[CONTRIBUTION NO. 36 FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

Reduction of Nitroguanidine. IX. The Reduction of Nitrosoguanidine to Aminoguanidine[1]

BY EUGENE LIEBER AND G. B. L. SMITH

Introduction

No quantitative studies on the reduction of nitrosoguanidine have appeared. Thiele,[2] who was the first to isolate and identify nitrosoguanidine as the first reduction product of nitroguanidine, stated that by reduction with zinc and acetic acid a "reichliche Ausbeute" of aminoguanidine was obtained, but gave no data. In the hydrogenation of nitroguanidine, Lieber and Smith[1c] found that the optimum conversion to aminoguanidine, over the temperature range 25 to 125°, took place in a medium of relatively high acid concentration. This was attributed to the fact that in acid media the reduction proceeded directly to aminoguanidine without the formation of nitrosoguanidine. This paper presents a study of the reduction of nitrosoguanidine to aminoguanidine, and correlates the data so obtained with the data from the reduction of nitroguanidine to aminoguanidine.

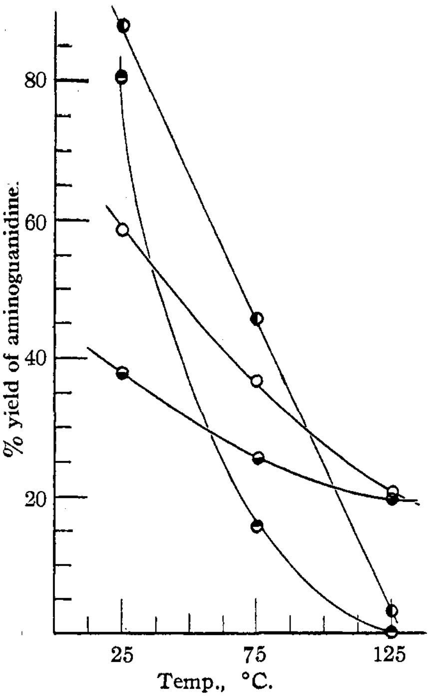

Fig. 1.—Hydrogenation of nitrosoguanidine at high pressure: ⊙, PtO_2 in 15% HAc; ◒, PtO_2 in H_2O; ◓, Raney Ni in H_2O; ◐, Raney Ni in CH_3OH.

Experimental

Preparation of Aminoguanidine from Nitrosoguanidine.—Twenty-two grams of nitrosoguanidine[1a] and 10 g. of Raney nickel catalyst suspended in 120 ml. of methyl alcohol was hydrogenated at 100 atmospheres pressure and room temperature. After the completion of the reduction the solution was filtered, diluted to 250 ml., and a portion titrated with potassium iodate,[3] a yield of 72.5% being indicated. The residual solution was saturated with carbon dioxide and the resulting voluminous white precipitate of aminoguanidinium bicarbonate was washed with cold water, alcohol and ether; yield, 24 g., 70.6%.

Anal. Calcd. for $CH_6N_4H_2CO_3$: N_2H_4, 23.53; CO_2, 32.34. Found: N_2H_4, 23.69, 23.47; CO_2, 32.79, 32.29.

Acidification of the bicarbonate followed by treatment with benzaldehyde and potassium hydroxide yields pearl-white plates of benzalaminoguanidine; m. p. found 177–178° (Dennis bar); reported, 178°.[4]

Factors Relating to the Formation of Aminoguanidine.—The variables studied in the reduction of nitrosoguanidine to aminoguanidine were *temperature* and *solvent media*, with both the platinum oxide and Raney nickel catalysts. The initial hydrogen pressure, on the individual runs, varied from 100 to 125 atmospheres. The reduction mixture comprised 8.8 g. (0.1 mole) of nitrosoguanidine and

TABLE I

FORMATION OF AMINOGUANIDINE BY HYDROGENATION OF NITRO- AND NITROSOGUANIDINE AT ELEVATED PRESSURES

Catalyst	Solvent	Temp., °C.	% Yield of aminoguanidine Nitro-	% Yield of aminoguanidine Nitrosoguanidine	Time of reduction, min. Nitro-	Time of reduction, min. Nitroso-
PtO_2	15% acetic acid	25	81.8	59.3	150	120
PtO_2	15% acetic acid	75	66.7	37.0	75	50
PtO_2	15% acetic acid	125	42.9	20.8	30	50
PtO_2	H_2O	25	2.7	38.2	180	420
PtO_2	H_2O	75	0.0	26.6	60	60
PtO_2	H_2O	125	..	20.6	...	20
Raney Ni	H_2O	25	57.0	80.9	140	150
Raney Ni	H_2O	75	10.5	15.9	40	60
Raney Ni	H_2O	125	0.0	0.0	30	30
Raney Ni	CH_3OH	25	75.7	88.7	150	180
Raney Ni	CH_3OH	75	35.0	46.2	25	40
Raney Ni	CH_3OH	125	0.0	3.2	30	30
Raney Ni	C_2H_5OH	75	50.6	59.1	30	80
Raney Ni	n-C_3H_7OH	75	48.7	27.0	30	100
Raney Ni	Dioxane	75	0.0	3.9	60	60

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[1] This paper is an abstract of a part of the thesis submitted by Mr. Lieber, to the Graduate Faculty of the Polytechnic Institute of Brooklyn, in partial fulfilment of the requirements for the degree of Doctor of Philosophy in June, 1937. For previous abstracts from this thesis see THIS JOURNAL, (a) **57**, 2479 (1935); (b) **58**, 1417; (c) 2170 (1936).

[2] Thiele, *Ann.*, **273**, 133 (1893).

[3] Jamieson, "Volumetric Iodate Methods," Chemical Catalog Co., New York, N. Y., 1926, p. 36.

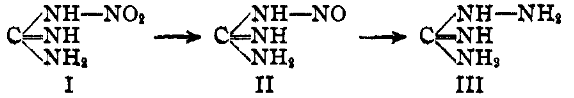
[4] Thiele, *Ann.*, **270**, 35 (1892).

either 0.4 g. of platinum oxide or 5 g. of Raney nickel catalyst. The volume of solvent medium was 120 ml. The reductions were carried out at 25, 75 and 125°. The aminoguanidine obtained was determined by titration.[3]

Figure 1 and Table I summarize the main results obtained. It will be observed that, except for platinum oxide catalyst in 15% aqueous acetic acid solution and Raney nickel catalyst in *n*-propyl alcohol, the yields of aminoguanidine are higher in starting from pure nitrosoguanidine than from nitroguanidine. This is especially evident for the platinum catalyst in neutral aqueous media.

Discussion

The data on the conversion of nitrosoguanidine to aminoguanidine indicate that the greatest loss in the reduction of nitroguanidine to aminoguanidine in neutral or basic media occurs in step I to II



$$\underset{\mathrm{I}}{\mathrm{C}\begin{cases}\mathrm{NH{-}NO_2}\\ \mathrm{=NH}\\ \mathrm{NH_2}\end{cases}} \longrightarrow \underset{\mathrm{II}}{\mathrm{C}\begin{cases}\mathrm{NH{-}NO}\\ \mathrm{=NH}\\ \mathrm{NH_2}\end{cases}} \longrightarrow \underset{\mathrm{III}}{\mathrm{C}\begin{cases}\mathrm{NH{-}NH_2}\\ \mathrm{=NH}\\ \mathrm{NH_2}\end{cases}}$$

Since in acid media the conversion is directly I to III without the formation of II, this factor is not operative and it will be observed that the yields of aminoguanidine, starting from nitrosoguanidine in acid media, are very much lower over the whole temperature range than when the starting material is nitroguanidine. This is due to the instability of nitrosoguanidine in acid solution.[5] From an examination of the last columns of Table I, it will be of interest to observe that nitrosoguanidine is much more resistant to reduction by catalytic hydrogenation than nitroguanidine, as measured by the times of reduction. The times as noted are for three molar proportions of hydrogen for nitroguanidine and two molar proportions of hydrogen for nitrosoguanidine to complete reduction to aminoguanidine. This probably accounts for the ability to isolate nitrosoguanidine as an intermediate product of reduction of nitroguanidine in neutral or basic media.[1a,5] As in the reduction of nitroguanidine,[1c] the yields of aminoguanidine for a nickel catalyst are conditioned by the type of solvent used. In absolute methyl alcohol, at room temperature, practically a quantitative conversion to aminoguanidine is obtained, while at 75°, the solvents may be placed in the order, ethyl, methyl and propyl alcohols, water and dioxane.

Summary

The reduction of nitrosoguanidine to aminoguanidine has been studied by the method of catalytic hydrogenation and the isolation of aminoguanidine described. The effect of temperature and solvent media on the yields of aminoguanidine have been determined and a comparison made with the conversion of nitroguanidine to aminoguanidine.

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[5] Sabetta, Himmelfarb and Smith, THIS JOURNAL, **57**, 2478 (1935).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

A Quantitative Study of the Influence of Certain Factors upon the Activity of the Amylase of Aspergillus Oryzae[1]

BY M. L. CALDWELL AND S. E. DOEBBELING

Recent work with the amylase of *Aspergillus Oryzae* made evident the need for more exact information concerning the influence upon its action of the hydrogen ion activities and electrolyte concentrations of its substrates, information which would establish the conditions necessary for the full activity of this enzyme at different stages in its purification and which would insure the attainment and consistent control of these conditions in comparative measurements of its activities. Such information is essential to further studies of the purification and properties of this enzyme and to comparisons of its characteristics with those of other amylases which have been investigated more intensively.[2] Results of work carried out to meet this need are briefly reported here.

Experimental

A number of amylase preparations of widely different degrees of concentration and purification were used. These included commercial products[3] and others, which

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[1] We are greatly indebted to The Takamine Ferment Company, New York, N. Y., for a grant in aid of this investigation.

[2] (a) Sherman, Caldwell and Adams, THIS JOURNAL, **50**, 2529, 2535, 2538 (1928); (b) *J. Biol. Chem.*, **88**, 295 (1930); (c) Sherman, Caldwell and Doebbeling, *ibid.*, **104**, 501 (1934); (d) Caldwell and Doebbeling, *ibid.*, **110**, 739 (1935).

[3] These products were kindly furnished by the Takamine Laboratory, Inc., Clifton, New Jersey.