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PROCESS OF PRODUCING NICOTINIC ACID

Adolph Zimmerli, Highland Park, N. J.

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The present invention relates to a process for producing nicotinic acid as the end product, but contemplates the formation of an intermediate product as the first phase of the treatment, which intermediate product constitutes the base material from which the end product is ultimately derived.

More particularly my invention relates to a process for producing nicotinic acid by the treatment of 5,7-dinitro-8-quinolinol, with nitric acid. The first phase of the treatment results in the production of quinolinic acid nitrate as an intermediate product, from which quinolinic acid may or may not be isolated, but which in either case serves as the base material for the production of nicotinic acid therefrom. From a chemical standpoint, it is immaterial whether the main process is carried out to its completion as a continuous process without interruption, or interrupted and subsequently continued by using the intermediate product as a base for the direct production of nicotinic acid, by merely utilizing a latter phase of the complete process as a separate process. In other words my complete process comprises several phases which has as the initial phase the production of quinolinic acid nitrate, by the action of nitric acid on 5,7-dinitro-8-quinolinol, as an intermediate product which latter may or may not be treated to isolate quinolinic acid therefrom. From this intermediate product nicotinic acid is produced as a continuous or separate phase of the entire process.

An object of the invention is the preparation of nicotinic acid cheaply, safely and in large quantities. A special object is to provide a process for producing nicotinic acid from a starting material that is readily available and renders a good yield.

Another object of the invention is the provision of a process for the production of nicotinic acid comprising several phases or steps, the initial phase resulting in the formation of an intermediate product which may or may not be isolated and constitutes the base from which nicotinic acid may be derived by practicing the complete process without interruption or in its separate phases.

Other objects of the invention will become manifest from the examples following hereinafter.

Nicotinic acid has been prepared according to the prior art from pyridines, substituted in the 3-position, by substitution or oxidation, or from quinolinic acid by the splitting off of CO_2 by heat or acids.

Quinolinic acid in turn, has been produced from numerous compounds of the quinoline series. The oxidation of unsubstituted quinoline gives very poor yields because the pyridine ring is as easily destroyed as the benzene ring.

Derivatives of quinoline, substituted in the benzene ring are attacked by acidic oxidizing agents more easily, leading to the destruction of the benzene ring while the pyridine ring remains intact. The oxidation of 8-quinoline-sulfonic acid, 8-quinolinol, and alizarineindigoblue has been described in the literature.

All of these methods are either using very expensive materials or materials available only in limited amounts, give low yields or proceed with extreme violence. For example, explosions have occurred when quinolinol was oxidized with nitric acid, the reaction being so strongly exothermic that it was impossible to keep the temperature within bounds, especially when working with batches of commercial size.

For successful operation on a large scale it was necessary to find a compound that could be oxidized safely, cheaply and give a good yield of nicotinic acid. My search for a quinoline derivative answering these specifications finally led me to the use of 5,7-dinitro-8-quinolinol as the starting material.

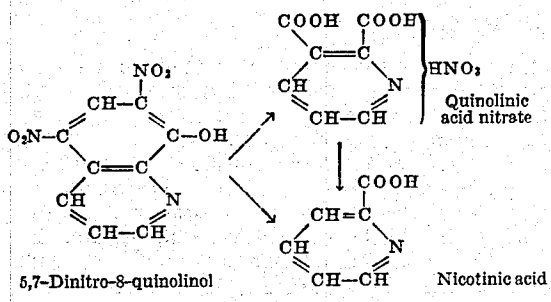
5,7-dinitro-8-quinolinol may be prepared in very good yield by the methods generally used for the nitration of phenols and naphthols. However, as prepared heretofore by workers of the prior art, there is no unanimity as to its properties. I have found that this could largely be corrected by a method of purification which consists in the recrystallization of the crude product as obtained by nitration of 8-quinolinol, from denaturing grade pyridine in which it is soluble at the boiling point to the extent of 13 parts in 100 parts of solvent. On cooling it crystallizes in thin elongated yellow leaflets, containing solvent of crystallization which evaporates on drying, leaving 5,7-dinitro-8-quinolinol as a yellow powder which decomposes suddenly without melting when heated to 320° C.

I have discovered that 5,7-dinitro-8-quinolinol offers enough resistance to oxidation so that it is attacked comparatively slowly by nitric acid of proper concentration. The reaction takes place stepwise and may be easily controlled by regulation of the concentration and temperature. It can be stopped, for example, when most of it has been converted into quinolinic acid nitrate, or it can be carried through to nicotinic acid without the isolation of an intermediate compound, such as quinolinic acid.

From 2 to 4 parts of 100% nitric acid or a corresponding amount of weaker acid are needed to complete the reaction. It proceeds slowly with very dilute acid, reaches a convenient speed with an acid of from 40% to 70% strength and has to be watched carefully if stronger acid is used.

The nitrous oxides formed by the reduction of the nitric acid may be reoxidized, absorbed and concentrated in known manner and used over and over so that only the comparatively small unavoidable loss through incomplete absorption has to be compensated by fresh nitric acid, thereby reducing the cost of the oxidizing agent to a small item.

My complete process in its major phases may be represented by the structure



5,7-Dinitro-8-quinolinol Nicotinic acid

In practicing my invention I may suspend crystals of 5,7-dinitro-8-quinolinol in dilute nitric acid. By proper control of acid concentration and temperature, hereinafter more fully illustrated by specific examples, I first produce quinolinic acid nitrate as an intermediate product, from which quinolinic acid may be isolated by the addition of water, but preferably is not isolated so as to allow the uninterrupted carrying out of the complete process to the end product.

In this latter phase I heat the quinolinic acid nitrate either alone or with more nitric acid to higher temperatures.

The invention, although not limited thereto, will be further illustrated by the following specific examples, the parts being by weight:

Example 1.—Nicotinic acid prepared directly, i. e., without isolation step

500 parts 5,7-dinitro-8-quinolinol are added gradually over a period of from 6 to 8 hours to 1800 parts 60% nitric acid at 100° C. After all the 5,7-dinitro-8-quinolinol has been added the temperature is raised gradually to 240° C. over an 8 hour period. At the beginning water and nitrous oxides distill over, then nitrous oxides and carbon dioxide while the mass thickens, then becomes liquid again. As soon as a uniform melt has been formed the mass is poured into shallow trays where it solidifies. The yield of crude nicotinic acid is from 220 to 260 parts.

Example 2.—Nicotinic acid prepared directly, i. e., without isolation step

The crude nitration product from quinolinol, consisting of a suspension of 5,7-dinitro-8-quinolinol in dilute nitric acid, is heated to boiling. The distilling water is replaced by nitric acid of 68% strength until all the 5,7-dinitro-8-quinolinol has disappeared, keeping the volume constant to this point. The heating and concentration is then continued as described in Example 1. The crude nicotinic acid, having a purity of 85–95% is then purified by sublimation or crystallization or a combination of both.

Example 3.—Quinolinic acid nitrate isolated

A suspension of 500 parts 5,7-dinitro-8-quinolinol in 500 parts nitric acid of 40% strength is heated to boiling. While refluxing, 900 parts 98% nitric acid are added gradually at such a speed that there is continuous evolution of nitrous fumes without ever allowing the reaction to become violent. After all the acid has been added the refluxing is continued until the evolution of nitrous fumes practically ceases. The solution is then emptied into a shallow steam heated kettle and the heating continued until the liquid solidifies into a cake of quinolinic acid nitrate. After cooling 1000 parts water are added and the suspension of quinolinic acid filtered off.

Example 4.—Nicotinic acid, as end product, including isolation step

500 parts 5,7-dinitro-8-quinolinol are added to 4500 parts nitric acid of 30% strength. Water and nitrous oxides are distilled until a clear solution of quinolinic acid nitrate is formed. This solution is then poured slowly into a vessel being kept at 200° C. to 240° C. After all has been added, the heating is continued until gassing ceases. After cooling, the nicotinic acid, weighing about 220 parts, is broken up and purified in any known manner.

It will be understood that the various examples herein set forth are given as merely illustrative of the various phases in which my invention may be practiced without departing from the spirit thereof. The invention in its broadest aspects comprises several phases or series of steps, the first phase resulting in the production of a substance which may be regarded as an intermediate product. Although my process permits of the isolation of such intermediate product, it is concerned primarily as affording a continuous process for producing the desired end product, and I wish protection of the process, practiced with or without interruption, as defined by the appended claims.

What is claimed is:

1. The process of producing quinolinic acid nitrate comprising adding in the absence of hydrochloric acid approximately 500 parts 5, 7, dinitro-8-quinolinol over a period of from 6 to 8 hours to about 1800 parts nitric acid of 60 percent strength at 100 degrees centigrade and evaporating to dryness.

2. The process of producing nicotinic acid, comprising adding in the absence of hydrochloric acid approximately 500 parts 5, 7, dinitro-8-quinolinol over a period of about 6 hours to about 1800 parts nitric acid of 60 percent strength at 100 degrees centigrades, then gradually heating the mixture in the absence of hydrochloric acid over a period of about 8 hours to 240 degrees centigrade until the evolution of nitrous fumes and carbon dioxide ceases.

3. The process of producing nicotinic acid, comprising heating 5,7-dinitro-8-quinolinol with nitric acid only of from 30 to 100 per cent strength until substantial quantities of nitrous oxide fumes are given off, this first phase of the treatment resulting in the production of quinolinic acid nitrate as an intermediate product, and continuing the treatment without isolating quinolinic acid by heating the quinolinic acid nitrate to 200–240 degrees centigrade until decarboxylation and denitration occurs with the evolution of carbon dioxide and nitrous oxide fumes, and recovering the nicotinic acid.

4. The process of producing nicotinic acid comprising treating 5,7-dinitro-8-quinolinol in the absence of hydrochloric acid with from 3 to 6 parts nitric acid of about 65 per cent strength, heating to boiling, adding concentrated nitric acid, evaporating to dryness, and heating to 200 to 240 degrees centigrade until the solid remelts.

5. The process of forming quinolinic acid nitrate as an intermediate product in the production of nicotinic acid comprising treating 5,7-dinitro-8-quinolinol in the presence of nitric acid of from 30 to 100 per cent strength and in the absence of hydrochloric acid by heating to temperatures of from 100 to 120 degrees centigrade until substantial quantities of nitric oxide fumes are given off.

6. The process of producing nicotinic acid comprising boiling 5,7-dinitro-8-quinolinol only with nitric acid of from 30 to 100 per cent strength to form quinolinic acid nitrate and continuing the treatment by heating to 200 to 240 degrees centigrade to convert the quinolinic acid nitrate into nicotinic acid.

7. The process of producing nicotinic acid comprising treating 5,7-dinitro-8-quinolinol in the absence of hydrochloric acid with nitric acid of from 30 to 100 per cent strength, heating to a temperature of about 100 degrees centigrade until substantial quantities of nitrous oxide fumes are given off, thereafter raising the temperature to from 200 to 240 degrees centigrade until decarboxylation and denitration occurs with the evolution of carbon dioxide and nitrous oxide fumes, and recovering the nicotinic acid.

ADOLPH ZIMMERLI.