

INVESTIGATION OF THE INDUSTRIALLY APPLICABLE SYNTHESIS OF IMINODIACETIC ACID

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The present paper deals with the synthesis of iminodiacetic acid, which is the basic material of the production of the plant-protecting agent *N*-phosphonomethyl glycine. The most economical procedure for the industrial preparation of iminodiacetic acid involves aminolysis of monochloroacetic acid, where the starting materials are monochloroacetic acid, ammonia and Ca(OH)₂. We improved the conversion of monochloroacetic acid into the target compound to 91 % from the present 67 % yield. Our results show that the rate-determining step is the formation of iminodiacetic acid, while a considerable amount of glycine is present. Our important recognition is that glycine, produced together with the desired iminodiacetic acid, can be converted with monochloroacetic acid to iminodiacetic acid after removal of the excess of ammonia from the reaction mixture.

Keywords: synthesis of iminodiacetic acid, concurrent consecutive, competitive reactions

Introduction

The industrial production of *N*-phosphonomethyl glycine, an important plant-protecting agent in agriculture, is based on either iminodiacetic acid, or glycine. Starting with iminodiacetic acid, *N*-phosphonomethyl glycine can be prepared in two steps. In the first step Mannich condensation of iminodiacetic acid, paraformaldehyde, and orthophosphorous acid gives *N*-phosphonomethyliminodiacetic acid [1-10].

In the second step, catalytic oxidation of *N*-phosphonomethyliminodiacetic acid leads to *N*-phosphonomethyl glycine.

N-phosphonomethyl glycine can also be synthesized directly from glycine. This procedure is based on treatment of a solution of glycine in methanol with paraformaldehyde and dimethylphosphite to obtain the sodium salt of *N*-dimethylphosphit methyl glycine. Addition of hydrochloric acid results in the precipitation of sodium chloride, and hydrolysis of *N*-dimethylphosphit methyl glycine sodium salt into *N*-phosphonomethyl glycine.

Because of the higher yield, the procedure starting from iminodiacetic acid appears to be more economical than that based on glycine.

The synthesis of iminodiacetic acid has been extensively studied, and most of the literature reports are patents. Iminodiacetic acid can be manufactured from the following starting materials:

- a. hydroxyacetoneitrile
- b. hydrogen cyanide and urotropine
- c. diethanolamine
- d. monochloroacetic acid

Table 1 Preparation of iminodiacetic acid

Starting material	Reagent added	Yield,%	Ref.
Hydroxyacetoneitrile	NaOH, H ₃ N	74	[1]
	H ₃ N	90	[2]
	Glycine, NaOH	45	[3]
	Glycine, NaOH	> 45	[4]
HCN, HMTA	HCN, HMTA	-	[5, 6]
	-	-	[6, 7]
Diethanolamine	CdO, NaOH	85	[8]
ClCH ₂ -COOH	H ₃ N (NaCN)	20-40	[9]
	H ₃ N, Ca(OH) ₂	85	[10]

It is well known that the reaction of monochloroacetic acid with ammonia in an aqueous

medium produces a mixture of primary, secondary and tertiary amines and glycolic acid. The iminodiacetic acid-content of the reaction mixture is ca. 20-40 %, depending on the reaction conditions. Glycine, as the primary product, may react with excess additional molecules of monochloroacetic acid to give iminodiacetic acid and then nitrilotriacetic acid [11-13].

Manufacturing of the product is presently based on a modified version of the protocol described in Ref. [10]. Thus, a 3.5 mol/dm^3 aqueous solution of monochloroacetic acid is neutralized with concentrated ammonium hydroxide at 18°C .

To this aqueous solution of the ammonium salt powdered caustic lime is added to liberate ammonia, which takes part in the nucleophilic substitution at elevated temperature. The resulting solution is filtered, concentrated to remove the excess of ammonia, and iminodiacetic acid is liberated from the salt by the addition hydrochloric acid. The product crystallizes from the solution in the form of its hydrochloride salt.

The above procedure is useful up to a ca. 67 % conversion of monochloroacetic acid into iminodiacetic acid. The technological process is uncontinuous, and a further disadvantage is the long reaction time (10 hours).

Experimental

Materials

Monochloroacetic acid, ammonia solution and $\text{Ca}(\text{OH})_2$ were purchased from Aldrich (Germany) and were used as received.

Investigation of the Reaction Rates

A solution of monochloroacetic acid (MCA) of 8 mol/dm^3 was neutralized with a solution of ammonia of 8 mol/dm^3 . The reaction was started by mixing 50 ml MCA ammonia salt solution with 50 ml of a suspension of $\text{Ca}(\text{OH})_2$ of 4 mol/dm^3 . The reaction mixture was thermostated at 40°C , 50°C , 60°C and 70°C . After a predetermined time interval samples were taken from the reaction mixture and the concentration of Cl^- , glycine and IMDA was determined.

Analytical Methods for Monitoring the Reactions

For the determination of the rate-equations of formation of iminodiacetic acid in a batch-type reactor, analytical methods suitable for the determination of the concentration of the components in time are required.

For this, key components/intermediates should be selected, and methods for their determination should be elaborated.

Quantitative Determination of Iminodiacetic Acid

For the quantitative determination of iminodiacetic acid various methods are known in the literature.

For simplicity, a spectrophotometric method was employed. This methodology is based on the nitrosation reaction of iminodiacetic acid carried out with two-fold molar excess of sodium nitrite under acidic conditions at room temperature.

Nitrosoiminodiacetic acid possesses an absorption maximum at 350 nm, which follows the Lamber-Beer law in the concentration interval of $5 \cdot 10^{-4}$ – 10^{-2} mol/dm^3 . Another components present in the system do not disturb the determination.

Simultaneous Determination of Glycine and Iminodiacetic Acid on a Layer of Strongly Acidic Cation Exchange Resin

Based on the results of Dévényi et al. [14], one-dimensional layer chromatography on a strongly acidic cation exchange resin was applied. The spots were developed by ninhydrin. Quantitative evaluation of the chromatograms is accomplished with a videodensitometer.

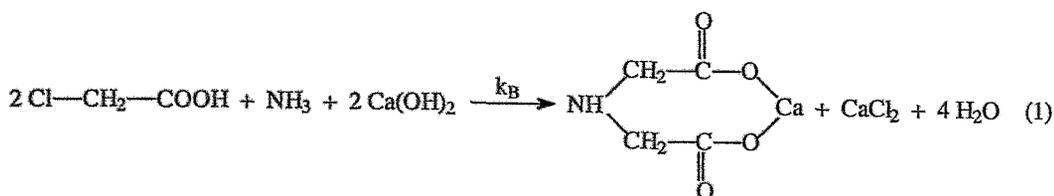
Monitoring of the Change of the Concentration of Monochloroacetic Acid with a Chloride Ion-Sensitive Membrane Electrode

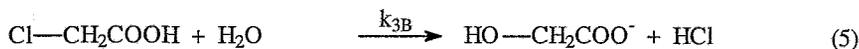
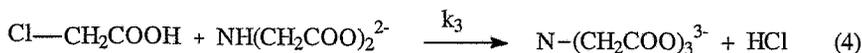
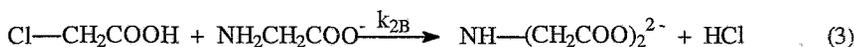
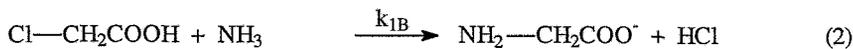
The chloride ion concentration in the system was measured with a chloride ion-selective electrode, which can be applied in a wide range of Cl^- concentration.

Results and Discussions

Investigation of the Reaction Rates in a Batch-type Reactor

No data were found in the literature concerning the kinetics, and equations describing the rate of formation of iminodiacetic acid. The complex chemical reaction (involving monochloroacetic acid, ammonium hydroxide, calcium hydroxide and water), which serves as the basis of manufacturing the target substance is given by the following series of equations:





The stoichiometry of the reaction is determined by a joint contribution of each of these processes. The equation does not represent all of the reactions proceeding in the complex system, and therefore, does not illustrate the contributing reactions which could be modified to obtain a desired better outcome. However, it is still possible to select a few processes which might be rate-determining because of their relatively low rate. Such an approach of discussing the reaction rate would permit description of the details of the complex reaction as a whole.

We supposed that the chemical process can be described with the following, simplified concurrent consecutive, competitive equations:

By investigating the elemental steps and conditions of the reaction of monochloroacetic acid with ammonia we can learn that the reaction system is concurrent, consecutive and competitive. The outcome is clearly a function of the ratio of the two nucleophiles, and also of the preponderance of the intermediary glycine. As no relevant data have been reported, we can thus suppose that apart from the molar ratio of the above components, the ratio of the rate of the two reactions may also be decisive on the formation of iminodiacetic acid. This latter is, naturally, a function of the molar ratio of monochloroacetic acid and ammonia.

The reaction of monochloroacetic acid with ammonia results in the formation of glycine as the primary product, which represents a second nucleophile in the system. Thus, glycine can react with monochloroacetic acid in a concurrent reaction to produce iminodiacetic acid. This concurrent consecutive reaction is accompanied by the hydrolysis of monochloroacetic acid as a parallel process. Under the initial conditions of the reaction the mixture contains calcium hydroxide in an equimolar quantity with that of monochloroacetic acid, thus hydrolysis must be taken into account more pointedly in this stage of the process.

To have an overall look on the reaction system we had to determine the rate constants of the individual partial reactions.

We have shown that the change of the concentration of monochloroacetic acid can be followed by measuring the chloride ion concentration, and that the effective conversion of this substance can be monitored by the determination of the concentration of iminodiacetic acid. Therefore, the progress of the reaction in time was followed by analyzing the quantities of the chloride ion, iminodiacetic acid and glycine at various periods.

Figure 1 shows the change of the concentration of iminodiacetic acid, glycine and monochloroacetic acid in the brutto chemical reaction, and one can see that the complete conversion of monochloroacetic acid is associated with a 65 % effective and utilizable transformation into iminodiacetic acid.

The chromatographic investigation on cation-exchange resin layer, followed by videodensitometric evaluation demonstrated that (depending on the reaction temperature) a considerable volume (20-27 %) of glycine is present in the reaction mixture. Therefore, further conversion of glycine (produced from monochloroacetic acid) into iminodiacetic acid does not proceed in the lack of monochloroacetic acid, as—for kinetic reasons—the concentration of ammonia has been selected higher than that of monochloroacetic acid.

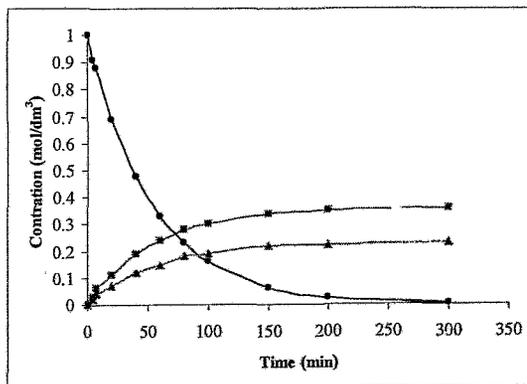


Fig.1 Change of the concentration of reactants and products versus time (● monochloroacetic acid, ■ iminodiacetic acid, ♦ glycine, at 60 °C)

According to the data of Figure 1, the apparent rate constants of the conversion of monochloroacetic acid (k_B) and the formation of iminodiacetic acid (k_{2B}) can be determined.

By plotting the logarithm of the relative concentration of monochloroacetic acid against the time a linear connection is obtained. Figure 2 shows this relation, i.e., the rate constants of the conversion of monochloroacetic acid in the brutto reaction.

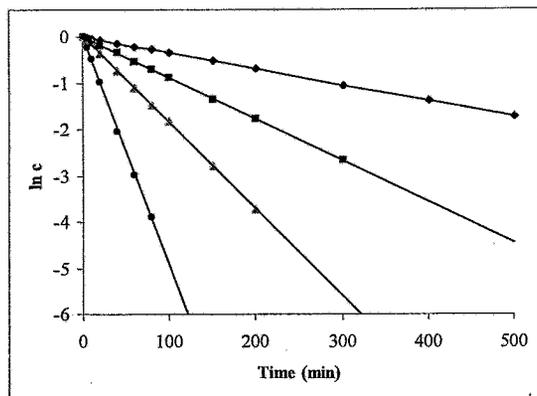


Fig. 2 Logarithm of the relative concentration of monochloroacetic acid versus time (\diamond 40, \blacksquare 50, \blacktriangle 60, \bullet 70 °C)

The observed linear relationship demonstrates the pseudo-first order of the reaction, and the dependence of the apparent rate constants on the temperature is expressed by Eq. 6.:

$$k_B = 3.27 \cdot 10^{10} \cdot \exp\left(-\frac{9354}{T}\right) \quad (6)$$

As the complete transformation of monochloroacetic acid in the brutto chemical reaction is of pseudo-first order, and due to the finding that glycine is in an excess compared to the concentration of monochloroacetic acid at the end of the reaction, formation of iminodiacetic acid can also be described by a pseudo-first order equation. For the determination of the k_{2B} rate constant, the logarithm of the concentration of iminodiacetic acid produced in the brutto process is plotted as a function of the reaction time. Figure 3 shows this relation, i.e. the rate constants of the formation of iminodiacetic acid in the brutto reaction.

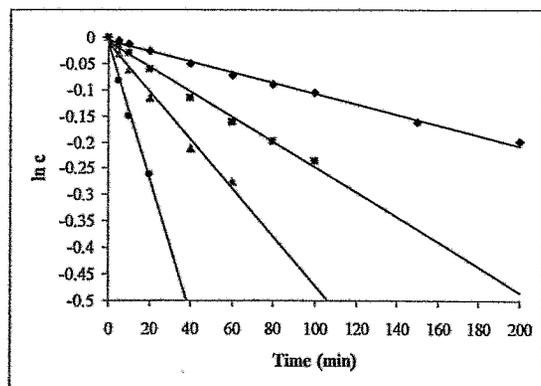


Fig. 3 Logarithm of the relative concentration of iminodiacetic acid versus time (\diamond 40, \blacksquare 50, \blacktriangle 60, \bullet 70 °C)

The observed linear relationship demonstrates the pseudo-first order of the reaction, and the dependence of the apparent rate constants on the temperature is expressed by Eq. 7.

$$k_{2B} = 1.18 \cdot 10^{10} \cdot \exp\left(-\frac{9337}{T}\right) \quad (7)$$

Determination of the Formation of Nitrilotriacetic Acid

The formation of nitrilotriacetic acid in the reaction of iminodiacetic acid with monochloroacetic acid is not significant under the applied experimental conditions.

Determination of the Rate Constant of the Hydrolysis of Monochloroacetic Acid

Under isolated conditions the rate constant k_{3B} of the hydrolysis was determined as follows: monochloroacetic acid was treated with an excess of calcium hydroxide, and the chloride ion-content of the reaction mixture was measured in given intervals. Thus the concentration of monochloroacetic acid can be readily determined in a given state of the reaction.

The change of the concentration of monochloroacetic acid as a function of the reaction time is shown in Figure 4.

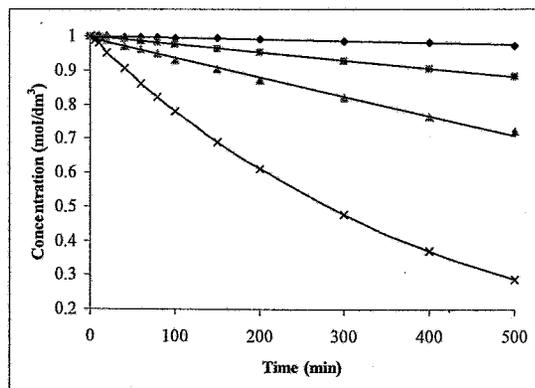


Fig. 4 Change of the relative concentration of MCA versus time (\diamond 40, \blacksquare 50, \blacktriangle 60, \times 70 °C)

By plotting the logarithm of the relative concentration of monochloroacetic acid as a function of time a linear relation is obtained, indicating the pseudo-first order of the reaction (see Figure 5).

The dependence of the apparent rate constants on the temperature is expressed by Eq. 8.

$$k_{3B} = 2.5754 \cdot 10^{14} \cdot \exp\left(-\frac{9805}{T}\right) \quad (8)$$

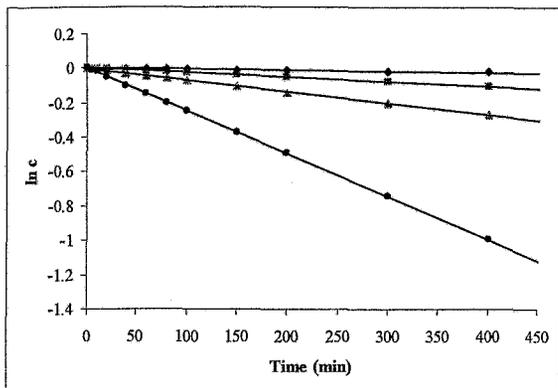


Fig.5 Logarithm of the relative concentration of MCA versus time
(♦40, ■ 50, ▲ 60, ● 70 °C)

Determination of the Rate Constant of the Formation of Glycine

The quantity of glycine, produced in the reaction mixture consisting of monochloroacetic acid, calcium hydroxide, ammonia and water cannot be measured directly, as a part of glycine is converted into iminodiacetic acid in a consecutive reaction. Therefore, the rate constant of the formation of glycine is determined by calculation.

According to the law of conservation of mass, the current composition of the reaction mixture can be described by the following equation:

$$[MCA]_0 = [MCA] + [GLY] + 2[IMDA] + [GA]$$

where $[MCA]$, $[GLY]$, $[IMDA]$ and $[GA]$ represent the concentration of monochloroacetic acid, glycine, iminodiacetic acid and glycolic acid, respectively, at a given t time, and the (0) subscript means the initial concentration of these materials.

The conversion of glycine from monochloroacetic acid can be calculated from the experimental data with the following equation:

$$[GLY]_s^* = [GLY]^* + [IMDA]^* = 1 - [MCA]^* - [IMDA]^* - [GA]^*$$

where

$[GLY]_s$ is the total concentration of glycine produced (i.e. the sum of the quantity present in the reaction mixture and that converted into iminodiacetic acid), and the * subscripts are for the relative concentrations of the components divided by $[MCA]_0$.

The calculations reveal the pseudo-first order of the formation of glycine, and the dependence of the apparent rate constants on the temperature is expressed by Eq. 9.:

$$k_{1B} = 5.66 \cdot 10^{10} \cdot \exp\left(-\frac{9805}{T}\right) \quad (9)$$

The apparent rate constant values of the brutto chemical reaction are summarized in Table 2.

Table 2 Apparent rate constants of the brutto chemical reaction.

T [°C]	k_B [min ⁻¹]	k_{1B} [min ⁻¹]	k_{2B} [min ⁻¹]	k_{3B} [min ⁻¹]
40	$3.469 \cdot 10^{-3}$	$1.346 \cdot 10^{-3}$	$1.25 \cdot 10^{-3}$	$0.530 \cdot 10^{-4}$
50	$8.950 \cdot 10^{-3}$	$4.296 \cdot 10^{-3}$	$3.22 \cdot 10^{-3}$	$2.550 \cdot 10^{-4}$
60	$18.490 \cdot 10^{-3}$	$11.08 \cdot 10^{-3}$	$6.65 \cdot 10^{-3}$	$6.740 \cdot 10^{-4}$
70	$50.24 \cdot 10^{-3}$	$20.85 \cdot 10^{-3}$	$18.09 \cdot 10^{-3}$	$24.80 \cdot 10^{-4}$

As the virtual rate constants are characteristic only of a given system, no suppositions concerning the kinetics can be drawn by their comparison. Under the given conditions (i.e. at a given ammonia concentration) $k_{1B} > k_{2B}$, which means that the reaction is shifted towards the formation of glycine.

Investigation of the Reaction of Monochloroacetic Acid with Glycine without Ammonia

It has been already mentioned that iminodiacetic acid is produced in a consecutive reaction: glycine, formed from monochloroacetic acid and ammonia reacts with monochloroacetic acid as the second nucleophilic reagent present in the reaction mixture according to equation (2).

As the value of the rate constant of the formation of glycine (k_{1B}) is higher than that of the formation of iminodiacetic acid (k_{2B}), a considerable amount (27-30 %) of glycine is left unreacted in the system at the end of the reaction. The rest of glycine can be utilized by the removal of the other nucleophilic partner, ammonia, from the system and by introducing an equimolar amount of monochloroacetic acid to ensure to react with glycine. The rate constant of the formation of iminodiacetic acid (k_{21}) under isolated conditions can be then determined by reacting monochloroacetic acid with glycine in the absence of ammonia, in a solution neutralized with calcium hydroxide.

The conversion of monochloroacetic acid and glycine is monitored by the determination of the concentration of the chloride ion and iminodiacetic acid. The data of these measurements are shown in Figure 6, by plotting the relative concentration values against the reaction time.

As Figure 6. represents, upon the action of calcium hydroxide, formation of glycolic acid also proceeds in a parallel reaction, and this is demonstrated by the difference in the actual concentration of the chloride ion and iminodiacetic acid.

By comparison of the data of Figures 1 and 6 one can recognize that the useful (effective) conversion of monochloroacetic acid (which may be as high as 80-90% depending on the temperature) is more favourable when iminodiacetic acid is produced with the reaction of glycine and monochloroacetic acid. However, the effective conversion is decreased by the formation of

glycolic acid, which can be restrained with ammonia. But such an alternative would lead to the decrease of the production of iminodiacetic acid, as well, due to a concurrent reaction of monochloroacetic acid with ammonia, to result in the increase of the glycine-content of the reaction system.

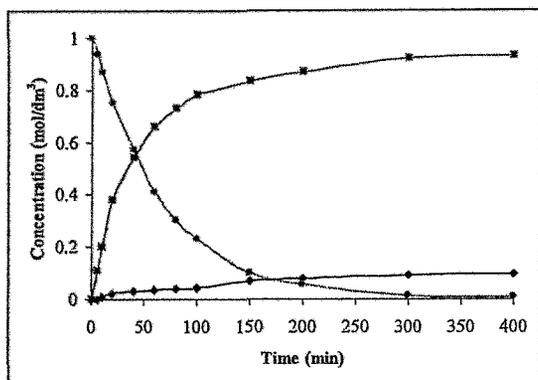


Fig. 6 Reaction of monochloroacetic acid with glycine under isolated conditions at 60 °C

(● monochloroacetic acid, ■ iminodiacetic acid, ◆ glycolic acid, at 60 °C)

The total conversion of monochloroacetic acid, including the effective conversion and hydrolysis of monochloroacetic acid, can be described with a pseudo-first order equation. Due to the hydration of glycine, the hydroxide ion concentration of the mixture is also increasing, which results in the increase of the rate of the hydrolysis of monochloroacetic acid, as well.

In Figure 7 the logarithm of the relative concentration values of monochloroacetic acid versus time is depicted. The roughly linear relation suggests that the transformation of monochloroacetic acid is of pseudo-first order, and that the dependence of the virtual rate constants on the temperature can be given by Eq. 10.

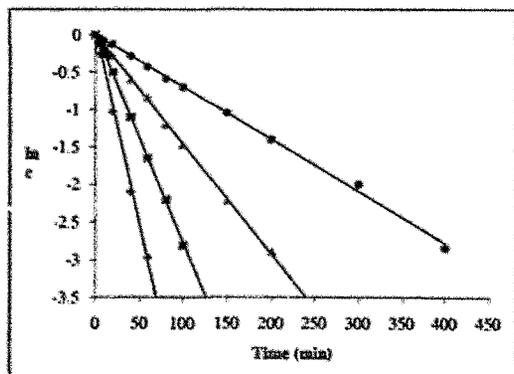


Fig. 7 Logarithm of the relative concentration of monochloroacetic acid versus time

(● 40, ▲ 50, ■ 60, ◆ 70 °C)

$$k_1 = 2.924 \cdot 10^7 \cdot \exp\left(-\frac{6921}{T}\right) \quad (10)$$

The reciprocal of the concentration of glycine (which is equal, with the opposite sign, with the change of the iminodiacetic acid concentration) as a function of the reaction time is shown in Figure 8.

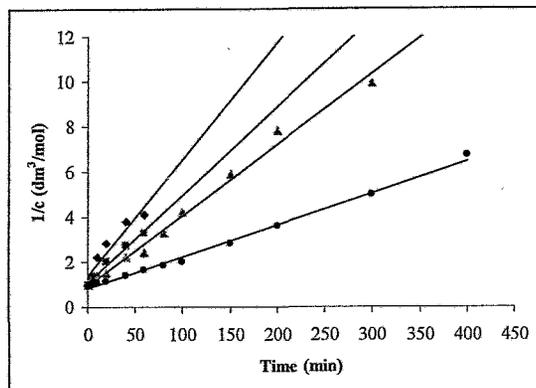


Fig. 8 Reciprocal of the concentration of iminodiacetic acid versus time.

(● 40, ▲ 50, ■ 60, ◆ 70 °C)

The obtained linear relation indicates a second order reaction, so that iminodiacetic acid is produced in a second order process. The dependence of the rate constant on the temperature can be approached by the k_{21} Arrhenius equation Eq. 11.

$$k_{21} = 3.523 \cdot 10^6 \cdot \exp\left(-\frac{6921}{T}\right) \quad (11)$$

The difference between the total and effective (useful) conversion of monochloroacetic acid comes from the production of glycolic acid, and thus the relative concentration of glycolic acid can be directly calculated.

The rate constant values k_{3B} , measured for the formation of glycolic acid, were in good agreement with the calculated rate constant values k_{31} on the basis of the reaction of glycine with monochloroacetic acid.

In Table 3 the apparent rate constants of the reactions carried out in the isolated chemical process are summarized.

Table 3 Apparent rate constants of the isolated reaction

T [°C]	k_1 [min ⁻¹]	k_{21} [dm ³ min ⁻¹ mol ⁻¹]	k_{31} [min ⁻¹]
40	$7.302 \cdot 10^{-3}$	$1.285 \cdot 10^{-2}$	-
50	$14.48 \cdot 10^{-3}$	$2.846 \cdot 10^{-2}$	$2.54 \cdot 10^{-4}$
60	$27.55 \cdot 10^{-3}$	$4.243 \cdot 10^{-2}$	$7.65 \cdot 10^{-4}$
70	$50.50 \cdot 10^{-3}$	$7.369 \cdot 10^{-2}$	$27.70 \cdot 10^{-4}$

Conclusion

During our work, inspection of the reaction system was carried out. In our working hypothesis we supposed that in the manufacturing system, consisting of monochloroacetic acid, ammonia, calcium hydroxide and water, concurrent consecutive, competitive reactions proceeded. We proved that the rate of the formation of nitriloacetic acid is immeasurably low. For monitoring the other three basic reactions, three key-components were selected, and analytical methods were elaborated for their determinations. The apparent rate constants of the processes were calculated from the concentrations of the key-components.

Comparison of the rate constants shows that the rate-determining step of the brutto conversion is the formation of iminodiacetic acid, and in agreement with the data of the measurements, a considerable amount of glycine is present.

Our important recognition is that glycine, produced together with the desired iminodiacetic acid, can be converted with monochloroacetic acid to iminodiacetic acid after removal of the excess of ammonia from the reaction mixture. During this latter process, the previously produced crop of iminodiacetic acid did not decompose.

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REFERENCES

1. U.S. Pat. 3,153,668 (1959)
2. U.S. Pat. 3,812,434 (1974)
3. Japan Pat. 71 40,611 (1971)
4. Japan Pat 76 19,718 (1976)
5. U.S. Pat. 3,904,668 (1978)
6. German Pat. 2,613,994 (1960)
7. German Pat. 2,527,120 (1966)
8. U.S. Pat. 3,842,081(1977)
9. SABORO T.: Bull. Chem. Research. Inst., Tohoku Univ. 1951, 1, 97-100
10. French Pat. 1,554,236 (1967)
11. PERKIN A.G. and DUPPA R.M.: Ann., 1853, 108
12. Orten J.M. and HILL M.: J. Am. Chem. Soc., 1931, 53, 2797
13. TOBIE W.C. AND AYRES G.B.: J. Am. Chem. Soc., 1942, 64, 725
14. DÉVÉNYI T.: Hung. Sci. Inst., 30, 1974