The effect of water on synthesis of triacetonamine from acetonine in acetone

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The effect of water on synthesis of 2,2,6,6-tetramethyl-4-piperidone (triacetonamine) from 2,2,4,6,6-pentamethyl-1,2,5,6-tetrahydropyrimidine (acetonine) in acetone under catalysis of acetic acid has been investigated. The results obtained indicate a considerable effect of water on selectivity of synthesis of triacetonamine from acetonine. The selectivity in a practically water-free medium was found to be more than 100 %. With the increasing amount of water in the reaction mixture at the outset of reaction the selectivity decreased. At the mole ratio $n(H_2O)/n(\text{acetonine}) = 3:1$ only 47 % selectivity was achieved, the reaction was shifted to formation of acetone and the amounts of by-products decreased. The possible sequence of reactions and the role of 4-amino-4-methyl-2-pentanone (diacetonamine), formed on decomposition of acetonine, are discussed.

В работе исследуется влияние воды на синтез 2,2,6,6-тетраметил-4- -пиперидона (триацетонамина) из 2,2,4,6,6-пентаметил-1,2,5,6-тетрагид-ропиримидина (ацетонина) в условиях катализа уксусной кислотой в ацетоне. Из полученных результатов следует, что вода сильно влияет на селективность синтеза триацетонамина из ацетонина. В практически безводной среде селективность более чем 100 %-на. С увеличением количества воды в реакционной системе в начале реакции селективность падает. При мольном отношении $n(H_2O)/n(\text{ацетонин}) = 3:1$ она представляет лишь 47 %, реакция сдвигается в сторону образования ацетона, количество побочных продуктов уменьшается. Обсуждается вероятный ход реакций и роль 4-амино-4-метил-2-пентанона (диацетонамина), который образуется при разложении ацетонина.

2,2,6,6-Tetramethyl-4-piperidone (triacetonamine, *I*) is an important starting compound in synthesis of polymer stabilizers, antioxidants, inhibitors of polymerization, free nitroxyl radicals, and also in preparation of some medicines and biologically active preparations.

The compound *I* can be prepared from 2,2,4,6,6-pentamethyl-1,2,5,6-tetrahydropyrimidine (acetonine *II*) and the latter by direct condensation of water-free

ammonia with acetone in the yield > 90 % [1—4]. The conversion of *II* to *I* is usually catalyzed with Lewis acids and is provided either in the presence of organic solvents or without them in water or water-free media [5—8]. The role of water in this reaction has not been explained so far, therefore, in the present work we focussed our attention to this problem.

Experimental

Chemicals

The compound *II* was prepared by condensation of acetone with ammonia [2]. The monohydrate was crystallized from diethyl ether. M.p. = 40—42 °C, $w(II) = 89.2$ % (GLC), $w(H_2O) = 10.5$ % (theor. 10.4 %). The compound *II* containing minimum water (water-free) was prepared by azeotropic distillation of water from the monohydrate and rectification. B.p. = 55—56 °C at 1300 Pa, $w(II) = 99.7$ % (GLC), $w(H_2O) = 0.12$ %.

Acetone and acetic acid (99 %) were of anal. grade.

Working procedure

Into a 500 cm³ three-necked round-bottom flask provided with a magnetic stirrer and reflux water-free *II* (92.6 g; 0.6 mol) or monohydrate of *II* (103.4 g), acetone (174.2 g; 3.0 mol), and acetic acid (18 g; 0.3 mol) were added. In the experiments with higher concentrations of water than corresponded to the monohydrate of *II* the appropriate amount of distilled water was added. The reaction mixture was refluxed at continuous stirring for 10 h. The water content of the samples was established by the method according to Fischer. The contents of *I*, *II*, 4-amino-4-methyl-2-pentanone (diacetonamine, *III*), acetone, and other by-products were established by gas—liquid chromatography (GLC) with a CHROM 41 apparatus on a column (1.2 m × 3.0 mm) of 10 % Carbowax 1500 on Chromaton N with 2 % KOH; detector FID, $t = 200$ °C; injection: $t = 130$ °C; column temperature: from 60 °C to 160 °C at the heating rate = 10 °C/min.

The selectivity of the reaction with regard to the formation of *I* (S_t) and conversion of *II* (C_r) were calculated.

$$S_t = \frac{n_v}{n_n} \cdot 100 \text{ mole } \% ; \qquad C_{II} = \frac{n_p}{n_n} \cdot 100 \text{ mole } \%$$

n_v = the amount of *I* formed,
n_n = the starting amount of *II*,
n_p = the amount of *II* converted.

Results and discussion

The compound *I* was synthesized from *II* according to the modified procedure by *Brandbury* [2]. The results obtained about the effect of water on the selectivity

of *I* and about conversion of *II* are summarized in Table 1 (reaction time 10 h). In assessing the results it is necessary to realize that the reaction was carried out in acetone. Acetone may, at the given reaction conditions, react with ammonia, arising from *II* on decomposition, to give *I* as the final product. Acetone was used with the aim to increase the selectivity of the reaction, not as an inert solvent. In ideal case the selectivity and yield of *I* might be 200 % when calculated to *II*. However, the results are related to formation of 1 mol *I* from 1 mol *II*.

Table 1

Selectivity, conversion, yield, and sum of by-products (without acetone) after 10 h reaction in dependence on the starting amount of water

$n(H_2O)$/mol	S_I/mole %	C_{II}/mole %	Yield/mole %	By-product mole %
0	116.0	96.0	111.0	19.0
1	97.2	99.2	96.4	10.1
2	80.0	99.5	79.6	7.0
3	47.2	99.9	47.1	5.1

The results obtained point to significant role of water in conversion of *II* to *I* catalyzed by acetic acid (Fig. 1). The selectivity of the reaction decreased with increasing concentration of water. The highest selectivity (116 %) was achieved in the case when the reaction started with minimum water content (given by the content in water-free *II*, acetone, and acetic acid). At the mole ratio $n(H_2O)/$ $/n$(acetonine) $= 3:1$ the selectivity decreased to 47 %. Conversion of *II* depended
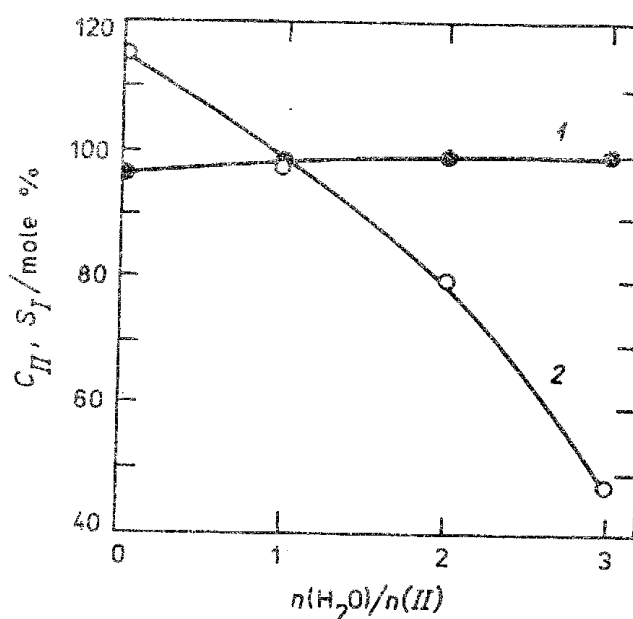

Fig. 1. Conversion *C* of *II* and selectivity *S* of the reaction to *I* in dependence on the starting amount of water (mole ratio $n(H_2O)/n(II)$) after 10 h reaction.
1. Conversion; *2.* selectivity.

only a little on water concentration and after 10 h was almost 100 % in the range of 0 to 3 mol of water per 1 mol of II (Figs. 1 and 5). However, simultaneously with the increasing water concentration less by-products were formed (Table 1, Fig. 2).
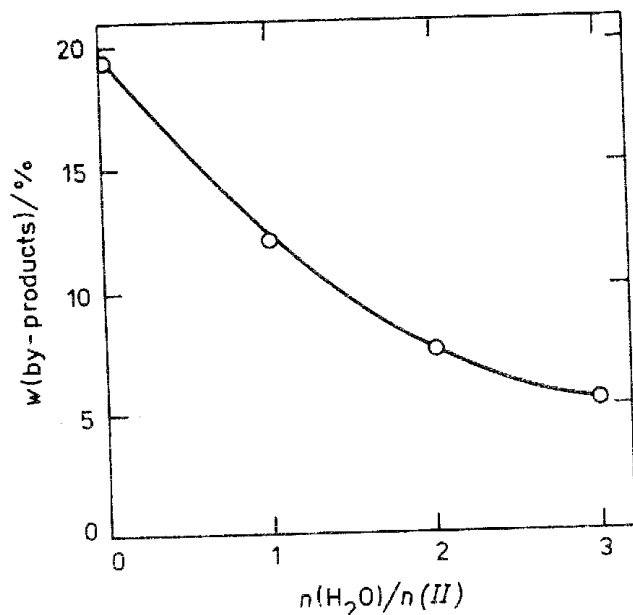

Fig. 2. Mass fraction of the formed by-products (except acetone) in dependence on the starting amount of water after 10 h reaction.

It is connected with hydrolysis of condensation products proceeding in aqueous medium to give acetone as the final product (the formed acetone was not included in the sum of by-products). On the contrary, in water-free medium condensation reactions of acetone proceeded, affording besides I also by-products and water. The amount of acetone in the reaction mixture decreased inversely with formation of water (Table 2).

Table 2

Increase and/or decrease of acetone and water in the reaction mixture after 10 h reaction in dependence on the starting amount of water

Starting amounts of acetone and water in the reaction mixture		Final amounts of acetone and water in the reaction mixture and their differences from the starting amounts			
$\dfrac{n(\text{acetone})}{\text{mol}}$	$\dfrac{n(\text{H}_2\text{O})}{\text{mol}}$	$\dfrac{n(\text{acetone})}{\text{mol}}$	$\dfrac{\Delta n(\text{acetone})}{\text{mol}}$	$\dfrac{n(\text{H}_2\text{O})}{\text{mol}}$	$\dfrac{\Delta n(\text{H}_2\text{O})}{\text{mol}}$
5	0	2.5	−2.5	1.2	+1.2
5	1	4.2	−0.8	1.5	+0.5
5	2	5.2	+0.2	1.7	−0.3
5	3	6.0	+1.0	2.3	−0.7

To obtain a better picture about the course of the reaction, other experiments have been provided with 1 and 3 mol of water per 1 mol of II where the reaction progress was followed in time dependence. The reason for choosing these two concentrations was the fact that in the preparation of II 3 mol of water were formed per 1 mol of II and that on purification the compound II crystallized as a monohydrate, i.e. from practical point of view only these two concentrations of water are significant. As can be seen in Figs. 3 and 4, the reaction was practically
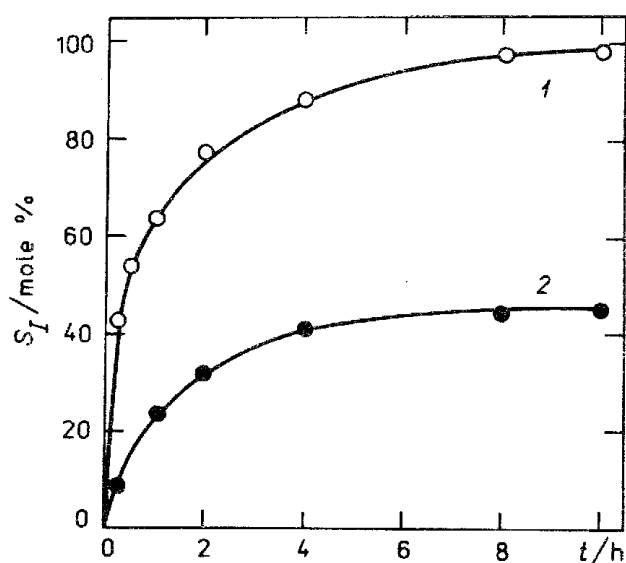
Fig. 3. Selectivity S of the reaction to I in time dependence.
1. Starting ratio $n(H_2O)/n(II) = 1:1$;
2. starting ratio $n(H_2O)/n(II) = 3:1$.
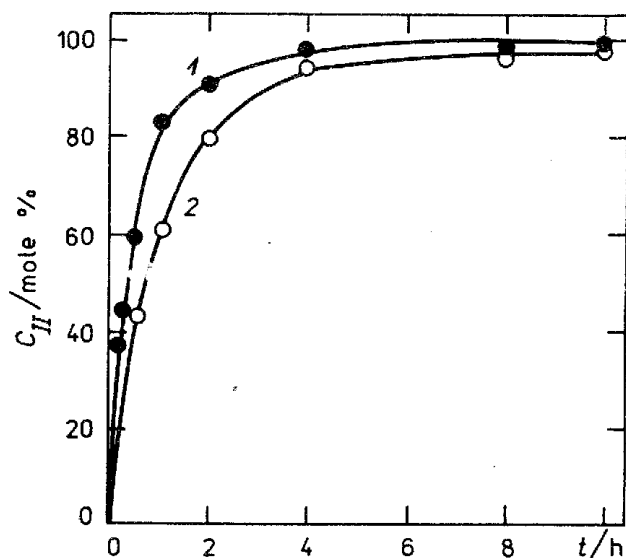
Fig. 4. Conversion C of II in time dependence.
1. Starting ratio $n(H_2O)/n(II) = 3:1$;
2. starting ratio $n(H_2O)/n(II) = 1:1$.

complete within 8 to 10 h and the concentrations of I, II, and other components of the reaction mixture were close to equilibrium concentration (Figs. 5 and 6). Decomposition of II was more rapid at higher water concentration (Figs. 5 and 6).
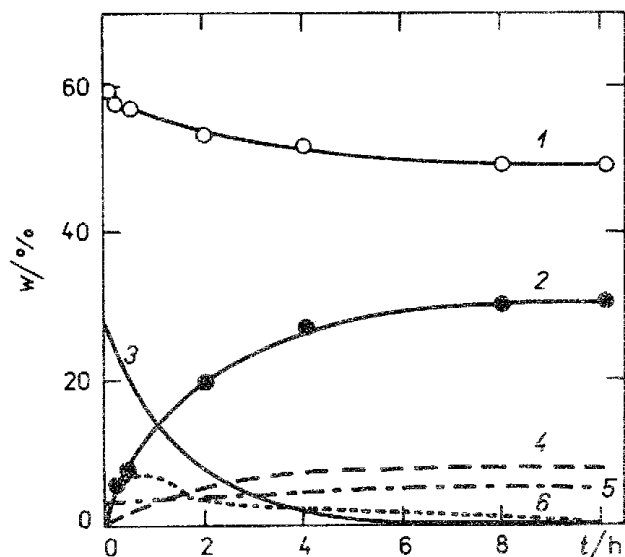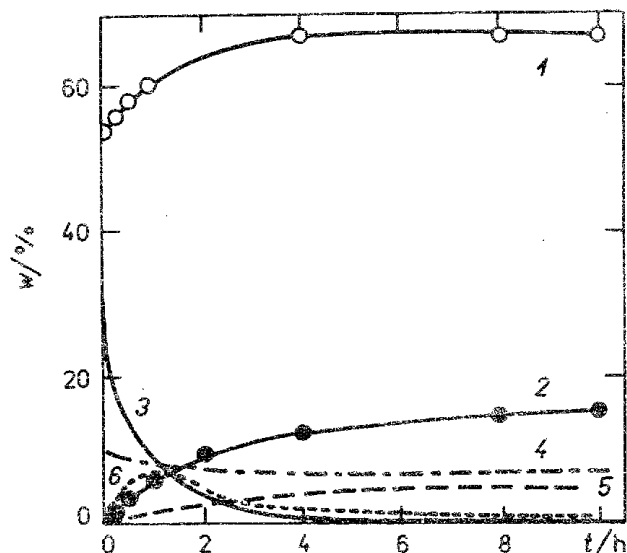
Fig. 5. Mass fraction of the reaction mixture in dependence on the reaction time at the starting ratio $n(H_2O)/n(II) = 1:1$.
1. Acetone ; *2. I* ; *3. II* ; *4.* by-products ; *5.* water ; *6. III*.

*Fig. 6.* Mass fraction of the reaction mixture in dependence on the reaction time at the starting ratio $n(H_2O)/n(II) = 3:1$.
1. Acetone ; *2. I* ; *3. II* ; *4.* by-products ; *5.* water ; *6. III*.

When the starting ratio $n(H_2O)/n(II) = 1:1$, water was formed, when it was $3:1$, water was consumed (Fig. 7). Figs. 5 and 6 illustrate that decomposition of *II* was accompanied by formation of *III* (Scheme 1). This is confirmed also by decomposition of 2,6-dipentamethylene-4,5-tetramethylene-1,2,5,6-tetrahydropyrimidine (condensation product of cyclohexanone and ammonia — corresponds to *II*). On decomposition of this product 2-(1-aminocyclohexyl)-cyclohexanone (corresponding to *III*), cyclohexanone, and ammonia were formed [9]. The compound *III* can react with acetone to give *I* (Scheme 1), mainly in shortage of water in the reaction medium. It is evidenced also by condensation reactions of *III* with carbonyl compounds (acetone, cyclopentanone, cyclohexanone, *I*) resulting in the appropriate piperidones [6]. The authors in [10] took *III* for an intermediate in the
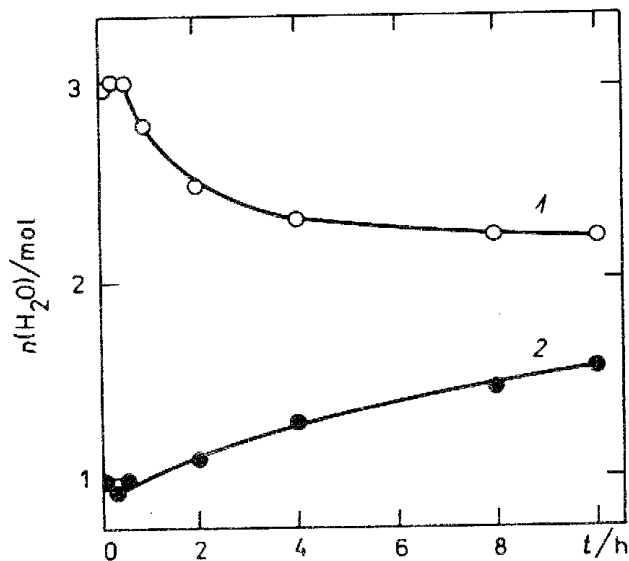
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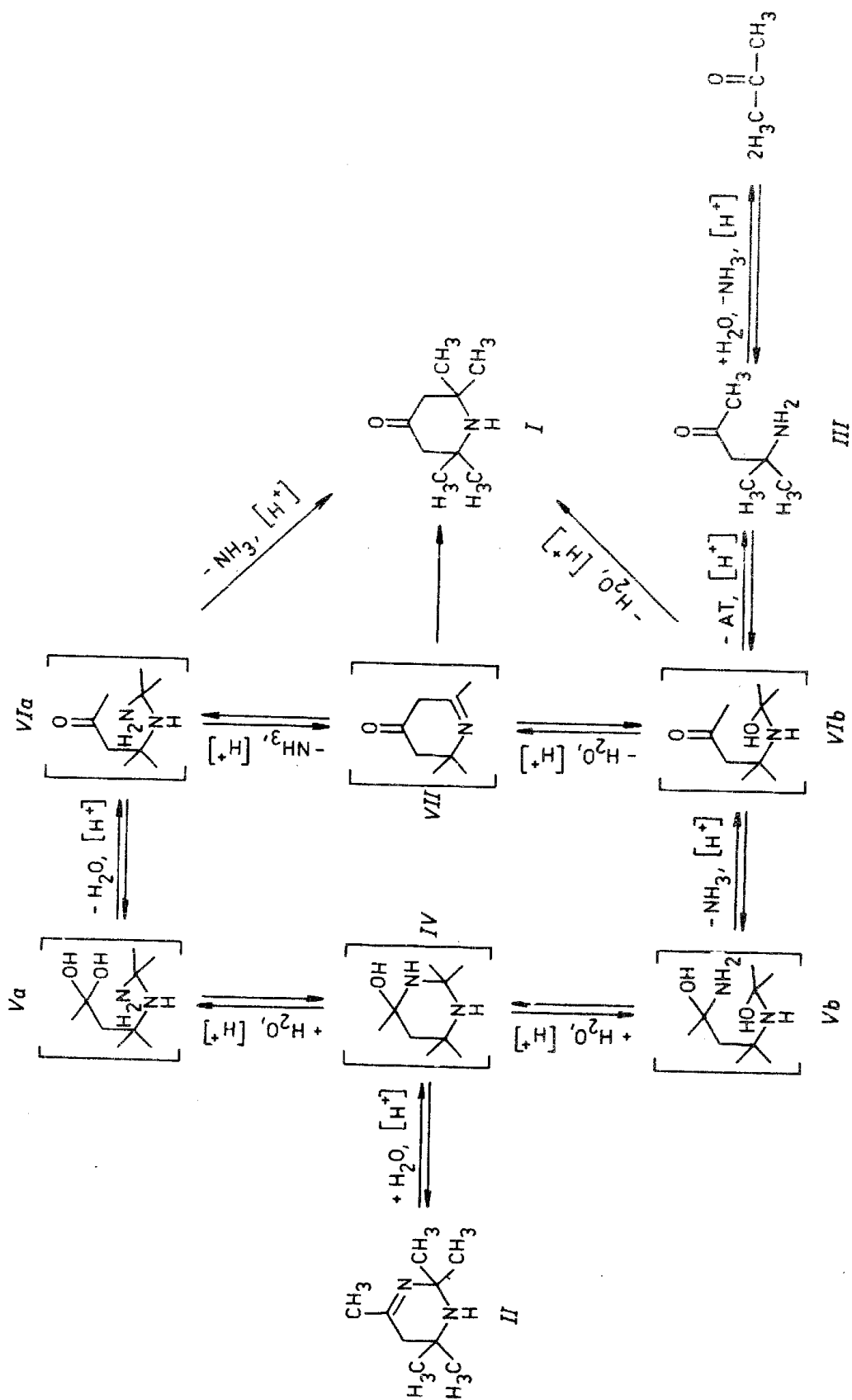
Scheme 1

Fig. 7. Decrease and increase of $n(H_2O)$ in the reaction mixture in dependence on the reaction time.
1. Starting ratio $n(H_2O)/n(II) = 3:1$;
2. starting ratio $nH_2O)/n(II) = 1:1$.

synthesis mentioned above. In the presence of excess water *III* decomposes to acetone and ammonia (Scheme 1).

Excess amount of acetone influenced the yield of the reaction not only by the reaction with ammonia but also by shifting the reaction equilibrium in favour of *I* (excess acetone shifts the equilibrium between *VIb* and *III* in favour of *VIb*, Scheme 1). On the contrary, water shifted the reaction equilibrium in favour of *III* or even of acetone.

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