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(29) It is not implied that endo double bond formation is prohibited. Hence there is no contradiction with results reported in ref 13.

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Nucleophilic Additions to Aldehydes and Ketones. 2.[1] Reactions of Heterocyclic Aldehydes with Hydroxide Ions

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Three groups of heterocyclic carboxaldehydes can be distinguished according to their reactivity toward hydroxide ions: to the first group belong nonhydrated five-membered heterocyclic aldehydes (derivatives of furan, thiophene, and N-substituted pyrrole) which add hydroxide ions to the carbon–oxygen double bond in a similar way as benzaldehydes. The second groups consists of pyrrole and indole derivatives where in alkaline media the NH group dissociates before the formyl group is attacked. Hydrated aldehydes (pyridine, thiazole, and imidazole derivatives) belonging to the third group show dissociation of the geminal diol. Equilibrium constants of these three types of reactions were measured spectrophotometrically. Most of the aldehydes studied undergo electrooxidation as geminal diol anions which was followed polarographically. Ring substituents and the nature of the heteroatom affect the values of equilibrium constants and half-wave potentials. In indole and pyrrole derivatives a specific interaction between the formyl group and the heterocycle is indicated.

In previous work[5] an acidity scale J_- has been developed to be used in strongly alkaline media for reactions involving addition of hydroxide ions. Some meta- and para-substituted benzaldehydes have been used as indicators for characterizing acidity of aqueous sodium hydroxide solutions. By means of this scale thermodynamic equilibrium constants for hydroxide ion additions to other meta- and para-substituted benzaldehydes were determined.[1] Corresponding pK values were correlated with Hammett substituent constants σ by means of a reaction constant $\rho = 2.76$ [$r = 0.994$, S (est) 0.012]. Later Greenzaid[6] also measured spectrophotometrically the ratio of concentrations of the anion of the geminal diol to that of the free aldehydic form. The concentration of an unspecified hydroxide was used in calculation of equilibrium constants of the reaction 1

$$\mathrm{ArCHO} + \mathrm{OH}^- \overset{K}{\rightleftharpoons} \mathrm{ArCH(OH)O}^- \qquad (1)$$

instead of acidity functions and the activity term $y_{\mathrm{ArCH(O^-)OH}}/y_{\mathrm{ArCHO}}y_{\mathrm{OH^-}}$ was neglected. This approach restricted the study to solutions of the unspecified base below 1.5 M and this in turn limited the investigation to compounds with electronegative substituents. Reported values could have been considered as practical equilibrium constants, provided that ionic strength was kept constant. As this was not the case, the values reported by Greenzaid[6] correspond for each compound to another ionic strength and hence can be considered only as "crude practical constants". Correlation of these approximate values for the limited group of monosubstituted and some disubstituted benzaldehydes accessible to measurement with Hammett substituent constants σ greater than zero, gave $\rho = 2.24$ ($r = 0.982$). The susceptibility of benzaldehydes to substituent effects for hydroxide addition is similar to that for methoxide addition, reported recently.[7]

The anion of the geminal diol has been proved[8] to be the electroactive form in the electrooxidation of benzaldehydes in alkaline media. Rate constants for the addition of the hydroxide ion and the reverse reaction obtained from polarographic data on benzaldehyde oxidations were about 1.5 orders of magnitude larger than values for 3- and 4-chlorobenzaldehydes measured by stopped-flow technique.[9] This difference might reflect different reaction conditions used, but also may be caused by the effect of the electric field in the vicinity of the electrode. Another electrochemical method, based on constant potential electrolysis of the corresponding aromatic acid at a rotating disc electrode at pH 6.2, was proposed.[10] The rate constants found[10] for 3-chlorobenzaldehyde which are seven to eight orders of magnitude smaller than those above were attributed to loss of water rather than OH$^-$. Since pH dependence of these constants has not been studied, it is not possible to comment on their attribution, but the value of the equilibrium constant, indicating that about 50% of 3-chlorobenzaldehyde exists in hydrated form, is clearly doubtful.

In this contribution both the studies of the equilibria involving addition of hydroxide and the electrooxidation of the aldehydic group are extended to heterocyclic compounds bearing an aldehydic group. Attention is being paid to the role of the nature of the heterocyclic ring and effect of substituents as well as to competitive reactions.

Experimental Section

Chemicals and Solutions. Fural, 5-methylfural, 5-hydroxymethylfural, 2-thiophenecarboxaldehyde, 3-methyl-2-thiophenecarboxaldehyde, 5-bromo-2-thiophenecarboxaldehyde, 2-pyrrolecarboxaldehyde, *N*-methyl-2-pyrrolecarboxaldehyde, 3-indolecarboxaldehyde, *N*-benzyl-3-indolecarboxaldehyde, *N*-ethyl-3-carbazolecarboxaldehyde, and 3-cinnolinecarboxaldehyde (Aldrich Chemical Co.), *N*-phenyl-2,5-dimethyl-3-pyrrolecarboxaldehyde

Table I. Oxidation Half-Wave Potentials and Equilibrium Constants of Addition of Hydroxide Ions to Nonhydrated Heterocyclic Aldehydes

							$E_{1/2}$,[d] V vs. SCE	
Registry no.	Aldehyde	λ_{max}, nm	$\epsilon \times 10^{-3}$, l. mol^{-1} cm^{-1}	pK'[a]	λ_{meas},[b] nm	Δ[c]	5.0 M NaOH	1.0 M NaOH
98-01-1	Fural	278	13.6	14.75	277	−1.09	−0.36	−0.24
620-02-0	5-Methylfural	293	15.8	15.65	293	−1.40	−0.37[e]	−0.22
698-63-5	5-Nitrofural	227	6.8	11.82	290	−1.08	−0.37	
		310	11.0					
67-47-0	5-Hydroxymethylfural	230	2.0	[f]	[f]	[f]	[f]	[f]
		280	14.8					
98-03-3	2-Thiophenecarboxaldehyde	264	23.0	15.21	290	−1.01	−0.45[e]	−0.30
		292	16.0					
4701-17-1	5-Bromo-2-thiophenecarboxaldehyde	270	5.0	14.64	302	−0.98	−0.47	−0.39
		302	12.0					
5834-16-2	3-Methyl-2-thiophenecarboxaldehyde	280	13.0	15.75	282	−1.08	−0.34	−0.22
1192-58-1	1-Methyl-2-pyrrolecarboxaldehyde	255	2.0	≈17.5	293	[g]	−0.23	−0.20
		293	16.0					
83-18-1	1-Phenyl-2,5-dimethyl-3-pyrrolecarboxaldehyde	260	8.5	≈16.0	260	[g]	[h]	[h]
		303	5.0					
7570-45-8	N-Ethyl-3-carbazolecarboxaldehyde	233	21.0	13.95	233	−0.94	−0.22	−0.14
		242	18.0		276			
		276	24.0		293			
		293	18.0					
		335[i]	10.0					
58503-24-5	N-Ethyl-3-carbazolecarboxaldehyde geminal diol anion	248	≈ 4.0	[j]	[j]	[j]	−0.22	−0.14
		275	≈ 4.0					
		300	12.0					
		350	10.0					
10511-51-0	N-Benzyl-3-indolecarboxaldehyde	248	7.0	[j]	[j]	[j]	[j]	[j]
		263	≈ 4.0					
		305	8.0					

[a] pK' = pK + pK_w; K = [ArCH(OH)O$^-$]/[ArCHO][OH$^-$]. [b] Wavelength at which the absorbance was measured for calculation of K. [c] Δ = slope of the plot of log[ArCHO]/[ArCH(OH)O$^-$] vs. acidity function J_-. [d] Polarographic half-wave potential of the anodic oxidation wave. [e] Polarographic curve shows a maximum. [f] Fast competitive homogeneous chemical reaction in alkaline media prevented measurement. [g] Only part of dissociation curve experimentally accessible. [h] No anodic wave observed before potential of mercury dissolution. [i] Wide band. [j] Reacts in alkaline media, but does not add OH$^-$ to CHO.

(Eastman Kodak), 5-nitrofural (Pfalz and Bauer), 2-indolecarboxaldehyde, and 1-methyl-2-imidazolecarboxaldehyde (kindly donated by Professor F. Popp, Clarkson College of Technology, Potsdam, N.Y.), 2-imidazolecarboxaldehyde, 2-thiazolecarboxaldehyde, and 2-benzothiazolecarboxaldehyde (kindly donated by Professor H. Lund, Aarhus University, Denmark) were freshly distilled, recrystallized, or sublimated. Purity was checked by gas–liquid chromatography. Stock solutions (0.01 M) of these aldehydes were prepared freshly in 96% ethanol.

Sodium hydroxide solutions were prepared from 0.1 and 1.0 M Baker reagent grade Dilut-it standardized solutions and from 50% Baker Analyzed sodium hydroxide containing less than 0.03% carbonate, shown to be 18.86 M by standardization with potassium acid phthalate. These standards, kept carbonate free, were diluted under nitrogen with distilled freshly boiled water cooled in a nitrogen stream.

All buffers used for pH < 12 were prepared from reagent grade chemicals.

Apparatus. Electronic spectra were recorded by means of a Unicam SP-800A recording spectrophotometer (Pye-Unicam, Cambridge, England). Cells (10 mm) were placed in a thermostated compartment and temperature maintained at 25 ± 0.01 °C.

Polarographic current–voltage curves (dc) were obtained with a Model 174 polarographic analyzer (Princeton Applied Research, Princeton, N.J.) in connection with a Hewlett-Packard 7004B X-Y recorder. The capillary used had in 1 M potassium chloride at 0.0 V (SCE) the following characteristics: rate of flow m = 1.9 mg/s, drop time t_1 = 3.4 s at h = 65 cm.

A modified Kalousek cell was used with a spectroscopic grade carbon rod immersed in 5 M sodium hydroxide as a separated reference cathode.[11] To minimize the effect of polarization of the reference cathode, the current–voltage curves were recorded from negative to positive potentials.

pH measurements were carried out with a Sargent-Welch Model NX pH meter with a Sargent S-30072-15 combination glass electrode as well as with a Radiometer electrode G-202B for measurements in alkaline region.

Procedures. For recording of the uv spectra an aliquot of the stock solution was added to an aqueous solution of a buffer or of sodium hydroxide so that the final aqueous solution contained 1 × 10^{-4} M aldehyde and 1% ethanol.

For each aldehyde spectra were recorded in buffers of varying pH or in sodium hydroxide solutions of varying concentration. For each aldehyde 10–15 spectra were recorded in solutions chosen so as to straddle the pK value. Spectra were always recorded within 2 min after mixing the solutions and then again after 5 min to check for any changes with time.

Polarographic anodic waves were recorded in 5 and 1 M sodium hydroxide solutions containing 2 × 10^{-4} M aldehyde and 2% ethanol. Solutions for polarographic electrolysis were freshly prepared from stock solutions and the curves were checked for any changes with time.

Evaluation of Equilibrium Constants. To evaluate the equilibrium constant K corresponding to reaction 1 in most cases the decrease of the absorbance of the free carbonyl form was followed. The values of wavelengths used are given for individual compounds in Tables I–III. In some cases the geminal diol anion has shown an absorbance (corresponding to aromatic system deprived of the conjugation with the carbonyl group) the increase of which was followed (cf. Table I–III). The ratio [ArCH(OH)O$^-$]/[ArCHO] was found at a given wavelength from $(A_0 - A)/(A - A_r)$ where A_0 is the absorbance due to pure carbonyl form (measured at sufficiently low sodium hydroxide concentration or in a buffer of sufficiently low pH), A_r absorbance of the pure geminal diol anion ArCH(OH)O$^-$ (measured at so high pH or sodium hydroxide concentration that conversion can be regarded as complete), and A absorbance of the solution in the acidity range between the two extremes.

The value of log ([ArCH(OH)O$^-$]/[ArCHO]) was then plotted against pH or J_- function.[5] For all aldehydes studied this plot was found linear with a slope (Δ) given in Tables I and III. The value of

Table II. Oxidation Half-Wave Potentials and Dissociation Constants of Heterocyclic Aldehydes Bearing on NH Group

Registry no.	Aldehyde	λ_{max}, nm	$\epsilon \times 10^{-3}$, l. mol^{-1} cm^{-1}	pK_N[a]	λ^N_{meas},[b] nm	pK'[c]	λ_{meas},[d] nm	$E_{1/2}$,[e] V vs. SCE 5 M NaOH	1 M NaOH
1003-29-8	2-Pyrrolecarboxalde-	250	≈ 3.0	13.65	293	>17		−0.22	−0.18
	hyde	293	16.0		315				
58503-25-6	2-Pyrrolecarboxalde-	265	≈ 1.0					−0.22	−0.18
	hyde iminate anion	315	22.0						
19005-93-7	2-Indolecarboxalde-	235	13.0	14.00	310	>17[f]		−0.40	−0.29
	hyde	310	23.0		335				
58503-26-7	2-Indolecarboxalde-	247	18.0					−0.40	−0.29
	hyde iminate	335	24.0						
	anion								
487-89-8	3-Indolecarboxalde-	244	13.0	12.33	324	>16		*h*	*h*
	hyde	261	13.0	12.36[g]					
		300	14.0						
58503-27-8	3-Indolecarboxalde-	265	22.0					*h*	*h*
	hyde iminate	324	22.0						
	anion								
10111-08-7	2-Imidazolecarboxalde-	215	4.0	10.08[i]	285		310	−0.21	−0.18
	hyde	287	5.0	10.34[i]	315				
58503-28-9	2-Imidazolecarboxalde-	310	8.0			≈13.5[i]			
	hyde iminate anion								

[a] K_N = [HetN$^-$][H$^+$]/[HetNH]. [b] Wavelength at which the absorbance was measured for calculation of K_N. [c] pK' = pK + pK_w; K = [ArCH(OH)O$^-$]/[ArCHO][OH$^-$]. [d] Wavelength at which absorbance was measured for calculation of K'_{CHO}. [e] Polarographic half-wave potential of the anodic oxidation wave. [f] In 4 M NaOH change of the solution and development of yellow coloration observed, but no time change found in 10 M NaOH. [g] Reference 10. [h] No anodic wave observed before potential of mercury dissolution. [i] Overall equilibrium constants, aldehydic group is present in equilibrium at least 70% in hydrated form.

Table III. Oxidation Half-Wave Potentials and Dissociation Constants of the Geminal Diol Group of Some Hydrated Heterocyclic Aldehydes

Registry no.	Aldehyde	λ_{max}, nm	$\epsilon \times 10^{-3}$, l. mol^{-1} cm^{-1}	pK_s[a]	λ_{meas}[b]	Δ[c]	$E_{1/2}$,[d] V vs. SCE 5 M NaOH	1 M NaOH
10200-59-6	2-Thiazolecarboxalde-	237	0.3	11.2[e]	295	−1.00	−0.38	−0.31
	hyde	295	0.4					
6639-57-2	2-Benzothiazolecar-	217	18.0	10.7[f]	315	−1.30	−0.55	−0.48
	boxaldehyde	255	7.0					
		296	2.0					
51073-57-5	3-Cinnolinecarboxal-	229	36.0	11.95[g]	250	−1.00	−0.38	−0.33
	dehyde	250	18.0					
		285	3.0					
		325	4.0					
	2-Imidazolecarboxal-	310	8.0	≈13.5[i]	310	−0.98	−0.21	−0.18
	dehyde iminate anion							
13750-81-7	*N*-Methyl-2-imidazole-	223	0.4	13.50[j]	289	−1.20	−0.23	−0.14
	carboxaldehyde	289	1.3					

[a] Overall equilibrium constant, K_s = [ArCH(OH)O$^-$][H$^+$]/([ArCHO] + (ArCH(OH)$_2$]). [b] Wavelength at which the absorbance was measured for calculation of K_s. [c] Δ = slope of the plot of log[ArCHO]/[ArCH(OH)O$^-$] vs. acidity function J_-. [d] Polarographic half-wave potential of the anodic oxidation wave. [e] About 80% hydrated form. [f] About 90% hydrated. [g] Strong hydration. [h] See also Table II. [i] At least 70% hydrated form. [j] Weak hydration.

pH or J_- where log ([ArCH(OH)O$^-$]/[ArCHO]) was equal to zero was considered equal to pK.

A completely analogous procedure was applied to determination of values pK_N corresponding to equilibrium 2:


(2)

In most cases both the decrease of the absorbance of the parent compound and the increase of the absorbance of the iminate ion (often stronger) was followed at wavelengths given in Table II.

Half-Wave Potentials. Measurements of half-wave potentials were made relative to that of the unsubstituted benzaldehyde as an internal standard the waves of which were recorded prior to and after recording of each series of waves. Values of half-wave potentials of benzaldehyde were taken[13] as −0.29 V in 1 M sodium hydroxide and as −0.44 V in 5 M sodium hydroxide, both expressed against SCE. Examples of polarographic curves are given in Figure 1.

Results and Discussion

Classification of Systems. Heterocyclic aldehydes studies can be divided into three groups: to the first two groups belong five-membered "neutral" aldehydes with an excess of π electrons;[12] to the third five- and six-membered "basic" aldehydes with a π-electron deficiency.

Formyl groups of aldehydes belonging to the first two groups show little hydration at lower pH values, in a way as most of the substituted benzaldehydes.[13] Values of molar absorptivities and their independence of solvent (when aqueous, DMF and Me$_2$SO solutions were compared) as well

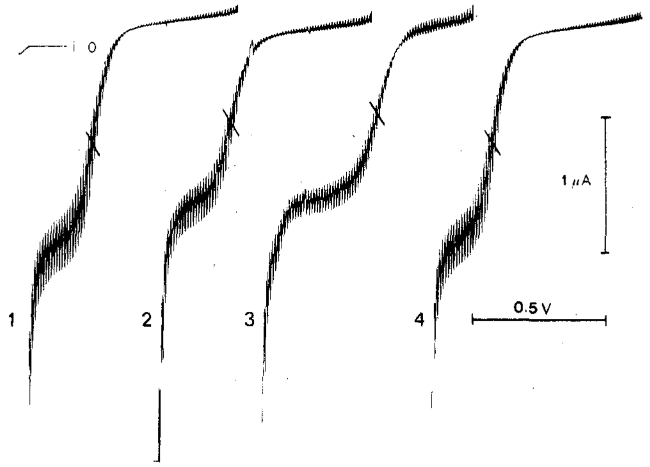


Figure 1. Anodic waves of heterocyclic aldehydes. 1 M sodium hydroxide, 2×10^{-4} M aldehyde, 2% ethanol. Compounds (half-wave potentials vs. SCE): (1) 2-thiophenecarboxaldehyde (−0.30 V); (2) 2-thiazolecarboxaldehyde (−0.31 V); (3) 2-benzthiazolecarboxaldehyde (−0.48 V); (4) benzaldehyde (−0.29 V). Curves recorded from −0.75 V (vs. Carbon rod in 5 M sodium hydroxide) to positive potentials, rate of scanning 200 mV/min.

as the height of polarographic reduction and oxidation waves indicate that less than 10% of these compounds in neutral or slightly acidic media exists in the geminal diol ($ArCH(OH)_2$) form.

The division of the first two groups is based on the nature of their acid–base properties. To the first group are assigned aldehydes which in strongly alkaline media add a hydroxide ion to the aldehydic group according to reaction 1, in a similar way as benzaldehydes.[5] Derivatives of furan and thiophene belong to this group as well as those derivatives of pyrrole which bear an alkyl or aryl group on the heterocyclic nitrogen.

To the second group belong such heterocyclic aldehydes where the attack of hydroxide ion in alkaline solution occurs preferentially on the heterocycle and results in the dissociation of the N–H bond. This group is represented by pyrrole and indole derivatives with an unsubstituted NH group. These compounds show thus the same type of acid–base properties as other indole and pyrrole derivatives.[14]

To the third group belong thiazole, imidazole, and pyridine derivatives which exist in aqueous solutions in an equilibrium in which a considerable fraction of the aldehyde is present in the hydrated form.

Differentiation between CHO and NH Reactions. Distinction between the type of reaction in these two groups of carboxaldehydes is possible on the basis of their spectral behavior: compounds belonging to the first group show with increasing hydroxide concentration a decrease of the absorption band in the 250–300-nm region as corresponds to the shift of equilibrium 1 in favor of the geminal diol anion. Reaction of the compounds belonging to the second group with bases yielding iminate anions—pyrrolate or indolate—is manifested by an appearance of a new absorption band at longer wavelength and with greater molar absorptivity than shown by the neutral molecule.

The change in spectra observed for systems involving formation of a geminal diol anion is due to an annihilation of conjugation between the aromatic ring and the carbonyl group. The resulting adduct—the geminal diol anion—is either practically transparent in the 250–300-nm range or shows a considerably weaker absorption band due to the transition involving only the π electrons of the aromatic ring.

The shift toward longer wavelength when compared with the conjugate acid and the increase in absorptivity accompanying the formation of the iminate ion resembles behavior of carbanions and carbanion enolates, where the effect is usually interpreted as due to the participation of the electrons of the unit charge in the conjugated system. Nevertheless, we have recently shown[15] that electronic spectra can be observed for anions containing only σ bonds and indicated that such spectra might involve photolysis and formation of hydrated electrons. Attempts are being made to prove or exclude such a possibility for iminate ions.

An alternative possibility for differentiation of proton abstraction from hydroxide ion addition would be to distinguish whether the dependence of the value of ratio of the concentrations of the conjugate acid and base fits better the H_- or the J_- acidity scales.[5,16] Nevertheless, significant differences between the two scales are observed at so high sodium hydroxide concentrations that this diagnostic tool cannot be practically applied to the study of most of the presently studied systems.

Evaluation. Equilibrium constants for reactions of nonhydrated aldehydes resulting in addition of the hydroxide ion are summarized in Table I, those for aldehydes where dissociation of the NH group occurs first in Table II. Half-wave potentials of anodic waves are also included.

For all compounds reported in Table I a decrease of the ArCO absorption band was observed, indicating addition of OH^- ions with the exception of *N*-benzyl-3-indolecarboxaldehyde, which undergoes a different reaction. Formation of a new band at longer wavelengths (at 315 nm) indicated the possibility of carbanion formation. For all aldehydes, where measurement of the ratio $[ArCH(OH)O^-]/[ArCHO]$ was possible over a sufficiently wide range of sodium hydroxide concentration, the plot of log $[ArCH(OH)O^-]/[ArCHO]$ as a function of J_- values was found linear. This allows the conclusion that all these aldehydes add hydroxide ion in a simple reversible reaction, as has been proved for substituted benzaldehydes.[5,13] Consecutive or competitive reactions like the Cannizzaro reaction or ring opening do not affect values in Table I. The slope of the aforementioned linear plot (Δ) varies for the majority of compounds studied between −0.94 and −1.09 (Table I) indicating that the application of the J_- acidity scale for these compounds is permissible. Deviations in the value of Δ (Table I) observed for methyl-substituted compounds (5-methylfural and 3-methyl-2-thiophenecarboxaldehyde) might be due to steric effects, but further data on larger alkyl groups and dependence on position would be needed before they can be discussed in more detail. Reversibility of the reaction has been proved in all instances by recovery of the aldehyde after acidification.

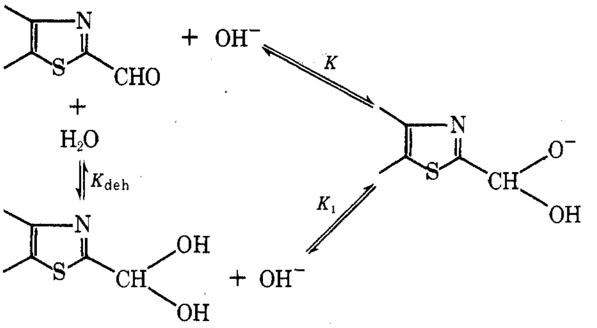
In addition to the rapidly established equilibrium corresponding to reaction 1, all furan derivatives have shown a considerably slower, consecutive reaction, fastest for 5-hydroxymethylfural. The nature of this process, considered to be a Cannizzaro or ring opening reaction, is under investigation.

Study of dissociation following reaction 2 (Table II) presented no complications, with the exception of the 2-imidazolecarboxaldehyde, which was present in the aqueous solutions also in hydrated form and will be discussed in the next section. Where comparison with literature was possible (i.e., for 3-indolecarboxaldehyde) agreement of our and reported[14] data was good.

Anodic waves of aldehydes which form the electroactive[8] geminal diol anion (Table I) correspond to oxidation of the aldehyde with formation of the corresponding carboxylic acid. Electrolysis products of the iminates (Table II) were not identified and the process involved is further studied.

Hydrated Aldehydes. Aldehydes derived from "basic" or π-deficient heterocyclic rings are strongly hydrated. The most typical representatives of this group, pyridinecarboxaldehydes, have been studied in sufficient detail[17–19] and were not thus included in this investigation. Quinolinecarboxaldehydes[17] are more strongly hydrated both in the protonated and uncharged form than the corresponding pyridinecarboxaldehydes. For thiazole- and imidazolecarboxaldehydes information about the position of the hydration–dehydration equilibria is rather scarce. 5-Imidazolecarboxaldehyde is estimated[20] to be about 50% hydrated in the protonated form and less in the uncharged form. 2-Imidazolecarboxaldehyde[21,22] and its *N*-alkyl derivatives[22] are more strongly hydrated than the 5 isomer. For 2-thiazolecarboxaldehyde stronger hydration of the cationic form than that of the free molecule is observed,[17] both being stronger than that for 5-imidazolecarboxaldehyde. Estimates from our spectral data (Table III) indicate that for the unprotonated forms of 2-thiazole, 2-benzothioazole, and 2-imidazole 70–90% of the aldehyde is in equilibrium present in hydrated form, whereas 1-methyl-2-imidazolecarboxaldehyde is only slightly, if at all, hydrated.

The reported value of pK_s (Table III) has different physical meaning for thiazole and imidazole derivatives. For thiazolecarboxaldehydes the overall acid–base reaction involves only the aldehydic group and eq 3 is operating (in the pH range studied, above pH 9):



(3)

The measured value K_s is related to the equilibrium constant of the addition of hydroxide ions (K) and to the dissociation constant of the hydrated form (K_1) by the expression $K_s = K_w K K_1 (K + K_1)$ and to the dehydration constant $K_{deh} = [\mathrm{ArCHO}]/[\mathrm{ArCH(OH)_2}]$ by relation $K_s = K_1/(1 + K_{deh})$. If, as indicated by the estimate of the hydration, $K_{deh} \ll 1$, then the measured value K_s is practically equal to K_1. The value of p$K_s \approx 11.2$ found for the two thiazole derivatives is of the same order of magnitude as values of dissociation constants of other compounds bearing the hydrated aldehydic group in the vicinity of an electronegative grouping (e.g., pK_1 about 10.0 for chloral[23] and trifluoroacetophenone[24] and 11.4 to 12.15 for the three pyridinecarboxaldehyde *N*-oxides[18]).

For 2-imidazolecarboxaldehyde dissociation of the NH group (Table II) and of the geminal diol (Table III) compete according to eq 4.

Formation of a new, more intense band at 310 nm in the pH range 9–11 indicates that paths 2a, 2b, and also 3a, 3b are not main contributors. The measured value of pK_N (Table II) is thus affected primarily by equilibria 1a and 4a. Consequently, the second acid–base process (pK_s in Table III) corresponds predominantly to equilibria 1b and 4b. For evaluation of relative contribution of path 1 and 4 information on position of hydration–dehydration equilibria both in neutral molecules and in imidazolate ions is essential.

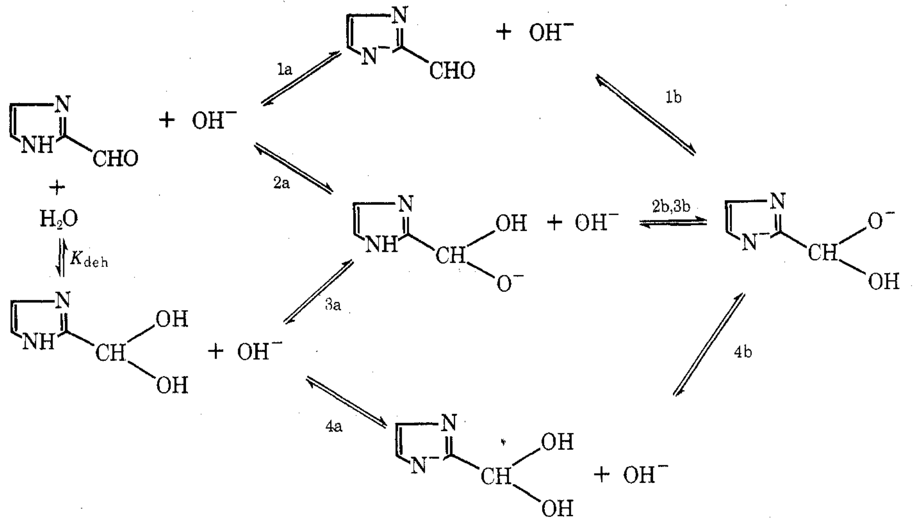
Anodic waves of the hydrated aldehydes (Table III) resembled those obsered for pyridinecarboxaldehydes[25] and correspond probably to the same process, i.e., oxidation of the geminal diol anion to carboxylic acid.

Structural Effects. Any comparison of structural effects on values of equilibrium constants and half-wave potentials (Tables I–III) must be carried out only inside of each of the specified groups, as only inside each of the groups the processes involved are analogous and hence the values measured comparable. This restricts the number of comparable compounds so that no attempt has been made to apply linear free energy or other theoretical treatment.

For addition of hydroxide ions to nonhydrated aldehydes (Table I) introduction of electropositive substituents into furan and thiophene rings results in an increase in pK' value, whereas electronegative substituents exert opposite effect. This is the same direction as observed for substituted benzaldehydes[13] and indicates a positive value of the reaction constant ρ. The difference in reactivity between fural and 2-thiophenecarboxaldehyde is relatively small, but both these aldehydes are considerably more reactive toward OH⁻ addition than N-substituted 2-pyrrolecarboxaldehydes. Extension of the condensed aromatic system in the carbazole derivative results in a marked shift in favor of the adduct.

Effect of substituents on the half-wave potentials of both furan and thiophene derivatives is small (Table I). Oxidation of 2-thiophenecarboxaldehydes occurs at somewhat more negative potentials (indicating easier oxidation) than that of fural and its derivatives. Half-wave potentials of 2-thiophenecarboxaldehyde are very close to those of benzaldehyde (Figure 1), indicating a similar level of interaction between the aromatic ring and the side chain.

Both N-substituted 2-pyrrolecarboxaldehydes and the carbazole derivative are oxidized at more positive potentials than furan and thiophene derivatives. The difference between N-substituted pyrrole and carbazole derivatives is relatively small, indicating that the conjugation extending effect of the



(4)

annelled rings is counterbalanced by another effect. The latter may be an effect of most suitable orientation at the electrode surface in the course of the electrode process, which the rigid carbazole derivative cannot achieve.

The value of pK_N for 3-indolecarboxaldehyde[14] has been shown to deviate from pK_N–σ plot, even when $\sigma^-_{p\text{-CHO}}$ was used. When the value of pK_N for 2-indolecarboxaldehyde (Table II) was correlated with $\sigma^-_{p\text{-CHO}}$, $\sigma_{m\text{-CHO}}$, or $(\sigma_p + \sigma_m)_{\text{CHO}}/2$, a small deviation in the same direction as for the 3-formyl derivative was observed. This clearly indicates a type of interaction between the formyl group and the indole ring, different from the interaction between the aniline ring and the aldehydic groups as expressed in the value of $\sigma^-_{p\text{-CHO}}$.

Specific interaction, not expressed by substituent constants, between the aldehydic group and the heterocycle is shown also by the comparison of the effect of an annelled benzene ring. Whereas pK_N value for the unsubstituted pyrrole is *0.54 units larger* than that for indole,[14] the effect of the annelled benzene ring on pK values of 2-carboxaldehydes is just opposite (Table II): the pK_N value for the pyrrole derivative is *0.35 units smaller* than that of the indole compound. In addition to the type of interaction observed for the 3-indolecarboxaldehyde[14] which would be in pyrrole even stronger than in indole (assuming comparable values of reaction constant ρ), it is impossible for the 2-carboxaldehydes to rule our direct interaction between the formyl group and the heterocyclic nitrogen.

The interaction between the formyl group and the indole ring, which increases the reactivity toward the OH^- attack on the NH group, seemingly decreases the reactivity of the formyl group to oxidation. This is shown by the absence of electroactivity of 3-indolecarboxaldehyde. Smaller interaction is shown by the 2-indolecarboxaldehyde, the electroactivity of which has not been impaired. Also the increase in the reactivity toward oxidation from pyrrole to indole derivative (Table II) is in the expected direction. Available data for these compounds do not allow us to distinguish if the changes in potentials are due to changes in formation of the electroactive geminal diol anion, in the electron transfer, or the hydrogen abstraction and more detailed analysis must be postponed.

All these results, nevertheless, indicate interaction between the formyl group and the indole ring, stronger for the 3 isomer than for the 2 isomer. Nevertheless, as such interaction operates not only in the 3 isomer, but also in the 2-carboxaldehyde it is indicated that the explanation by enol formation, offered for 3-carboxaldehyde,[14] might not be complete.

Presence of a unit negative charge on the heterocyclic ring decreases reactivity toward the hydroxide attack on the carbonyl group in a similar way as N-substitution. This follows from comparison of pK' values in Table II with values for N-substituted pyrrole derivatives (Table I).

For hydrated aldehydes the small effect of the annelled benzene ring in the thiazole derivatives as well as of *N*-methyl substitution in 2-imidazolecarboxaldehyde on values of pK_s (Table III) is probably due to the absence of conjugation in both the predominating geminal diol and its anion.

On the other hand, the ease of oxidation is increased by the added benzene ring in the 2-benzothiazolecarboxaldehyde and decreased by N-methylation in the imidazole derivative, as follows from comparison of polarographic half-wave potentials (Table III). As such change cannot reflect the position of the equilibrium yielding geminal diol anion, it must be caused by structural effects either on the electron transfer or hydrogen abstraction.

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Nucleophilic Additions to Aldehydes and Ketones. 3.[1] Reactions of Ortho-Substituted Benzaldehydes and Their Polarographic Oxidations

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Ortho-substituted benzaldehydes add in strongly alkaline media hydroxide ions in a reversible, rapidly established equilibrium reaction, in which an anion of the geminal diol [$ArCH(OH)O^-$] is formed. Extrapolation to zero ionic strength and use of acidity function J_- made it possible to determine thermodynamic equilibrium constants for benzaldehydes bearing both electropositive and electronegative substituents. Correlation of pK_a with $\sigma_{o\text{-X}}$ and dissociation constants of benzoic acids were explained by similarity in structures of the geminal diol anion and carboxylate ion or the transition state in ester hydrolysis. Structural effects on polarographic half-wave potentials of anodic waves indicated quantitative or qualitative changes in the heterogeneous portion of the electrode process, seemingly involving the hydrogen abstraction step [$ArCH(OH)O^- \rightleftharpoons ArCOOH + 2e + H^+$].

Previously[1,3] the acidity scale J_- for reactions involving addition of hydroxide ion in strongly alkaline media has been used for determination of thermodynamic values of equilibrium constants for additions to meta- and para-substituted benzaldehydes[3a] as well as to some heterocyclic aldehydes.[1] In this paper the study was extended to some ortho-substi-