cyanoacetate and αβ-unsaturated nitriles coordinated to ruthenium(III) are also hydrated to the corresponding amides.

The rate constants for the reactions of the pentamminerhodium(III) and pentammineiridium(III) complexes of benzonitrile with OH^- ions have been determined.[21] Comparison with the reaction of the corresponding cobalt(III) complex under analogous conditions[11] showed that the rate constants decrease in the sequence Co > Rh > Ir, i.e. in the homologous series of complexes with the same central ion electron configuration completion the reactivity decreases with increasing the ionic radius. This confirms the significant influence of the electrostatic attraction between the central ion and the nitrile ligand on the ability of the latter to be subjected to nucleophilic attack.[21]

As a consequence of the high stability of cobalt(III), ruthenium(III), and other tervalent metal complexes[22–25] of carboxylic acid amides, the isolation of the free amides requires the reduction of the central ion in these complexes to the II-state, which gives much less stable complexes. A method has also been proposed[22–24] for the preparation of amides from pentammineaquoruthenium(II) trifluoroacetate and nitriles in accordance with the scheme

$$[Ru(H_2O)(NH_3)_5]^{2+} + RCN \xrightarrow[-H_2O]{} [Ru(NH_3)_5NCR]^{2+} \underset{-e}{\rightleftarrows} [Ru(NH_3)_5NCR]^{3+} \xrightarrow{H_2O} \rightarrow$$

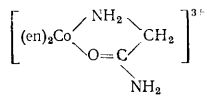
$$\rightarrow [Ru(NH_3)_5NH_2\overset{O}{\overset{\|}{C}}R]^{3+} \xrightarrow{+e,H_2O} [Ru(NH_3)_5(H_2O)]^{2+} + RCONH_2.$$

The addition of water to acetonitrile and benzonitrile coordinated to platinum(II) in the *trans*-acetonitrilebis(triphenylphosphino)methylplatinum cationic complex in an alkaline medium has been described.[26] Analogous results were obtained later[27] starting with similar complexes having other tertiary phosphine ligands:

$$[PtMe(NCMe)L_2]^+ \xrightarrow{H_2O,OH^-} PtMe(\overset{O}{\overset{\|}{H}}NCMe)L_2.$$

The interaction of $[PtCl_4]^{2-}$ with acetonitrile combined with the oxidation of the central ion by oxygen leads to the formation of the acetamide complex of platinum(IV). It has been suggested[28] that the reaction proceeds via the intermediate formation of the complexes $[Pt(NCMe)Cl_3]^-$ and $Pt(H_2O)\cdot(NCMe)Cl_2$.

Studies of the hydration of the nitrile group incorporated in the inner sphere of a complex but not linked directly to the central ion are of interest. It has been shown[29] that the CN group of the aminoacetonitrile ligand in the complex *cis*-$[Co(H_2O)(en)_2(H_2NCH_2CN)]^{3+}$ is hydrated in neutral and alkaline media with formation of a five-membered chelate compound:



The reaction is regarded as a process within the complex involving hydration by the water molecule coordinated to the cobalt ion. In the analogous complex based on 3-aminopropionitrile hydration does not occur under these conditions and the corresponding six-membered chelate compound is not therefore formed. In an acid medium the complexes of both nitriles are hydrated, but the rate of hydration of the first is ~10^5 times greater. The presence of mercury(II) ions makes it possible to increase the rate of hydration of the aminoacetonitrile and 3-aminopropionitrile ligands to the same extent (by a factor of ~10^7). The different types of behaviour during hydration of aminoacetonitrile and 3-aminopropionitrile incorporated in complexes shows that the presence of the nitrile and water in the same coordination sphere is not a sufficient condition for hydration within the complex; the appropriate disposition of the reacting groups in space is also necessary (in the case considered there must be a possibility of the formation of a five-membered chelate compound). The combination of the accelerating effect induced by the possibility of chelation and of the presence of mercury ions permits, overall, an increase in the rate of hydration in a neutral medium by a factor of 10^{15}–10^{18}. The catalysis by mercury(II) ions can be explained by the fact they they form a complex with the nitrile group, withdrawing electron density to themselves: this facilitates nucleophilic attack by the hydroxide ion and the formation of an unstable Hg^{2+} complex with the amide group.[30] The Ag^+ ion is a less effective catalyst of hydration within the complex, but it is in its turn greatly superior to Zn^{2+} and Cd^{2+}.[29]

The hydration of the nitrile group in the presence of mercury(II) ions in the complexes *cis*-$[Co(en)_2(H_2NCH_2CH_2CN).X]^{2+}$, where X = Cl or Br, is based on the removal of a halide ion under the influence of Hg^{2+}, the occupation of the liberated coordination site by the OH^- ligand, and subsequent catalysis by the Hg^{2+} ion of the nucleophilic attack by the OH ligand on the nitrile group within the complex and the formation of a chelate compound. In the analogous complexes based on aminoacetonitrile the hydration also proceeds partly via this mechanism.[25,29,31]

In the absence of Hg^{2+}, the complexes $[Co(en)_2(H_2NCH_2CN).X]^{2+}$ (at pH 7.3 and above) are not hydrated; instead, rapid intramolecular addition of the deprotonated amino-group, located *trans* to the halide ion and to the non-coordinated nitrile group takes place and complexes in which the amidine substituent has a coordination capacity of three are obtained: $\{Co(en)[H_2NCH_2C(NH_2)=NCH_2CH_2NH_2]X\}^{2+}$. The reaction is of first order with respect to both the initial aminoacetonitrile complex and OH^- ions.[31,32]

III. HOMOGENEOUS-CATALYTIC HYDRATION

It was stated above that bivalent cobalt, nickel, and copper chelate complexes of pyridine-2-carboxamide and other amides with similar structure are extremely stable under the conditions of their synthesis. However, conditions have been found under which the amide ligands in these complexes are substituted by nitriles, which makes it possible to employ such complexes as hydration catalysts.

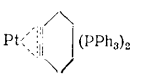
Bivalent nickel, copper, and cobalt complexes of picolinic acid or its amide[33–35] proved to be effective and highly selective catalysts of the hydration of 2-cyanopyridine (pH 5.5 to 8.5, reaction temperature 60 °C and above). In most cases the catalysts remained unchanged after the reaction. The same complexes showed no catalytic activity when an attempt was made to hydrate 3- and 4-cyanopyridines. On the other hand, 2-cyanopyridines are not hydrated in the presence of cobalt(III) and platinum(IV) complexes, although the former reacts with 2-cyanopyridine on heating in aqueous solution.[35] The catalysis of the hydration of 2-cyanopyridine is evidently based on the displacement of the 2-carboxypyridine or pyridine-2-carboxylate ligand from the complex by a 2-cyanopyridine molecule, the subsequent hydration of the coordinated nitrile, and the repeated substitution of the amide ligand formed by the nitrile.[35]

The complex used as the hydration catalyst can be formed in the reaction mixture *in situ*. It is obtained using as the starting material the salts of metals† capable of giving rise to complexes with 2-carboxypyridines and their derivatives. Thus, when aqueous solutions of 2-cyanopyridine[33] and also 4-substituted 2-cyanopyridines[38] were heated with a large excess of nickel(II) or copper(II) chloride, chelates were obtained in which two molecules of the corresponding pyridine-2-carboxamide were present as ligands for each central ion. In the presence of a smaller amount of metal chloride, free amides are also produced together with the chelate complexes. The formation of a chelate complex which catalyses hydration directly also accounts for the conversion of 2,6-dicyanopyridine into pyridine-2,6-dicarboxamide when a mixture of this dinitrile and water is boiled in the presence of catalytic amounts of cobalt(II) acetate.[39]

A study of the hydration of substituted 2-cyanopyridines in the presence of the complex $[Cu(H_2O)(en)_2]Cl_2$ in a nearly neutral medium established that the reactivity decreases in the sequence[38] 2-cyano-4-methylpyridines > 2-cyanopyridine > 2,4-dicyanopyridine. Since an electron-donating substituent in the 4-position promotes and an electron-accepting substituent hinders hydration, it can be assumed that the rate-limiting stage of the process is the nucleophilic reaction involving the incorporation of the nitrile in the inner sphere of the complex. 2-Cyanoquinoline proved to be much less reactive than 2-cyanopyridine, apparently because of the lower capacity of the nitrogen atom of the pyridine ring to form a coordinate bond with the central ion. Whereas the 2-cyano-group in 2,4-dicyanopyridine is selectively hydrated while the 4-cyano-group is inert, in 2,6-dicyanopyridine both cyano-groups react and the product is pyridine-2,6-dicarboxamide. It is noteworthy that an increase of temperature (up to boiling of the reaction mixture) and of the duration of heating of aqueous solutions of nitriles and complex catalysts leads to the hydrolysis of pyridinecarboxamides and the formation of the corresponding carboxylic acids.[38]

Thus the hydration of nitriles with the cyano-group in the 2-position in the pyridine ring in the presence of certain bivalent metal complexes can be used to synthesise the corresponding amides. There is so far little information about the successful homogeneous catalytic hydration of other nitriles in the molecules of which there are no groups capable of chelating the ligands.

In the presence of catalytic amounts of zerovalent platinum complexes of phosphines and cyclohexyne, for example,



acetonitrile is converted into acetamide in a low yield after prolonged heating.[26,40] Benzonitrile is hydrated analogously.[40] It has been suggested that a coordinated hydroxo-group, appearing in the platinum complex under the reaction conditions, is responsible for the catalysis. Phenylacetonitrile,[26] which is a stronger CH acid than acetonitile, is not hydrated under these conditions and is merely incorporated in the inner sphere of the complex $Pt(C_6H_9)[CH(CN)Ph](PPh_3)_2$. When non-ionic phosphonocyclohexyne complexes of platinum react with αβ-unsaturated nitriles, the complexes exhibit a capacity to catalyse the addition of water to the C=C bond. Mainly di(2-cyanoethyl) ether and 3-hydroxyproprionitrile and only 8% of acrylamide have been obtained from acrylonitrile.[26]

The strong hydroxo-bases, formed when zerovalent platinum complexes of phosphines, for example $[Pt(P(t\text{-}Bu)_2Ph]_2$ and $Pt[P(iso\text{-}Pr)_3]_3$, are treated with water, were found to catalyst nitrile hydration.[41] After the reaction, the catalysts are isolated and changed. It has been suggested that complexes containing nitriles coordinated to platinum in the corresponding amido-complexes formed from them as a result of attack by OH^- ions are intermediates in the reaction. The degree of conversion of the initial nitriles is low and in the hydration of αβ-unsaturated nitriles the addition of water is not regioselective; in a number of cases the hydration of the C=C bond predominates. Under the conditions of acrylonitrile hydration, the dimer $CH_2=C(CN)CH_2CH_2CN$ was also formed.

† The metal salts are not usually catalysts of nitrile hydration, although it has been reported that various amides have been obtained from nitrile complexes with $PdCl_2$ on boiling with water[36] and also on treatment of solutions of nitriles in acetic acid with $TiCl_4$ and water.[37] However, it is noteworthy that the mechanisms of these reactions have not been studied, so that it is not clear to what extent the complexes and the hydrogen chloride, produced by the hydrolysis of $PdCl_2$ and $TiCl_4$ are each responsible for the hydration.

The hydration of acetonitrile at 80 °C in the presence of different hydroxophenyl and hydroxomethyl complexes $PtRL_2(OH)$ and the analogous acetamido-complexes $PtRL_2$. .(NHCOMe) has been described.[42] The phenyl complexes are more active than the methyl complexes. When R = Ph, the activity of the complexes decreases in the following sequence as a function of the nature of the ligand L:

$$PEt_3 > P(t\text{-}Bu)Me_2 > PPh_3 \simeq PMe_2Ph > P(t\text{-}Bu)_2Me \gg P(C_6H_{11})_3 .$$

When the catalytically most active complex $PtPh(PEt_3)_2(OH)$ was used, 173 moles of acetamide per mole of the catalyst were obtained for a low degree of conversion of acetonitrile (~11%). Under the same conditions, acrylonitrile gives rise to products of the hydration of both the C≡N and C=C bonds. Higher saturated aliphatic nitriles and benzonitriles are hydrated to a lesser extent than acetonitrile, partly because of the inhomogeneity of the reaction medium. Methyl cyanoacetate reacts with the above hydroxo-complexes, forming methoxycarbonyl(keten imino)- or cyanomethoxycarbonylmethyl complexes, for example:

$$PtPh(PEt_3)_2(N{=}C{=}CHCOOMe) \text{ or } Pt(Me)(dppp)[CH(CN)COOMe] ,$$

where dppp = 1,3-bis(diphenylphosphino)propane.

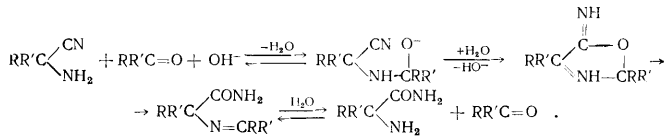
The catalytic hydration of benzonitrile has been carried out also in the presence of the cationic complex $[cis\text{-}Pt(PPh_3)_2.(o\text{-}CH_2C_6H_4CONH_2)]_2(BF_4)_2$. However, not more than 5 moles of benzamide were then obtained per mole of the catalyst. It has been shown[9] that the loss of catalytic activity in the given system is associated with the conversion of the initial complex into the complex $[cis\text{-}Pt(PPh_3)_2(o\text{-}CH_2C_6H_4CONH)]_2$.

The phosphine complexes of zerovalent rhodium and iridium, *trans*-$Rh(CO)(PPh_3)_2(OH)$ and *trans*-$Ir(CO)(PPh_3)_2(OH)$, are more active in the hydration of acetonitrile than the analogous phosphine complexes of platinum. In the presence of the iridium complex, nitriles such as phenylacetonitrile, acrylonitrile, and crotononitrile are also hydrated to the amides.[40]

An appreciable increase of the yields in the homogeneous-catalytic hydration has been achieved in a number of studies.[43–45] The authors began with the results of a study[46] according to which acetonitrile is hydrated to acetamide in a satisfactory yield and with a high selectivity in the presence of sodium chloropalladate and 2,2′-bipyridyl (bipy) at pH 10.4. It was shown[43] that a number of products of the reaction of sodium chloroplatinate [chloropalladate?] and 2,2′-bipyridyl, among which the neutral complex $Pd(bipy)Cl_2$ proved to be a most active catalyst of the hydration reaction are formed under the reaction conditions. Treatment of this complex with an equivalent amount of hydroxide ion yielded the complex $Pd(H_2O)(bipy)(OH)Cl$, which exhibits an even higher catalytic activity. The latter is retained when the chloride ion in the palladium complex is replaced by other anions ($MeCOO^-$, Br^-, OH^-) and bipyridyl is replaced by other bidentate nitrogen-containing ligands.[44] The hydration (at 76 °C and pH 5.5) of acetonitrile and butyronitrile in the presence of an excess of water and catalytic amounts of the above complexes afforded the amides in yields of 70–84% for a selectivity of 100%. The yields of adipamide, benzamide, and phenylacetamide in the hydration of the corresponding nitriles are low. Acrylamide is formed in 80% yield from a heterogeneous mixture of acrylonitrile and water at 60 °C in the presence of a catalytic amount of the complex $Pd(H_2O).(bipy)(OH)_2$ soluble in the nitrile.[45] In order to isolate the amide from the reaction mixture, the catalyst was decomposed with acid, the precipitated complex of the palladium salt of this acid and bipyridyl was filtered off, and the filtrate was evaporated. Study of the hydration kinetics of acetonitrile has established[44] that the amide formed inhibits the addition of water to the nitrile group. The results also support the view that the hydration involves the intramolecular attack by the OH group on the coordinated CN group.

Dichlorobis(η-cyclopentadienyl)zirconium apparently catalyses the hydration of α-hydroxyisobutyronitrile.[118]

Hydration specific to α-aminonitriles, which proceeds in an alkaline medium and is catalysed by carbonyl compounds, has been described. The reaction has been studied in relation to a series of α-aminonitriles with the amino-group at a secondary or tertiary carbon atom, acetaldehyde, isobutyraldehyde, acetone, etc. being used as the carbonyl compounds.[47–49] A carbonyl compound can be formed directly in the reaction mixture together with ammonia and hydrocyanic acid as a result of the hydrolytic decomposition of the α-aminonitrile. The hydration reaction proceeds in accordance with the following mechanism:



Its rate is determined by the rates of the reversible formation of the geminal aminoalkoxide anion and subsequent cyclisation to a substituted 5-imino-oxazolidine. The rate of cyclisation (in the presence of isobutyraldehyde as the catalyst) is then ~10^8 times higher than the rate of nucleophilic attack by OH^- ions on the nitrile group, which is the reason for the catalytic effect of carbonyl compounds.[49] Hydrolysis of the reaction mixtures (without the isolation of the α-aminoamides) makes it possible to obtain α-aminoacids in almost quantitative yields.[50]

IV. HETEROGENEOUS-CATALYTIC HYDRATION

The heterogeneous-catalytic hydration of nitriles can take place in the presence of acids or bases insoluble in the reaction mixture. Anion-exchange resins were frequently used previously as catalysts and 3- and 4-cyanopyridines were hydrated. Under these conditions, 85–96% of 3-cyanopyridine is converted into the amide. The subsequent hydrolysis results in the simultaneous formation of 3-carboxypyridine bound chemically to the catalyst (up to 5–10%), which lowers its activity and necessitates its periodic regeneration.[1,51–55] Attention is concentrated below on new trends in the hydration of nitriles in the presence of heterogeneous catalysts whose action is not based on their acidity and basicity (or not solely on these factors) but on other properties.

1. Hydration in the Presence of Metal Oxides

Among metal oxides, manganese(IV) oxide is the most effective catalyst of the hydration of nitriles. As early as 1934, the formation of benzamide was observed when benzonitrile came into contact with active MnO_2 at room temperature.[56,57] It was suggested[57] that the reaction proceeds by virtue of the water bound to MnO_2 and that the yield of the amide (~3%) is limited by its content. Subsequently the hydration was carried out in methylene chloride[58] and dioxan[59] in the presence of a large amount of MnO_2 containing sufficient bound water to satisfy the stoichiometry of the reaction. It was not until the 1970's that it was established that manganese(IV) oxide is the catalyst and that there is no necessity for its preliminary "saturation" with water for effective hydration.[60,61]

The study of the hydration of benzonitrile in the presence of the β- and γ-modifications of MnO_2 showed that the activity of the catalyst is not determined by its crystal lattice type but by its specific surface,[62] which is usually 30–80 $m^2 g^{-1}$. The catalytic activity of MnO_2 depends on its method of preparation[55] in so far as the conditions of the synthesis influence the surface area of the oxide. The catalyst is used in a powdered or pelleted form. Because of the low degree of coverage of the manganese(IV) oxide surface by the nitrile in the hydration reaction,[63] the yield of the amide per unit mass of the catalyst and per unit time is low and for this reason a comparatively large amount of MnO_2 is used to synthesise the amides, its mass in the hydration reaction carried out by the periodic method usually exceeding severalfold the mass of the nitrile.

Aromatic nitriles, including *o*-substituted nitriles, and water, taken in molar proportions of 1 : 1.2 at 100–140 °C in the presence of MnO_2, form amides in high yields. Hydrolysis takes place to a very slight extent (1–2%),[60,64] but on raising the temperature the yield of the acid increases (it reaches 28% in the reaction with benzonitrile at 200 °C). Aromatic nitriles are hydrated extremely smoothly also in organic solvents—methylene chloride[58] and dioxan.[59]

Halogenoacetonitriles are hydrated to the amides in the presence of MnO_2 in high yields and with a high selectivity at temperatures below 100 °C. At higher temperatures side reactions play a significant role. Thus the hydration of trichloroacetonitrile yielded, together with the amide, appreciable amounts of ammonia, hydrogen chloride, carbon dioxide, and chloroform. The formation of the last compound can be accounted for by the hydrolysis of trichloroacetamide, the decarboxylation of the trichloroacetate anion, and the reaction of the trichloromethyl anion with water.[64]

The hydration of aliphatic nitriles in the presence of MnO_2 in the presence of small amounts of water proceeds to an appreciable extent only on heating to 140–170 °C.[60,64] This results in low yields of amides contaminated by products of side reactions—hydrolysis and oxidation.[65] (The simultaneous reduction of Mn^{4+} to Mn^{2+} leads to the deactivation of the catalyst.) The formation of NH_3 and CO_2 on hydration of acetonitrile is caused mainly by the hydrolysis of acetamide and subsequent "oxidative decarboxylation"[66] of acetic acid:

$$MeCN \xrightarrow{H_2O} MeCONH_2 \xrightarrow[-NH_3]{H_2O} MeCOOH \xrightarrow[-H_2O]{O} [HOOCCOOH] \xrightarrow{O} 2CO_2 + H_2O .$$

Slow acetamide and acetonitrile oxidation reactions also take place and the oxidation of acetonitrile results in the formation of hydrogen cyanide and carbon dioxide. In the hydration of isobutyronitrile the main side products are hydrogen cyanide and acetone, which are formed via α-hydroxyisobutyronitrile; acetone is also formed in the oxidation and decarboxylation of α-hydroxyisobutyric acid.[65]

Satisfactory yields of amides derived from unsubstituted and β-hydroxy- and β-methoxy-substituted aliphatic nitriles are achieved as a result of hydration in the presence of MnO_2 under mild conditions (60–80 °C) in dilute aqueous solutions.[61,67]

When the nitriles are sparingly soluble in water, the initial reaction mixtures are homogenised by organic solvents or the reaction is carried out in the presence of emulsifying agents.

The hydration of succinonitrile in dilute aqueous solutions results in the initial formation of 3-cyanopropionamide, which then combines with a water molecule and is converted into succinamide. Conditions have been found under which each of these compounds is obtained in a high yield.[67] At 60 °C, the rate constants for the addition of the first (activation energy 56 kJ mol^{-1}) and second water molecules are in the ratio 4 : 1. This ratio shows that the influence of the substituents in both reactions is based mainly on the inductive effect. On the other hand, the direct influence of the neighbouring $CONH_2$ group, which leads to a significant alteration of the rate (as for 2-cyanobenzamide coordinated to cobalt[16]), and what is more to a change in the reaction pathway (as in the hydration of succinonitrile in the presence of a copper-containing catalyst[68]), is not observed. At the same time the influence of substituents in the molecules of nitriles on their reactivity is not caused solely by polar effects.[63,67] Thus the effective rate constants (at 60 °C) for the hydration of 3-cyanopropionamide, 3-hydroxypropionitrile, and 3-methoxypropionitrile are in the proportions 2.1 : 1.3 : 1, although the polar constant $\bar{\sigma}^*$ for all three substituents are similar (1.75, 1.60, and 1.73).[69] The causes of the above ratios will be examined below in the discussion of the hydration mechanism.

Under the influence of MnO_2 both in the presence of small amounts of water and in its absence, acrylonitrile and methacrylonitrile partially polymerise via the C=C bonds. In the macromolecules of the polymer based on methacrylonitrile, amide groups as well as short conjugated segments $(\rangle C{=}N{-})_n$ were identified together with the nitrile groups. It has been suggested[64] that the polymerisation proceeds via a radical mechanism and is initiated directly by the free radicals formed as a result of the oxidation of organic compounds by manganese oxide.[70] Acrylamide has been obtained as the main reaction product (70%) from acrylonitril in aqueous solution in the presence of a radical reaction inhibitor, but under these conditions, too, side reactions involving oxidation by manganese oxide take place, which leads to the rapid deactivation of the oxide.[71]

The nitrile groups of polyacrylonitrile in an aqueous solution of potassium thiocyanate at 80 °C are hydrated in the presence of MnO_2 (a degree of conversion of 50% has been achieved).[72]

3-Cyanopyridine in aqueous solution at 85 °C in the presence of MnO_2 is converted into nicotinamide, a product of practical importance, in a high yield (96%). Under the proposed conditions, the reaction takes place in the kinetic region and is described satisfactorily by a first order equation.[62] Similar results were later obtained in other studies[55,73] for the hydration of 3-cyanopyridine in the presence of MnO_2. The cyano-group of cyanamides is hydrated in aqueous solutions in the presence of the same oxide.[74,75]

When phenyl- and diphenyl-acetonitriles were heated with water and MnO_2, the corresponding amides were not obtained because the oxidation reactions predominated.[76] A polymer, soluble in organic solvents, whose molecules incorporated the conjugated (C=N−) chains as well as amide, nitrile, and carboxy-groups, was formed from phenylacetonitrile in the presence of MnO_2 at 80–125 °C (the reaction mechanism has been published[76]). Oxidation of diphenylacetonitrile, having only one hydrogen atom in the α-position, with manganese oxide afforded a high yield of tetraphenylsuccinonitrile.[76]

α-Hydroxynitriles whose OH groups are located at a primary or secondary carbon atom are hydrated selectively and in high yields to α-hydroxyamides in dilute aqueous or aqueous dioxan solutions at room temperature in the presence of MnO_2.[77] An increase of reaction temperature promotes the hydrolysis of the amides formed. Attention has been drawn to the appreciable adsorption of α-hydroxyamides on manganese(IV) oxide. The reactivity of the α-hydroxynitriles RCH(OH)CN decreases in the following sequence in terms of the substituent R: H > Me > Et > n-Pr > iso-Pr. The hydration of α-hydroxynitriles which are tertiary alcohols proceeds in a more complex manner. The hydroxynitriles undergo simultaneous dehydrocyanation under the reaction conditions,[78] which lowers the yield of α-hydroxyamides.

Since α-hydroxyisobutyramide, formed on hydration of α-hydroxyisobutyronitrile, can be used as the starting material for the synthesis of methacrylic monomers,[79-81] most attention has been devoted to the study of the reactions of this nitrile.[63,82,119] It has been found that dehydrocyanation, which is reversible in the absence of MnO_2, becomes almost irreversible in the presence of this oxide. The hydrocyanic acid formed is rapidly adsorbed on the surface of manganese(IV) oxide and is then comparatively slowly oxidised to cyanogen, which gives rise to oxamide on hydration. Under dehydration conditions, dehydrocyanation proceeds until the attainment of equilibrium over a period shorter than 5 min. In the course of approximately the same time, adsorption equilibrium is established between the dissolved hydrocyanic acid and the hydrocyanic acid on the surface of MnO_2. The hydration of α-hydroxyisobutyronitrile as well as the oxidation of HCN take place much more slowly, i.e. the dehydrocyanation and adsorption period in the main separated in time from the hydration and oxidation period. In the hydration of α-hydroxyisobutyronitrile in an aqueous medium the yield of amide does not therefore exceed 70%. When the reaction is carried out in a less polar medium (in aqueous dioxan solutions), where the dehydrocyanation is appreciably retarded, it is possible to increase the yield of α-hydroxyisobutyramide. The addition of acetone to the reaction medium, which shifts the equilibrium towards hydrocyanation with reformation of the starting material, is even more effective. An important feature of the hydration in the presence of acetone is the presence of an extremum in the relation between the effective rate constants and the water content in the aqueous acetone mixture (there is a minimum at a water mole fraction of 0.8), which can be attributed to a change in the internal structure of the water–acetone mixture.[82] The optimisation of the process taking into account its inhibition by the α-hydroxyisobutyramide formed (adsorption on MnO_2) revealed the conditions (45 °C, 1.3 M nitrile, 3.4 M acetone, 7–8 h) under which α-hydroxyisobutyramide is obtained in 95% yield with a selectivity of 96% in the presence of the catalyst specimen employed. The shift of the dehydrocyanation equilibrium by the introduction into the reaction mixture of the ketone formed as a result of the reaction is effective also in the hydration of other α-hydroxynitriles unstable in water.[63,82]

In aqueous solutions in the presence of manganese(IV) oxide, α-aminoisobutyronitrile is converted into α-aminoisobutyric acid, α-aminoisobutryamide, α-hydroxyisobutyramide, acetone, ammonia, hydrocyanic acid, and its oxidation products. Evidently the hydration of α-aminoisobutyronitrile is accompanied by the hydrolysis of both this compound and of the hydration product as well as secondary reactions of the hydrolysis products:[63]

$$Me_2C(NH_2)CN \left\{ \begin{array}{l} \xrightleftharpoons[-NH_3]{H_2O} Me_2C{=}O + HCN \rightleftarrows Me_2C(OH)CN \xrightarrow{H_2O,\,MnO_2} Me_2C(OH)CONH_2, \\ \xrightarrow[MnO_2]{H_2O} Me_2C(NH_2)CONH_2 \xrightarrow{H_2O,\,MnO_2} Me_2C(NH_2)COOH + NH_3. \end{array} \right.$$

The replacement of α-aminoisobutyronitrile in the above system by its hydrochloride rules out hydrolysis almost completely and appreciably accelerates the hydration, which leads to a virtually quantiative yield of α-aminoisobutryamide hydrochloride (45 °C, 1 h). The subsequent binding of the hydrogen chloride by a strong base and an increase of the temperature of the reaction mixture to 90 °C make it possible to achieve with the same yield the hydrolysis of the resulting amide, catalysed by manganese(IV) oxide, to α-aminoisobutyric acid. 2-Amino-2-methylbutyramide and 2-amino-2-methylbutyric acid are formed analogously from 2-amino-2-methylbutyronitrile.[63]

Data on the kinetics and mechanism of the hydration of nitriles in the presence of manganese(IV) oxide are of interest. S-Shaped kinetic curves for the hydration of benzonitrile in the presence of MnO_2 and small amounts of water, the acceleration of the reaction by the preliminary treatment of the catalyst with benzonitrile, its retardation as a result of a similar treatment with water, and other kinetic features of the hydration reaction suggested that the first stage of the process is the formation of an intermediate complex of the nitrile with MnO_2, which is then subjected to nucleophilic attack by water.[83] It follows from the relations presented above between the rate of hydration and the polar properties of the substituents in the nitrile molecules that, in the hydration in the presence of an excess of water, the rate-limiting stage is the second.[63,67] Kinetic data have shown[63] that the complex of the nitrile with MnO_2 is then attacked by water from the bulk phase.

In the reactions of hydroxynitriles the hydroxy-group as well as the nitrile group can react with the catalyst surface, for example, via the formation of hydrogen bonds. Under the conditions of the hydration α-hydroxynitriles with a tertiary OH group, such interaction is probably the cause of the acceleration of the dehydrocyanation side reaction in the presence of manganese oxide, which was mentioned above.

In view of the appreciable electron-accepting capacity of the group $\alpha\text{-}\overset{+}{N}H_3$, it was to be expected that the hydration of α-ammonianitrile, like the hydrolysis of α-ammonia-amide, will proceed at a higher rate than the corresponding reactions of the α-amino-compounds. However, as shown above, this happens only in the case of the hydrolysis. The opposite behaviour in the hydration reaction can be attributed to the fact that the α-aminonitrile is adsorbed on the acid centres of the catalyst via the highly basic NH_2 groups; since both σ-bonds in the group $C{-}C{\equiv}N$ are colinear,[1] contact between the CN group in the adsorbed α-aminonitrile, whose position is to a large extent fixed, and the surface of the catalyst is hindered for geometrical reasons with a consequent retardation of its reaction with water. In the hydration of α-ammonianitrile adsorbed on the catalyst via the nitrile group such steric hindrance does not arise.

Depending on their position in the nitrile molecule, the same functional groups have exerted the opposite influence on the reactivity of the nitrile group. Whereas substituents in the α-position in the nitrile capable of interacting with the catalyst play a negative role in the hydration, the β-substituents accelerate the hydration as a result of their interaction with the catalyst. Presumably the higher reactivity of 3-aminocarbonyl- and 3-hydroxy-propionitriles compared with 3-methoxypropionitrile (see above) is due to the interaction of both the $CONH_2$ or OH group and the CN group with the surface of the catalyst, which leads to the formation of energetically favourable closed structures and to an increase of the surface concentration of the substrate.

It is striking that hydrocyanic acid is not hydrated in the presence of MnO_2 and is instead oxidised to cyanogen. This may be a consequence of the formation of the hydrogen bond between the hydrogen atom of HCN and the oxygen-containing groups on the surface of the catalyst with subsequent elimination of the hydrogen atom from the HCN molecule.[63]

Despite the fact that manganese(IV) oxide proved to be a highly active catalyst of the hydration of nitriles, in some cases its application is limited, as shown above, by its high oxidising capacity, as a result of which the addition of water to the nitrile group is not always the main pathway in the

reaction between reactants. Hydration in the presence of other metal oxides is therefore of interest.

Numerous oxides proposed as hydration catalysts are inactive or their activity is low[120] in the temperature range where hydration takes place in the presence of MnO_2. The study of the interaction of benzonitrile with water in the presence of various oxides under comparable conditions[84] showed that hydration proceeds at an appreciable rate as a rule only at 175–225 °C. Hydration is induced by almost all transition metal oxides, but, not counting MnO_2, the oxides of the iron subgroup elements proved to be the most active. Results of practical interest have been obtained with iron(III) oxide. At 225 °C benzamide has been obtained in 71% yield (the yield of benzoic acid was 7.5%); when Fe_2O_3 is re-used, its activity does not fall. In contrast to MnO_2, iron(III) oxide proved to be an extremely effective catalyst of the hydration of readily oxidisable nitriles such as phenylacetonitrile and diphenylacetonitrile. It has been shown that the hydration of nitriles in the presence of Fe_2O_3, as in the presence of MnO_2, is preceded by the interaction of the catalyst with the CN group.[84] Cobalt(III) and nickel(III) oxides are no less active in the hydration of benzonitrile than Fe_2O_3, but, under the conditions investigated (Co_2O_3 at 225 °C and Ni_2O_3 already at 175 °C), they interact to an appreciable extent with the reaction products, which rules out their reuse. After prolonged refluxing of aqueous solutions of 3- and 4-cyanopyridines in the presence of NiO, high yields of the amides were obtained.[33] On the other hand, in the reaction of 2-cyanopyridine under the same conditions, the amide obtained hydrolyses to 2-carboxypyridine, which forms a chelate compound with a catalyst. It has been suggested that the geminal positions of the nitrogen atoms of the pyridine ring and of the amide group of this compound are responsible for their simultaneous and specific adsorption on the same catalytic surface centre, which is the cause of the ready hydrolysability of the amide group.[33] At the same time the hydration of 2,4- and 2,6-dicyanopyridines to the corresponding dicarboxamides has been achieved in another study[38] in the presence of NiO.

In the hydration of benzonitrile (at 225 °C) copper(II) and zinc oxides proved to have activities similar to those of the oxides of the iron subgroup elements. However, in the presence of CuO the reaction products interact with the catalyst, while in the presence of ZnO the hydration is accompanied to a large extent by the hydrolysis of the benzamide formed.[84] Under milder conditions (refluxing of the aqueous solutions), copper(II) oxide proved to be a weak catalyst of the hydration of 3- and 4-cyanopyridines, but, like NiO, it induces appreciable hydrolysis of 2-cyanopyridine and the formation of a chelate compound.[33] Zinc oxides accelerates slightly the hydrolysis of stearonitrile at 180 °C.[85]

The analogues of zinc oxide in the subgroup, namely the cadmium and mercury(II) oxides, undergo irreversible changes in the course of the reaction.[84] It has been shown[86] that cadmium oxide is bound in the form of a salt to the benzoic acid formed. The interaction of benzonitrile and of *p*-substituted benzonitriles with water and CdO has been directed towards the formation of diamminecadmium benzoates in quantitative yields:

$$2RC_6H_4CN + 3H_2O + CdO \rightarrow (RC_6H_4COO)_2Cd\cdot 2NH_3.$$

The reactions catalysed by metal oxides are frequently catalysed also by the sulphides of the same metals. In the presence of copper(II) sulphide 25% of benzamide has been obtained from benzonitrile at 225 °C. The instability of CuS in the presence of water was also manifested under these conditions.[87]

The activity of the oxides of Group IIA elements proved to be low and approximately the same.[84] Among the oxides of Group III elements, alumina proved to be a weak but extremely selective hydration catalyst.[84] The adsorption of nitriles on this oxide is accompanied by their partial conversion into amides.[88,89] High yields of aromatic and saturated aliphatic amides have been obtained[90] on refluxing solutions of the corresponding nitriles in t-butyl alcohol in the presence of alumina modified by treatment with potassium fluoride.[91] The water required for hydration is present in the catalyst. Alumina and potassium fluoride taken separately do not induce an appreciable hydration of the nitriles, other conditions being equal.

Among the oxides of Group IV elements, a satisfactory yield of benzamide (59%) is obtained in the presence of lead(II) oxide. Zirconium and germanium(IV) oxides exhibit a weak catalytic activity, while titanium(IV) and silicon oxides are almost inactive. Among the oxides of Group V elements, a tendency has also been observed towards an increase of activity with increase of the atomic weight. In the presence of Bi_2O_3 and V_2O_5 benzamide has been obtained in almost identical satisfactory yields and both oxides also give rise to an appreciable hydrolysis of benzamide.[84] (The hydrolysis of amides in the presence of V_2O_5 at 150–180 °C has been used as a preparative method of synthesis of carboxylic acids.[92]) The activity of the oxides of Group VI metals increases in the sequence $Cr_2O_3 < MoO_3 < WO_3$. In the presence of the last oxide 41% of benzamide was obtained at 225 °C (with a selectivity of 95%).[87]

Comparison of the hydrating capacities of various higher and lower oxides of the same metals showed that in all cases the higher oxides are more active. A relation between the activities of various oxides and their acid–base properties has not been discovered. Thus the activities of Bi_2O_3 and V_2O_5, the first of which has basic properties and the second has acid properties, are similar.[84] Nor has it been possible to correlate the activities of various metal oxides with the electronic configurations of the corresponding cations. Overall, the oxides of transition metals with moderate acid–base properties proved to be the most active and selective in the reaction considered.

2. Hydration in the Presence of Metal-Containing Catalysts

Among the known metal-containing catalysts, the most active in the hydration of nitriles are those based on copper. It is known that metallic copper is a catalyst of the alkaline hydrolysis of polyacrylonitrile.[93] However, the first attempts at the hydration of nitriles in the presence of catalysts based on metallic copper were described subsequently.[33,94,95] The best results were achieved in the hydration of 2-, 3-, and 4-cyanopyridines in aqueous solutions: the yield of the amides reached 50% for a low selectivity. Later the first patent was published[96] on the hydration of acrylonitrile and other nitriles in the presence of catalysts incorporating, together with copper salts, which the authors erroneously assumed to be the main carriers of catalytic properties, also zerovalent copper. Since then numerous versions of copper catalysts for the hydration of nitriles (copper on oxide and organic polymeric carriers,[97] Raney copper, and powdered copper with a high surface area) have been described mainly in the patent literature.[2] The catalysts are obtained in the usual way, i.e. by reducing mixtures of finely dispersed copper(II) oxide and other oxides, for example the Atkins catalyst, prepared beforehand. Copper(II) oxide is usually reduced at 170–250 °C with hydrogen, the activity of the catalyst increasing with decrease of the hydrogen content in

its mixture with nitrogen or another inert gas.[98] At a reduction temperature of 210 °C the optimum hydrogen content in the hydrogen–nitrogen mixture is 3 mole %. The rate of hydration increases with increase of the degree of reduction of CuO, but the presence of small amounts of CuO and Cu_2O in the copper catalyst does not exert an appreciable influence on its activity.[99,100] The rate of hydration is influenced also by inorganic salts present as admixtures in the liquid component of the reaction mixture and in the catalyst.[121,122]

In order to obtain active copper powders, copper salts (sulphates, chlorides, acetates, etc.) are also reduced by metal hydrides, alkali metal tetrahydroborates, metals, hydrazine, formaldehyde, and other reductants.[2] As a rule, there is no direct relation between the activity of the catalysts and their surface area (10–120 $m^2\ g^{-1}$). The nature of the carrier has a greater influence on the activity.

After prolonged use in continuous processes, copper containing hydration catalysts are gradually deactivated, which is accounted for by the oxidation of copper by the traces of atmospheric oxygen dissolved in the reaction mixture and by the blocking of the catalyst surface by copper(II) oxide. The regeneration of oxide catalysts consists in their reduction, in the first place by hydrogen, as described above. Additional oxidation of the partly spent catalyst by atmospheric oxygen before its reduction may prove useful.

The efficiency of the regeneration of catalysts which have lost their activity depends to a large extent on the nature of the carrier. Thus the catalyst obtained by the thermolysis (in the presence of hydrogen) of copper formate deposited on the cross-linked copolymer of 4-vinylpyridine and 1,4-divinylbenzene contains finely dispersed copper and exhibits a high initial activity in the hydration reaction.[97] However, after its deactivation, it is impossible to restore fully its activity by passing hydrogen, while less dispersed copper catalysts obtained under the same conditions on metal oxides are readily regenerated. It has been suggested[97] that the finely dispersed copper on the polymeric carrier becomes partially aggregated on contact with atmospheric oxygen. It is also possible that the carrier undergoes chemical changes in the course of the high temperature reduction and this is responsible for the alteration of its influence on the activity of copper.

One of the ways of increasing the lifetime of copper-containing catalysts involves the introduction of halide ions into the reaction mixture,[101] in particular of potassium bromide.[102] The catalytic activity of the oxidised copper is almost fully restored after it has been treated with potassium iodide.[103]

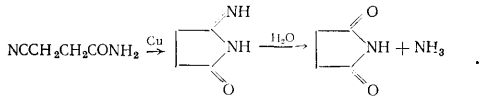
Aromatic and unsubstituted aliphatic nitriles are hydrated with a high selectivity in the presence of various copper-containing catalysts; appreciable amounts of side products have not been detected. The yields of aliphatic amides at 100–110 °C are close to theoretical values.[104] The synthesis of benzamides with a substituted amino-group in the 2-position from 2-chlorobenzonitrile and piperidine or another cyclic base in the presence of a bronze is apparently based on the hydration of aromatic nitriles in the presence of copper.[105]

The kinetics of the hydration of aromatic nitriles for a molar ratio of water and the nitrile of 1.5 : 1 in dioxan in the presence of the Cu–MgO catalyst are described by a second-order equation. The effective specific rate constants for the hydration increase with increase of the electron-accepting capacity of the substituent in the benzene ring of the nitrile. A satisfactory correlation has been established between these constants and the Hammett σ constants (ρ = +0.33).[104] The kinetics of the hydration of aliphatic nitriles in an excess of water in the presence of the Cu–MgO catalyst obey a first-order equation. A satisfactory correlation between the effective specific rate constants and the Taft σ^* constants (ρ = +1.78) has been observed for the hydration of acetonitrile, propionitrile, butyronitrile, 3-hydroxypropionitrile, and acrylonitrile. The low absolute reaction constants show that the polarity of the transition state in the hydration of nitriles in the presence of copper catalysts is low.[104]

In the presence of the Cu–MgO catalyst chloroacetonitrile partly undergoes side reactions with evolution of hydrogen chloride, which interacts with the catalyst. On lowering the hydration temperature to room temperature, it was possible to suppress to a large extent the formation of HCl and to obtain a high yield of chloroacetamide. In the presence of this catalyst 3-chloropropionitrile undergoes dehydrochlorination together with hydration, which leads to the formation of acrylamide as the main reaction product.[104]

In contrast to 2-hydroxynitriles, 3-hydroxypropionitrile is hydrated smoothly in the presence of copper (activation energy E_a = 60 kJ mol^{-1} at 90–110 °C).[104,106] 2-Methoxyisobutyronitrile is also hydrated, although the reaction is very slow owing to steric hindrance.[107]

The hydration of the nitriles of dibasic aliphatic acids in an excess of water in the presence of the Cu–ZnO–Al_2O_3 catalyst has been described.[68] Adiponitrile is hydrated, as in the presence of manganese(IV) oxide, initially to 5-cyanovaleramide, which is then converted into adipamide. The hydration of succinonitrile involves the formation of 3-cyanopropionamide and succinimide (instead of succinamide as in the presence of MnO_2). Malononitrile is hydrated to 2-cyanoacetamide and at the same time is partly converted into a polymeric product. In the presence of an excess of water the ratios of the rate constants for the addition of the first water molecule to adipo-, succino-, and malono-nitriles are 1.35 : 1 : 9. The highest reactivity of malononitrile can be naturally accounted for by the mutual activation of the two cyano-groups. However, the lower rate constant for succinonitrile than in the hydration of adiponitrile is unexpected, since the negative polar effect of the 2-cyanoethyl group of succinonitrile is somewhat greater than that of the 4-cyanobutyl group of adiponitrile. Presumably the hydration of succinonitrile is preceded by the interaction of the active centres of the catalyst, in close proximity, with both cyano-groups of the dinitrile with formation of a cyclic complex, in which at least one cyano-group is π-bonded to the metal. On the other hand, in the hydration of adiponitrile such a cyclic complex would be strained and in this case electron-donating properties are therefore shown only by the *n* electrons of the cyano-group, which is the reason for the higher reactivity of adiponitrile. The unusual interaction of succinic acid derivatives with the copper catalyst may be responsible also for the fact that 3-cyanopropionamide is not hydrated but undergoes cyclisation in an aqueous solution in the presence of zerovalent copper:



It is noteworthy that the rate constant for the hydration of adiponitrile is greater by a factor of ~1.7 than for 5-cyanovaleramide.[68] A greater reactivity of the cyano-group in the adiponitrile molecule than in the compound where one cyano-group has already reacted has been observed also in a number of other reactions of adiponitrile.[1]

The hydration of acrylonitrile in the presence of copper-containing catalysts has been studied more thoroughly than for any other nitrile. The numerous varieties of catalysts based on zerovalent copper described have been proposed primarily for the hydration of acrylonitrile. In the presence

of copper-containing catalysts acrylamide is formed in high yields. In the presence of the $Cu-Cr_2O_3$ catalyst at temperatures not exceeding 120 °C up to 90% of acrylonitrile is converted into acrylamide when the catalyst is used repeatedly.[108] The Cu–MgO and $Cu-ZnO-Al_2O_3$ catalysts as well as Raney copper also exhibit a high activity in the hydration of acrylonitrile.[97,108,109] After prolonged hydration in the presence of the $Cu-SiO_2-MgO$ catalyst, the yield of acrylamide is 85%.[97] Certain technological aspects of the hydration of acrylonitrile in the presence of $Cu-ZnO-Al_2O_3$ in an excess of water and, in particular, the quantitative dependence of the rate of hydration in a continuous process on temperature, the linear flow rate in the reactor, and the initial concentration of acrylonitrile in the reaction mixture, as well as the phase equilibria in the systems formed by the initial nitrile, the amide, water, and other substances have been examined.[71,108,110,111] The hydration of acrylonitrile in the presence of Raney copper in a flow-circulation system has been described[112] and the same paper also presents an empirical equation for the process kinetics.

The hydration of acrylonitrile in the presence of copper-containing catalysts is not fully regioselective. Together with the hydration of the cyano-group, water adds to the C=C bond under the reaction conditions with formation of 3-hydroxypropionitrile, which then partially reacts with a second acrylonitrile molecule or undergoes hydration. This leads to the formation of di(2-cyanoethyl) ether and 3-hydroxypropionamide.[106] These reactions have been studied quantitatively in the hydration reaction in the presence of the $Cu-ZnO-Al_2O_3$ catalyst.[106] It has been found that, by virtue of their occurrence in the temperature range 80–120 °C, the selectivity of the hydration to acrylamide is 97–93%. At 100 °C in a continuous process the selectivity increases to 99.5% (for a degree of conversion of acrylonitrile of 90%) as a consequence of the elution from the catalyst of traces of alkali, which catalyse the addition of water to the C=C bond. The hydration of the double bonds is also accelerated by copper(II) oxide, which is incorporated to a greater or lesser extent in the catalysts based on metallic copper.[123] However, the possibility of the side reaction involving the formation of 3-hydroxypropionitrile depends not only on the admixture in the catalyst but also on the structure of the latter. Whereas in the hydration reaction in the presence of Raney copper carefully washed with water acrylamide is virtually the only reaction product, when catalysts deposited on certain carriers are employed 3-hydroxypropionitrile is formed in appreciable amounts; under these conditions, the more basic the carrier the lower the selectivity of the hydration to acrylamide (for example, water adds to the C=C bond particularly vigorously in the presence of the Cu–MgO catalyst).[71,97] The replacement of the basic MgO by the SiO_2-MgO carrier, which exhibits acidic properties, made it possible to suppress to a large extent the formation of 3-hydroxypropionitrile: under comparable conditions in the preparation of the catalysts and their tests, the selectivity in the formation of acrylamide increased from 75% to 97%.[97] It is therefore undesirable to employ catalysts containing basic components for the hydration of the C≡N group in unsaturated nitriles capable of combining with water via the C=C double bond, although these catalysts may be entirely suitable for the synthesis of amides from other nitriles.

Small amounts of other side products are also formed in the hydration of acrylonitrile. Thus traces of acrylamide hydrolysis products, namely, acrylic acid and ammonia, have been found in the reaction mixture.[106,113] Only above 120 °C are these admixtures formed in more appreciable amounts.[108] Microadmixtures of a number of unsaturated amides, namely heptatrienamide, pentadienamide, and 5-cyanopent-2-enamide, which may be the products of the catalytic hydration of the corresponding nitriles present as admixtures in the initial acrylonitrile, have been detected in acrylamide.[114] Under the conditions of the hydration reaction in the presence of Raney copper containing adsorbed hydrogen, there is a possibility of side reactions involving the hydrogenation of acrylonitrile, which leads to the appearance of admixtures of n-propylamine in acrylamide.[2]

The kinetics in the initial period of the hydration of acrylonitrile in an excess of water are described by an equation which is of first order with respect to the nitrile ($E_a = 75.8–86.7$ kJ mol^{-1}).[100,108] In an excess of acrylonitrile the reaction is also of first order with respect to water.[100] In the hydration of acrylonitrile as well as other nitriles in an excess of water up to high degrees of conversion the reaction kinetics do not obey the equation derived for the initial period of the hydration process, which can be explained by the inhibition of the reaction by the amides formed, through preferential adsorption of acrylamide on the catalyst surface.[71,97,100,109,122] Calculation based on the kinetic data for high degrees of conversion using different copper catalysts on carriers[97] showed that the ratios of the adsorption coefficients for a number of amides and the corresponding nitriles are 10 : 1–50 : 1. It has been shown recently that acrylamide is not the only reaction product inhibiting the hydration of acrylonitrile. The acrylic acid formed in the hydrolysis of acrylamide in an amount as much as 0.7 mole % of the initial nitrile reduces the rate of hydration under comparable conditions by more than a factor of two. Under the influence of acrylamide, the same effect is attained when its content is ~15%. Another side product, namely 3-hydroxypropionitrile, does not affect the rate of hydration of acrylonitrile.[100]

Under conditions of the hydration of methacrylonitrile in the presence of copper-containing catalysts, side reactions do not occur to an appreciable extent, in contrast to acrylonitrile; methacrylamide (96%), which is an industrial monomer, and the nitrile which has failed to react have been isolated from the reaction products. The first order reaction rate constant diminishes during hydration with increase of the content of the amide in the reaction mixture. The activation energy in the temperature range 61–90 °C is 55.7 kJ mol^{-1}.[115]

Raney copper has been used as the catalyst of the hydration of the cyano-groups of polyacrylonitrile in a saturated aqueous solution of potassium thiocyanate. A polymer containing up to 34% of acrylamide elementary units was obtained. Polymerisation via the cyano-groups with formation of azapolyene sections in the macromolecules also occurs under the hydration conditions.[71,72]

The data for the hydration of nitriles in the presence of oxide catalysts (see above) suggest that the hydration in the presence of copper includes a stage in which the nitrile interacts with the catalyst (activation of the cyano-group) with subsequent addition of water. The data presented above for the kinetics of the hydration of dinitriles[68] agree with the hypothesis that the cyano-group interacts with the catalyst surface. Important evidence in support of this is provided by the polymerisation via the cyano-groups of polyacrylonitrile under the influence of a hydration catalyst, i.e. the occurrence on copper of a reaction in which water is not involved. The positive reaction constants ρ in the Hammett and Taft equations presented above show that the rate of hydration of nitriles is limited by the rate of nucleophilic attack by water on the CN group.[104] If the interaction of the catalyst with the nitrile, for example the formation of a complex, were the rate-limiting stage, then the constant ρ would have had the opposite sign. The mechanism proposed by Elsemongy and Onsager,[109] according to which the catalyst

activates both the nitrile and water, is also inconsistent with the observed correlations. Thus the sequence of the principal stages of the hydration process is apparently clear. However, it has been shown[100] that, in order to refine the reaction mechanism, it is necessary to carry out additional studies on the adsorption and other processes occurring during hydration.

An attempt has been made to hydrate the thiocyanate group in organic compounds in the presence of a copper catalyst.[116] However, when an aqueous solution of methyl thiocyanate was heated in the presence of Raney copper, only insignificant amounts of *S*-methyl thiocarbamate were found in the reaction products. It was discovered that the main reactions of methyl thiocyanate involve the hydrolysis of the SCN and $SCONH_2$ groups at the sulphur–carbon bond and the homolytic reactions of the SCN group induced by the presence of copper.

Catalysts based on metallic nickel have also been used for the hydration of nitriles.[33,94,95,117] Urushibara nickel (nickel on a zinc carrier) and Raney nickel proved to be the best catalysts. The hydration was carried out by prolonged refluxing of nitriles with an excess of water in the presence of these catalysts. The amides have been obtained in high yields from benzonitrile, a series of *p*-substituted benzonitriles, and 3-, 4-, and 2-cyanopyridines. *o*-Substituted benzonitriles and aliphatic nitriles have been converted into amides in moderate yields. The hydration of nitriles entails the simultaneous formation of acids and amines (the latter evidently as a consequence of the hydrogenation by the hydrogen adsorbed on the catalyst). The hydration of amino- and nitro-benzonitriles is accompanied by side reactions of the resulting amides with the catalyst. Only nickel and zinc complexes have been obtained in the case of *p*-hydroxy- and *o*- and *p*-cyano-benzonitriles, *p*-cyanobenzoic acid, ethyl *p*-cyanobenzoate, and *p*-cyanobenzaldehyde. The introduction of pyridine into the reaction mixture increases the yield of the amides, while the introduction of thiophen and organic acids lowers their yield. It has been suggested[95] that the hydration is preceded by the adsorption of the cyano-groups on nickel, mainly on its basic centres.

The studies of the hydration reaction in the presence of the nickel catalysts examined above were carried out in the 1960's. In view of major practical advances achieved in the employment of copper as a hydration catalyst, subsequently nickel catalysts attracted little attention.[55]

Among other metallic catalysts, mention has been made of "activated iron"[55] and iron–zinc[2] and platinum[1] catalysts.

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Thus the present review shows that the advances in various new aspects of the hydration of nitriles are not all of equal value. Significant results have been obtained in the homogeneous hydration of coordinated nitriles. It has been established that coordination is responsible for a very considerable increase of the rate of hydration (by a factor up to $\sim 10^{18}$). Considerable experimental data have now accumulated on the synthesis in these reactions of amides (coordinated to different ions) in high yields. In a number of instances the study of the hydration kinetics made it possible to examine in detail the reaction mechanism and to put forward entirely feasible mechanisms for the reactions of the initial complexes. It has also been found that the coordinated nitriles also enter into other reactions in aqueous solutions, the latter being determined by the structure of the nitriles and sometimes by the reaction conditions. At the same time there have been no systematic studies of the hydration of a sufficiently wide range of nitriles and of the influence of the structure of the initial complexes on the characteristic features of the hydration process. The preparative value of the hydration reaction under consideration is as a rule limited, because the isolation of the free amides requires the chemical modification or even the decomposition of the amide-containing complexes obtained.

The homogeneous-catalytic hydration of nitriles in the presence of complexes as catalysts, which leads to the formation of amides not linked chemically to the complexes present in the reaction mixture, has so far been comparatively little studied. There have been as yet no kinetic investigations of the reaction and high rates of hydration and degrees of conversion approaching quantitative values have not been achieved. However, the proposed fundamental mechanism of the catalytic action of complexes appears to be correct. Apparently the main task in this field is the choice of new catalytically more active complexes and the develoment of conditions for the isolation of the amides formed, which will make it possible to increase the preparative values of the method.

The best practical results have so far been achieved in the heterogeneous-catalytic hydration of nitriles. This hydration method has undoubted advantages over other considered in this review and also those described previously[1] in view of its simplicity, high yields of the amides, and also because reactants other than nitriles are hardly consumed in the synthesis of the amides. All these factors have served as a basis for the employment of heterogeneous-catalytic hydration of nitriles in industrial organic synthesis. During the last 5–10 years, studies have been made of the kinetics and mechanism of the hydration reaction and many of its features in the presence of manganese(IV) oxide and copper-containing and other catalysts have become understood, which made it possible to propose reliable reaction mechanisms, but these require a certain amount of experimental confirmation and specification in greater detail. In view of the similarity of the characteristics of the hydration of certain substituted nitriles under the conditions of heterogeneous catalysis and in a homogeneous medium containing complexes with the same nitriles as ligands and also in view of the weak dependence of the activation energies for the hydration of nitriles on the method of hydration, it is to be expected that the achievements in the study of the mechanism of homogeneous hydration will promote the solution of urgent problems in the heterogeneous-catalytic hydration of nitriles.

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