

THE REACTION OF α -AMINO KETONES WITH NITROUS ACID

by

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TITLE

THE REACTIONS OF α -AMINO KETONES

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PREVIEW

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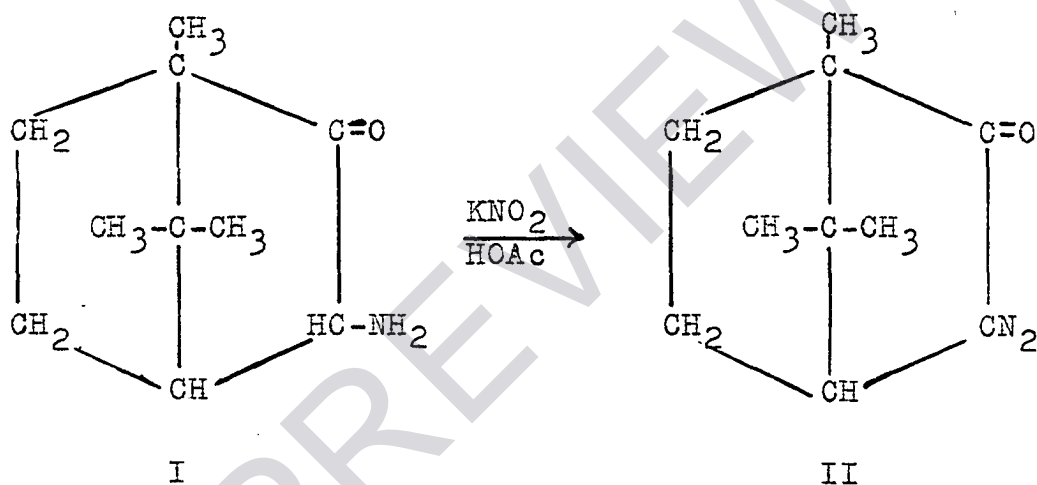
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INTRODUCTION

Although the reaction of amines with nitrous acid has been studied extensively, the reaction of α -amino ketones with nitrous acid has received little attention. It has been used to a small extent in the preparation of α -diazoketones.

In 1881, Schiff and Maissen¹ treated α -aminocamphor (II) with potassium nitrite and acetic acid to obtain α -diazocamphor (I).

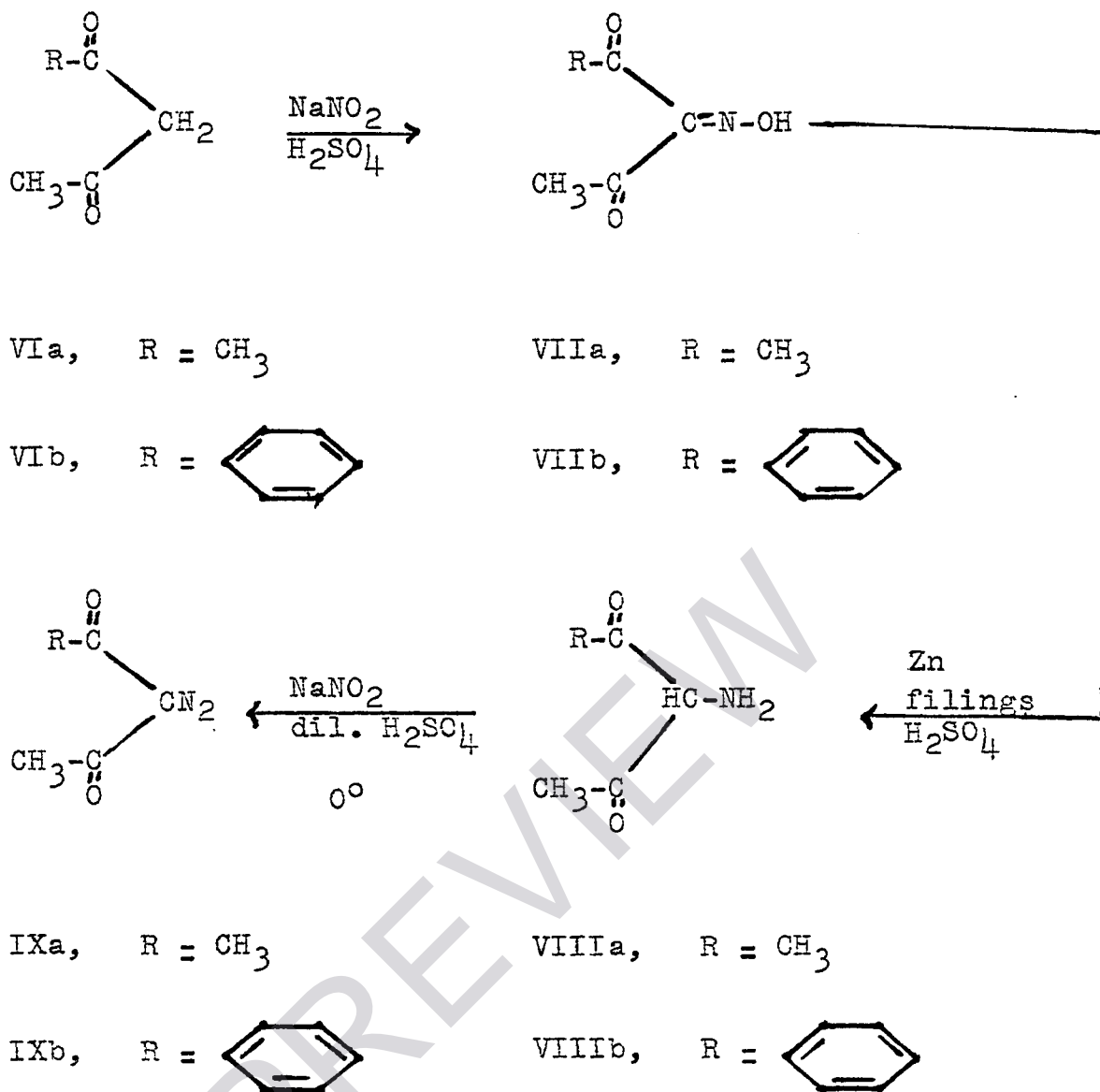


A short time later, Angeli^{2,3} reinvestigated this reaction. α -Diazocamphor and α -diazacetophenone were prepared by the treatment of α -aminocamphor and phenacylamine, respectively, with sodium nitrite and acetic acid. In another paper, Angeli⁴ described the treatment of α -aminocamphor with sodium nitrite and dilute sulfuric acid, substituted for acetic acid, from which α -diazocamphor was obtained again.

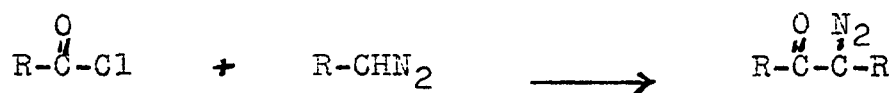
Because of the instability of diazo ketones to acid, the ether solution of the diazo ketone was removed from the acidic reaction mixture rapidly and immediately extracted with a sodium carbonate solution. In a later paper, Angeli⁵ reported that in the diazotization of phenacylamine to α -diazoacetophenone, acidification of the sodium carbonate extraction yielded benzoic acid. Two possible routes were proposed to explain the formation of the benzoic acid. One route involved the oxidation of α -diazoacetophenone by the nitrous acid to yield benzoic acid as one of the products. The other route involved the decomposition of diazoacetophenone (III) to benzoic acid (IV) and diazomethane (V).



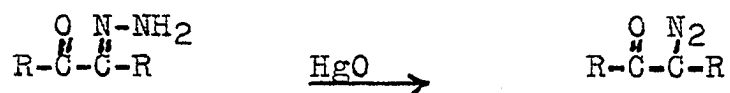
In 1902, Wolff⁶ prepared diazoacetylacetone (IXa) and diazobenzoylacetone (IXb) by this same reaction in the following manner. Acetylacetone (VIa) and benzoylacetone (VIb) were treated with sodium nitrite and sulfuric acid to obtain isonitrosoacetylacetone (VIIa) and isonitrosobenzoylacetone (VIIb), respectively. Aminoacetylacetone (VIIIa) and aminobenzoylacetone (VIIIb) were prepared by the reduction of VIIa and VIIb, respectively, with zinc filings and sulfuric acid. The treatment of VIIIa and VIIIb with sodium nitrite and dilute sulfuric acid yielded IXa and IXb, respectively.



In more recent years, there have been few examples of this method of preparation of diazoketones^{7,8}. This is mainly due to the fact that there are now two methods for preparing diazoketones which give much better yields than the diazotization of α -amino ketones. The first of these involves the reaction of acyl chlorides with diazoalkanes⁹.



The second is the oxidation of the mono hydrazone of an α -diketones, usually using mercuric oxide as the oxidizing agent.¹⁰



PREVIEW

STATEMENT OF PROBLEM

The purpose of this investigation was to determine the products obtained from the reaction of α -amino ketones with nitrous acid and attempt to discover the probable reaction routes by which these products were obtained.

PREVIEW

DISCUSSION

Although Angeli⁵ proposed two possible reaction routes as possible explanations for the production of benzoic acid from the reaction of phenacylamine hydrochloride with nitrous acid, nothing further had been published to substantiate the formation of the benzoic acid or to determine the actual reaction route. In both of the reaction routes proposed by Angeli, α -diazacetophenone formed initially and then reacted further in one of two ways. The first involved the oxidation of the α -diazacetophenone by the nitrous acid; the second involved the decomposition of the α -diazacetophenone to yield benzoic acid and diazomethane.

In the present investigation, phenacylamine hydrochloride was treated with sodium nitrite and dilute sulfuric acid following the procedure utilized by Womack and Nelson¹¹ in the preparation of ethyl diazoacetate. The dilute sulfuric acid was added in portions at 0° C. to a solution of the amine salt and a slight excess of sodium nitrite with ether present to dissolve the products as they were formed. The ether portion was removed and extracted with a 10% aqueous solution of sodium carbonate. A bright yellow solid was obtained on evaporation of the ether solution. Recrystallization of this yellow solid from petroleum ether yielded α -diazacetophenone (16%). On acidification with concentrated hydrochloric acid, the sodium carbonate solution yielded benzoic acid (32%).

Since this procedure required a great deal of manipu-

lation, an attempt was made to utilize an alternative procedure. The new procedure involved the dropwise addition of the dilute sulfuric acid to a solution of phenacylamine hydrochloride and sodium nitrite in water with ether again present to dissolve the products as formed. The ether portion was extracted with sodium carbonate from which, on acidification, benzoic acid (46%) was obtained. On evaporation of the ether, a yellow solid was obtained. The infrared spectrum of this solid contained no diazo band thus indicating the absence of α -diazoacetophenone. The infrared spectrum did contain the bands obtained from the spectrum of a pure sample of phenacyl alcohol, notably the OH band (3600 cm^{-1}) and the carbonyl band (1700 cm^{-1}). Other bands also were present indicating the presence of other material besides phenacyl alcohol. Therefore, the absence of α -diazoacetophenone in this case was attributed to an acid-catalyzed hydrolysis to the corresponding hydroxy compound, phenacyl alcohol (XIV). A portion of XIV also could have arisen as a result of the acid-catalyzed hydrolysis of the intermediate keto diazoic acid (XIII).

