Translated from *Uspekhi Khimii*, **46**, 1757-1786 (1977) U.D.C. 543.253

Polarographic Study of the Reactions of Carbonyl Compounds with Ammonia and Its Derivatives and Their Application in Polarographic Analysis

Ya.I.Tur'yan

The theoretical principles and the experimental results of the application of polarography to the study of equilibria in single- and multi-stage reactions of carbonyl compounds with ammonia and its derivatives and of the acid-base properties of their products are examined. A comparison is made with data obtained by other research techniques. More than 100 reactions are analysed taking into account the nature of the carbonyl compound and the nucleophile.
The mechanism of the polarographic electrochemical reduction of the reaction products, including aminocarbinols, is considered. The analytical application of the reactions in the indirect polarographic determination of carbonyl and nitrogen compounds is discussed.
The bibliography includes 207 references.

CONTENTS

I.	Introduction	925
II.	Reaction equilibria and acid-base properties of products	925
III.	The mechanism of the polarographic reduction of reaction products	933
IV.	Analytical applications	936

I. INTRODUCTION

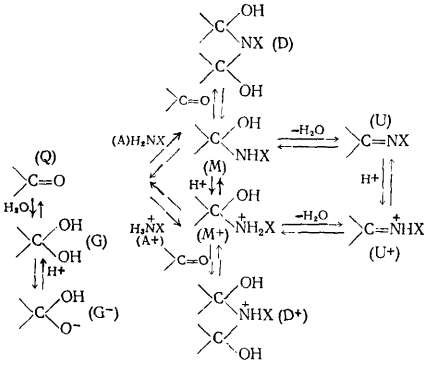
The use of the reactions of carbonyl compounds with ammonia and its derivatives in polarography makes it possible to investigate the physicochemical parameters of these reactions [1-3] and to achieve in many instances important indirect determinations of the substances involved. The latter is very important for the understanding of the mechanism of the nucleophilic interaction [4,5], which is widely used in other branches of analytical chemistry [6,7].

Among the physicochemical parameters of the reactions of carbonyl compounds with ammonia and its derivatives, the equilibrium constants and the acid–base dissociation constants of the products have been most widely investigated with the aid of polarography. These applications of the polarographic method are examined in the present review together with the mechanism of the reduction of the reaction products and the analytical applications.

II. REACTION EQUILIBRIA AND ACID–BASE PROPERTIES OF PRODUCTS

An extensive application of polarography in the study of the reactions of carbonyl compounds with ammonia and its derivatives was achieved for the first time by Zuman [8-11] and by Zuman and Březina [12,13]. However, in the majority of the early studies [8-21] the polarographic method was used to investigate the simpler single-stage interaction and Matoušek [22] was the first to use polarography to characterise quantitatively the multistage interaction on the basis of the reactions with formaldehyde. This research was developed further [23-29] and now involved the determination of quantitative reaction parameters. The development of the theoretical and experimental principles of the application of polarography to the study of single-stage and partly multistage interactions was continued in other studies [30-35].

Among the reactions involved in the given equilibrium, it is possible to isolate the main and side reactions. The main reactions, which are observed in aqueous solution, can be described by the following general mechanism [36-38]:

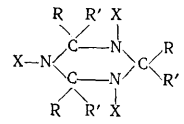


(1)

where Q, G, and G′ are respectively the carbonyl compound, its hydrated form, and its anion, A and A^+ are ammonia or an ammonia derivative and its form protonated at the nitrogen atom, M, D, and D^+ are adducts—hydroxyalkyl- and bishydroxyalkylamines (there is also a possibility of trishydroxyalkylamines T and T^+ in the reaction between HCHO and NH_4^+ [28])—and the corresponding forms protonated at the nitrogen atom, and U and U^+ represent the dehydration products—an unsaturated compound and its form protonated at the nitrogen atom.

The reaction of secondary amines HNXX′ with formaldehyde leads to the formation, apart from M(M^+), of the corresponding cation of the quaternary amino-derivative [39-41] $X'X\overset{+}{N}(CH_2OH)_2$. A similar reaction is also characteristic [39] of tertiary amines $XX'X''\overset{+}{N}CH_2OH$, although according to Matoušek [22] there is also a possibility of the formation of the compound $XX'X''\overset{+}{N}CH_2O^-$ under these conditions.

Together with the main reactions (1), numerous side reactions have been noted[36], among which those involving the formation of the cyclic trimer



(2)

and the diamine $\diagdown C(HNX)_2$ are the most important[38,39].

We shall use the following notation for the equilibrium constants of the main reactions:

$$L_G = [G]/[Q], \quad (3)$$
$$L_M = [M]/[A][Q], \quad (4)$$
$$L_{M^+} = [M^+]/[A^+][Q], \quad (5)$$
$$L_D = [D]/[A][Q]^2, \quad (6)$$
$$L_{D^+} = [D^+]/[A^+][Q]^2, \quad (7)$$
$$L_T = [T]/[A][Q]^3, \quad (8)$$
$$L_{T^+} = [T^+]/[A^+][Q]^3, \quad (9)$$
$$L_U = [U]/[A][Q], \quad (10)$$
$$L_{U^+} = [U^+]/[A^+][Q], \quad (11)$$

and for the acid dissociation constants:

$$K_G = [G^-][H^+]/[G], \quad (12)$$
$$K_{A^+} = [A][H^+]/[A^+], \quad (13)$$
$$K_{M^+} = [M][H^+]/[M^+], \quad (14)$$
$$K_{D^+} = [D][H^+]/[D^+], \quad (15)$$
$$K_{T^+} = [T][H^+]/[T^+], \quad (16)$$
$$K_{U^+} = [U][H^+]/[U^+]. \quad (17)$$

If the reaction involves the anion of the carbonyl compound (for example, the anion of pyruvic acid) or with the anion of the nucleophile (for example, the anion of an aminoacid), then L_M, L_D, K_{M^+}, K_{D^+}, and K_{U^+} are replaced by L_{M^-}, L_{D^-}, $K_{M^\pm}$, $K_{D^\pm}$, and $K_{U^\pm}$. For the reaction of the anion of the carbonyl compound with the nucleophile anion, we have $L_M =$ and $K_{M^\pm}$. In a fairly acid pH range, Eqns. (5), (7), and (13)–(15) hold also for aminoacids. Here it is necessary to bear in mind that the constant K_{A^+} has not been determined experimentally and is usually assumed[42] to be equal to the acid dissociation constant of the methyl or ethyl ester of the aminoacid. On the other hand, the acid dissociation constants of the carboxy-group in the protonated form of the aminoacid K'_{A^+} as well as the acid dissociation constants $K_{A^\pm}$ of the protonated nitrogen atom in the aminoacid dipolar ion have been determined experimentally[42]. Some of the above constants are interrelated:

$$K_{M^+} = K_{A^+}L_M/L_{M^+}, \quad (18)$$
$$K_{D^+} = K_{A^+}L_D/L_{D^+}, \quad (19)$$
$$K_{T^+} = K_{A^+}L_T/L_{T^+}, \quad (20)$$
$$K_{U^+} = K_{A^+}L_U/L_{U^+}. \quad (21)$$

In view of the insignificant influence[42] of the carbonyl compound undergoing the addition reaction on the constant K'_{A^+}, we obtain a similar relation also for aminoacids:

$$K_{M^\pm} = K_{A^\pm}L_{M^-}/L_{M^+}. \quad (22)$$

We shall now consider equations for the determination of equilibrium constants from the average limiting polarographic current $\bar{i}_{lim}$ for the reduction of the reaction products. If G^-, D, and D^+ are neglected in mechanism (1) for $c_Q =$ const. (c is the overall concentration, the subscript indicates the substance involved, and the square brackets represent the equilibrium concentration), we obtain the equation[32]:

$$L_e = \frac{[M]+[M^+]+[U]+[U^+]}{([Q]+[G])([A]+[A^+])} = (L_{M^+}+L_{U^+})\frac{K_{A^+}\{(L_M+L_U)/(L_{M^+}+L_{U^+})\}+[H^+]}{(1+L_G)(K_{A^+}+[H^+])} =$$
$$= \frac{\bar{i}_{lim}\cdot\bar{i}^0_{lim}}{(\bar{i}^0_{lim}-\bar{i}_{lim})(c_A\bar{i}^0_{lim}-c_Q\bar{i}_{lim})}. \quad (23)$$

The sums of the constants $L_M + L_U$ and $L_{M^+} + L_{U^+}$ (for the reaction between HCHO and NH_2NH_2)[33] were determined from the dependence of the effective equilibrium constant L_e on pH and the individual equilibrium constants were found with the aid of additional investigations[33,34]. In Eqn. (23), $\bar{i}^0_{lim}$ is the limiting current in the presence of an excess of nucleophile such that a further increase of c_A does not lead to an increase of $\bar{i}_{lim}$, i.e. under these conditions virtually the entire carbonyl compound is converted into products which can be polarographed; $\bar{i}_{lim}$ and $\bar{i}^0_{lim}$ can have both diffusional and kinetic origins[30,32]. The dehydration product U^+ is reduced[1,32,34] and, if a diffusion current obtains, the stages involving the protonation of M and U and the $M(M^+)$ dehydration stages are fairly rapid and there is insufficient time for the equilibrium in the stages involving the formation of the adduct $M(M^+)$ to be appreciably displaced at the surface of the dropping electrode. The latter condition should also be observed in the presence of a kinetic current[30–35], which is due to slow stages involving either the protonation of U or the dehydration of M^+ (see below).

If the study is performed with $c_A =$ const., $\bar{i}_{lim}$ is determined in the presence of an excess of the carbonyl compound and Eqn. (23) then has the same form, but c_A and c_Q must be interchanged.

Under the conditions such that $L_U \gg L_M$ and $L_{U^+} \gg L_{M^+}$ (M and M^+ may be neglected), Eqn. (23) assumes a simpler form when account is taken of Eqn. (21):[32]

$$L'_e = \frac{[U]+[U^+]}{([Q]+[G])([A])+[A^+])} = L_{U^+}\frac{K_{U^+}+[H^+]}{(1+L_G)(K_{A^+}+[H^+])} =$$
$$= \frac{\bar{i}_{lim}\cdot\bar{i}^0_{lim}}{(\bar{i}^0_{lim}-\bar{i}_{lim})(c_A\bar{i}^0_{lim}-c_Q\bar{i}_{lim})}. \quad (24)$$

The equilibrium constants for the individual stages can now be found directly from Eqn. (24) (for the reactions of various carbonyl compounds with NH_2NH_2, with the exception of HCHO).[31,33,35]

A further simplification of Eqn. (24) is achieved when $c_A \gg c_Q$:[12,13,17,30,34]

$$L'_e = L_{U^+}\frac{K_{U^+}+[H^+]}{(1+L_G)(K_{A^+}+[H^+])} = \frac{\bar{i}_{lim}}{(\bar{i}^0_{lim}-\bar{i}_{lim})c_A}. \quad (25)$$

When $c_Q \gg c_A$ ($c_A =$ const.), it is necessary to replace c_A by c_Q in Eqn. (25). Eqn. (25) has been used in a number of studies[12,13,17] but without taking into account the hydration of the carbonyl compound. Furthermore, the limiting diffusion current $\bar{i}_d$ for the carbonyl compound was used in some investigations[8,10–13] instead of $\bar{i}^0_{lim}$, which is less accurate, because the constants of the $U(U^+)$ and Q diffusion currents may differ. On the other hand, in the case of the kinetic current the replacement of $\bar{i}^0_{lim}$ by $\bar{i}_d$ is altogether inadmissible.

If $L_M \gg L_U$ and $L_{M^+} \gg L_{U^+}$ (i.e. U and U^+ may be neglected), then [U], $[U^+]$, L_{U^+}, and K_{U^+} in Eqns. (24) and (25) must be replaced by [M], $[M^+]$, L_{M^+}, and K_{M^+} respectively. M^+ may then be reduced at the electrode instead of U^+.

Retaining M, M^+, D, and D^+ in Eqn. (1), introducing T and T^+ (for the reaction between HCHO and NH_4^+),[28] and

neglecting A, G^-, U, and U^+, the present author and Cheremukhina [28] obtained the equation

$$\frac{\bar{i}_{\lim}}{\bar{i}^0_{\lim}-\bar{i}_{\lim}} = L_{M^+}\frac{K_{M^+}[H^+]}{(1+L_G)[H^+]}c_Q + L_{D^+}\frac{K_{D^+}[H^+]}{(1+L_G)^2[H^+]}c_Q^2 + L_{T^+}\frac{K_{T^+}+[H^+]}{(1+L_G)^3[H^+]}c_Q^3, \quad (26)$$

but no account was taken of the hydration of Q. In the derivation of Eqn.(26), it was assumed that $c_Q \gg c_A$ (c_A = const.) and that the sum of the products $M^+ + D^+ + T^+$ is reduced. The current $\bar{i}^0_{\lim}$ was determined in the presence of a large excess of Q. If A is also involved in mechanism (1), then $[H^+]$ in the denominators of all the terms on the right-hand side of Eqn.(26) must be replaced by $K_{A^+} + [H^+]$. When $[H^+] \gg K_{A^+}(K_{M^+}, K_{D^+}, K_{T^+})$ or $[H^+] \ll K_{A^+}(K_{M^+}, K_{D^+}, K_{T^+})$, then Eqn.(26) and the corresponding equation with $K_{A^+} + [H^+]$ in the denominators can be greatly simplified [23,24,26,41]. Furthermore, the trishydroxyalkyl derivative $T(T^+)$ was not involved in the equilibrium [reactions of formaldehyde with aminoacids [24,25], $\overset{+}{N}H_3OH$, [26] and $(CH_3)_2\overset{+}{N}H_2$ [40,41]] and the third term in Eqn.(26) (with c_Q^3) was eliminated. The equilibrium constants were found with the aid of equations of type (26) [23-26,28,41] using a graphical method analogous to the methods of determining the equilibrium constants for stepwise complex-formation reactions based on the study of potentials [43] (potentiometry) or half-wave potentials [44] (polarography).

Eqn.(25) can be used to describe the equilibrium in the reactions involving $NH_2NHCONH_2$ [17,30] without any changes (because $U + U^+$ predominates). On the other hand, in the studies [8,10-13] of the reactions involving NH_3, NH_2RCOO^-, and $NH_2CH_2CH_2OH$ in the presence of an excess of the nucleophile, the adduct M [8,10,11] or $M + M^+$ [12,13] was the dominant species and $L_{M^+}(L_M)$ and K_{M^+} were apparently determined from Eqn.(25) [8,10-13] rather than $L_{U^+}(L_U)$ and K_{U^+}, as believed by the authors [8,10-13]. We shall return to this problem later.

The single-stage interaction (the dominance of M^+ in the reactions of formaldehyde with aminoacids in an acid medium [29] and of M in the reaction of formaldehyde with $NH_2CH_2CH_2OH$ [45,46] in the presence of an excess of the latter) has been investigated polarographically using Eqns. (26), in which only the first term (the aminoacid term) was retained and (25) in which L_{U^+} and K_{U^+} were replaced by L_{M^+} and $K_{M^+}(NH_2CH_2CH_2OH)$ respectively. The insignificant concentration of D^+ in the reactions involving aminoacids with a primary amino-group in an acid medium [29] is apparently due to the relatively low value of L_{D^+}, which has been confirmed by data obtained using kinetic [24,29] and other methods [47].

It is noteworthy that, in a polarographic study [24] of the reactions of formaldehyde with aminoacids in an alkaline medium, samples were polarographed in an acid medium in order to increase $\bar{i}_{\lim}(\bar{i}^0_{\lim})$. Under these conditions, the limiting current decreased with time t and values of $\bar{i}_{\lim}(\bar{i}^0_{\lim})$ extrapolated by $t = 0$ were used in the calculations. The extrapolation was facilitated by the fact that the kinetic equation relating $\bar{i}_{\lim}(\bar{i}^0_{\lim})$ to time was of first order [24], which can be explained by the rapid and almost complete decomposition of D^+ to M^+ and the reduction of $M^+(L_{D^+}/L_{M^+} \ll L_{M^+})$. Thus, although only the M^+ wave was observed in the acid solution, its height corresponded to the sum of the concentrations of the adducts [M] + [D] formed in the alkaline medium.

In contrast to these reactions, the $HCHO-\overset{+}{N}H_3OH$ [26] and $HCHO-\overset{+}{N}H_4$ [28] equilibria in an acid medium, i.e.

$$Q + A^+ \underset{k_{-1}}{\overset{k_{+1}}{\rightleftarrows}} M^+ + Q \underset{k_{-2}}{\overset{k_{+2}}{\rightleftarrows}} D^+, \quad (27)$$

which were also investigated by the polarographic method, are characterised by the opposite relation: $L_{D^+}/L_{M^+} \gg L_{M^+}$, which is probably due to the much smaller influence of steric hindrance than in the reactions with aminoacids. When account is taken of the relation $k_{-1} \gg k_{+2}$, [27] which is most likely to be characteristic of aminoacids (steric effect), the decomposition reaction between M^+ and D^+ (aminoacids) involving the reformation of the initial substances via a first-order mechanism cannot be accounted for by postulating the attainment of equilibrium in the $D^+ \rightleftharpoons M^+ + Q$ stage. As stated above, here it is necessary to assume (bearing in mind the very low value of L_{D^+}/L_{M^+}, so that $k_{-2} \gg k_{+2}$) a rapid and almost complete decomposition of D^+ to M^+ and a slow decomposition of M^+ into the initial substances Q and A^+ in accordance with a first-order kinetic equation [24]. It is noteworthy that, when the reactions between formaldehyde and aminoacids were carried out in an alkaline medium and samples were polarographed in an acid medium [24] in the presence of an excess of formaldehyde, the currents $\bar{i}^0_{\lim}$ were readily attained. On the other hand, when the reactions were carried out in the acid medium used in the polarographic experiments [29], $\bar{i}^0_{\lim}$ could not be attained even in the presence of a very large excess of formaldehyde, because of the low value of L_{M^+}. The values of $\bar{i}^0_{\lim}$ obtained by carrying out the reactions in an alkaline medium [24] were therefore used to calculate L_{M^+}. [29]

Equilibria (1) can be investigated polarographically also on the basis of the wave of the carbonyl compound [14,16,19], but the scope of the method is then limited: (1) the use of only an excess of the nucleophile hinders the study of the equilibrium involving the formation of D(D^+) and even more so of $T(T^+)$; (2) the wave of the carbonyl compound may be distorted by the superposition of the reduction of the reaction product [22].

Since either the reaction products or the starting material are consumed at the electrode during the polarographic experiment, there is a possibility of a shift of the equilibrium at the electrode surface. This results in exaltation of the limiting current [48] and the values of $\bar{i}_{\lim}$ are no longer suitable for a sufficiently accurate determination from the latter of the equilibrium constants for the reactions investigated. The degree of such exaltation of $\bar{i}_{\lim}$ is greater the larger are the rate constants for the first stages of reactions of type (27) under conditions corresponding to the reduction of M, D, and T (M^+, D^+, and T^+). It has been shown [48] that the above influence cannot introduce a major error if $k_{-1} \leq 0.1-0.2\ s^{-1}$, while in the reduction of the initial substance Q and in the presence of only the stage involving the formation of M, [14,16] we have $k_{+1}[A] \leq 0.1-0.2\ s^{-1}$. This rule holds [48] in the reduction (and also oxidation) of substances subject to both diffusional and kinetic limitations, but in the latter case the limitations should not be associated with the displacement of the equilibria in the test reactions at the electrode surface. The kinetic limitation may be caused either by the slow protonation of the adducts M (D, T) [28] or of the dehydration product [31-35] (the adducts D and T are absent and U is reduced or hydrogen is evolved catalytically under the influence of U^+ [30]). This conclusion can be extended to the limiting kinetic current due to the slow dehydration of the adduct M (U is reduced) [32,33].

We may note that the rate constants for the decomposition of the adducts M^+ into the initial substances (the reactions between formaldehyde and aminoacids), which have been investigated by the polarographic method [24], remained sufficiently low in an acid solution (Table 1) to cause the undesirable exaltation of $\bar{i}_{\lim}$ in the study of the

equilibrium [24]. Under these conditions, the constants k_{+1} and k_{-1} depended appreciably on the nature of the amino-acid and the observed increase of k_{-1} with increase of both the $-I$ and $+I$ effects of the substituent X (Table 1) can be explained on the basis of the kinetic scheme of Cordes and Jencks [56]:

$$\overset{+}{\mathrm{N}}\mathrm{H}_2\mathrm{CH}_2\mathrm{OH} \overset{-\mathrm{H}^+}{\rightleftarrows} \mathrm{X}\overset{+}{\mathrm{N}}\mathrm{H}_2\mathrm{CH}_2\mathrm{O}^- \xrightarrow[\text{slow}]{} \mathrm{HCHO} + \mathrm{NH}_2\mathrm{X} \overset{\mathrm{H}^+}{\rightleftarrows} \mathrm{X}\overset{+}{\mathrm{N}}\mathrm{H}_3\mathrm{X}. \qquad (28)$$

The substituent X with a $-I$ effect accelerates the slow stage (the inductive effect facilitating the dissociation of the $C-\overset{+}{N}$ bond predominates); the acceleration of the reaction with increase of the $+I$ effect of the substituent X is due to the dominance of the steric factor, which is manifested by the displacement of the initial equilibrium stage to the right. The steric effect also predominates in glycine and, since it is smaller, the result is a relatively low value of k_{-1} (Table 1). The correlation between k_{-1} and K'_{A^+} (Table 1) confirms the above role of the inductive and steric factors. It is also possible to follow the influence of the steric factor on k_{+1} (Table 1). With the exception of glycine, this effect predominates at the equilibrium stage involving the deprotonation of the nucleophile (the increase of k_{+1} with increase of the $+I$ effect). The reduced steric hindrance in glycine is apparently manifested to a greater extent in the slow stage involving interaction with formaldehyde, which in fact leads to a relatively larger value of k_{+1} (Table 1). Mechanism (28) also makes it possible to understand the reason why k_{-1} increases with pH [24] without the need to take into account the appreciable amount of the doubly protonated M^{2+} species [24] (protonated at the nitrogen and oxygen atoms).

Table 1. The limiting current constants (I^0_{lim}, μA mmole^{-1} mg$^{-2/3}$ s$^{1/2}$) for the reduction of the adduct $CH_2(OH)\overset{+}{N}H_2X$, [24] the rate constants for the formation of the adduct from formaldehyde monohydrate and an amino-acid (k_{+1}), [29] the rate constants for its decomposition (k_{-1}) [24] into the initial substances, and the dissociation constants of the carboxy-groups of the corresponding aminoacids (K_{A^+}) [49] (the rate constants were determined at pH ~ 1 and 25°C).

Aminoacid	X	I^0_{lim}	$10^4 k_{+1}$, litre mole^{-1} s^{-1}	$10^3 k_{-1}$, s^{-1}	pK'_{A^+}
β-Alanine	CH_2CH_2COOH	0.55	—	0.19	3.55
Glycine	CH_2COOH	0.91	5.6	3.0	2.35
α-Alanine	$CH(COOH)CH_3$	1.5	0.68	3.4	2.35
Norvaline	$CH(COOH)(CH_2)_2CH_3$	2.7	1.4	3.8	—
Norleucine	$CH(COOH)(CH_2)_3CH_3$	2.5	1.1	4.5	2.34
Leucine	$CH(COOH)CH_2CH(CH_3)_2$	2.5	—	5.2	2.33
α-Aminoadipic acid	$CH(COOH)(CH_2)_3COOH$	2.4	—	6.7	—
Valine	$CH(COOH)CH(CH_3)_2$	(3.1)	2.9	8.8	2.29
Glutamic acid	$CH(COOH)(CH_2)_2COOH$	2.5	—	12.8	2.30
β-Phenyl-α-alanine	$CH(COOH)CH_2C_6H_5$	2.7	—	17.6	2.11
Aspartic acid	$CH(COOH)CH_2COOH$	2.7	—	26.0	1.99

The reaction between formaldehyde and $\overset{+}{N}H_3OH$ is also fairly slow because the limiting current has a diffusional origin [51]. Only the rate constant for the decomposition of D^+ into M^+ and Q ($k_{-2} = 2 \times 10^{-4}$ s^{-1}) has been obtained for this reaction (by the polarographic method) [26,27].

With increase of pH, the rate of formation of M (D, T) and U increases appreciably. Thus, on the basis of kinetic data (polarographic method) [10] for the reaction between CH_3COCOO^- and NH_3 (pH 9.25), one may assume [48] that the author [10] worked under the conditions corresponding to the limit of a fairly reliable application of the method to the study of the equilibrium in this reaction on the basis of the values of $\bar{i}_{lim}$. The rate of formation of the adduct M in the reaction between pyridine-4-aldehyde and methylamine at pH 10.5 is so high that the kinetics are controlled in this case by the carbonyl dehydration step [52]. $k_{-1} = 58$ s^{-1} was obtained [52] for this dehydration stage (by the stopped-flow method), which implies that, during the polarographic reduction of M, there is an appreciable exaltation of $\bar{i}_{lim}$ and the polarographic method becomes unsuitable for the investigation of the equilibrium in the formation of this adduct.

The pH dependence of the rates of the reactions $Q + A(A^+) \rightarrow U(U^+)$ is more complex because these reactions proceed via the formation and dehydration of $M(M^+)$ and involve a change in pH, as shown by Jencks [37,53]; there is also a change in the rate-determining stage. However, here too the problem of the degree of the distorting influence of the reactions involving the formation of an intermediate aminocarbinol (the reduction of U [17,31-35]) at the electrode surface can be in many instants solved comparatively simply. The point is that, in the majority of reactions of this kind, the equilibrium concentrations of $M(M^+)$ may be neglected compared with the concentrations of $U(U^+)$ and in the calculations one must therefore use the overall equilibrium constant and the effective rate constant for the reaction $Q + A(A^+) \rightarrow U(U^+)$ and not the equilibrium and kinetic parameters of the individual stages. The maximum value of k_{-1} is obtained [37] for the reaction between $(CH_3)_2CO$ and NH_2OH. .($\overset{+}{N}H_3OH$) under fairly acid conditions (the value of L_{U^+} for the calculations was taken from Conant and Bartlett [54]), but this value too ($k_{-1} = 3.5 \times 10^{-3}$ s^{-1}) is much lower than the lowest permissible limit [48]. This conclusion can probably be extended also to reactions of aliphatic carbonyl compounds with hydrazine (the formation and reduction of hydrazones) [31-35], although no direct kinetic measurements have been made. This is indicated by the invariance of the equilibrium constants over a wide range of nucleophile concentrations [31-35].

The equilibrium constants for the side reactions between nucleophiles and carbonyl compounds [the formation of a cyclic trimer (2) and a diamine], found in a number of studies [38,39,47,55,56], show that the concentrations of these products are insignificant under the conditions of the polarographic study [24,29]. Only the glycinate anion gives rise to an appreciable concentration of the trimer under the given conditions (alkaline solution) [24], but here too it does not exceed 9%.

The acid dissociation of the hydrated form of the carbonyl compound is also indicated in mechanism (1), but in the majority of studies $[H^+] \gg K_G$, so that this process may be neglected. On the other hand, polarographic data [24] for the reactions of formaldehyde with aminoacids in an alkaline medium were recently revised [25] taking into account the acid dissociation of $CH_2(OH)_2$.

It is noteworthy that, under the conditions of the polarographic study at ordinary temperatures and relatively low concentrations of the carbonyl compound, the influence of the additional (apart from hydration) deactivation of the carbonyl compound (for example owing to polycondensation [57], aldol condensation, or the Cannizzaro reaction [58]) can also be usually neglected, at any rate for the usual accuracy of the equilibrium constants (±10-30%). In the determination of $\bar{i}^0_{lim}$, the concentration of formaldehyde reached [28] a fairly high value in some cases (7.0 M), but under these conditions the side reactions of

Table 2. The equilibrium constants (L_M) for the reactions RR'CO + $H_2NX \rightleftharpoons$ RR'C(OH)NHX at 20–30°C.

H_2NX		NH_3 (pK_{A+}=9,25)			α-Alanine $CH_3CH(NH_2)COO^-$ ($pK_{A\pm}$=9,87)			Glycine $H_2NCHNCOO^-$ ($pK_{A\pm}$=9,88)		
RR'CO	L_G	L_M, litre mole^{-1}	method	references	L_M^c, litre mole^{-1}	method	references	L_M^d, litre mole^{-1}	method	references
Cyclopentanone	—	$1.6\cdot10^{-3}$	P	13	$8.0\cdot10^{-2}$	P	13	0.190	P	13
α-Methylcyclohexanone	—	$4.5\cdot10^{-3}$	P	13	—	—	—	$2.4\cdot10^{-2}$	P	13
$(CH_3)_2CO$	$2.0\cdot10^{-3}$	$4.0\cdot10^{-3}$	P	12	—	—	—	$6.8\cdot10^{-2}$	P	12
Cyclohexanone	—	$9.8\cdot10^{-3}$	P	13	$3.0\cdot10^{-2}$	P	13	$7.2\cdot10^{-2}$	P	13
$C_6H_5COCOO^-$	—	L_{M^-}=0.10	P	8	—	—	—	—	—	—
C_6H_5CHO	—	0.15	P	8	—	—	—	—	—	—
$CH_3COCOCH_3$	2,0	0.15	P	8	—	—	—	—	—	—
CH_3COCOO^-	$5.4\cdot10^{-2}$	L_{M^-}=0,26	P	8, 10	$L_{M^{2-}}$=0.98	P	8, 11	$L_{M^{2-}}$=2.6	P	8, 11
$CH_3(CH_2)_2CHO$	0.48	11.6	S	59	—	—	—	—	—	—
CH_3CH_2CHO	0.72	18.1	S	59	—	—	—	—	—	—
CH_3CHO	1.4	$1.1\cdot10^{2}$	S	59	26	Pt, Su	38	47	Pt, Su	38
»	»	8.9[a]	Pt	38	—	—	—	—	—	—
»	»	1.3	P	8	—	—	—	—	—	—
HCHO	$2.0\cdot10^{3}$	$1.5\cdot10^{6}$[b]	P	28	$4.8\cdot10^{4}$	Pt	60	$3.2\cdot10^{5}$	Pt	60
»	»	—	—	—	$4.4\cdot10^{4}$	Pt	61	$1.2\cdot10^{5}$	Pt	61
»	»	—	—	—	$4.6\cdot10^{4}$	Pt	62	$1.3\cdot11^{5}$	P	24, 25
»	»	—	—	—	$4.8\cdot10^{4}$	P	24, 25	$1.8\cdot10^{5}$	Su, Pt, I	47
»	»	—	—	—	$4.2\cdot10^{4}$	Pt	39	—	—	—
»	»	—	—	—	$4.4\cdot10^{4}$	Su, I, Pt	47	—	—	—

Methods: P = polarographic; S = spectrophotometric; Pt = potentiometric (pH); Su = sulphite; I = iodometric. [a] $L_D = 1.9\times10^{2}$ from Ref. 38; [b] $L_D = 5.2\times10^{9}$ and $L_T = 1.4\times10^{13}$ from Ref. 28; [c] L_{M^-} for HCHO and $L_{D^-} = (1.4-3.0)\times10^{8}$ from Refs. 24, 25, 39, 47, 60, and 61; [d] L_{M^-} for HCHO and $L_{D^-} = (1.2-4.4)\times10^{9}$ from Refs. 24, 25, 47, and 61.

Table 3. The equilibrium constants (L_M) for the reactions RR'CO + $H_2NX \rightleftharpoons$ RR'C(OH)NHX at 20–25°C.

H_2NX		Leucine $(CH_3)_2CHCH_2CH(NH_2)COO^-$ ($pK_{A\pm}$=9,74)			Aspartic acid $-OOCCH_2CH(NH_2)COO^-$ ($pK_{A\pm}$=10,00)			CH_3NH_2 (pK_{A+}=10,62)			$(CH_3)_2CHNH_2$ (pK_{A+}=10,63)		
RR'CO	L_G	L_M^d, litre mole^{-1}	method	References	L_M^e, litre mole^{-1}	method	References	L_M, litre mole^{-1}	method	References	L_M, litre mole^{-1}	method	References
$(CH_3)_2CO$	$2.0\cdot10^{-3}$	—	—	—	—	—	—	0.22	S	63	$4.9\cdot10^{-2}$[c]	T	65
$(CH_3)_2CHCHO$	0.44	—	—	—	—	—	—	$1.3\cdot10^{2}$[b]	S, Pt	64	48[b]	S, Pt	64
CH_3CHO	1.4	55	Pt, Su	38, 56	47	Pt, Su	38, 56	—	—	—	—	—	—
HCHO	$2.0\cdot10^{3}$	$3.4\cdot10^{4}$	Pt	60	$3.1\cdot10^{4}$	P	24, 25	$3.0\cdot10^{6}$	Cr, Su, I	55	—	—	—
»	»	$4.0\cdot10^{4}$	Pt	62	$3.0\cdot10^{4}$	Pt, Su	47	—	—	—	—	—	—
»	»	$4.8\cdot10^{4}$	P	24, 25	$5.2\cdot10^{4}$[a]	P	61	—	—	—	—	—	—
»	»	$4.2\cdot10^{4}$	Pt, Su	47	—	—	—	—	—	—	—	—	—

Methods: Cr = cryoscopic; T = acid–base titration; the remaining symbols have the same significance as in Table 2. [a] 30°C; [b] 35°C; [c] in C_2H_5OH; [d] L_{M^-}; $L_{D^-} = (1.2-1.8)\times10^{8}$ for HCHO was taken from Refs. 24, 25, 47, 60, and 62; [e] $L_{M^{2-}}$; $L_{D^{2-}} = (0.92-2.2)\times10^{8}$ for HCHO was taken from Refs. 24, 25, 47, and 61.

Table 4. The equilibrium constants (L_M) for the reactions RR'CO + $H_2NX(HNXX') \rightleftharpoons$ RR'C(OH)NHXRR'C(OH)NXX' at 20–25°C.

$H_2NX(HNXX')$		n-$C_4H_9NH_2$ (pK_{A+}=10,60)			NH_2OH (pK_{A+}=5,97)			$H_2NC_2H_4OH$ (pK_{A+}=9,50)			Morpholine O(CH₂—CH₂)NH(CH₂—CH₂) (pK_{A+}=8,7)		
RR'CO	L_G	L_M, litre mole^{-1}	method	references	L_M, litre mole^{-1}	method	references	L_M, litre mole^{-1}	method	references	L_M, litre mole^{-1}	method	references
$(CH_3)_2CO$	$2.0\cdot10^{-3}$	$8.4\cdot10^{-2}$	P	20	1.0[c]	S	37	—	—	—	—	—	—
CH_3COCOO^-	$5.4\cdot10^{-2}$	—	—	—	60[d]	S	37	3.3[d]	P	8	—	—	—
$(CH_3)_2CHCHO$	0.44	$1.0\cdot10^{2}$[a]	S, Pt	64	—	—	—	—	—	—	—	—	—
CH_3CHO	1.4	—	—	—	—	—	—	—	—	—	25	Pt	38
HCHO	$2.0\cdot10^{3}$	$1.2\cdot10^{6}$[b]	Pt	39	—	—	—	$5.8\cdot10^{4}$	P	45, 46	$1.6\cdot10^{6}$	Pt	38, 39
Cyclohexanone	—	—	—	—	6.5	S	37	—	—	—	—	—	—
C_6H_5CHO	—	—	—	—	11.3	S	37	—	—	—	—	—	—

For the significance of the symbols designating the methods, see Table 2. [a] 35°C; [b] reaction with t-$C_4H_9NH_2$; [c] $L_U = 1.1\times10^{6}$ and $L_{U^+} = 63$;[54] [d] L_{M^-}.

the carbonyl group were disregarded, since the aim of the experiments was merely to achieve a virtually complete conversion of the nucleophile into the polarographed products.

Table 5. The equilibrium constants L_U for the reactions $RR'CO + H_2NX \rightleftharpoons RR'C{=}NX + H_2O$ at 25 °C.

H_2NX		$NH_2NHCONH_2$ (pK_{A^+}=3,43)			NH_2NH_2 (pK_{A^+}=8,1)		
RR'CO	L_G	L_U, litre mole^{-1}	method	references	L_U, litre mole^{-1}	method	references
Glucose	—	16	P, I, S	21	—	—	—
$(C_2H_5)_2CO$	—	38	I	66	—	—	—
$CH_3(OH)COCH_2OH$	—	$1.4\cdot10^2$	P	30	—	—	—
Cyclopentanone	—	$6.8\cdot10^2$	I	66	—	—	—
»	—	56	P	17	—	—	—
Cyclohexanone	—	$5.0\cdot10^2$	I	54	—	—	—
»	—	$4.9\cdot10^2$	I	66	—	—	—
»	—	$1.9\cdot10^2$	P	17	—	—	—
$CH_3COC_2H_5$	—	—	—	—	$1.3\cdot10^3$	P	33
$(CH_3)_2CO$	$2.0\cdot10^{-3}$	$3.2\cdot10^2$	I	54	$2.4\cdot10^3$	P	33
»	—	$3.1\cdot10^2$	I	66	—	—	—
»	—	76	P	17	—	—	—
$C_6H_5COCH_3$	—	$3.8\cdot10^2$	P	17	—	—	—
$CH_3CO(CH_2)_2COO^-$	—	—	—	—	$3.5\cdot10^3$	P	35
CH_3COCOO^-	—	$2.1\cdot10^{5a}$	I	54	b	—	—
CH_3CH_2CHO	0 72	—	—	—	$2.5\cdot10^5$	P	33
$CH_2(OH)CHO$	—	$4.0\cdot10^4$	P	30	—	—	—
$CH_3(OH)CH(OH)CHO$	—	$4.0\cdot10^4$	P	30	—	—	—
CH_3CHO	1.4	$7.7\cdot10^4$	I	54	$1.9\cdot10^6$	P	31, 33
»	»	$9.1\cdot10^4$	P	17	—	—	—
$(CH_3)_3CCHO$	0,24	$6.2\cdot10^4$	I	54	—	—	—
Furfural	—	$1.3\cdot10^{5c}$	I	54	—	—	—
C_6H_5CHO	—	$3.2\cdot10^5$	I	54	—	—	—
»	—	$>5\cdot10^4$	P	17	—	—	—
»	—	$4.5\cdot10^{5d}$	S	67	—	—	—
HCHO	$2.0\cdot10^3$	$1.2\cdot10^7$	Pt	52	$5.8\cdot10^{8e}$	P	33, 34

For the significance of the symbols designating the method, see Table 2.

[a] L_U, $L_{M^-} = 10.5$ from Ref. 37; [b] $L_{M^-} = 25.5$ from Ref. 37; [c] $L_M = 1.1$ from Ref. 37; [d] $L_M = 1.3$ from Ref. 68; [e] $L_M = 1.9 \times 10^9$ from Ref. 34.

Tables 2–7 present the equilibrium constants, including those obtained by nonpolarographic methods, for the reactions of nucleophiles with various carbonyl compounds. A fairly complete compilation of equilibrium constants (Tables 6 and 7) is available for protonated species, since the polarographic method is particularly promising, because of its high sensitivity, for the investigation of equilibria of this kind. It is noteworthy that the study of the equilibria involving the protonated forms of the nucleophile and the products, carried out for the first time in polarographic investigations [12,17,25], makes it possible to eliminate to a considerable degree the distorting influence of the cyclisation of the product [39,47]. In order to take into account the hydration of carbonyl compounds (which has been done in only a few studies; the effective equilibrium constants are more difficult to compare), the present author selected the most reliable values for L_G [69] (Tables 2–7). In the calculations for carbonyl compounds those values of L_G have not been determined, it was assumed that $L_G \ll 1$, although this was not apparently valid in all cases [for example, in the reactions involving $CH_2(OH)COCH_2OH$, $CH_2(OH)CH(OH)CHO$, and $CH_2(OH)CHO$ in Tables 5 and 7]. Tables 1–7 also list the acid dissociation constants of the initial nucleophiles taken from Ref. 49. Furthermore, the values of K_{A^+} are indicated for certain aminoacids in an acid medium; as mentioned above, they were assumed equal to the values of K_{A^+} for the methyl or ethyl esters of the corresponding aminoacids [70–72].

Table 6. The equilibrium constant L_{M^+} for the reactions $RR'CO + H_3\overset{+}{N}X(H_2\overset{+}{N}XX') \rightleftharpoons RR'C(OH)\overset{+}{N}H_2X[RR'C(OH)\overset{+}{N}HXX']$ at 20–25 °C.

RR'CO		HCHO, L_G=2,0·10^3			CH_3CHO, L_G=1,4		
$H_3\overset{+}{N}X(H_2\overset{+}{N}XX')$	pK_{A^+}	L_{M^+}, litre mole^{-1}	method	references	L_M, litre mole^{-1}	method	references
$\overset{+}{N}H_3OH$	5.97	$(1.7—1.8)\cdot10^{4a}$	P	26	—	—	—
Aspartic acid	—	$8.0\cdot10^2$	Pt, Su, I	47	0.34	Pt, Su	38, 56
Leucine	7.57	$1.8\cdot10^2$	Pt, Su	47	0.41	Pt, Su	38, 56
Glycine	7.64	$5.0\cdot10^2$	P	29	—	—	—
»	»	$1.3\cdot10^3$	Pt, Su, I	47	0.72	Pt, Su	38, 56
α-Alanine	7.74	60	P	29	—	—	—
»	»	$2.8\cdot10^2$	Pt, Su, I	47	0.17	Pt, Su	38, 56
Norvaline	—	90	P	29	—	—	—
Norleucine	—	90	P	29	—	—	—
Valine	—	96	P	29	—	—	—
»	—	72	Pt, Su, I	47	—	—	—
Morpholine	8.7	$(3.8—4.2)\cdot10^3$	Cr, Su, M	55	0.17	Pt, Su	38
»	»	$1.8\cdot10^3$	Pt	39	—	—	—
β-Alanine	9.06	—	—	—	0.65	Pt, Su	38, 56
$\overset{+}{N}H_4$	9.25	26[b]	P	28	$\leqslant 2.4\cdot10^{-2}$	Su	38
γ-Aminobutyric acid	9.71	—	—	—	0.62	Pt, Su	38, 56
ε-Aminocaproic acid	10.30	—	—	—	0.65	Pt, Su	38, 56
Sarcosine	—	$4.4\cdot10^2$	Pt	39	—	—	—
Proline	—	$1.0\cdot10^3$	Pt	39	—	—	—
$CH_3\overset{+}{N}H_3$	10.62	$2.6\cdot10^3$	Cr, Su, M	55	—	—	—
$(CH_3)_2\overset{+}{N}H_2$	10.71	$(3.2—4.0)\cdot10^3$	Cr, Su, M	50	—	—	—
»	»	$3.4\cdot10^3$	Pt	39	—	—	—
»	»	$6.0\cdot10^3$	P	40, 41	—	—	—
Piperidine	11.12	$3.0\cdot10^3$	Pt	39	—	—	—
Pyrrolidine	11.27	$2.8\cdot10^3$	Pt	39	—	—	—

Method: M = mercurimetric; for the significance of the remaining symbols designating the methods, see Tables 2 and 3.

[a] $L_{D^+} = (6-12) \times 10^3$ from Refs. 26; [b] $L_{D^+} = 7.2 \times 10^4$; $L_{T^+} = 1.6 \times 10^3$ from Ref. 28.

Table 7. The equilibrium constant L_{U^+} for the reaction $RR'CO + H_3\overset{+}{N}X \rightleftharpoons RR'C{=}\overset{+}{N}HX + H_2O$ at 25 °C.

$H_3\overset{+}{N}X$		$\overset{+}{N}H_3NHCONH_2$ (pK_{A^+}=3,4)		$\overset{+}{N}H_3NH_2$ (pK_{A^+}=8,19)	
RR'CO	L_G	L_{U^+}, litre mole^{-1}	references	L_{U^+}, litre mole^{-1}	references
$C_6H_5COCH_3$	—	0.38	17	—	—
Cyclopentanone	—	0.40	17	—	—
$CH_3COC_2H_5$	—	—	—	0.63	33
$(CH_3)_2CO$	$2.0\cdot10^{-3}$	1.5*	54	1.1	33
»	—	0.55	17	—	—
Cyclohexanone	—	1.04	17	—	—
$CH_2(OH)CHO$	—	5.0	30	—	—
$CH_3CO(CH_2)_2COO^-$	—	—	—	1.6**	35
$CH_3CO(CH_2)_2COOH$	—	—	—	2.3	35
$CH_3(OH)CH(OH)CHO$	—	6.6	30	—	—
CH_3CH_2CHO	0.72	—	—	86	33
CH_3CHO	1.4	$3.2\cdot10^2$*	54	$4.3\cdot10^2$	31, 33
»	»	42	17	—	—
C_6H_5CHO	—	$6.7\cdot10^2$*	54	—	—
»	—	>40	17	—	—
Furfural	—	$8.3\cdot10^2$*	54	—	—
$CH_3COCOOH$	2.4	$1.0\cdot10^3$*	54	—	—
HCHO	$2.0\cdot10^3$	—	—	$7.4\cdot10^4$***	33, 34

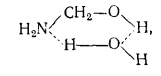
*Measured by the iodometric method; in the remaining cases, the polarographic method was used.

**L_{U^+}.

***$L_{M^+} = 2.4 \times 10^5$ from Ref. 33.

The reproducibility of the equilibrium constants in various studies using polarographic and other methods is quite satisfactory in many instances: the reactions of formaldehyde with α-alanine and glycine (Table 2), with leucine and aspartic acid (Table 3), and dimethylamine (Table 6). On the other hand, in some cases it is so far

difficult to regard the constants as reproducible within one order of magnitude, this being particularly true of the equilibrium constants L_D (Tables 2 and 3). The values of L_M for reactions between RR'CO and NH_3 taken from Ogata and Kawasaki[59] (Table 2) are probably too high owing to failure to take into account, as suggested by Gaux and Le Henaff[38], the cyclisation of the adduct. The value of L_M (Table 2) found from L_{M^+} and K_{M^+} for the reaction between formaldehyde and ammonia also appears too high[28]. However, the stoichiometry of the reactions in an acid medium, established by the present author and Cheremukhina[28], rules out the likelihood of the cyclisation of the adduct, particularly since one of the possible cyclisation products (hexamethylenetetramine) is polarographically inactive[73]. The hypothesis of the formation in the reaction between formaldehyde and NH_4^+ of a similar cyclisation product with several nitrogen atoms of type (2) or of hexamethylenetetramine must be rejected also because of the observation of two titration jumps corresponding to strong and weak ($pK_{A^+} \simeq 5$ for the reaction product) acids. On the other hand, one cannot assume the similarity of the pK_{A^+} for several groups in the cyclisation product, protonated at the nitrogen atom, because of the strong inductive effect (for example $pK_{A^{2+}} = 5.57$ and $pK = 9.81$ for piperazine). However, the formation of mono-, bis-, and tris-hydroxymethyl derivatives of ammonia with similar pK_{A^+} values in the range 4.3 to 4.5 in the reaction between formaldehyde and NH_4^+ [28] fully justifies the single-stage titration of the adducts as acids whose strength is close to that of acetic acid. Another possible factor causing an unduly high value of L_M(HCHO + NH_3) [25] is the formation of the dehydration product NH=CH_2 and not the adduct NH_2CH_2OH. However, the existence of NH=CH_2 in solution is hardly possible in an appreciable concentration owing to the marked tendency of this compound to cyclise[36]. The formation of the fairly stable cyclic hydrate



(29)

on the basis of the adduct appears more probable, which leads to an increase of L_M.

Other nucleophiles (Table 2) as well as other carbonyl compounds form less stable cyclic hydrates of type (29) owing to steric hindrance, and an anomalously high value of L_M is therefore characteristic of such compounds (Table 2). This can also be said of the protonated form of the adduct, including the adduct obtained in the reaction between formaldehyde and NH_4^+.[28] The enhanced overall hydration of both the initial protonated nucleophile and of the protonated adduct under these conditions rules out a significant influence of the formation of the cyclic hydrate on L_{M^+}. The values of L_{M^+} for the reaction between formaldehyde and NH_4^+ and other analogous reactions are therefore fairly comparable (Table 6). Admittedly, the cause of the lower values of L_{M^+} for the reactions of formaldehyde with $\overset{+}{N}H_3CH_2COOH$ and $CH_3CH(\overset{+}{N}H_3)COOH$, taken from the study of Zhantalai and the present author[29], compared with the data of Feraud and Le Henaff[47] is not altogether clear, particularly since the values of L_{M^+} in these studies are similar for the reactions involving valine (Table 6). It is noteworthy that the reliability of the data from Ref. 29 was also confirmed by kinetic measurements (Table 1).[24,29].

The relation between the reactivity and the nature of the carbonyl compound in reactions with the same nucleophile was considered on the basis of the Hammett equation (aromatic carbonyl compounds[67]) and the Taft equation (aliphatic carbonyl compounds[33,59]). An increase of the equilibrium constants with increase of the positive charge on the carbonyl carbon was demonstrated (Tables 2–7).

In the reactions of aliphatic carbonyl compounds with ammonia, primary amines, aminoalcohols, and amino-acids, the concentrations of the dehydration products $U(U^+)$ can usually be neglected. When aliphatic aldehydes are considered, the main cause of the low capacity of the adducts $M(M^+)$ formed under these conditions for dehydration is due to the overall electron-accepting effect of the substituents at the carbonyl group[4], which hinders the protonation of the oxygen of the hydroxy-group in M and even more so in the M^+ species protonated at the nitrogen atom. It would appear that aliphatic ketones should have led to a shift of the equilibrium towards dehydration products, which has in fact been suggested[8-13,63]. However, here too (probably owing to the insufficient electron-donating effect) the equilibrium involves the preferential formation of the adducts $M(M^+)$, as shown by a comparison with other equilibrium constants (Tables 2 and 6).

The values of L_M and L_U have been found separately[37] for the reactions involving NH_2OH. The higher values of L_M for NH_2OH, $NH_2NHCONH_2$, and NH_2NH_2 compared with other nucleophiles are noteworthy, which has been explained[37] by the stabilisation of the adduct in the former case owing to an intramolecular hydrogen bond. The lower values under these conditions of L_M for furfural and benzaldehyde (Table 5) are caused[37] by the conjugation of the carbonyl group and the aromatic ring. The influence of the intramolecular hydrogen bond in the initial carbonyl compound on the kinetics of reactions with NH_2CH was noted by Knorre and Emanuel'.[74]

There are many reactions (Tables 5 and 7) where the equilibrium between $M(M^+)$ and $U(U^+)$ is almost completely displaced towards the dehydration product $U(U^+)$, which is characteristic of nucleophiles containing nitrogen or oxygen next to the NH_2 group (the compounds NH_2NH_2, $NH_2NHCONH_2$, and NH_2OH). In these reactions, with the exception of those between formaldehyde and $NH_2NH.CONH_2$ (NH_2NH_2, $\overset{+}{N}H_3NH_2$, $\overset{+}{N}H_3OH$),[26,32,33,52] the relation $L_U \gg L_M$ or $L_{U^+} \gg L_{M^+}$ holds (Tables 5 and 7). Under these conditions, the thermodynamic stabilisation of the dehydration products owing to the presence of conjugated systems in the latter apparently has the main influence[5,53]. The higher values of L_U for furfural and benzaldehyde (Table 5) have been explained[37] by the additional stabilisation of the dehydration product as a result of the conjugation of the azomethine group with the aromatic ring. On the other hand, in the reactions of formaldehyde with $NH_2NHCONH_2$ (NH_2NH_2, $\overset{+}{N}H_3NH_2$, $\overset{+}{N}H_3OH$), the electron-accepting effect of the two hydrogen atoms at the carbon atom of the CH_2OH group of the aminocarbinol to a large extent prevents the protonation of the oxygen in the hydroxy-group and hence hinders the dehydration of the aminocarbinol. For example, $L_U/L_M \simeq L_{U^+}/L_{M^+} = 0.31$ for $NH_2NH_2(\overset{+}{N}H_3NH_2)$.[33] Since the values of L_M and L_U may be expected to be similar also for the reaction of formaldehyde with $NH_2NHCONH_2$, the observed[52] equilibrium constant, which the authors[52] believed to be L_M, was included in Table 5 (see L_U).

The problem of the relation between reactivity and the nature of the nucleophile is more complex. Apart from the effects of the intramolecular hydrogen bond and conjugation discussed above (NH_2NH_2, $NH_2NHCONH_2$, NH_2OH), attention was directed[37] to the absence of any correlation between $L_M(L_U)$ and K_{A^+} (Tables 2–7). Jencks[37] and Kallen and Jencks[39] explained the latter by the similarity

of the values of σ^* for the hydrogen atom and the RR'COH group substituting it, as a result of which the polar effects of the substituents in the nucleophile should not influence $L_M(L_U)$ appreciably. This is the difference [39] between the reactions under consideration and those of carbonyl compounds with nucleophiles such as CH acids [75-77]. Nevertheless the problem of the role of the polar effect of substituents in nitrogen-containing nucleophiles is apparently more complex. Thus the relations $L_M \gg L_{M^+}$ and $L_U \gg L_{U^+}$ (Tables 2 and 7), the increase of L_M [38,56] in the series of aminoacids $NH_2(CH_2)nCOO^-$ with increase of n, and the influence of the nature of the substituents in amides on the rates of reaction with formaldehyde [78] can be explained [38,78] by the polar effect. Furthermore, a distinct correlation between L_{M^+} and K_{A^+} (Table 6) and between L_{M^+} and σ^* for the substituent X in $\overset{+}{N}H_3X$ has been observed for several nucleophiles ($\overset{+}{N}H_4$, $\overset{+}{N}H_3CH_2COOH$, $\overset{+}{N}H_3OH$) with a primary amino-group in the protonated state [79]. For reasons which are obscure, $CH_3\overset{+}{N}H_3$ deviates significantly from this correlation (Table 6). Protonated secondary amines and also aminoacids of the type $H_3\overset{+}{N}(CH_2)nCOOH$ likewise failed to show a correlation between L_{M^+} and K_{A^+} (Table 6).

Sander and Jencks [52] obtained a correlation (also confirmed by Hine and Redding [80]) between the reactivity and the nature of the nucleophile using a set of constants expressing the ratios of the equilibrium constants for the given series to the equilibrium constant for a standard nucleophile (methylamine). However, these data are insufficient for reactions involving aliphatic carbonyl compounds, particularly since formaldehyde exhibits an appreciable deviation from the correlation [52].

The reactivity of the nucleophile depends appreciably on steric factors [36,38,39]. This is manifested in the series of aminoacids [36], for example, on passing from glycine to α-alanine, and also in the relation $L_{M^-} > L_{D^-}/L_{M^-}$ (Tables 2 and 3). It is noteworthy that the relation $L_{M^+} < L_{D^+}/L_{M^+}$ holds for protonated forms (Table 6), which is most probably due to the dominant influence of the decrease of the degree of hydration on passing from A^+ to M^+. However, the dominance of steric factors may also be expected for aminoacids ($L_{M^+} \gg L_{D^+}/L_{M^+}$), since the formation of D^+ could not be observed experimentally [29,47,56]. It has been noted [38] that the steric factors of nucleophiles are manifested to a lesser extent in the reactions of acetaldehyde compared with those of formaldehyde. Apparently for this reason we have $L_M < L_D/L_M(CH_3CHO)$ (Table 2).

On the basis of Eqns. (18)-(22) and using the equilibrium constants L_M, L_U, L_{M^+}, and L_{U^+}, the acid dissociation constants of adducts protonated at the nitrogen atom (Table 8) and of the dehydration products (Table 9) were found in a number of studies. Some of the results have been revised using the average equilibrium constants (when different equilibrium constants are quoted in the literature for the same reaction). Furthermore, Tables 8 and 9 present some of the results of direct measurements of K_{M^+} and K_{U^+}. It is necessary to consider the considerable discrepancies between the results [54,67] (see K_{U^+} for $C_6H_5CH{=}N\overset{+}{N}H_2CONH_2$; Table 9) and also the considerable variation of K_{M^+} for the adduct obtained in the reaction between RR'CO and NH_4^+ as a function of the nature of the carbonyl compound (Table 8). In contrast to other nucleophiles, in the latter case the formation of a cyclic hydrate of type (29) and the sensitivity of this factor to the nature of the carbonyl residue (the steric effect) show a more significant influence; the sensitivity is lowest for formaldehyde. On the other hand, a somewhat low value of K_{M^+} for $\overset{+}{N}H_3C(CH_3)_2CH$ was apparently found [12] (Table 8). Nucleophiles which themselves introduce an appreciable steric hindrance (for example α-aminoacids) form adducts for which the difference between the K_{M^+} as a function of the nature of the carbonyl compound are small (Table 8). The dependence of K_{U^+} for the dehydration product on the nature of the carbonyl compound (reactions with NH_2NH_2 and $\overset{+}{N}H_3NH_2$) is described by the Taft equation [33].

Table 8. The acid dissociation constants of the nucleophiles $H_3\overset{+}{N}X(H_3\overset{+}{N}\overset{-}{X}$; $H_2\overset{+}{N}XX')$ (K_{A^+}) and the adducts (K_{M^+}) in reactions with RR'CO at 20-25 °C.

RR'CO	$H_3\overset{+}{N}X(H_3\overset{+}{N}\overset{-}{X}$; $H_2\overset{+}{N}XX)$	pK_{A+}	pK_{M+}	References
HCHO	Morpholine	8.7	6.0	38,39,55
CH_3CHO	»	»	6.5	38
HCHO	NH_4^+	9.25	4.5	28
CH_3CHO	»	»	6.9	8,38
$(CH_3)_2CO$	»	»	9.0	12
HCHO	Valine	9.72[a]	7.0[b]	24,25,29,47,60,61
HCHO	Leucine	9.74[a]	7.4[b]	24,25,47,60,62
CH_3CHO	»	»	7.6[b]	38,56
HCHO	α-Alanine	9.87[a]	7.4[b]	24,25,29,39,47,60—62
CH_3CHO	»	»	7.7[b]	38,56
$(CH_3)_2CO$	»	»	8.4[b]	12
HCHO	Glycine	9.88[a]	8[b]	42
HCHO	»	»	7.6[b]	24,25,29,47,60,61
CH_3CHO	»	»	8.1[b]	38,56
HCHO	Aspartic acid	10.00[c]	8.4[d]	24,25,47
CH_3CHO	Ditto	»	7.9[d]	38,56
CH_3CHO	β-Alanine	10.24[a]	7.5[b]	38,56
CH_3CHO	γ-Aminobutyric acid	10.56[a]	7.7[b]	38,56
HCHO	$CH_3\overset{+}{N}H_3$	10.62	7.5	55
HCHO	Proline	10.64	7.9	39,60
HCHO	Sarcosine	10.7	7.7[b]	39,60
HCHO	$(CH_3)_2\overset{+}{N}H_2$	10.71	8.0	39
HCHO	Piperidine	11.12	8.1	39
HCHO	Pyrrolidine	11.27	8.6	39

[a] $pK_{A^\pm}$; [b] $pK_{M^\pm}$; [c] $pK_{A^\pm}$; [d] $pK_{M^\pm}$.

Table 9. The acid dissociation constants of the nucleophiles $H_3\overset{+}{N}X$ (K_{A^+}) and the dehydration products (K_{U^+}) in the interaction of the nucleophiles with RR'CO at 25 °C.

RR'CO	pK_{U+}	References
$\overset{+}{N}H_3NHCONH_2$; pK_{A+} 3.43=		
$CH_2(OH)CHO$	−0.5	30
$CH_2(OH)CH(OH)CHO$	−0.4	30
CH_3CHO	0.8	17,54
C_6H_5CHO	0.8[a]	54
C_6H_5CHO	−1.05	67
Furfural	1.2[a]	54
$(CH_3)_2CO$	1.2	17,54,66
Cyclopentanone	1.3	17
Cyclohexanone	0.9	17,54,66
$(CH_3)_2CO$ $\overset{+}{N}H_3OH$; pK_{A+} = 5.97	1.7[b]	54
HCHO $\overset{+}{N}H_3NH_2$; pK_{A+} = 8.15	4.21	33,34
CH_3CHO	4.45	31,33
CH_3CH_2CHO	4.64	33
$CH_3CO(CH_2)_2COO^-$	4.76	35
$(CH_3)_2CO$	4.76	33
$(CH_3)_2CO$	5.1[c]	81
$CH_3COC_2H_5$	4.79	33

[a] Adjusted for pK_{A^+} = 3.43; [b] adjusted for pK_{A^+} = 5.97; [c] in methanol; [d] pK_{A^+} = 8.19 was used in Refs. 31, 33, and 35; here the values of pK_{U^+} have been adjusted to pK_{A^+} = 8.1.

The main conclusion which can be drawn from Tables 8 and 9 is the occurrence of the relations $K_{M^+} \gg K_{A^+}$ and $K_{U^+} \gg K_{A^+}$, which is very important for the acid–base titration of the reaction products [6,7]. Under these conditions, K_{M^+} ($K_{M^\pm}$) is greater by 1.5–3.0 orders of magnitude than K_{A^+} ($K_{A^\pm}$), while K_{U^+} is greater than K_{A^+} by 2.0–4.0 orders of magnitude. Whereas the higher values of K_{U^+} compared with K_{A^+} can be readily explained (by the polar effect of the azomethine group), the reason for the appreciably higher values of K_{M^+}($K_{M^\pm}$) is still insufficiently clear, because, as stated by Kallen and Jencks [39], polar effects do not change very greatly when the hydrogen atom is replaced by the C(OH)RR′ group. The above authors' hypothesis of the significant role in this case of the common hydration factor is quite justified (by analogy with amines [82]), but the formation under these conditions of a cyclic hydrate of type (29), particularly for the adduct involving HCHO and NH_4^+, which causes an additional enhancement of the acid function of the protonated nitrogen, is probably also important. Aminocarbinols where the amino-group is not in the 1-position apparently form less stable hydrates (with more than 6 units) and the role of this factor is reduced. Naturally, the direct electron-accepting effect of the R″C(OH)RR′ group in such aminocarbinols is less pronounced, which also reduces their acid properties.

III. THE MECHANISM OF THE POLAROGRAPHIC REDUCTION OF REACTION PRODUCTS

The mechanism of the reduction of the dehydration products (hydrazones, oximes, etc.) has been investigated in greater detail (Lund [83,84], Kitaev and coworkers [85–87]). This mechanism was recently considered in Kitaev and Buzykin's review [88] and will be only briefly described in the present review, with the exception of the problem of the kinetics of the limiting current which has not been dealt with adequately. The possible mechanisms of the electrochemical reduction of adducts (aminocarbinols) have been considered in the literature in less detail, particularly since their reduction via the formation of the usual dehydration product U (the adduct of a nucleophile with a secondary or tertiary amino-group) is frequently ruled out.

As stated in Section II, the presence of conjugated systems [5] is characteristic of the dehydration product U having the structure RR′C=NYR″, where Y is either a nitrogen atom (hydrazones) or an oxygen atom (oximes), which, together with protonation, facilitates the dissociation of the N–Y bond during their reduction. Under these conditions, four-electron reduction is usually observed in an acid solution [83–87]:

$$\begin{aligned} RR'C{=}N{-}YR'' \xrightarrow{H^+} (RR'C{=}N{-}YR'')^+ H \xrightarrow{2\bar{e};2H^+} \\ \rightarrow R''YH + RR'C{=}\overset{+}{N}H_2 \xrightarrow{2\bar{e};2H^+} RR'CH\overset{+}{N}H_3. \end{aligned} \qquad (30)$$

It has recently been shown [34] that unsubstituted hydrazones of aliphatic carbonyl compounds also undergo a four-electron reduction reaction at pH ≤ 8. Since hydrazones of this kind are to a large extent hydrolysed, a microcoulometric study has been carried out [34] in the presence of a very large excess of hydrazine.

If Y is a carbon atom in the compounds RR′C=NYR″ (azomethines), only the double bond is reduced (a two-electron process) [83]:

$$RR'C{=}NYR'' \xrightarrow{2\bar{e};\,2H_2O} RR'CHNHYR'' + 2OH^-. \qquad (31)$$

The mechanism of the generation of the kinetic limiting current in the reduction of hydrazones when the solution contains the corresponding adducts has been considered [34] on the basis of the scheme

$$\begin{array}{ccccc} M & \xrightarrow{\text{diff.}} & M & & \\ \uparrow\downarrow & & \uparrow\downarrow k'_{-1}\ \ k'_{+1} & & \\ & & H^+;\ k''_{+1} & & \\ U & \xrightarrow[\text{diff.}]{} & U & \rightleftarrows & U^+ \xrightarrow{\text{red.}} \\ & & & k''_{-1} & \end{array}, \qquad (32)$$

which takes into account both the slow protonation of U and the slow dehydration of M. A kinetic equation has been derived (in the presence of a large excess of the nucleophile when virtually the entire carbonyl compound is converted into M and U): [34]

$$\lg \frac{\bar{i}^0_{lim}}{(\bar{i}^0_{lim})_d - \bar{i}^0_{lim}} = \lg \frac{k''_{+1}[k'_{+1}(L_M + L_U) + \bar{\varkappa} L_U]}{\bar{\varkappa}\,(k'_{+1}(L_M + L_U) + (k'_{-1} + \bar{\varkappa})(L_M + L_U) + k''_{+1} L_M [H^+])} - pH, \qquad (33)$$

where $(\bar{i}^0_{lim})_d$ is the limiting diffusion current and $\bar{\varkappa}$ is the Ilkovič constant. Since under these conditions $k'_{-1} \gg k'_{+1}[H^+]$ and $k'_{-1} \gg \bar{\varkappa}$ or $k'_{-1} \gg k''_{+1}[H^+]$ and $k'_{+1} \gg \bar{\varkappa}$ (enhancement of base catalysis at the hydration–dehydration stages) [89,90], Eqn.(33) assumes the following form [34] with increase of pH ($L_U/L_M = k'_{+1}/k'_{-1}$):

$$\lg \frac{\bar{i}^0_{lim}}{(\bar{i}^0_{lim})_d - \bar{i}^0_{lim}} = \lg \frac{k''_{+1} L_U}{\bar{\varkappa}(L_M + L_U)} - pH; \qquad (34)$$

when $L_U \gg L_M$, whereupon the dehydration product predominates {[U] ≫ [M]}, we obtain

$$\lg \frac{\bar{i}^0_{lim}}{(\bar{i}^0_{lim})_d - \bar{i}^0_{lim}} = \lg \frac{k''_{+1}}{\bar{\varkappa}} - pH. \qquad (35)$$

It is noteworthy that Eqns.(33)–(35) are applicable to both bulk-phase and surface protonation processes [91] when the Henry adsorption isotherm holds. Eqns.(34) and (35) correspond to mechanism (32) with a fairly rapid adduct dehydration stage. Here kinetic inhibition is due solely to the stage involving the protonation of the dehydration product U.

Eqn.(33) has been confirmed [34] for the reduction of the products of the reaction of formaldehyde with NH_2NH_2. .($\overset{+}{N}H_3NH_2$) in the pH range 5.5–8.0. Thus formaldehyde hydrazone is reduced even in the acid pH range with considerable kinetic limitation owing to the slow dehydration of the adduct present in a considerable amount (Table 5). With increase of pH, the retardation of the process at the protonation stage was also observed. This inhibition predominated at pH ≥ 7.0 [see Eqn.(34)]. [34] Since the concentration of the adduct was extremely low, the limiting current for the hydrazones of other aliphatic carbonyl compounds at pH ≤ 6.5 had a diffusional origin, while at pH > 6.5–7.0 kinetic process inhibition, due to the retardation of the stage involving the protonation of the dehydration product, was manifested. The applicability of the usual equation for the polarographic dissociation curve [Eqn.(35)] to these hydrazones has been demonstrated [34], this being characteristic also of thiosemicarbazones [92].

In order to find the true rate constants from Eqns. (33)–(35), the Koutecký equation has been used [34,92]. For the formaldehyde adduct, the true dehydration rate constant $k' = 0.4\ s^{-1}$ at pH ~ 6, which is close to the result obtained from a chronopotentiometric study [93]. The rate constants for the protonation reaction are listed in Table 10. Surface protonation [34,87,91,92] with participation of adsorbed species is characteristic of the majority of these compounds, as shown by the unduly high rate constants (Table 10). The rate constant for the bulk-phase process may have been

found only for the anions of levulinic acid owing to the insignificant adsorption of the hydrazone anion at $E = -1.3 - -1.6$ V (here and henceforth potentials relative to the normal calomel electrode are quoted) (Table 10). Surface protonation is also characteristic of oximes [94]. The semicarbazonium ion may participate in the protonation reaction [95,96].

Table 10. The true (K_{U^+}) and apparent (polarographic) (K'_{U^+}) acid dissociation constants of the dehydration products and the rate constants k (based on the Koutecky equation with a coefficient of 0.886) for their protonation at 25°C.

Dehydration product	pK_{U+}	pK'_{U+}	k, litre mole^{-1} s^{-1}	Refs.
Acetophenone thiosemicarbazone	0.92	7.5	$5 \cdot 10^{13}$ a	92
Cyclohexanone thiosemicarbazone	1.04	7.0	$4 \cdot 10^{12}$ a	92
Acetaldehyde semicarbazone	0.8	6.5	$6 \cdot 10^{11}$ a	92
Benzaldehyde semicarbazone	0.8	7.2	$2 \cdot 10^{13}$ a	92
Formaldehyde hydrazone	4.21	6.7	$2 \cdot 10^{10}$ b	34
Acetaldehyde hydrazone	4.45	7.8	$6 \cdot 10^{10}$	34
Propionaldehyde hydrazone	4.64	7.8	$5 \cdot 10^{10}$	34
Acetone hydrazone	4.76	7.8	$3 \cdot 10^{10}$	34
Ethyl methyl ketone hydrazone	4.79	7.8	$3 \cdot 10^{10}$	34
Hydrazone of levulinate anion	4.76	7.4	$5 \cdot 10^{9}$	35

[a] The dropping period of the dropping mercury electrode was $t_1 = 3.0$ s; [b] Eqn.(34), $L_M = 1.9 \times 10^9$ and $L_U = 5.8 \times 10^8$ (Table 5).

The plot of $\bar{i}_{lim}$ against pH for the limiting current corresponding to the equilibrium $Q + A(A^+) \rightleftharpoons M(M^+) \rightleftharpoons U(U^+)$ passes [30,34] through a maximum, which has been explained [30,34], on the one hand, by the increase of the concentration of the reaction products with increasing pH (because $L_M \gg L_{M^+}$ and $L_U \gg L_{U^+}$) and, on the other hand, by the opposed effect due to the enhancement of inhibition at the product U protonation stage. The calculated $\bar{i}_{lim}$–pH curves obtained with the aid of Eqn.(23) (for $c_A \gg c_Q$) are close to the experimental curves [34]. Expressions have also been found [34] for pH_{max} {subject to the condition $d\bar{i}_{lim}/d[H^+] = 0$} at which $\bar{i}_{lim}$ reached a maximum value. The expression for pH_{max} corresponding to reactions involving the appreciable formation of M (formaldehyde) together with U is [34]

$$pH_{max} = -\frac{1}{2} \lg \frac{(L_M + L_U)(k'_{+1} + k'_{-1} + \bar{\varkappa})\bar{\varkappa} c_A}{k''_{+1}(k'_{+1} + \bar{\varkappa})(1 + L_G)}. \quad (36)$$

The following expression has been obtained for reactions where the concentration of M compared with U may be neglected [34]:

$$pH_{max} = -\frac{1}{2} \lg \frac{K_{A+}(1 + L_G + c_A L_U)\bar{\varkappa}}{k''_{+}(1 + L_G)}. \quad (37)$$

The values of pH_{max} have been calculated [34] with the aid of Eqns.(36) and (37) and the maximum limiting currents $(\bar{i}_{lim})_{max}$ have been obtained with the aid of Eqn.(22) for $c_A \gg c_Q$ using the values of $\bar{i}^0_{lim}$ and $[H^+]_{max}$. pH_{max} and $(\bar{i}_{lim})_{max}$ are close to the experimental values for a series of hydrazones (Table 11) (the values of L_G were taken from Tables 2–7).

The influence of the nature of the hydrazones of aliphatic carbonyl compounds on the half-wave potential $E_{1/2}$ is determined to a large extent (Table 12) by the inductive effects of the substituents in the carbonyl compound, as shown by the shift of $E_{1/2}$ towards negative values with increase of the electron-donating effect of the substituents. A similar conclusion follows also from the correlation analysis of the half-wave potentials for many other compounds with the azomethine group [97]. With the exception of formaldehyde hydrazone, the limiting current constants in the acid pH range (Table 12) correspond to a diffusion process.

Table 11. Comparison of the experimental and calculated values of pH_{max} and $(\bar{i}_{lim})_{max}$ [34] ($c_Q = 1.0 \times 10^{-4}$ M; $c_A = 1.0 \times 10^{-3}$ M).

Hydrazone	pH_{max}		$(\bar{i}_{lim})_{max}$, μA	
	expt.	calc.	expt.	calc.
Of formaldehyde	6.0	6.1	1.18	1.17
Of acetaldehyde	6.6	6.6	2.26	2.27
Of propionaldehyde	6 9	7.1*	1.75	1.77*
Of acetone	7.8	7.9	0.60	0.49

*It was assumed in the calculations that $L_G = 0.72$, which is more accurate than the value adopted in Ref. 34.

Table 12. The half-wave potentials ($E_{1/2}$, pH = 7.4) and the limiting current constants (I^0_{lim}, μA mmole^{-1} mg$^{-2/3}$ s$^{1/2}$; pH = 3.5–5.5) for the reduction of RR'C=NH$_2$.

R	R'	$-E_{1/2}$, V	I^0_{lim}	R	R'	$-E_{1/2}$, V	I^0_{lim}
CH_2=CH	H	1.05	—	CH_3CH_2	H	1.30	9.8
CH_2=C(CH_3)	H	1.15	—	CH_3	CH_3	1.47	9.6
CH_3CH=CH	H	1.22	—	CH_3	C_2H_5	1.46	9.4
H	H	1.17	6.4	CH_3	$(CH_2)_2COO^-$	1.49*	10.5*
CH_3	H	1.32	9.8				

Data from Ref. 35; in the remaining cases, data from Ref. 93 were used.

We shall now proceed to the consideration of the mechanism of the polarographic reduction of adducts–aminocarbinols. For the formation of aminocarbinols with participation of formaldehyde, Matoušek [22] proposed a mechanism involving the reduction of the adduct M with dissociation of the C–O bond (first wave):

$$\text{>NCH}_2\text{OH} \xrightarrow{H^+} \text{>NCH}_2\overset{+}{\text{O}}\text{H} \rightarrow H_2O + \text{>N}\overset{+}{\text{C}}\text{H}_2 \xrightarrow{2\bar{e};\ H^+} \text{>NCH}_3. \quad (38)$$

and reduction with dissociation of the N–C bond (second wave, which coincides with the formaldehyde reduction wave):

$$\text{>NCH}_2\text{OH} \xrightarrow{H^+} \text{>}\overset{+}{\text{N}}\text{HCH}_2\text{OH} \rightarrow \text{>NH} + \overset{+}{\text{C}}\text{H}_2\text{OH} \xrightarrow{2\bar{e};\ H^+} \text{CH}_3\text{OH}. \quad (39)$$

These mechanisms are based [22] on data concerning the nature of the chemical reduction of the corresponding hydroxymethyl derivatives and also pulse volt-amperometric data at different frequencies. In addition to reaction (38), attention should also be directed to the possibility of the intermediate formation and reduction of an ammonium derivative:

$$\text{>NCH}_2\text{OH} \xrightarrow{H^+} \text{>NCH}_2\overset{+}{\text{O}}\text{H} \rightarrow H_2O + \text{>}\overset{+}{\text{N}}\text{=CH}_2 \xrightarrow{2\bar{e};\ H^+} \text{>NCH}_3. \quad (40)$$

The occurrence of a two-electron process of type (38) or (40) was demonstrated[26] by a microcoulometric study of the sum of the products of the reaction between formaldehyde and $\overset{+}{N}H_3OH$. Since this reaction gives rise[26] to the mono- and bis-hydroxymethyl derivatives $HO\overset{+}{N}H_2 . CH_2OH$ and $HO\overset{+}{N}H(CH_2OH)_2$, the reduction of only one hydroxymethyl group in both the mono- and bis-hydroxymethyl derivative should correspond to the two-electron process:

$$HO\overset{+}{N}H(CH_2OH)_2 \xrightarrow{H^+} HO\overset{+}{N}H(CH_2OH)\,CH_2\overset{+}{O}H \rightarrow H_2O + HO\overset{+}{N}H(CH_2OH)\,\overset{+}{C}H_2 \xrightarrow{2e;H^+} \rightarrow HO\overset{+}{N}H(CH_2OH)\,CH_3. \quad (41)$$

This is most probably associated with the fact that there is insufficient time for the product of the two-electron reduction, namely $HO\overset{+}{N}H(CH_2OH)CH_3$ to undergo a repeated dehydration stage with further reduction at the electrode surface.

Presumably the reduction with dissociation of the C–O bond [reaction (38)] or the C–N bond [reaction (39)] is activated by the formation of a six-membered cyclic hydrate of type (29). Although protonation is inhibited under these conditions, the enhancement of the mutual inductive effect of the RR'N and OH groups facilitates the reduction. This probably constitutes the main difference in the electrochemical behaviour of aminocarbinols with the amino-group in the 1-position compared with other aminocarbinols, which are incapable of being electrochemically reduced.

Table 13. Polarographic characteristics of the hydroxymethyl derivatives of aminoacids[100] at 25°C ($\bar{i}$lim, $\mu A\ mmole^{-1}\ mg^{-2/3}\ s^{1/2}$).

Aminoacid	$K_{A\pm}$	$pK_{M\pm}$	$c_{HCHO}=0{,}6M$		$c_{HCHO}=6{,}0M$		$c_{HCHO}=2{,}0M$ pH=7,8
			pH_{max}	$(\bar{i}_{lim})_{max}$	pH_{max}	$(\bar{i}_{lim})_{max}$	$-E_{1/2}$, V
β-Phenyl-β-alanine	5.4	—	7.6	1.4	5.8	1.8	1.13
β-Alanine	10.24	—	7.4	0.60	4.7	1.7	1.18
β-Phenyl-α-alanine	8.6	—	7.8	1.4	6.2	2.9	1.16
Valine	9.72	7.0	8.2	1.0	6.8	(1.9)	1.17
Leucine	9.74	7.4	7.9	0.92	6.3	2.6	1.18
Norleucine	9.83	—	8.2	0.86	6.4	2.4	1.18
Norvaline	—	—	8.2	0.80	6.4	2.4	1.18
α-Alanine	9.87	7.4	8.0	0.57	6.0	1.6	1.19
Glycine	9.88	7.6	6.8	0.60	4.4	2.2	1.20
α-Aminoadipic acid	—	—	8.0	0.38	6.3	1.2	1.22
Glutamic acid	9.95*	—	7.8	0.45	6.2	1.2	1.25
Aspartic acid	10.00**	8.4	8.0	0.32	6.4	1.3	1.26

* $pK_{A\pm}$; $pK_{A\pm}=4{,}51$.
** $pK_{A\pm}$; $pK_{A\pm}=3{,}9$

In an acid medium (pH ≤ 2), where the adduct M(D, T) is almost completely protonated at the nitrogen atom, the dehydration stage preceding the electrochemical reduction process is either catalysed by repeated protonation (at the oxygen atom[24]) or there is intramolecular catalysis owing to a hydrogen bond:

$$RR'C(HO\cdots H)-N^+HX \rightleftarrows RR'C(HO-H^+)-NHX \quad (42)$$

Since the limiting kinetic current is independent of pH in this range of the latter for many hydroxymethyl derivatives of aminoacids[24], intramolecular catalysis appears to be more likely. The independence of $\bar{i}$lim of pH in fairly acid solutions also shows that the kinetic current is caused by inhibition at the dehydration stage [mechanism (38)],[22] while the stage involving the protonation of the oxygen atom [mechanism (42)] is fairly rapid (is close to equilibrium). The nature of the substituent X in the nucleophiles (Table 1) has an effect under these conditions, manifested mainly by displacement of equilibrium (42) [the distance from the dissociating $C-\overset{+}{O}$ bond than in the decomposition of the adduct into the initial substances is greater]. An increase of the $-I$ effect of the substituent X (the inductive and steric influences) as well as an increase of the $+I$ effect (the dominance of steric influences) displaces equilibrium (42) to the right; hence follows an increase of $\bar{i}$lim and its correlation with the constants k_{-1} and K'_{A^+} (Table 1). Starting with norvaline, $\bar{i}$lim approaches the diffusion value (Table 1).

Table 14. The half-wave potentials for the reduction of $RR'C(OH)\overset{+}{N}H_2X$.

R	R'	X	pH	$-E_{1/2}$, V	References
H	H	OH	~0	0.49*	26,51
H	H	H	2.5	0.84*	28,99
H	H	H	7.8	1.11	99
C_6H_5	COC_6H_5	H	9.25	0.58	8
CH_3	$COCH_3$	H	9.25	0.66	8
C_6H_5	COO^-	H	9.25	0.88	8
CH_3	COO^-	H	9.25	1.04	8
CH_3	H	H	9.25	1.44	8
CH_3	CH_3	H	9.25	1.56	8
CH_3	COO^-	CH_2COO^-	9.88	1.09	8
CH_3	CH_3	CH_2COO^-	9.88	1.50	8
CH_3	COO^-	$CH(CH_3)COO^-$	9.87	1.10	8
CH_3	COO^-	CH_2CH_2OH	9.50	1.04	8
H	H	CH_2CH_2OH	10.0	1.3	73

* $RR'C(OH)\overset{+}{N}H_2X$.

Over a wide range of pH values with c_Q = const. and c_A = const., $\bar{i}$lim passes through a maximum as a function of pH,[22,28,73,95,96,98-101] as in the reduction of semicarbazones[30] and hydrazones[34] in an equilibrium mixture. This is caused by the increase of the concentrations of the adducts ($L_M \gg L_{M^+}$, $L_D \gg L_{D^+}$, $L_T \gg L_{T^+}$) with increasing pH, the opposite effect due to the decrease of the concentrations of the forms of the adducts protonated at the nitrogen atom, and inhibition either at stage (42) or at the stage involving the protonation of the adduct at the nitrogen atom. The occurrence of one of the above inhibiting effects with increasing pH is indicated by the confirmation of the validity[28] of Eqn.(35) for the reduction of M + D + T (for the reaction of formaldehyde with NH_4^+). Under these conditions, the $\bar{i}$lim–pH curve is described by Eqn.(26) when account is taken of Eqn.(35). As for hydrazones[34], pH_{max} was found from the condition $d\bar{i}lim/d[H^+] = 0$[28] and it was shown theoretically that pH_{max} should shift towards lower pH values with increasing c_Q, which agrees with experimental data[99]. This is also characteristic[100] of the adducts obtained by the reaction of formaldehyde with aminoacids (Table 13). In the presence of a not unduly large excess of formaldehyde, the changes in $(\bar{i}lim)_{max}$ and in $E_{1/2}$ at a constant pH (Table 13) are caused mainly by the inductive and steric effects of substituents in similar (α- or β-) aminoacids, which leads to a correlation between $(\bar{i}lim)_{max}$ and $E_{1/2}$ and between $K_{A\pm}$ and $K_{M\pm}$ (Table 13). The influence of the inductive effect on $E_{1/2}$ at a constant pH (the displacement of $E_{1/2}$ towards positive values with increasing $-I$ effect) is also illustrated by the data in Table 14.

IV. ANALYTICAL APPLICATIONS

The reactions under consideration are widely used for the indirect polarographic determination of carbonyl and nitrogen compounds. Distinct polarographic waves are observed, while under the usual conditions the reduction of many compounds is either partly or fully masked by the discharge of the supporting electrolyte. This applies particularly to nitrogen compounds and many aliphatic and cyclic carbonyl compounds. Even when the carbonyl compound is reduced relatively readily (formaldehyde, etc.), a valuable feature of the reaction is that the reduction wave of the product M(D, T) or U occurs at potentials much more positive than the reduction potentials of the carbonyl compounds, which makes it possible to use a large excess of the latter and hence increase the sensitivity of the determination of the nitrogen compounds. On the other hand, in the determination of the carbonyl compounds, a large excess of the nitrogen compound (ammonia, semicarbazide, hydrazine, etc.) is also permissible, because the nucleophile employed is frequently polarographically completely inactive under the given conditions.

It must be emphasised that, in the selection of the concentration of the reactant, one need not endeavour to ensure the complete conversion of the component being analysed into the polarographed product. It is sufficient to obtain an equilibrium mixture, because the limiting current in the presence of an excess of the reactant at a constant concentration of the latter and a constant pH is proportional to the concentration of the substance analysed [Eqns. (25) and (26)]. Naturally, in the analysis it is important to achieve reaction equilibrium rapidly, which is usually done by selecting the optimum pH in the solution. For this purpose and also in order to increase the sensitivity of the determination of the carbonyl compound, a supporting electrolyte buffer solution was used with a pH close to the pK_{A^+} of the nucleophile present in excess [8,12,13]. The optimum pH of the supporting electrolyte corresponding to the maximum limiting current is frequently selected for analysis [98-101]. In order to attain equilibrium rapidly and increase the sensitivity of the determination, the reaction has been carried out [102,103] in an alkaline medium and the polarographic measurements have been made in an acid solution. This method is suitable only when the reaction products are very slowly decomposed in the acid solution into the initial substances (aminoacids with the amino-group not in the α-position) [24,102,103]. It has been shown [104] that the rate of equilibration in the carbonyl–amine interaction increases sharply in anhydrous acetic acid, which is probably due mainly to catalytic factors.

The selectivity of the methods is achieved either by selecting appropriate reagents (*N*-alkylhydroxylamines [105], hydrazine [106]) or by altering the pH of the supporting electrolyte [107,108].

From the analytical point of view, it is also important that, with the aid of the reactions under consideration, it is possible to trap easily the component analysed in the gas phase [109,110] or extract it fairly completely from a non-aqueous solution [106,111]. One should also note that suitable direct analytical reactions with carbonyl compounds have not been found for many nitrogen compounds [51,73,98,102,112-117], because of their weak nucleophilic properties, so that it has been suggested (see below) that the nitrogen compounds be subjected to preliminary hydrolysis with subsequent conversion of the hydrolysis products in the presence of the carbonyl compound into the polarographed substances. Preliminary hydrolysis has also been used [118] for vinyl acetate with conversion of the resulting acetaldehyde (reaction with hexamethylene-1,6-diamine) into the polarographed product. The conversion of organic nitrogen compounds into the inorganic ammonium ion with its subsequent polarographic determination in the presence of formaldehyde has been achieved [119] in order to improve the familiar Kjeldahl method. The nitrogen-containing reagent (an aminoacid) to be used for the determination of a carbonyl compound has been obtained [120] by the hydrolysis of the substance to be analysed—polycaproamide.

Analytical determinations are usually based on cathodic waves, but anodic waves for the products of the interaction of carbonyl compounds with *o*-phenylenediamine have also been used [121-124].

1. Determination of Carbonyl Compounds

Reactions with Girard reagents (the formation of hydrazones) have been used [101,125-132] to determine aliphatic and cyclic ketones, ketosteroids, terpenes, and other carbonyl compounds. Analytical reactions belonging to an analogous class have been carried out on the basis of hydrazine [15,21,106,114,133-142], phenylhydrazine [143], semicarbazide [17,21,109,110,144-150], maleic acid monohydrazide [151], aminoguanidine [151], and 2,4-dinitrophenylhydrazine [152-155] (either an excess of the reagent [153] was determined [153,154] or an amperometric titration was carried out [154]). It is noteworthy that, whereas the use of hydrazine for the determination of aliphatic carbonyl compounds was unsuccessful owing to the use of an unduly acid supporting electrolyte [133] (in contrast to the determination of sugars [134]), starting with the work of Baranova et al. [114] and Yuan-Hsiao Lin and Chen-Ya Wang [135] the problem has been solved successfully (determination of carbonyl compounds in the wash water from the manufacture of isoprene [114] and determination of acetone in vinyl acetate [135]; supporting electrolytes at pH 6.3 [114] and 7.2 [135] have been used).

This application has been developed in other investigations [106,136-142] and included the separate determination of a series of aliphatic aldehydes and ketones in the manufacture of synthetic rubber monomers [106,136,139], formaldehyde has been determined in cellulose ethers [140,141], and a highly sensitive method has been developed for the determination of acetaldehyde in commercial ethanol without the need for the preliminary concentration (distillation) of the former [142]. The use [156] of reactions based on semicarbazide, thiosemicarbazide, and phenylhydrazine for the adsorption concentration of aliphatic and aromatic aldehydes on a stationary mercury drop, which permitted an appreciable increase of the sensitivity of the determination (oscillographic polarography), is of interest. An increase of the sensitivity of the determination with the aid of similar reagents has also been achieved by using oscillographic difference polarography [157].

The reactions with hydroxylamine and its alkyl derivatives (the formation of oximes) have been used for the polarographic determination of carbonyl compounds: the determination of aliphatic aldehydes [105], aldoses [21,144], pyridoxals [158], vanillin [159,160], furfural [161,162], crotonaldehyde [163], and acetone [164].

The reactions with ammonia [8,12,13,165-167], glycine [8,12,13,168], methylamine [13], n-butylamine [20], isobutylamine [124], ethylenediamine [169], 1,6-hexamethylenediamine [118,169-172], monoethanolamine [73,173], and *o*-phenylenediamine [121,124,174-178] are also of definite importance in the polarographic determination of carbonyl compounds. Nevertheless, in many cases preference must be given to substituted and

unsubstituted hydrazines and hydroxylamines as reagents because of the much larger reaction equilibrium constant (see Section II).

2. Determination of Nitrogen Compounds

The possibility, in principle, of the polarographic determination of an aminoacid on the basis of its reactions with pyruvic acid or acetone was already demonstrated in earlier investigations [11,12]. Subsequently methods were developed for the determination of methylamine in the presence of dimethylamine (reaction with piperonal) [179], aminoacids and ammonium ions (reactions with phthalic anhydride) [180,181], hydrazine and its derivatives (reactions with benzaldehyde) [182], and primary amines (reaction with isobutyraldehyde) [183].

Starting with the work of Matoušek [22] and Tur'yan and coworkers [28,102], formaldehyde has found extensive applications as a reagent in the indirect polarography of nitrogen compounds. It is used to determine aminoacids [98,100,102,103,107,108,184,185], caprolactam [98,102,103,186,187] (hydrolysis to ϵ-aminocaproic acid), *N*-methylpyrrolidinone [116] (hydrolysis to *N*-methylaminobutyric acid), ammonium ions [28,99,108,119,188], hexamethylenetetramine [73,113] (hydrolysis to ammonium ions, but is can also be determined from the formaldehyde formed—reaction with monoethanolamine [73])†, acetonitrile [40,115] (hydrolysis to ammonium ions), primary and secondary amines [40,114,190-195], dimethylformamide [40,114] (hydrolysis to methylamine), hydroxylamine [26,51,196,197], cyclohexanone oxime [26,51,112,197] and other oximes [117] (hydrolysis to hydroxylamine), hydrazine, and formylhydrazine [138]. The successful employment of formaldehyde is due, firstly, to the high equilibrium constants for the reactions (Section II) combined with the possibility of creating a relatively high concentration of the reagent in the supporting electrolyte and, secondly, the fact that, in the presence of an excess of formaldehyde, several polarographically active products are formed (in the general case, mono-, bis-, and tris-hydroxymethyl derivatives), which also increases the sensitivity of the methods. Even in a very acid medium, where the nucleophile is almost completely protonated, formaldehyde behaves as a fairly active reagent [26,51,112,196].

Certain nitrogen compounds (diamines [198,199], hydrazine and its derivatives [200], semicarbazide [200], and hydrazides [201,202]) have been determined successfully using acetone as the reagent. Other carbonyl compounds have also been employed to determine hydrazides [203-205] and thiosemicarbazides [206].

The determination of 2,2'-bis-(3-amino-4-hydroxyphenyl)propane in polymers on the basis of its reaction with benzaldehyde has been reported [207].

REFERENCES

1. P. Zuman, Chem. Listy, 46, 688 (1952).
2. Ya. I. Tur'yan and V. F. Romanov, Zavod. Lab., 28, 5 (1962).
3. P. Zuman, "Organická Polarografie Metodika a Pouziti", Statni Nakladatelstvi Technické Literatury, Prague, 1966, p. 114.
4. W. P. Jencks, "Catalysis in Chemistry and Enzymology" (Translated into Russian), Izd. Mir, Moscow, 1972, p. 349.
5. C. K. Ingold, "Theoretical Foundations of Organic Chemistry" (Translated into Russian), Izd. Mir, Moscow, 1973, p. 820.
6. I. M. Kolthoff and V. A. Stenger, "Volumetric Analysis" (Translated into Russian), Goskhimizdat, Moscow, 1950, Vol. 1; 1952, Vol. 2.
7. M. R. F. Ashworth, "Titrimetric Organic Analysis" [Vol. XV of "Chemical Analysis" by W. Walisch] (Translated into Russian), Izd. Khimiya, Moscow, 1968, Part I; 1972, Part II.
8. P. Zuman, Coll. Czech. Chem. Comm., 15, 839 (1950).
9. P. Zuman, Chem. Listy, 45, 40 (1951).
10. P. Zuman, Chem. Listy, 45, 65 (1951).
11. P. Zuman, Chem. Listy, 46, 516 (1952).
12. P. Zuman and M. Březina, Chem. Listy, 46, 599 (1952).
13. M. Březina and P. Zuman, Chem. Listy, 47, 975 (1953).
14. G. A. Crowe, Jr. and C. C. Lynch, J. Amer. Chem. Soc., 70, 3795 (1948); 71, 3731 (1949).
15. G. Sartori and A. Gaudiano, Gazzetta, 78, 77 (1948).
16. G. A. Crowe, Jr. and C. C. Lynch, J. Amer. Chem. Soc., 72, 3622 (1950).
17. P. Souchay and M. Graizon, Chim. Anal., 36, 85 (1954).
18. D. M. Coulson, Anal. Chim. Acta, 19, 284 (1958).
19. K. Dušek, J. Polymer Sci., 30, 431 (1958).
20. R. E. Van Atta and D. R. Jamieson, Anal. Chem., 31, 1217 (1959).
21. J. W. Haas, Jr. and R. E. Kadunce, J. Amer. Chem. Soc., 84, 4910 (1962).
22. L. Matoušek, Dissertation, Karlova Univ., Prague, 1949.
23. Ya. I. Tur'yan, "Tezisy Dokladov na 4-m Soveshchanii po Elektrokhimii Organicheskikh Soedinenii" (Abstracts of Reports at the Fourth Conference on the Electrochemistry of Organic Compounds), Inst. Elektrokhim. Akad. Nauk SSSR, Moscow, 1962, p. 22.
24. Ya. I. Tur'yan and B. P. Zhantalai, Kinetika i Kataliz, 3, 325 (1962).
25. Ya. I. Tur'yan, Zhur. Obshch. Khim., 45, 2107 (1975).
26. Ya. I. Tur'yan and V. V. Smekalova, Zhur. Anal. Khim., 17, 1117 (1962).
27. V. V. Smekalova and Ya. I. Tur'yan, Symposium, "Polyarografiya i Kinetika Khimicheskikh Reaktsii" (Polarography and Kinetics of Chemical Reactions), IREA, Moscow, 1964, p. 112.
28. Ya. I. Tur'yan and T. A. Cheremukhina, Zhur. Anal. Khim., 19, 815 (1964).
29. B. P. Zhantalai and Ya. I. Tur'yan, Kinetika i Kataliz, 6, 761 (1965).
30. D. Fleury, M. B. Fleury, and P. Souchay, Compt. rend., 267C, 477 (1968).
31. Ya. I. Tur'yan and O. A. Tolstikova, Zhur. Anal. Khim., 26, 378 (1971).
32. Ya. I. Tur'yan and O. A. Tolstikova, Reakts. Sposobn. Org. Soed., 9, 785 (1972).
33. Ya. I. Tur'yan and O. A. Tolstikova, Reakts. Sposobn. Org. Soed., 9, 795 (1972).

† The products of the interaction of ammonium ions with formaldehyde, formed on hydrolysis of hexamethylenetetramine, were apparently also polarographed in a study [189] where a very acid supporting electrolyte was used in the determination of hexamethylenetetramine.

34. Ya. I. Tur'yan and O. A. Tolstikova, Zhur. Obshch. Khim.. 45, 688 (1975).
35. I. A. Kuzovnikova, L. A. Badovskaya, Ya. I. Tur'yan, and V. G. Kul'nevich, Reakts. Sposobn. Org. Soed., 12, 103 (1975).
36. D. French and J. T. Edsall, "Advances in Protein Chemistry", Acad. Press, Inc., New York, 1945, Vol. II, p. 277.
37. W. P. Jencks, J. Amer. Chem. Soc., 81, 475 (1959).
38. B. Gaux and P. Le Henaff, Bull. Soc. chim. France, 2501 (1972).
39. R. G. Kallen and W. P. Jencks, J. Biol. Chem., 241, 5864 (1966).
40. T. V. Mekryukova and Ya. I. Tur'yan, Zhur. Anal. Khim., 23, 1712 (1968).
41. Ya. I. Tur'yan, Zhur. Obshch. Khim., 45, 2487 (1975).
42. R. B. Martin, "Introduction to Biophysical Chemistry" (Translated into Russian), Izd. Mir, Moscow, 1966, pp. 89, 91.
43. I. Leden, Z. phys. Chem., 188A, 160 (1941).
44. D. D. Deford and D. N. Hume, J. Amer. Chem. Soc., 73, 5321 (1951).
45. P. M. Zaitsev and Z. V. Zaitseva, Ukrain. Khim. Zhur., 31, 820 (1965).
46. Ya. I. Tur'yan, Zhur. Obshch. Khim., 45, 2105 (1975).
47. P. F. Feraud and P. Le Henaff, Bull. Soc. chim. France, 1968 (1968).
48. Ya. I. Tur'yan, Paper deposited at the All-Union Institute of Scientific and Technical Information (VINITI), No. 3068-76, from 10th August, 1976.
49. "Spravochnik Khimika" (The Chemist's Handbook), Izd. Khimiya, Moscow, 1964, Vol. III, p. 82.
50. E. H. Cordes and W. P. Jencks, J. Amer. Chem. Soc., 85, 2843 (1963).
51. Ya. I. Tur'yan and V. V. Smekalova, Zavod. Lab., 28, 923 (1962).
52. E. G. Sander and W. P. Jencks, J. Amer. Chem. Soc., 90, 6154 (1968).
53. W. P. Jencks, Symposium, "Sovremennye Problemy Fizicheskoi Organicheskoi Khimii" (Modern Problems in Physical Organic Chemistry) (Translated into Russian), Izd. Mir, Moscow, 1967, p. 342.
54. J. B. Conant and P. D. Bartlett, J. Amer. Chem. Soc., 54, 2881 (1932).
55. P. Le Henaff, Bull. Soc. chim. France, 3113 (1965).
56. B. Gaux and P. Le. Henaff, Compt. rend., 271C, 1093 (1970).
57. M. I. Siling and B. Ya. Aksel'rod, Zhur. Fiz. Khim., 42, 2780 (1968) [Russ. J. Phys. Chem., No. 11 (1968)].
58. V. Pojunen, Suomen Kem., 21B, 21 (1948); Chem. Abs., 42, 8155 (1948).
59. Y. Ogata and A. Kawasaki, Tetrahedron, 20, 855, 1573 (1964).
60. E. W. Balson and A. Lavson, Biochem. J., 30, 1257 (1936).
61. M. Levy and D. E. Silberman, J. Biol. Chem., 118, 723 (1937).
62. E. H. Frieden, Ph. D. Thesis, Univ. California, Los Angeles, 1942; quoted after Ref. 36.
63. A. Williams and M. L. Bender, J. Amer. Chem. Soc., 88, 2508 (1966).
64. J. Hine and Chuen Yuan Yeh, J. Amer. Chem. Soc., 89, 2669 (1967).
65. A. Le Bris, G. Lefevre, and F. Coussemant, Bull. Soc. chim. France, 1366 (1964).
66. F. P. Price, Jr. and L. P. Hammett, J. Amer. Chem. Soc., 63, 2387 (1941).
67. R. Wolfenden and W. P. Jencks, J. Amer. Chem. Soc., 83, 2763 (1961).
68. M. Anderson and W. P. Jencks, J. Amer. Chem. Soc., 82, 1773 (1960).
69. P. Greenzaid, Z. Luz, and D. Samuel, J. Amer. Chem. Soc., 89, 749 (1967).
70. O. H. Emerson and P. L. Kirk, J. Biol. Chem., 87, 597 (1930).
71. J. T. Edsall and M. H. Blanchard, J. Amer. Chem. Soc., 55, 2337 (1933).
72. A. Neuberger, Biochem. J., 30, 2085 (1936).
73. B. P. Zhantlai and N. I. Ruch'eva, Zhur. Prikl. Khim., 39, 2339 (1966).
74. D. G. Knorre and N. M. Emanuel', Dokl. Akad. Nauk SSSR, 91, 1163 (1953).
75. T. N. Hall, J. Org. Chem., 29, 3587 (1964).
76. V. M. Belikov, Yu. N. Belokon', N. S. Martinkova, and N. G. Faleev, Izv. Akad. Nauk SSSR, Ser. Khim., 2136 (1969).
77. Ya. I. Tur'yan, Zhur. Obshch. Khim., 45, 2106 (1975).
78. H. Imoto and M. Kobayashi, Bull. Chem. Soc. Japan, 33, 1651 (1960).
79. Ya. I. Tur'yan, Zhur. Obshch. Khim., 44, 2365 (1974).
80. J. Hine and R. W. Redding, J. Org. Chem., 35, 2769 (1970).
81. H. F. Harnsberger, E. L. Cocharan, and H. H. Szmant, J. Amer. Chem. Soc., 77, 5048 (1955).
82. H. K. Hall, J. Amer. Chem. Soc., 79, 5441 (1957).
83. H. Lund, Acta Chem. Scand., 13, 249 (1959).
84. H. Lund, Tetrahedron Letters, 3651 (1968).
85. Yu. P. Kitaev and T. V. Troepol'skaya, Izv. Akad. Nauk SSSR, Ser. Khim., 1903 (1967).
86. Yu. P. Kitaev, G. K. Budnikov, T. V. Troepol'skaya, and I. M. Skrebkova, Zhur. Obshch. Khim., 37, 1437 (1967).
87. G. K. Budnikov, S. Yu. Baigil'dina, and Yu. T. Kitaev, Elektrokhimiya, 2, 1263 (1966).
88. Yu. P. Kitaev and B. I. Buzykin, "Gidrazony" (Hydrazones), Izd. Nauka, Moscow, 1974, p. 343.
89. K. Veselý and R. Brdička, Coll. Czech. Chem. Comm., 12, 313 (1947).
90. R. Bieber and G. Trümpler, Helv. Chim. Acta, 30, 706, 2000 (1947).
91. S. G. Mairanovskii, "Katalicheskie i Kineticheskie Volny v Polyarografii" (Catalytic and Kinetic Waves in Polarography), Izd. Nauka, Moscow, 1966.
92. Yu. P. Kitaev and G. K. Budnikov, Zhur. Obshch. Khim., 33, 1396 (1963).
93. O. A. Tolstikova, Candidate's Thesis, Yaroslavl' Technological Institute, 1972.
94. C. Degrand, Bull. Soc. chim. France, 2100 (1972).
95. D. Fleury, Bull. Soc. chim. France, 2922 (1969).
96. D. Fleury and M. B. Fleury, Coll. Czech. Chem. Comm., 36, 331 (1971).
97. P. Zuman, "Substituent Effects in Organic Polarography", Plenum Press, New York, 1967, p. 172.
98. Ya. I. Tur'yan and B. P. Zhantalai, Zavod. Lab., 27, 1211 (1961).
99. Ya. I. Tur'yan and B. P. Zhantalai, Zavod. Lab., 28, 1431 (1962).
100. B. P. Zhantalai and Ya. I. Tur'yan, Zhur. Anal. Khim., 23, 282 (1968).
101. M. Březina, J. Volke, and V. Volkova, Coll. Czech. Chem. Comm., 19, 894 (1954).

102. Ya. I. Tur'yan, Yu. M. Tyurin, and B. P. Zhantalai, Zhur. Anal. Khim., **16**, 352 (1961).
103. I. I. Turian, I. M. Tiurin, and B. P. Jantalai, Anal. Romino Sovietice, Chimie, **1**, 147 (1962).
104. L. V. Kononenko, V. M. Dmitrieva, and V. D. Bezuglyi, Zhur. Obshch. Khim., **38**, 223 (1968).
105. Masaichiro Masui and Chino Yijima, Bunseki Kagaku, **15**, 1350 (1966); Ref. Zhur. Khim., 13G213 (1967).
106. O. A. Tolstikova, Ya. I. Tur'yan, and N. A. Strelkova, Zavod. Lab., **35**, 1320 (1969).
107. B. P. Zhantalai, Biokhimiya, **29**, 1009 (1964).
108. B. P. Zhantalai and N. I. Kobylina, Zavod. Lab., **31**, 668 (1965).
109. A. V. Khoroshin, Zavod. Lab., **28**, 420 (1962).
110. O. Manaušek and Z. Kučerova, Veda Vyzkum Prumyslu potravinarskem, **16**, 59 (1965); Chem. Abs., **64**, 4168 (1966).
111. Yu. A. Davydovskaya and N. M. Rotenshtein, Symposium, "Metody Analiza Khimicheskikh Reaktivov i Preparatov" (Methods for the Analysis of Chemical Reagents and Preparations), Izd. IREA, Moscow, 1971, No. 19, p. 52.
112. Ya. I. Tur'yan and V. V. Smekalova, USSR P. 156 743 (1962); Byul. Izobret., No. 16, 70 (1963).
113. B. P. Zhantalai, USSR P. 168 043 (1965); Byul. Izobret., No. 3, 71 (1965).
114. V. G. Baranova, A. G. Pankov, and Ya. I. Tur'yan, "Osnovy Fiziko-khimicheskikh Metodov Analiza i Kontrol' Proizvodstva Izoprena" (Principles of the Physicochemical Methods for the Analysis and Control of the Manufacture of Isoprene), NIITEKhIM, Moscow, 1965.
115. Ya. I. Tur'yan, T. A. Cheremukhina, and T. V. Mikhailova, Zhur. Prikl. Khim., **39**, 463 (1966).
116. Yu. A. Vakhrushev, P. M. Zaitsev, N. M. Chetverikova, and B. P. Zhantalai, Khim. Prom. Ukrainy, Nauchno-Proizv. Sbornik, No. 2 (32), 50 (1967).
117. M. S. Rusakova, V. A. Podgornova, B. F. Ustavshchikov, and Ya. I. Tur'yan, Uch. Zap. Yaroslavsk. Tekhnol. Inst., **11**, 78 (1969).
118. Yu. S. Ignat'ev, M. T. Strukova, N. Yu. Miloshevich, and V. A. Solov'eva, Zhur. Anal. Khim., **23**, 1888 (1968).
119. B. P. Zhantalai, K. P. Petrishchev, and M. M. Karavaev, Symposium, "Promyshlennost' Khimicheskikh Rekativov i Osobo Chistykh Veshchestv" (Industrial Manufacture of Chemical Reagents and Specially Pure Substances), NIITEKhIM, Moscow, 1968, No. 12, p. 99.
120. M. P. Strukova, Yu. S. Ignat'ev, L. N. Smirnov, and S. P. Smirnova, Zhur. Anal. Khim., **27**, 1647 (1972).
121. T. Wasa and S. Musha, Bull. Chem. Soc. Japan, **40**, 1624 (1967).
122. T. Wasa and S. Musha, Bull. Chem. Soc. Japan, **41**, 1578 (1968).
123. W. Tamotsu and M. Soichiro, Bull. Univ. Osaka Prefect., **A17**, 139 (1968); Ref. Zhur. Khim., 20G223 (1969).
124. M. Fedoreňko, J. Königstein, and M. Bullova, Chem. Zvesti, **22**, 25 (1968).
125. J. K. Wolfe, E. B. Hershberg, and L. F. Fieser, J. Biol. Chem., **136**, 653 (1940).
126. E. B. Hershberg, J. K. Wolfe, and L. F. Fieser, J. Biol. Chem., **140**, 215 (1941).
127. O. Bjornson and M. Ottensen, Quart. J. Pharm. and Pharmacol., **19**, 519 (1946).
128. V. Prelog and O. Häfliger, Helv. Chim. Acta, **32**, 2088 (1949).
129. S. Shimizu, Jr., Shinshu Univ., No. 4, 307 (1954); Chem. Abs., **50**, 10 346 (1956).
130. J. R. Young, J. Chem. Soc., 1516 (1955).
131. B. Fleet and P. N. Keliher, Analyst., **94**, 659 (1969).
132. M. D. Booth and B. Fleet, Analyst., **95**, 649 (1970).
133. J. M. Lupton and C. C. Lynch, J. Amer. Chem. Soc., **66**, 697 (1944).
134. J. W. Haas, Jr. and C. C. Lynch, Anal. Chem., **29**, 479 (1957).
135. Yuan-Hsiao Lin and Chen-Ya Wang, Hua Hsueh Hsueh Pao, **31**, 419 (1965); Chem. Abs., **64**, 7368 (1966).
136. O. A. Tolstikova, T. V. Shiryaeva, A. G. Pankov, O. P. Yablonskii, A. F. Moskvin, and M. F. Knyazeva, Prom. Sintetich. Kauchuka, No. 6, 29 (1968).
137. N. L. Burnaev, V. M. El'gort, and E. M. Klyachkova, Symposium, "Materialy II Nauchno-tekhnicheskoi Konferentsii po Voprosam Stroitel'nykh Materialov dlya Zheleznodorozhnogo Promyshlennogo i Grazhdanskogo Stroitel'stva" (Proceedings of the IInd Science and Engineering Conference on Problems of the Constructional Materials for Railway, Industrial, and Civic Buildings), Izd. Uzorgtekhstroi, Tashkent, 1969, p. 159.
138. B. P. Zhantalai and A. A. Kirilovich, Symposium, "Novye Issledovaniya v Polyarografii" (New Research in Polarography), Izd. Shtiintsa, Kishinev, 1972, p. 260.
139. R. Geyer, H. Bormann, and S. Pettemeridon, Z. Chem., **13**, 346 (1973).
140. G. A. Petropavlovskii and Z. D. Chernova, Zhur. Prikl. Khim., **47**, 2506 (1974).
141. Z. D. Chernova, G. G. Vasil'eva, and G. A. Petropavlovskii, Zhur. Anal. Khim., **30**, 1438 (1975).
142. V. E. Strukova, Yu. E. Fal'kovich, Ya. I. Tur'yan, V. I. Grinfel'd, and Z. A. Lisetskaya, Izv. Vys. Ucheb. Zaved., Pishchevaya Tekhnol., No. 4, 170 (1976).
143. G. P. Tikhomirov and G. G. Belous, Zhur. Anal. Khim., **27**, 173 (1972).
144. J. W. Haas, Jr. and J. D. Storey, Anal. Chem., **34**, 145 (1962).
145. L. Vignoli, B. Cristau, F. Gouezo, and C. Fabre, Chim. analyt., **45**, 439 (1963).
146. B. Fleet, Anal. Chim. Acta, **36**, 304 (1966).
147. L. Súcha, Coll. Czech. Chem. Comm., **33**, 1375 (1968).
148. M. D. Booth and B. Fleet, Analyst., **34**, 844 (1969).
149. M. Přibyl and J. Nedbálkova, Fresenius Z. Analyt. Chem., **244**, 244 (1969).
150. Yu. A. Davydovskaya, M. M. Rotenshtein, and Yu. I. Vainshtein, Trudy. VNII Khim. Reaktivov i Osobo Chistykh Khim. Veshchestv., No. 35, 203 (1973).
151. J. Barrett and C. Morris, Biochem. J., **40**, 450 (1946).
152. W. J. N. Neish, Rev. Trav. chim., **72**, 105, 1098 (1953).
153. L. I. Petrova and E. N. Novikova, Zhur. Prikl. Khim., **28**, 219 (1955).
154. E. V. Zobov and Yu. S. Lyalkov, Zhur. Anal. Khim., **11**, 459 (1956); Izv. Akad. Nauk Turkmen. SSR, No. 1, 93 (1958).
155. V. Kemula, "Progress in Polarography", Intersci. Publ., New York, 1962, Vol. II, p. 397.
156. Yu. A. Davydovskaya, M. M. Rotenshtein, and Yu. I. Vainshtein, Symposium, "Novye Issledovaniya

v Polarografii" (New Research in Polarography), Izd. Shtiintsa, Kishinev, 1972, p. 281.
157. B. K. Afghan, A. V. Kulkarni, and J. F. Ryan, Anal. Chem., 47, 488 (1975).
158. O. Manoušek and P. Zuman, J. Electroanalyt. Chem., 1, 324 (1960).
159. J. Davidek, Fresenius Z. anal. Chem., 179, 165 (1961).
160. J. Davidek, Nature, 190, 1003 (1961).
161. J. Davidek, Nature, 197, 378 (1963).
162. A. N. Bagaev and Yu. V. Vodzinskii, Zavod. Lab., 32, 1461 (1966).
163. J. Paściak and B. Przybyla, Chem. Anal., 19, 345 (1974).
164. I. G. Dermanova, N. N. Andreeva, and V. A. Simonov, Zhur. Anal. Khim., 29, 1032 (1974).
165. P. Zuman, Chem. Listy, 46, 521 (1952).
166. V. Růžička, Z. Matušů, and V. Medonos, Sci. Papers Inst. Chem. Technol., Prague, 633 (1958).
167. E. Hakoila, Suomen Kem., 43, 109 (1970).
168. P. Zuman and F. Santavy, Coll. Czech. Chem. Comm., 18, 28 (1953).
169. M. E. Hall, Anal. Chem., 31, 2007 (1959).
170. T. S. Ivcher, E. M. Perepletchikova, and E. N. Zil'berman, Zhur. Prikl. Khim., 39, 227 (1965).
171. Yu. S. Ignat'eva, M. P. Strukova, L. E. Volkova, and L. A. Mikheeva, Zhur. Anal. Khim., 24, 1389 (1970).
172. Yu. S. Ignat'ev, M. P. Strukova, and V. P. Dolbanova, Zhur. Anal. Khim., 29, 1434 (1974).
173. E. P. Kovsman, P. M. Zaitsev, Z. V. Zaitseva, E. A. Karavaeva, and Yu. M. Tyurin, Symposium, "Promyshlennost' Khimicheskikh Reaktivov i Osobo Chistykh Veshchestv" (The Industrial Manufacture of Chemical Reagents and Specially Pure Substances), NIITEKhIM, Moscow, 1966, No. 5, p. 135.
174. T. Wasa, M. Takagi, and S. Ono, Bull. Chem. Soc. Japan, 34, 578 (1961).
175. S. Musha, T. Wasa, and T. Naito, Bull. Chem. Soc. Japan, 39, 1902 (1966).
176. M. Takagi, Y. Gotoh, R. Hosogaki, S. Amono, and S. Ono, Starke, 20, 215 (1968); Ref. Zhur. Khim., 12R381 (1969).
177. M. Takagi, T. Nishio, K. Dan-ura, K. Takahashi, and S. Ono, Starke, 20, 251 (1968); Ref. Zhur. Khim., 14G210 (1969).
178. B. N. Kolokolov, L. V. Bychkova, M. S. Brodskii, and Yu. A. Yalter, Zavod. Lab., 37, 904 (1971).
179. M. Leclerc, Mem. Poudres, 35, 365 (1953).
180. D. R. Norton and N. H. Furman, Anal. Chem., 26, 1116 (1954).
181. D. R. Norton and C. K. Mann, Anal. Chem., 26, 1180 (1954).
182. G. C. Whitnack, J. E. Yong, H. H. Sisler, and E. St. C. Gantz, Anal. Chem., 28, 833 (1956).
183. N. F. Alekseev, Zavod. Lab., 24, 684 (1958).
184. B. P. Zhantalai, Zhur. Vses. Khim. Obshch. im Mendeleeva, 9, 238 (1964).
185. Y. Kobayashi, Bull. Chem. Soc. Japan, 40, 1391 (1967).
186. S. S. Shtal', V. N. Dmitrieva, and V. D. Bezuglyi, Plast. Massy, No. 9, 61 (1968).
187. P. N. Kovalenko, Zh. P. Anisimova, M. M. Evstifeev, and L. T. Azhipa, Symposium, "Problemy Analiticheskoi Khimii" (Problems of Analytical Chemistry), Izd. Nauka, Moscow, 1970, Vol. 1, p. 185.
188. P. Ya. Yakovlev and R. D. Malinina, Zavod. Lab., 28, 1434 (1962).
189. B. Tökés and G. Suciu, Chim. anal., No. 3, 193 (1972); Ref. Zhur. Khim., 13G201 (1973).
190. Ya. I. Tur'yan and Yu. A. Vakhrushev, Symposium, "Poluprodukty dlya Sinteza Poliamidov" (Intermediates for the Synthesis of Polyamides), Gos. Nauchno-tekh. Izd. Khim. Lit., Moscow, 1963, p. 252.
191. V. P. Zhantalai and N. I. Kobylina, Symposium, "Promyshlennost' Khimicheskikh Reaktivov i Osobo Chistykh Veshchestv" (The Industrial Manufacture of Chemical Reagents and Specially Pure Substances), NIITEKhIM, Moscow, 1966, No. 5, p. 94.
192. M. Masui, K. Fujitz, and H. Ohmari, Chem. Comm., No. 3, 182 (1970).
193. M. P. Strukova, Yu. S. Ignat'ev, N. Yu. Miloshevich, and N. Yu. Zamelin, Zhur. Anal. Khim., 25, 1833 (1970).
194. J. D. McLean and O. L. Daniels, J. Assoc. Offic. Anal. Chem., 54, 555 (1971).
195. T. B. Argova, L. V. Veshova, and L. S. Reishakhrit, Vestnik Leningrad. Univ., No. 16, 146 (1972).
196. Ya. I. Tur'yan and V. V. Smekalova, USSR P. 156 744 (1962); Byul. Izobret., No. 16, 70 (1963).
197. P. M. Zaitsev and I. P. Nesterova, Gigiena i Sanitariya, No. 6, 80 (1969).
198. Yu. S. Ignat'ev, Zavod. Lab., 31, 1188 (1965).
199. T. V. Argova, L. V. Vesheva, and L. S. Reishakhrit, Vestnik. Leningrad. Univ., No. 4, 157 (1971).
200. D. K. Banerjee, G. C. Riechmann, and C. C. Budke, Anal. Chem., 36, 2220 (1964).
201. C. C. Budke, D. K. Banerjee, and F. D. Miller, Anal. Chem., 36, 523 (1964).
202. L. Schlitt, M. Rink, and Von M. Stackelberg, J. Electroanalyt. Chem., 13, 10 (1967).
203. M. Deželič, A. Lachovič, and M. Trkovnik, Croat. Chem. Acta, 32, 31 (1960).
204. G. Alessandro and E. Mecarelli, Bull. Chim. farmac., 103, 427 (1964).
205. B. Bobarevič, M. Deželič, and V. Jovanovič, Glasnik hem i tehnol. BiH, No. 13–14, 47 (1964–1965) [Ref. Zhur. Khim., 22G153 (1956).
206. S. Biliński, J. Matusik, and T. Urban, Ann. Univ. M. Curie-Sklodowska, A19, 49, 1964 (1966); Ref. Zhur. Khim., 23G194 (1967).
207. L. V. Kononenko, V. N. Dmitrieva, A. I. Pavlov, G. M. Tseitlin, V. D. Bezuglyi, and V. V. Korshak, Zhur. Anal. Khim., 23, 1032 (1968).

Department of Analytical Chemistry,
Krasnodar Polytechnic Institute