[CONTRIBUTION FROM THE ORGANIC CHEMISTRY DEPARTMENT, RESEARCH DIVISION, ABBOTT LABORATORIES]

Inhibition of Catalytic Reduction with Rhodium by Compounds Leading to Strong Nitrogen Bases. I. Hydrogenation of the C=N Linkage and the Promoter Effect of Certain Organic Acids

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This work on the catalytic hydrogenation of benzylidenebutylamine to benzylbutylamine is the first report of the inhibitory effect of nitrogen bases on reductions with rhodium catalysts. The effect of certain acids on the rate and extent of reduction is discussed. Taking the *p*Ka as a criterion of acid strength, the acids within the range of 2.88 (tartaric acid) and 4.64 (acetic acid) are effective promoters or catalyst detoxicants for this reduction with rhodium on alumina. Propionic acid (*p*Ka 4.70) is slightly less effective than acetic acid, while with trimethylacetic acid (*p*Ka 5.05) the effect is considerably decreased. Acids stronger than tartaric acid have little or no effect.

There are no references in the literature which describe the effect of nitrogen bases on hydrogenation in the presence of rhodium catalysts. Work in this laboratory on the reduction of various substituted aliphatic nitriles in the presence of ammonia[1] and in the conversion of cycloheptanoneoxime to cycloheptylamine[2] led us to believe that these catalysts should be excellent ones for the hydrogenation of compounds leading to strong bases.

However, more recent work with them on the reduction of *N*-benzylidenecyclopropylamine to *N*-benzylcyclopropylamine gave results which were not in keeping with the high activity noted in our previous work.

To determine whether the product of the reduction of *N*-benzylidenealkylamines were catalyst poisons or inhibitors *N*-benzylidenebutylamine (A) was selected as starting material. In this way possible steric effects of the cyclopropyl group would be eliminated and more straightforward results could be obtained.

The rather moderate rate of hydrogenation and the incomplete disappearance of the C=N band in the infrared spectrum of benzylbutylamine (B) suggested that rhodium catalysts might be inactivated by nitrogen containing compounds in the same manner as platinum.[3]

Since it has been shown that acids prevent catalyst poisoning,[3,4] it seemed logical to use those of varying strength in the reduction of A to B and observe the effect of each.

From the results obtained (see Table I) it appears that acids of moderate strength facilitate the catalytic reduction of benzylidenebutylamine to benzylbutylamine. The most active ones lie in the range between tartaric acid and acetic acid. Propionic acid is slightly less effective than acetic acid and trimethylacetic acid, the weakest one used, is much less effective. Experiments show that with these promoter acids (or detoxicants) the rate of hydrogenation is increased five to eight fold. Cinchomeronic, *p*-toluenesulfonylacetic and malonic acids, whose *p*Ka values are close to tartaric acid, are ineffective. From these results it could be expected that the stronger acids also would be ineffective. This is indicated by acids II to VI. With some of the strong acids, when only half an equivalent was used, there was little change in their effect. When 0.05 mole of acetic acid per 0.1 mole of A was used the rate was close to that in the experiment with an equimolar amount of acetic acid up to about 50% of hydrogen uptake. Thereafter the rate decreased appreciably. Of particular interest were the experiments with the dibasic acids, tartaric and succinic, when only 0.05 mole of acid was used. The *p*Ka value of second carboxyl group in tartaric acid (3.94–4.16) should place it in the range of the effective acids. The second carboxyl group of succinic acid has a *p*Ka value of 5.28, higher than that of trimethylacetic acid. On the basis of acid strength one might be led to believe that in this experiment tartaric acid should be effective. Actually, there was little difference between the two acids. Uptake of hydrogen followed that of acetic acid for about 50% of the total after which the rate decreased until uptake was complete in two and a half to three hours.

DISCUSSION

It appears then that benzylbutylamine indeed acts as a mild catalyst poison or inhibitor toward rhodium.[5] It is likely that the effective acids combine with B to prevent chemisorption and allow normal adsorption and desorption to take place at the catalyst surface. The result showing the reaction time where half a molar equivalent of acetic acid is used appears to further substantiate this

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[1] M. Freifelder, *J. Am. Chem. Soc.*, **82**, 2386 (1960).

[2] Unpublished work from this laboratory.

[3] E. B. Maxted and A. G. Walker, *J. Chem. Soc.*, 1093 (1948); E. B. Maxted and M. S. Biggs, *J. Chem. Soc.*, 3844 (1957).

[4] T. S. Hamilton and R. Adams, *J. Am. Chem. Soc.*, **50**, 2260 (1928).

[5] Unpublished work in this laboratory on the reduction of other nitrogen bases with rhodium seems to indicate that most strong bases have this same inhibitory action.

TABLE I

ACIDS USED IN REDUCTION

	Acid	pKa[a]	Reduction Time, hr.	Product[b]
I.	—		6	B + 10% A
II.	Hydrochloric[c]		5–6	B + 10% A
III.	Oxalic[c]	1.25	4.5 (incomplete)	
IV.	Cyclohexylsulfamic	1.3[d]	3–4 (incomplete)	
V.	Dichloracetic	1.30–1.45	6	B + 5% A
VI.	Isophthalic	2.30	incomplete	
VII.	Cinchomeronic	2.6[e]	8 (incomplete)	
VIII.	*p*-Toluenesulfonacetic	2.7[e]	5 (incomplete)	
IX.	Malonic	2.69–2.85	4	B
X.	Tartaric[d]	2.88	1	B
XI.	Salicylic	2.97	0.85	B + trace of A
XII.	Phthalic	3.10	<1	B + trace of A
XIII.	Mandelic	3.41	1	B
XIV.	Formic	3.77	1.0–1.1	B
XV.	Succinic[d]	4.19	1	B
XVI.	Acetic[d]	4.64	1.25[f,g]	B
XVII.	Propionic	4.70	1.35–1.5	B
XVIII.	Trimethylacetic	5.05	2.0–2.5	B
XIX.	A + 10% B		>6	B + 10% A

[a] Except where noted all values were obtained from *Stability Constants, Part I: Organic Ligands; Part II, Inorganic Ligands.* Compiled by J. Bjerrum, G. Schwarzenback, and L. G. Sillen under the auspices of the International Union of Pure and Applied Chemistry, published in 1957, by The Chemical Society, London. [b] Assayed by comparison with the infrared spectrum of A and B. [c] Similar results obtained with 0.05 mole of acid per 0.1 mole of A. [d] When tartaric and succinic each was used in the ratio of 0.05 mole per mole of A, reduction was complete in 2.5–3.0 hr. With acetic acid under the same conditions hydrogen uptake was incomplete after 4 hr. Observation of these reactions and comparison with the normal run with an equivalent of XVI showed that uptake of hydrogen in each case was similar up to 50%. Thereafter the rate of uptake decreased appreciably. [e] Value determined by Mr. R. Robinson, Physical Chemistry Dept., this laboratory. [f] When absolute methanol was used as solvent no change in time was noted. [g] When rhodium on carbon was used as the catalyst reduction time was decreased. When it was used in experiment one complete hydrogen uptake was accomplished in less than 6 hr.

mode of action. After 50% uptake the reaction rate decreases appreciably. The same phenomenon is observed with half a molecular equivalent of tartaric or succinic acids. That tartaric acid does not act as a promotor in less than molecular quantities is not surprising. It is well known that many dibasic organic acids do not form salts in the ratio of two moles of base to one of acid. In this instance complete detoxification therefore should not be expected.

The reason for the ineffectiveness of the acids stronger than tartaric acid is not clear. The results would suggest that these acids might be chemisorbed at least as firmly as B,[6] the product of reduction. If such is the case the stronger acids should act as inhibitors in the reduction of non-nitrogenous compounds with rhodium. Hydrogenation of toluene or benzoic acid in alcohol in the presence of II, III or IV refute this mode of action. Only hydrochloric acid acted as a powerful inhibitor (see Experimental).

EXPERIMENTAL

All hydrogenations were carried out in two Parr low pressure hydrogenators whose shaking speeds were identical (255 revolutions per minute). Each piece of apparatus was calibrated and required the same drop in pressure for 0.1 mole of compound. The solvent, denatured ethyl alcohol, consisted of 100 parts of 95% ethanol and 5 parts of methanol. In one experiment anhydrous methanol was used to see whether there was any difference between anhydrous and non-dried solvent when an acid promoter was used. The catalyst, 5% rhodium on alumina,[7] was used in a ratio of one part catalyst to ten parts by weight of compound. In a few experiments 5% rhodium on carbon[7] was tried for comparison. The acids used in this work were either commercially available or prepared in the laboratory and were purified when necessary.

Benzylidenebutylamine. n-Butylamine (146.2 g., 2.0 moles) was added in a thin stream to a stirred solution of 212.1 g. (2.0 moles) of distilled benzaldehyde in 150 cc. of dry benzene. The solution was refluxed and the water removed by means of a separator. When the calculated amount of water was separated (2.5 hr.) the solution was concentrated under reduced pressure. The residue was then distilled. It boiled at 71–75° (0.2 mm.), n_D^{25} 1.5230–1.5232 and weighed 242.1 g. (75% yield.)[8] A second lot of material was prepared in the same manner. The combined products were redistilled before use in hydrogenation.

Standard experiment. One and six tenths grams of 5% rhodium on alumina was added to a solution of 16.1 g. (0.1 mole) of benzylidenebutylamine in 75 cc. of denatured alcohol. The mixture was then hydrogenated under a pressure of 2 atm. until uptake was complete and the time required for completion noted.

Effect of addition of benzylbutylamine. N-Benzylbutylamine (1.6 g.) was added to the standard experimental run and the same procedure followed.

Addition of acid. An equimolecular amount of the appropriate acid was added to the described standard experiment

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(6) Some preliminary studies on the heat of adsorption of solutions of A and B with rhodium catalysts seem to indicate a low value for A indicating physical adsorption and a considerably higher value for B suggesting chemisorption. More complete details including work with some of the acids in Table I will be reported at a later date.

(7) Available from Engelhard Industries, Newark, N. J.

(8) C. W. C. Stein and A. R. Day, *J. Am. Chem. Soc.*, **64,** 2569 (1942), report a 34% yield.

and the same procedure followed. Time of reduction was noted and compared with the standard experiment. In addition, half a molecular equivalent was used in experiments with hydrochloric, oxalic, cyclohexylsulfamic acids in the strong acid group, and with acetic, tartaric, and succinic acids in the milder acid group and the effects noted.

In order to determine whether hydrogen uptake was complete, the solution, after reduction, was filtered from the catalyst and concentrated. If acid was not used in the reduction, the residue was dissolved in dry chloroform and made up to 50 cc. with that solvent. A sample of the solution was submitted for infrared analysis and comparison with known standards of benzylbutylamine and benzylidenebutylamine.[9] When the procedure using acid was followed, the residue obtained after work up was treated with water and excess sodium hydroxide. The base was then extracted with benzene and the extract dried over anhydrous magnesium sulfate. After filtration and removal of solvent the residue was dissolved in chloroform and made to 50 cc. total volume. A sample was then submitted for infrared examination.

Effect of acids on reduction of toluene or benzoic acid. Toluene or benzoic acid (0.1 mole) in 100 cc. of analytical reagent methyl alcohol was hydrogenated in the presence of 20% by weight of 5% rhodium on alumina (or 5% rhodium on carbon) under 2 atm. pressure. Uptake of hydrogen was complete in 90 min. In similar reductions in the presence of 0.1 mole of III or IV no change in time was noted. However, with either toluene or benzoic acid and 0.1 mole of hydrochloric acid uptake of hydrogen was only 25% of $3H_2$ in 6 hr.

NORTH CHICAGO, ILL.

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(9) Carried out by W. Washburn of Abbott Laboratories.

[CONTRIBUTION FROM THE UNITED STATES DEPARTMENT OF THE INTERIOR, BUREAU OF MINES, REGION V]

The Lithium-Ethylenediamine System. III. Formation of Imidazole Derivatives and Cleavage of Certain Carbon-Carbon Bonds[1]

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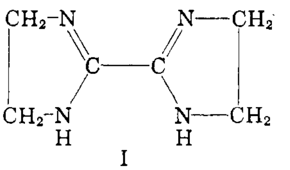
Hydrocarbons such as tetralin and isopropylbenzene, in the presence of *N*-lithioethylenediamine, $H_2NCH_2CH_2NHLi$ catalyze the self-condensation of ethylenediamine to give bis(Δ^2-2-imidazolinyl), hydrogen, and ammonia. In the presence of *N*-sodioethylenediamine, $H_2NCH_2CH_2NHNa$, a similar reaction takes place and in addition yields an unidentified compound, $C_6H_8N_4$. Stilbene with *N*-lithioethylenediamine gives bis(Δ^2-2-imidazoinyl), toluene, and 1,2-diphenylethane; under the same conditions, 1,2-diphenylethane is unchanged.

We have shown[1] that reaction of certain dienes, such as *d*-limonene, with *N*-lithioethylenediamine, $H_2NCH_2CH_2NHLi$ (NLA), leads to the evolution of hydrogen and the formation of the corresponding aromatic hydrocarbon. This paper describes experiments designed to extend the scope of the dehydrogenation reaction.

When tetralin was heated at 90–100° with *N*-lithioethylenediamine in solution in excess ethylenediamine, there was a slow evolution of hydrogen and ammonia. Only one organic product, other than recovered tetralin, was isolated from the mixture; it was identified as bis(Δ^2-2-imidazolinyl), I.[4] Similar results were obtained when toluene, ethylbenzene, or isopropylbenzene was used in place of tetralin.[5] The formation of I appeared to be fastest with tetralin and slowest with toluene. In one experiment with tetralin, the rate of gas evolution at the end of eighty-three hours of intermittent heating was approximately the same as at the start.



I

Woodburn and O'Gee[4] obtained I from the reaction of ethylenediamine with cyanogen at 0°. The over-all reaction can be written:

$$C_2N_2 + 2\ C_2H_8N_2 \longrightarrow C_6H_{10}N_4 + 2\ NH_3 \qquad (1)$$

In the present work, the over-all reaction seems to be:

$$3\ C_2H_8N_2 \longrightarrow C_6H_{10}N_4 + 2\ NH_3 + 4\ H_2 \qquad (2)$$

The dehydrogenation of ethylenediamine to cyanogen by *N*-lithioethylenediamine does not seem likely; nor would this pathway explain the need for the aromatic hydrocarbon. It is more likely that some reaction occurs which produces various intermediate compounds, and that the aromatic hydrocarbon, perhaps in the form of some metallated derivative, plays a part. The relative proportions of

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[1] For the previous paper, see L. Reggel, S. Friedman, and I. Wender, *J. Org. Chem.*, **23**, 1136 (1958). A portion of the material in the present paper was presented before the Division of Organic Chemistry at the 129th Meeting, American Chemical Society, Dallas, Tex., April 1956.

[2] Bureau of Mines, U.S. Department of the Interior, Pittsburgh, Pa.

[3] Union Carbide Corp., South Charleston, W. Va. This work was carried out as part of a cooperative agreement between the Bureau of Mines and the Union Carbide Corp.

[4] H. M. Woodburn and R. C. O'Gee, *J. Org. Chem.*, **17**, 1235 (1952). We wish to thank Dr. Woodburn for supplying a sample of this material.

[5] In the presence of decalin, a very small amount of I was formed; this may have arisen from a trace amount of tetralin in the decalin.