

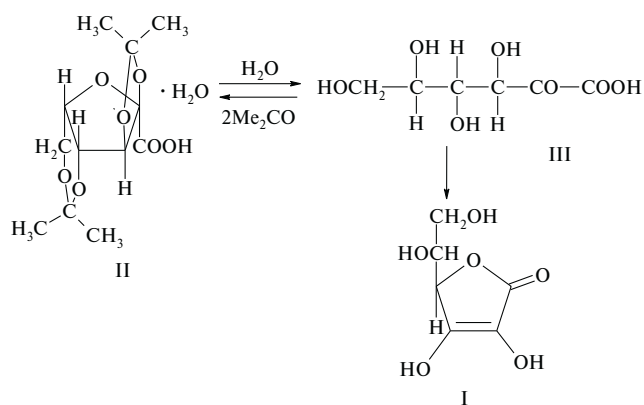
SYNTHESIS OF ASCORBIC ACID FROM DIACETONE-2-KETO-L-GULONIC ACID

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The commercial production of ascorbic acid (vitamin C) is based on the method proposed in 1934 by Reichstein and Grussner [1]. This process, with insignificant modifications, is still used for the synthesis of ascorbic acid (I) throughout the world. In the final stage of this process, diacetone-2-keto-*L*-gulonic acid hydrate (II) is converted into I via 2-keto-*L*-gulonic acid (III) in the presence of an acid catalyst. The mechanism of this conversion is unknown and the optimum conditions were selected empirically.



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The conversion of diacetoneketogulonic acid II into ascorbic acid I includes two main stages. First, the protective isopropylidene groups are detached with the formation of ketogulonic acid III and two acetone molecules. The complete hydrolysis of acid II requires two water molecules. One of these is taken from the initial hydrate II and another is liberated upon the cyclization of acid III into ascorbic acid.

We have developed a method for obtaining I from II in toluene in the presence of concentrated hydrochloric acid as a catalyst. Important factors determining the yield of I are the hydrogen chloride concentration and the process duration. An increase in the concentration of HCl leads to an increase in the yield of I, which reaches a maximum for $[HCl] = 5.75 \times 10^{-2}$ mole/liter (Table 1) and then decreases, probably because of decomposition of I in the strongly acidic medium. Table 2 illustrates the dependence of the yield of I on the duration of reaction mixture heating. Here, maximum yield is reached after heating for 5.5 h, and then the yield decreases somewhat.

Since the conversion of II into III is reversible, removal of acetone from the reaction zone favors a shift of the equilibrium toward the formation of III. As a result, the yield of I may reach up to 94%. Table 3 illustrates the dependence of the ascorbic acid yield on the reaction duration upon acetone removal. As seen, a maximum is reached after heating for 6 h, after which the yield of I decreases. This pattern is analogous to that observed without acetone removal, which is ev-

TABLE 1. Dependence of the Ascorbic Acid Yield on the HCl Concentration (Temperature, 70°C; Process Duration, 5 h)

$[HCl] \times 10^{-2}$, mole/liter	Yield, %
4.00	73
4.85	77.5
5.125	78.5
5.425	81
5.75	83
6.125	77.5

TABLE 2. Dependence of the Ascorbic Acid Yield on the Duration of Heating at 70°C (HCl Concentration, 0.05 mole/liter)

Process duration, h	Yield, %
2.0	53
3.5	70
5.0	72.5
5.5	75
6.5	72.5

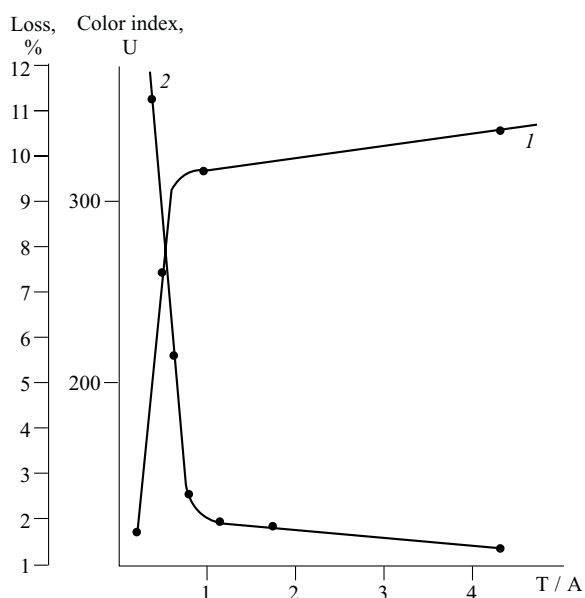


Fig. 1. Plots of (1) solution color index and (2) product I loss versus the T/A ratio in the mixture used to wash the TAA precipitate.

idence that the stage determining the target product yield is the stage of compound III cyclization into I.

The final purpose of the commercial synthesis of I is obtaining medicinal ascorbic acid (MAA). The conversion of ascorbic acid from technical (TAA) to medicinal (MAA) grade is an important final stage of the whole commercial process. TAA precipitated upon cooling of the reaction mixture is filtered, washed with a toluene – acetone (T – A) mixture, and dissolved in water. This solution is used for obtaining MAA. An important factor in the TAA to MAA conversion is the color of this aqueous TAA solution: for successful

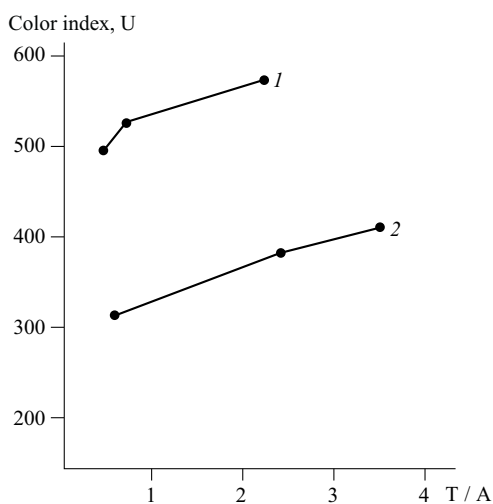


Fig. 2. Plots of the final solution color index versus the T/A ratio in the mixture used to wash an aqueous TAA solution with the initial color index of (1) 600 U and (2) 450 U.

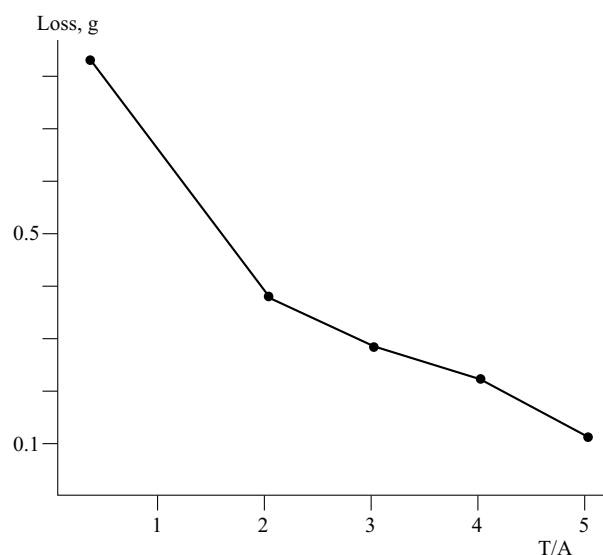


Fig. 3. Plot of product I loss versus the T/A ratio in the mixture used to wash the aqueous TAA solution.

conversion, the color index of the TAA solution must not exceed 300 units (U).

In the stage of TAA washing, the product is partly lost as a result of dissolution in the washing solvent mixture. An increase in the acetone proportion decreases the color index, but increases the TAA loss. The optimum T/A ratio ensuring a sufficiently low solution coloration and small TAA losses is 1 : 2 (Fig. 1).

We have developed a method for obtaining MAA without isolating TAA. For this purpose, the reaction mass upon heating is treated with water, after which the aqueous layer is washed with a T – A mixture and MAA is isolated. Treatment of the reaction mass with water yields an aqueous solution of I with a color index within 400 – 600 U, depending on the quality of initial II and reaction conditions. The color index of the aqueous solution obtained upon washing depends on the T/A ratio in the washing mixture (Fig. 2): the index drops when the T/A ratio decreases from 3.0 to 0.33. However, a TAA solution suitable for MAA isolation (i.e., possessing a color index below 300 U) can be obtained only

TABLE 3. Dependence of the Ascorbic Acid Yield on the Duration of Heating upon Acetone Removal (Temperature, 70°C; [HCl] = 0.05 mole/liter)

Process duration, h	Yield, %
3	72.5
4	82
5	88
6	94
7	92
8	72

provided that the initial TAA solution possesses a color index of 400 U or below. Solutions with a higher initial coloration should be preliminarily clarified by treating with activated charcoal [2].

Figure 3 shows a plot of the TAA loss from solution versus the T/A ratio. A comparison of the product loss and the TAA solution color level reached upon washing with a T – A mixture leads to the conclusion that the optimum T/A ratio is 1 : 2.

EXPERIMENTAL PART

Technical ascorbic acid (TAA). Method A. To a mixture of 50 g (0.17 mmole) of diacetoneketogulonic acid hydrate (II) and 50 ml toluene is added 5.4 ml hydrochloric acid ($d = 1.165$ g/ml) and the mixture is heated for 5 h at 70°C. Upon cooling, the precipitate is filtered and dried to obtain 24.85 g of TAA.

Method B. To 50 g (0.17 mmole) of diacetoneketogulonic acid hydrate (II) melted on heating to 70°C is added 3.5 ml of hydrochloric acid ($d = 1.165$ g/ml). The mixture of acetone, hydrogen chloride, and water (about 10 ml) is distilled off. To the residue was added 50 ml of toluene and

3.5 ml of hydrochloric acid and the mixture was heated for 6 h at 70°C. Upon cooling, the precipitate is filtered and dried to obtain 24.14 g of TAA.

Medicinal ascorbic acid (MAA). Method A. A solution of 20 g of TAA in distilled water (color index, 350 U) is washed with 20 ml of a toluene – acetone mixture (1 : 2). The aqueous layer is separated and analyzed for color and ascorbic acid content: color index, 276 U; content of I, 19.1 g.

Method B. The reaction mass with TAA obtained by heating 50 g of II is cooled to 50°C. To this mass is added 20 ml of distilled water, and the aqueous layer is separated and analyzed for color and ascorbic acid content (for example: color index, 400 U; content of I, 16.0 g). Washing the solution with 40 ml of a toluene – acetone mixture (1 : 2) yields a MAA solution with a color index of 300 U, containing 15.2 g of ascorbic acid.

REFERENCES

1. T. Reichstein and A. Grussner, *Helv. Chim. Acta*, **17**, 311 (1934).
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