MECHANISM OF THE ULLMANN CONDENSATION

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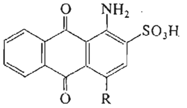
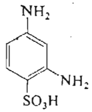
It has been found that the condensation rate of 1-amino-4-bromoanthraquinone-2-sulphonic acid (*I*) with 1,3-diaminobenzene-4-sulphonic acid (*II*) giving 1-amino-4-(3'-amino-4'-sulphoanilino)anthraquinone-2-sulphonic acid (*III*) in media of $NaHCO_3$-CO_2 and $NaHCO_3$–Na_2CO_3 with catalysis by CuI obeys the kinetic relation $v = k[I][II][Cu^+][CO_3^{2-}]$, being controlled by the kinetic relation $v = k[I][II][Cu^+]^2[PO_4^{3-}]$ in media of NaH_2PO_4–Na_2HPO_4 buffers. The suggested reaction mechanism presumes formation of a bifunctional catalyst $CuCO_3^-$ or $Cu_2PO_4^-$ which splits off the proton and bromide anion from the reaction intermediate in the rate-limiting step.

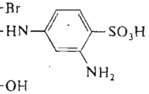
In spite of its considerable industrial importance the reaction of 1-amino-4-bromoanthraquinone-2-sulphonic acid (*I*) with aromatic amines (the so called Ullmann condensation which is used for production of blue and green substantive, reactive and acid dyestuffs) has been little studied theoretically so far. There exists extensive patent literature describing the condensations of the compound *I* with various amines, but a deeper study of the reaction and search for its possible mechanism are only dealt with in a series of reports by Tuong and Hida[1-3]. These authors followed the condensation of *I* with aniline and found it to be first order in each of the reactants. They also paid considerable attention to the catalyst effects. Initially they supposed Cu^{2+} ion to be the most effective catalyst, then they accepted the idea that Cu^+ ion only was efficient, which followed from the finding that the reaction is slowed down by the presence of compounds which form stable complexes with Cu^+ (chlorides, bromides, iodides, cyanides *etc.*). The reaction order with respect to the catalyst was not found; in suggesting the possible mechanism the authors supposed a first order reaction.

The present paper starts from the results of the authors cited. The main attention was paid to elucidation of effects of catalysts and bases. The condensation of *I* with 1,3-diaminobenzene-4-sulphonic acid (*II*) was chosen as model reaction due to suitable reactivity of *II* and excellent solubility of the main product, 1-amino-4-(3'-amino-4'-sulphoanilino)anthraquinone-2-sulphonic acid (*III*). Besides, the reaction produced small amounts of 1-amino-4-hydroxyanthraquinone-2-sulphonic acid (*IV*), and in some cases formation of 1-aminoanthraquinone-2-sulphonic acid (*V*) was observed, too[4].





I, R= —Br

III, R= 

IV, R= —OH

V, R= —H

II

EXPERIMENTAL

Reagents. 1-Amino-4-bromoanthraquinone-2-sulphonic acid (*I*), 1,3-diaminobenzene-4-sulphonic acid (*III*) and 1-amino-4-(3'-amino-4'-sulphoanilino)anthraquinone-2-sulphonic acid (*III*) in the form of the corresponding sodium salts were recrystallized twice from water, dried at 100°C and submitted to elemental analysis. Their purity was checked chromatographically.

Analysis. 1-Amino-4-hydroxyanthraquinone-2-sulphonic acid (*IV*) and 1-aminoanthraquinone-2-sulphonic acid (*V*) were identified chromatographically by comparison with the authentic substances (hue, R_F value on Silufol with ethyl acetate–methanol-25% ammonia 8 : 2 : 1 as eluent: *I*, reddish orange, 0·51- *III*, blue, 0·05; *IV*, violet, 0·48; *V*, orange, 0·46).

pH *Values* were measured with a Radelkis OP-204 apparatus using a glass electrode Polymetron 8405 at 25°C after each experiment.

Potential values E were measured with a copper electrode (made of high-conductivity copper) and a saturated calomel electrode at 25°C in the reaction mixtures which were prepared anew after finishing the whole series of the kinetic runs.

Kinetics measurements. Sodium 1,3-diaminobenzene-4-sulphonate (1·5 . 10^{-2} mol) was mixed with the calculated amount of $NaHCO_3$ and, in certain cases, a chosen amount of NaBr or a calculated volume of 0·5M-KI was added thereto. In the experiments using phosphate buffers the chosen volumes of 1·5M-H_3PO_4 and 2·5M-NaOH were added. Constant ionic strength was adjusted by addition of Na_2SO_4. Volume of the mixture was made up to 90 ml by addition of water. The solution was placed in a four-necked flask with a stirrer, reflux condenser, thermometer and an inlet tube, and it was heated to 40°C in a thermostat. In the cases using hydrogencarbonate buffers CO_2 was introduced (0·1 l/min) into the mixtures, whereas in the runs using $NaHCO_3$–Na_2CO_3 and NaH_2PO_4–Na_2HPO_4 we introduced N_2. The used gases were saturated with water vapour at 40°C before introduction. After 15 min introducing CO_2 (N_2), we added 0·1 g CuI and 0·3 g Cu bronze and, after further 15 min, 10 ml 0·1M solution of 1-amino-4-bromoanthraquinone-2-sulphonic acid preheated at 40°C was added. At definite time intervals 5 ml samples were withdrawn, and the reaction was stopped by addition of the sample into 5 ml 2·5M-NaOH and dilution with water to 100 ml. The separated copper compounds and the hydroxy compound *IV* were removed by filtration through a dense sintered glass. Content of the compound *III* in the filtrate was determined spectrophotometrically at 600 nm using a Spekol apparatus (Zeiss, Jena). The reactions were followed within a time of about five reaction half-lives.

Rate constants k_{exp} were calculated from the relation

$$k_{exp} = -(c_\infty / c_0 t) \ln (1 - c/c_\infty) , \qquad (1)$$

where c and c_∞ mean the concentrations of *III* at a time t and after the completed reaction, respectively, and c_0 stand for the concentration of *III* after the completed reaction under the presumption of 100% yield of the condensation, *i.e.* the initial concentration of the compound *I*.

The equation (*1*) was derived[11] with the presumption of the overall pseudo-first order of the main amination reaction as well as of the both side reactions. This condition was fulfilled with respect to the reaction conditions chosen (considerable excess of *II* and bases compared to *I*, constant pH and constant catalyst amount).

RESULTS AND DISCUSSION

First of all, it was found that the reaction without the catalyst does not take place at all. With small amounts of copper(I) chloride or iodide the kinetic measurements showed considerable lack of reproducibility; the reaction rate decreased in the course of the reaction. Satisfactory results were obtained after increasing the catalysts amounts and addition of copper (Tables I–IV), the catalytic effects of CuCl, CuI and Cu_2O being the same. In the kinetic runs we used copper(I) iodide only.

Tuong and Hida[2] found that the reaction rate is markedly decreased by additions of halogenides, which is undoubtedly due to decrease of concentration of univalent copper. For obtaining quantitative data we followed the dependence of the condensation rate of *I* and *II* on concentrations of the added potassium iodide and sodium bromide. The results are given in Table I. If relation (*2*) is obeyed,

$$k_{exp} = k_1[Cu^+]^n \qquad (2)$$

TABLE I

Dependence of Reaction Rate on Concentration of KI and NaBr

$[NaHCO_3] = 5 \cdot 10^{-1}$ mol/l; introduction of CO_2; $c_\infty/c_0 = 0.95$; μ(KI) = 0.8 mol/l; μ(NaBr) = 1.4 mol/l.

[KJ] . 10^3, mol/l	0·2	1	2	3	4	6	8	10
$k_{exp} \cdot 10^4$, s^{-1}	10·93	10·93	7·92	5·00	3·84	2·18	1·08	0·65
[NaBr] . 10, mol/l	1	2·5	4	5	5·6	6·7		
$k_{exp} \cdot 10^4$, s^{-1}	12·60	12·65	12·60	9·88	8·00	6·90		

then introduction of the solubility product leads to relation (3) between k_{exp} and iodide (bromide) ion concentration.

$$\log k_{exp} = -n \log [X^-] + \text{const.} \quad (3)$$

The results obtained show that the n value does not remain constant within the whole studied halogenide concentration range. In the I^- concentration range 0 to $1{\cdot}4 \cdot 10^{-3}$M the reaction rate does not change ($n = 0$), within $1{\cdot}4 \cdot 10^{-3}$M to $5 \cdot 10^{-3}$M $I^{(-)}$ it is $n = 1$, and at still higher iodide concentrations the n value is increased ($n = 2$). In the presence of sodium bromide the k_{exp} of the condensation is unchanged until 0·4M Br^-, at higher bromide concentrations the slope n is equal to unity. The reaction could not be followed within a broader NaBr concentration range, because higher electrolyte concentrations (necessary for appropriate ionic strength adjustment) cause separation of the compound *I* ($\mu = 1{\cdot}6$M).

We found a noteworthy difference between the "limit" concentrations of the two halogenides, *i.e.* the concentrations above which the reaction rate begins to decrease.

TABLE II

Dependence of Reaction Rate on Concentration of $NaHCO_3$ (buffer $NaHCO_3$–CO_2; $\mu = 0{\cdot}8$ mol/l)

$[NaHCO_3] \cdot 10$, mol/l	0·5	0·75	1	2	3	4	5	6·5	10
$k_{exp} \cdot 10^4$, s^{-1}	0·93	1·65	2·08	4·30	6·26	9·46	10·80	14·70	21·50
pH	6·72	6·92	7·04	7·42	7·66	7·83	7·97	8·14	8·45
—E (S.C.E.), V	0·046	0·052	0·054	0·076	0·090	0·103	0·114	0·125	0·141
c_∞/c_0	0·62	0·73	0·73	0·83	0·89	0·95	0·95	0·95	0·95

TABLE III

Dependence of Reaction Rate on Concentration of $NaHCO_3$ (buffer $NaHCO_3$–Na_2CO_3; $\mu = 1{\cdot}4$ mol/l; $c_\infty/c_0 = 0{\cdot}95$)

$[NaHCO_3] \cdot 10$, mol/l	3·25	3·30	2·50	1·25
$[Na_2CO_3] \cdot 10$, mol/l	1·12	1·60	2·50	3·75
$k_{exp} \cdot 10^4$, s^{-1}	5·50	5·50	4·50	2·26
pH	9·60	9·70	10·05	10·55

This fact can obviously be explained by the great difference between the solubility products of CuBr and CuI ($P_{CuBr} = 4\cdot15 . 10^{-8}$, ref.[5]; $P_{CuI} = 5\cdot06 . 10^{-12}$, ref.[7]). At lower concentrations of the halogenides the Cu^+ concentration is constant being determined by the solubility product of copper(I) hydroxide ($P_{CuOH} = 7\cdot18 . 10^{-14}$, ref.[8]). According to presumptions, ratio of the "limit" concentrations ($[Br^-]_{lim}/[I^-]_{lim} = 290$) should be equal to ratio of the solubility products of the both halogenides ($P_{CuBr}/P_{CuI} = 8200$). The difference between the both values is due to the fact that the results given in literature were obtained under different conditions from those used in the present study.

Increase in the reaction order with respect to Cu^+ at higher iodide anion concentrations is only apparent, because Cu^+ concentration can be affected by some complexation equilibrium, *e.g.* $Cu^+ + 2 I^- \rightleftharpoons CuI_2^-$.

The technical-scale condensations of *I* with various amines are carried out practically invariably in the presence of $NaHCO_3$ or its mixture with Na_2CO_3. In this study we have followed effects of some other bases, too, *viz.* NaH_2PO_4–Na_2HPO_4 buffer and sodium acetate. The results are given in Tables II–IV and Figs 1–4.

From Fig. 2 it is seen that in $NaHCO_3$–CO_2 (and perhaps also in $NaHCO_3$–Na_2CO_3) buffers the reaction rate is proportional to the HCO_3^- anion concentration, *i.e.*

$$k_{exp} = k_2[HCO_3^-] \,. \tag{4}$$

TABLE IV

Dependence of Reaction Rate on Concentration of NaH_2PO_4 and Na_2HPO_4

$\mu = 1\cdot0$ mol/l.

$k_{exp} . 10^4$, s^{-1}	c_∞/c_0	$[NaH_2PO_4] . 10$ mol/l	$[Na_2HPO_4] . 10$ mol/l	pH	$-E$ (S.C.E.) V
6·77	0·37	5·287	0·712	6·40	0·075
3·53	0·48	0·713	0·525	6·95	0·107
6·73	0·58	1·460	1·075	6·95	0·107
8·28	0·58	1·800	1·325	6·95	0·107
6·32	0·67	1·175	1·325	7·15	0·117
2·25	0·68	0·225	0·525	7·50	0·127
4·66	0·76	0·450	1·050	7·50	0·127
6·40	0·85	0·675	1·575	7·50	0·127
7·75	0·79	0·605	2·195	7·65	0·136
1·52	0·71	0·125	0·625	7·80	0·141
2·66	0·77	0·205	1·035	7·80	0·141
4·11	0·83	0·315	1·575	7·80	0·141
4·96	0·83	0·415	2·075	7·80	0·141
6·87	0·85	0·520	2·595	7·80	0·141

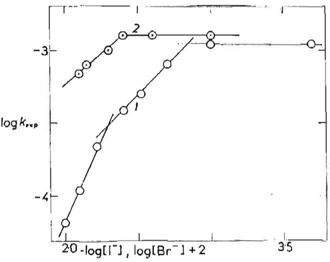


FIG. 1

Dependence of log k_{exp} on log $[I^-]$ *1* and log $[Br^-]$ *2*.

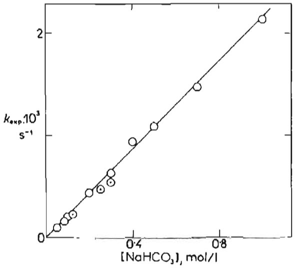


FIG. 2

Dependence of k_{exp} on Concentration of $NaHCO_3$

Buffer $NaHCO_3$-CO_2 ○, $NaHCO_3$-Na_2CO_3 ⊙.

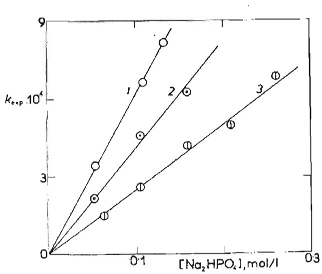


FIG. 3

Dependence of k_{exp} on Concentration of Na_2HPO_4

Ratio $NaH_2PO_4 : Na_2HPO_4 = 1 : 0{\cdot}74$ *1*; $1 : 2{\cdot}33$ *2*; $1 : 5{\cdot}00$ *3*.

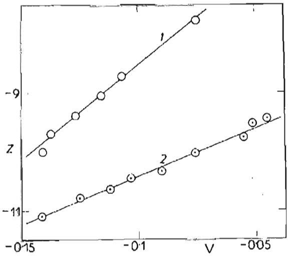


FIG. 4

Dependence of Reaction Rate on Potential of Copper Electrode

1 $Z = \log k_{exp} - \text{pH} - \log [HPO_4^{2-}]$, *2* $Z = \log k_{exp} - \text{pH} - \log [HCO_3^-]$.

Furthermore, the reaction rate was found to be dependent on the potential of Cu electrode, *i.e.* on a quantity depending immediately on the Cu^+ ion concentration. From the measurements carried out it follows that the dependence of k_{exp} on the potential E of copper electrode is expressed by the Eq. (*5*) which can be transformed into Eq. (*6*) by introduction of dissociation equilibrium of carbonic acid. Using Eq. (*1*) and the Nernst equation, the relation (*6*) can be transformed into Eq. (*7*).

$$\log k_{exp} - \mathrm{pH} - \log [HCO_3^-] = k \, . \, E + \text{const.} \tag{5}$$

$$\log k_{exp} - \log [CO_3^{2-}] = k \, . \, E + \text{const.} \tag{6}$$

$$\log k_{exp} - \log [CO_3^{2-}] = nFE/2\cdot303RT + \text{const.} \tag{7}$$

In Eq. (*7*) n means the reaction order with respect to Cu^+ ion, and the factor $F/2\cdot303RT = 16\cdot95 \ V^{-1}$ at 25°C.

Experimentally it was found $n = 1\cdot03$ (Fig. 4), hence k_{exp} can be expressed by Eq. (*8*).

$$k_{exp} = k_3[Cu^+][CO_3^{2-}] \tag{8}$$

The same result is obtained by introduction of solubility product of CuOH and dissociation equilibria of water and carbonic acid into Eq. (*4*).

From Table II it is obvious that decreasing of the $NaHCO_3$ concentration below 0·3–0·4 mol/l results in decrease of the (c_∞/c_0) value, *i.e.* decrease of yields of the condennsation product *III*. The yield decrease is not due to a higher proportion of the hydrolytic product *IV* but to that of the redox reaction product *V*. Whereas in the experiments using the $NaHCO_3$ concentrations above 0·3 mol/l the compound *V* was not detected chromatographically, decreasing of the $NaHCO_3$ concentration below 0·3 mol/l resulted in gradual increase of amounts of the compound *V*. Semiquantitative chromatographic assessment showed that amount of the hydrolysis product did not change within the range studied.

In NaH_2PO_4–Na_2HPO_4 buffers the reaction rate was found to be proportional to the buffer concentration at constant pH value (*i.e.* constant ratio of the buffer components) (Fig. 3). Under these considitions the copper electrode potential remained unchanged, too.

In the experiments using different ratios of the buffer components we found linear dependence between $(\log k_{exp} - \mathrm{pH} - \log [HPO_4^{2-}])$ and E (Fig. 4), but its slope was $32\cdot8 \ V^{-1}$, *i.e.* double what it was in the previous case. Hence the reaction rate is proportional to the square of concentration of univalent copper. After modification it can then be written:

$$k_{exp} = k_4[Cu^+]^2[PO_4^{3-}] \, . \tag{9}$$

The relatively low values (c_∞/c_0), *i.e.* low yields of the condensation product *III*, show that phosphate buffers will hardly be of any use in synthesis of *III*. Mutual ratio of the side products *IV* and *V* was not followed in this study.

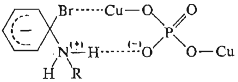
Application of acetate anion as the base was also investigated, but the results were negative. In an experiment carried out under the conditions given in Table I but without NaBr it was found $k_{exp} = 12{\cdot}40 \,.\, 10^{-1}\,s^{-1}$, practically the same value being obtained ($k_{exp} = 12{\cdot}28 \,.\, 10^{-3}\,s^{-1}$) in an experiment carried out under the same conditions but with addition of 0·6 mol/l sodium acetate.

If the Eqs (*8*) and (*9*) are extended by the dependence of the reaction rate on the concentrations of *I* and *II* (the 1. order with respect to *II* is obvious from analogy to the results of Tuong and Hida[1]), then final forms of the kinetic dependences of the reactions in carbonate and phosphate buffers are given in Eqs (*10*) and (*11*), respectively.

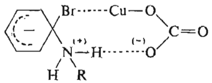
$$v = k_5[I][II][Cu^+][CO_3^{2-}] \qquad (10)$$

$$v = k_6[I][II][Cu^+]^2[PO_4^{3-}] \qquad (11)$$

So far most ideas[3] about the course of the Ullmann condensation have been derived from the mechanism suggested by Bunnett and Zahler[6]. The authors presumed a primary formation of a complex between Cu^+ ion and aryl halogenide in which the increased electrophilicity of the leaving group facilitates the proper nucleophilic substitution. No assistance of base was considered. This mechanism agrees with the found kinetic relation (*10*) provided the rate-limiting step is splitting off of the proton from the reaction intermediate (schematically represented as $(I.II.Cu)^+$) by action of carbonate anion. The relation (*11*), however, cannot be explained in this way, the found reaction order with respect to Cu^+ cation being contradictory. A possible explanation is that the proper catalyst is the $Cu_2PO_4^-$ or $CuCO_3^-$ anion which acts as a bifunctional catalyst: with its nucleophilic centre it facilitates splitting off of the proton from nitrogen, and with its electrophilic centre it facilitates splitting off of the leaving group. The transition state can be represented then as *VIa* or *VIb*.



VIa



VIb

The Eqs (*10*) and (*11*) correspond to the reaction course represented in Scheme 1, provided the concentration of the reaction intermediate is low and constant during the reaction, and provided the equilibria (*12*) and (*13*) are established.

SCHEME 1

$$B = Cu_2PO_4^- \text{ or } CuCO_3^-$$

$$2\,Cu^+ + PO_4^{3-} \rightleftharpoons Cu_2PO_4^- \quad (12)$$

$$Cu^+ + CO_3^{2-} \rightleftharpoons CuCO_3^- \quad (13)$$

In this reaction, acetate anion is inefficient due to its inability to form a compound type B.

Bifunctional action of some catalysts in aromatic nucleophilic substitution was first observed by Bitter and Zollinger[9] in a study of the condensation of cyanuric chloride with aniline catalyzed with α-pyridone and some carboxylic acids. Later, similar action was found by Pietra and Vitali[10] in the reaction of 2,4-dinitrochlorobenzene and piperidine catalyzed with α-pyridone, too[11].

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