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2,843,598

PROCESS FOR PREPARING 3-PYRAZOLIDONES

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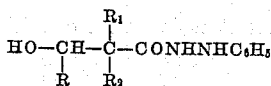
3 Claims. (Cl. 260—310)

This invention relates to a process for the preparation of 3-pyrazolidones and more particularly for the preparation of 1-phenyl-3-pyrazolidones.

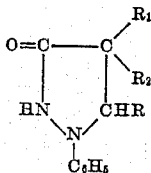
The Reynolds et al. U. S. Patent 2,743,279, granted April 24, 1956, described a process for the preparation of 3-pyrazolidones which includes heating a hydrazide such as *N*-β-hydroxypropio-*N'*-phenylhydrazide in an inert organic solvent having a boiling point of at least 110° C. in the presence of the "dehydration catalysts" hydrochloric acid, sulfuric acid, *p*-toluene sulfonic acid and methane sulfonic acid. The temperature of reaction was said to be critical.

I have discovered a process for preparing 3-pyrazolidones from hydrazides such as that mentioned above in higher yield and purity and which process may be carried out at relatively low temperatures of the order of less than 110° C. in the absence of organic solvent. In fact, when my process is carried out at elevated temperatures, inferior product results.

The process of my invention includes heating hydrazides, such as *N*-β-hydroxypropio-*N'*-phenylhydrazide, having the general formula



wherein R, R₁ and R₂ each represent hydrogen atoms or alkyl groups of from 1 to 4 carbon atoms such as methyl, ethyl, propyl and butyl groups, at a temperature below about 110° C. in the presence of phosphoric acid as a cyclodehydration agent to obtain 3-pyrazolidones having the general formula



One important advantage of my process compared to the process of the Reynolds et al. invention resides in the fact that appreciably higher yields of the 3-pyrazolidone compounds are obtained. For example, in the process of the patent Example 2, a 66 percent yield of 1-phenyl-3-pyrazolidone was obtained by heating *N*-β-hydroxypropio-*N'*-phenylhydrazide in xylene in the presence of *p*-toluene sulfonic acid. In the process of the present invention described in more detail hereinafter, when the same hydrazide is heated with phosphoric acid at temperatures below 110° C. yields of about 70 to 90 percent of the theoretical amount are readily obtainable and the product has such high purity that recrystallization is not necessary. Moreover, it has been found to be impossible to produce one of the products of the present invention

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1-phenyl-4,4-dimethyl-3-pyrazolidone by employing the hydrazide β-hydroxypivalylphenylhydrazide in the process of the patent without extensive decomposition setting in, whereas this same hydrazide readily yielded 1-phenyl-4,4-dimethyl-3-pyrazolidone when employed in the low-temperature process of the present invention.

The process of the invention can be carried out in numerous ways with some effect upon yield, although yield is maintained at a relatively high level. For example, when the hydrazides are heated in the absence of organic solvent in the presence of polyphosphoric acid as a cyclodehydration agent, the highest yields are obtained. When other phosphoric acids such as the usual 85 percent ortho-phosphoric acid are used in the process, the yields are somewhat lowered although the addition of concentrated sulfuric acid to the 85 percent phosphoric acid in an amount of the order of about 2 to 50 percent by volume preferably 2 to 25 percent by volume appreciably increases the yield. It will be noted that when the process of the invention is carried out using sulfuric acid alone in place of phosphoric acid, little if any 3-pyrazolidone compound is obtained.

The concentration of the hydrazide in the reaction mixture also has an effect upon yield; that is, the highest yields are obtained when from about 0.1 to 0.7 gram of the hydrazide are present per cc. of phosphoric acid used in the reaction mixture.

As will be apparent from the examples hereinafter, an inert organic solvent or diluent is not required in the reaction mixture, and best results are obtained in its absence.

As mentioned, the temperature for carrying out the reaction is critical insofar as the upper temperature limit is concerned, and satisfactory yields are obtained by carrying out the reaction at from about 60 to less than 110° C. At temperatures above about 110° C. product purity is adversely affected. Little product is obtained by allowing the reactants to stand at about 20° C. Reaction times of the order of 5 hours are suitable and 24 hours reaction time has little effect one way or another.

The following examples will serve to illustrate the process of my invention:

EXAMPLE 1

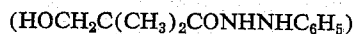
1-phenyl-3-pyrazolidone

Nine grams of *N*-β-hydroxypropio-*N'*-phenylhydrazide were added to 40 grams of polyphosphoric acid (115 percent H₃PO₄), and the mixture stirred while heating on a steam bath to 85° C. Heating and stirring was continued for 5 hours when the pale yellow mixture was diluted to 400 ml. volume with cold water. A white crystalline precipitate appeared, and was filtered off after one hour standing, washed with cold water, and dried. M. P. 120.5–121.5° C. Yield 6.4 g., 79% of theory.

EXAMPLE 2

4,4-dimethyl-1-phenyl-3-pyrazolidone

20.8 grams of β-hydroxypivalylphenyl hydrazide



(Bull. Soc. 31 124 (1904)) were added to 80 grams of polyphosphoric acid (115 percent H₃PO₄) and the mixture mechanically stirred, and heated to 85° C. on the steam bath for about 5 hours. The reaction mixture was then diluted with cold water with stirring to 650 ml. volume. After standing one hour in the cold, the white crystalline precipitate was removed by filtration, washed with cold water, and dried. M. P. 167.5–170° C. Yield: 18.2 g. or 95.8% of theory.

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EXAMPLE 3

*5-ethyl-1-phenyl-3-pyrazolidone*10.4 grams of β -hydroxyvalerylphenylhydrazide

were added to 20 ml. of polyphosphoric acid (104 percent H_3PO_4) and the mixture mechanically stirred while heating at 85° C. for 5 hours on the steam bath. The reaction mixture was then diluted to 400 ml. with cold water, and, after 1 hour, the white crystalline precipitate was removed by filtration, washed with cold water, and dried. M. P. 120–121° C. Yield: 86.3% of theory.

The effect of variations in the cyclodehydration agent and concentration of hydrazide in the reaction mixture is illustrated in the following examples:

EXAMPLE 4

Anhydrous phosphoric acid

10.4 g. β -hydroxypivalylphenylhydrazide were added to 20 ml. anhydrous phosphoric acid (made by heating 85 percent phosphoric acid to 150° C. for 3 hours), and the mixture stirred and heated on the steam bath at 85° C. for 24 hours. The mixture was diluted to 400 ml. with cold water, and the white crystalline precipitate removed by filtration, washed with water, and dried. Yield: 8.5 g. or 89.5% of theory.

EXAMPLE 5

85% phosphoric acid

10.4 grams of β -hydroxypivalylphenylhydrazide were added to 25 ml. 85 percent phosphoric acid and the mixture stirred and heated at 85° C. for 5 hours. It was then diluted to 400 ml. with cold water, the white crystalline precipitate removed after 1 hour, washed with water, and dried. Yield: 6.1 g. or 64% of the theoretical.

EXAMPLE 6

85% phosphoric acid and sulfuric acid

10.4 grams of β -hydroxypivalylphenylhydrazide were added to a mixture of 20 ml. 85 percent phosphoric acid and 1 ml. concentrated sulfuric acid (4.5 percent by volume of sulfuric acid), and the mixture heated at 85° C. for 24 hours. It was then diluted to 400 ml. with cold water, and after 1 hour the white crystalline product was removed by filtration, washed with water and dried. Yield: 6.8 g. or 71.5% of theory.

EXAMPLE 7

85% phosphoric acid and sulfuric acid

The procedure of Example 6 was repeated except that

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the acid mixture consisted of 15 ml. 85 percent phosphoric acid and 5 ml. concentrated sulfuric acid (25 percent by volume of sulfuric acid). The yield in this case was 7.4 g. or 77.8% of theory.

EXAMPLE 8

Five grams of β -hydroxypivalylphenylhydrazide were heated at 85° C. for 5 hours in a mixture of 40 ml. 85 percent phosphoric acid and 24 ml. concentrated sulfuric acid. The mixture was then diluted to 400 ml. with cold water and the crystalline precipitate filtered off after 1 hour, washed with water and dried. Yield: 2.6 g. or 56.7% of theory.

In the manner of the above examples, other 3-pyrazolidones can be prepared using the corresponding hydrazide. Accordingly, 1-phenyl-4-methyl-3-pyrazolidone is readily prepared from the corresponding β -hydroxybutyrophénylhydrazide having the above formula in which R and R₁ are hydrogen atoms and R₂ is a methyl group. While the course of the reaction has not been investigated further, it would appear that the reaction would readily lend itself to the production of other 3-pyrazolidone compounds in which the phenyl group in the 1-position of the pyrazolidone nucleus is substituted with inert radicals such as alkyl groups and halogen atoms whose presence in the initial hydrazide molecule does not interfere with the course of the reaction.

What I claim is:

1. The process for the preparation of 1-phenyl-4,4-dimethyl-3-pyrazolidone which comprises heating β -hydroxypivalylphenylhydrazide at a temperature less than about 110° C. in the presence of phosphoric acid as a cyclodehydration catalyst.

2. The process of claim 1 wherein the acid is polyphosphoric acid.

3. The process for the preparation of 1-phenyl-4,4-dimethyl-3-pyrazolidone which comprises heating from about 0.1 to 0.7 gram of β -hydroxypivalylphenyl hydrazide per cc. of phosphoric acid at a temperature less than about 110° C.

References Cited in the file of this patent

UNITED STATES PATENTS

2,743,279 Reynolds et al. ----- Apr. 24, 1956

OTHER REFERENCES

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