HYDRAZINE AS A REDUCING AGENT FOR ORGANIC COMPOUNDS (CATALYTIC HYDRAZINE REDUCTIONS)

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CONTENTS

I. INTRODUCTION

A. SCOPE AND LIMITATION

Hydrazine has been used as a reducing agent under two sets of conditions.

1. Solutions of hydrazine or hydrazine hydrate have been used in various solvents with or without potassium or sodium hydroxide or other bases such as potassium *t*-butoxide for the reduction of carbonyl compounds. The well-known Wolff–Kishner reduction reviewed by Todd (176) is one example.

2. Catalytic hydrazine reduction, effective mainly in the presence of finely divided metals, can be employed to reduce aromatic nitro compounds or to dehalogenate halo compounds. It was the introduction of the hydrogenation catalysts, Pd (49, 140), Pt (108), and Ni (18), which made this technique a convenient laboratory procedure since no pressure apparatus is required.

This review is limited to a survey of the literature covering these two methods through 1963.

B. PREVIOUS REVIEWS

The literature of hydrazine in general includes two books (10, 37) written in the past 15 years, and five extensive reviews (33, 56, 112, 151, 181), as well as sections in a recent monograph (9). Articles have been published dealing with the reduction of inorganic ions (23), especially for gold plating (76) and the production of finely divided metals (10) or thin films (113). In spite of an extensive literature, the quantitative determination of hydrazine leaves much to be desired. Few of the common oxidizing agents are useful (61), including Chloramine-T (25). Although hydrazine reduces a variety of oxidizing agents like permanganate, iodate, and ceric ions, the reaction does not go to completion. Audrieth and Ogg (10) have reviewed this aspect of hydrazine chemistry.

C. PRECAUTIONS

Hydrazine and hydrazine hydrate are violent poisons since they inhibit certain enzyme systems, thus causing reduced body metabolism. They are basic compounds and cause irritation of the skin, mucous membrane, and eyes (125). Rubber corks and certain plastics are attacked. Investigators using hydrazine or hydrazine hydrate should take precautions to avoid inhalation or contact. Also, the literature under section B above should be studied. Mixtures of hydrazine and nitric acid are explosive and a solution of hydrazine in ethanol in the presence of 0.5 to 0.05% copper decomposes hydrogen peroxide vigorously (Helman catalyst used in V-2 rockets). Note also the following discussion.

D. CATALYTIC DECOMPOSITION

Hydrazine is thermodynamically unstable, but the thermodynamic properties of hydrazine (10, 37, 110) *per se* are not useful in predicting the nature of the organic products obtained when hydrazine is used as a reducing agent. In the presence of finely divided hydrogenation catalysts, nickel, palladium, or platinum, hydrazine will decompose spontaneously. The composition of the gases liberated will depend upon the nature of the catalysts employed. There is no universal agreement on the stoichiometry of the decomposition. Early studies (summarized in ref. 10) in 1902 (170) showed that hydrazine spontaneously decomposed in contact with active Pt to liberate ammonia, nitrogen, and hydrogen. The equation proposed was

$$2N_2H_4 \xrightarrow{Pt} 2NH_3 + N_2 + H_2$$

If hydroxyl ion was present, the proportion of hydrogen increased and the ratio of gases obtained approached the equation

$$3N_2H_4 \xrightarrow[OH^-]{Pt} 2NH_3 + 2N_2 + 3H_2$$

Two years later Gutbier and Neundlinger (77) showed that in the absence of the hydroxyl ion pure hydrazine in contact with oxygen-free platinum black decomposed to form

$$3N_2H_4 \xrightarrow{Pt} 4NH_3 + N_2$$

Neither hydrogen nor nitrous oxide was formed.

Addition of barium hydroxide increased the amount of hydrogen obtained and the representative equation became

$$N_2H_4 \xrightarrow[Ba(OH)_2]{Pt} N_2 + 2H_2$$

Thus decomposition products obtained seem to be a function of the concentration of the hydroxyl ion present. Increased concentration of base lowers the amount of ammonia and increases the proportion of nitrogen and hydrogen. This would bear out the hypothesis (10) that hydrogen is a primary decomposition product which could in turn reduce more hydrazine to ammonia. In the presence of hydroxyl ion, the hydrazine dissociation is hindered and the ability of hydrogen to effect reduction is greatly reduced with the result that it is liberated as a gas.

Dzhardamalieva (53) using PtO_2 at 50° got only nitrogen and hydrogen as spontaneous decomposition products of hydrazine.

Raney nickel influences the catalytic decomposition of hydrazine relative to the amount of catalyst present. In large amounts the reaction approaches (53, 89)

$$3N_2H_4 \xrightarrow{Ni} 2NH_3 + 2N_2 + 3H_2$$

Irrera (89) claimed that water also plays a role in this decomposition. Palladium over calcium carbonate as a catalyst was not studied until 1963, and then it was reported that almost stoichiometric amounts of nitrogen and hydrogen were obtained (89).

$$N_2H_4 \xrightarrow[CaCO_3]{Pd} N_2 + 2H_2$$

However, over Ni or Pd–C or Ru–C, ammonia was also reported (156).

For the catalytic hydrazine reduction, the implication is that the nature of the catalyst may play a role in determining the final product isolated when an aromatic nitro compound is reduced. Yet in the examples collected for this review, it seems to make no difference which metal catalyst is present during the complete reduction of an aromatic nitro compound to the corresponding aniline when an excess of hydrazine is used. Slight differences are noted in the reduction of the aromatic nitro compounds to the intermediate coupled products. To date, the one major difference noted is in the dehalogenation reaction (68), for a specific catalyst, Pd, is required here.

Both Pietra (141) and Rottendorf and Sternhell (156) have suggested that the reactivity of hydrazine in the presence of the catalysts, Ni, Pd, Pt, or Ru, is simply due to the hydrogen liberated.

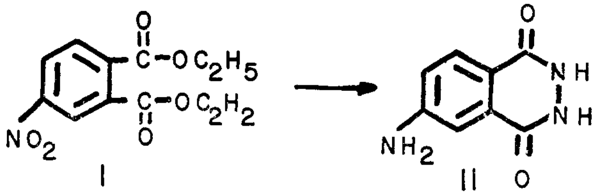
II. REDUCTION OF AROMATIC NITRO COMPOUNDS BY HYDRAZINE

A. DIRECT REDUCTION TO ANILINES

1. *Reductions without Catalysts*

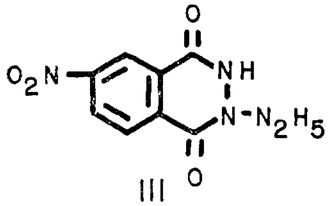
A few years after the isolation of hydrazine hydrate (44), it was tried as a reducing agent for nitro, nitroso, and isonitroso groups by Rothenburg (155). The reaction medium was refluxing alcohol; only limited success was achieved with this reaction. Over a period of years, other attempts were made to reduce nitrobenzene by hydrazine also in the absence of a catalyst, and again moderate yields were obtained (45, 74). In 1907 Curtius tried to reduce ethyl 3,5-dinitrobenzoate and obtained only the acid hydrazide (48); thus were discovered the hydrazides, azides, and rearrangement of the latter compounds to isocyanates. This sequence of reactions is known today as the Curtius reaction. Smith (163) has summarized this work.

Curtius reduced 2,4-dinitrobenzoic acid to 2-nitro-4-aminobenzoic acid (45, 46) and also a nitrophenol to the corresponding aminophenol. 4-Aminophthalhydrazide (II) was obtained from diethyl 4-nitrophthalate (I) (45), as well as a compound called "4-nitrophthalylhydrazide" (III) (47).



I

II



III

In an attempt to increase the yields of the amine compounds by the reduction of nitrobenzoic acids, nitrotoluene, and nitroaniline, Müller and Zimmerman (134) used sealed tubes. They noted no dehalogenations when reducing *m*-chloronitrobenzene. Chloroaniline was obtained in 84% yield; the 2,4-dinitrotoluene was reduced stepwise to the corresponding diamine.

Good yields (89%) were obtained when 2,2′-dinitrodiphenyl sulfide was reduced with hydrazine in refluxing alcohol without a catalyst (127). This yield was not obtained by others (152), and only 56% yield was reported 34 years later. A detailed procedure is given in the book by Shirley (162).

2. *Reductions with Catalysts*

The first use of a catalyst for hydrazine reductions was reported by Busch and Schulz (31) in 1929. A variety of nitro compounds, including nitrosubstituted toluenes, phenols, sulfonic acids, and anilines, were treated in neutral or basic solution with hydrazine and Pd–$CaCO_3$ (1%). The reactions were more vigorous in methanol than ethanol. Intermediate reduction products were also noted, but few yields were given. No further work was reported until platinum, prepared by reducing Adams oxide in an atmosphere of hydrogen, was introduced as a catalyst by Kuhn (108) who also reinvestigated 5% Pd–C. Complete reduction of aromatic nitro compounds to anilines, and nitrite and nitrate esters to the corresponding alcohols, could be achieved using these catalysts. Cyclohexene was not reduced. No reactions took place without catalysts. Balcom and Furst (18) introduced Raney nickel as the catalyst, and a series of nitrobenzenes and nitrobiphenyls were reduced to the corresponding amines in yields of 80–99%.

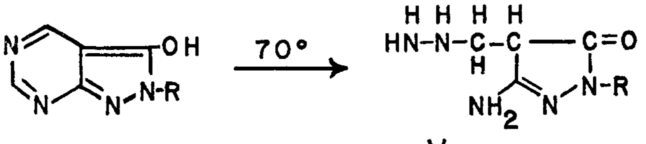
Subsequently, Pietra (140) independently published the use of Pd–C as a catalyst and a variety of aromatic nitro compounds were reduced. Dewar and Mole (49) also came upon this catalyst almost simultaneously, using the system to reduce a series of nitro polynuclear hydrocarbons to amines.

Since that time a large variety of aromatic and heterocyclic nitro compounds have been reduced to amines. Many polyfunctional aromatic nitro compounds may undergo more complex reactions than simple reduction. Tables I and II summarize the types of compounds completely reduced.

Only a few failures have been reported; these have been heterocyclic compounds, including nitropyrimidines (59, 66). The reduction of 5-nitrofurfural diacetate is in doubt. This has been reported (131, 132) but could not be reproduced (177).

3. *Side Reactions*

A few side reactions have been reported when hydrazine was a reactant independent of the use of a catalyst. In cases of two fused nitrogen ring systems containing pyrimidine, this ring was cleaved. A pyrazolo-[3,4-*d*]pyrimidine (IV) was cleaved under mild conditions to form a substituted pyrazolone (V) (26).



IV

V

Taylor (172) cleaved the pyrimidine ring of a pteridine. This reaction may account for the failure of Fanta and Hedman (59) to obtain any recognizable product on reducing 2-nitro-5-phenylpyrimidine.

The conditions of the reaction, more than the presence of other functional groups, seem to influence the yields and products obtained in the catalytic hydrazine reduction. Balcom and Furst (18) reduced nitro derivatives of diphenyl ether without ether cleavage, cinnamic acid without double bond hydrogenation, and benzophenone without carbinol formation.

Ikawa (88) cleaved 1-nitro-1′-hydroxydiphenyl ether after heating in 99% ethanol and hydrazine in a sealed tube for 10 hr. It is noteworthy that the nitro was not reduced and yields were exceedingly poor.

Without catalysts, 4,4′-dinitrodiphenyl sulfide is smoothly reduced to the diamine with no thioether cleavage (127, 152).

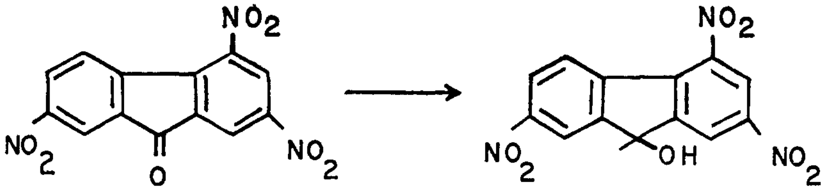
TABLE I

COMPLETE REDUCTION OF AROMATIC NITRO COMPOUNDS

Compound	Catalyst	Yield, %	Ref.
A. Without potential hydrazine reacting group			
Nitrobenzene	Cu or Fe	. . .	107
	Ni, Ni	80–90+, . . .	18, 128
	Pd–C, Pd–C, Pd–C	91.9, 95, . . .	19, 140, 144
	Pt or Pd, . . .	. . ., . . .	74, 108
2-(*m*-Substituted benzyl)nitromesitylenes	Ni	. . .	1
Nitromesitylenes	Ni	. . .	75
4-Amino-4′-nitrodiphenylamine	Ni	Quant.	3
N-Benzoyl-3-morpholino-4-nitroaniline	Ni	65.3	3
N-Benzoyl-3-anilino-4-nitroaniline	Ni	32	3
1-Nitroaniline	Pd–C, Ru–C	88, 61	140, 147
3-Nitroaniline	. . ., Ru–C, Pd–C	. . ., 70, 95	134, 147, 155
2-Nitrophenol	Pd–C, . . ., Cu or Fe	88, . . ., . . .	19, 31, 107
3-Nitrophenol	Pd–CaCO$_3$, Cu or Fe	. . ., . . .	31, 107
4-Nitrophenol	. . ., Cu or Fe	. . ., . . .	31, 107
4,6-Dinitro-*m*-xylene	Pd–C	87	19
3-Nitrobenzaldehyde	. . .	66.6	84
4-Nitrobenzaldehyde	. . .	70.8 (KOH)	
		41.3	84
Nitrofluorenes	Ni	90	135
1- or 2-nitrotriphenylene	Ni	. . .	21
1-Nitronaphthalene	Pd–C, Pd–C	60, 88	49, 140
2-Nitronaphthalene	Pd–C	62	49
1-Nitro-2-naphthylamine	Pd–C	85	19
1-, or 2-, or 3-, or 9-nitrophenanthrene	Pd–C	60–81	49
2-Nitro-*x*-substituted fluorene	Ni	80–95	63
2-Nitrofluorene	Pd–C, Pd–C, Ni	97, 93–96, 99+	19, 20, 115
3-Nitropyrene	Pd–C	64	49
2-Nitrochrysene	Pd–C	65	49
3-Nitroperylene	Pd–C	67	49
4-Nitroanisole	Pd–C	63	49
2-Nitrobenzoic acid	Ru–C	. . .	147
3-Nitrobenzoic acid	Cu, . . .	. . ., . . .	107, 134
4-Nitrobenzoic acid	. . ., Pd–C	. . ., 84	135, 140
2,4-Dinitrobenzoic acid (to monoamine)	. . .	. . .	46
2,4-Dinitrobenzoic acid ethyl ester	. . .	. . .	46
4-H-, or methyl-, or hydroxy-1,3-dinitrobenzene (to monoamine)	Cu	. . .	107
2-Nitrotoluene	Cu or Fe, Pd–C, . . .	. . ., . . ., 95	107, 134, 140
3-Nitrotoluene	Cu or Fe, Pd–C, . . ., . . .	. . ., 95, 77–80, . . .	84, 107, 134 140
4-Nitrotoluene	Cu or Fe, Pd–C, . . ., . . .	. . ., 82, 89.2, . . .	84, 107, 134, 140
2,4-Dinitrotoluene	. . .	. . .	134
2-Nitro-*p*-toluic acid	Pd–C	88	180
4,4′-Dinitrobibenzyl	. . .	99	84
4,4′-Dinitrostilbene-2,2′-disulfonic acid	. . .	70–73.3	84
4,4′-Dinitrobibenzyl-2,2′-disulfonic acid	. . .	70	84
4-Nitropropylbenzene	. . .	. . .	84
Bis(2-nitrophenyl) disulfide	. . .	56	152
1-Carboxy-2-(2-nitrostyryl)tropolone	Ni	60	171
2,2′-Dinitrodiphenylmethane	Ni	. . .	100
2-, or 3-, or 4-nitroaniline	Pd–CaCO$_3$	. . .	31
3-Nitrobenzenesulfonic acid	Pd–CaCO$_3$	. . .	31
2-Amino-5′-nitrobiphenyl	Ni	86	3
4-Amino-4′-nitrodiphenylamine	Ni	90+	3
2-Methyl-4′-nitrobiphenyl	Ni	80–99+	18
6,6′-Dimethyl-2,2′-dinitrobiphenyl	Pd–C	63	19
4-Nitrobiphenyl	Ni	80–99+	18
2- or 4-nitrobiphenyl	Pd–C	89–92	19
3-Nitrobiphenyl	Ni	. . .	55
4-Nitrodiphenyl ether	Ni	80–99+	18
4,4′-Dinitrodiphenyl ether	Ni	80–99+	18
2,2′-Dinitrodiphenylmethane	Ni	. . .	110
1,2-Dinitrodiphenyl sulfide	. . .	89	127
Bis(2-nitrophenyl) disulfide	. . .	56	152

TABLE I (*Continued*)

Compound	Catalyst	Yield, %	Ref.
B. With potential hydrazine reacting group			
4-Nitrocinnamic acid	Ni	80–99+	18
3-Nitrostyrene	Ni	12	8
3-Nitrobenzophenone	Ni	80–99+	18
Nitrofluorescein	Pd–C	85	140
C. Without dehalogenation			
3-Chloro-1-nitromesitylene	Ni	94	2
2-Fluoro-5-nitrotoluene	Pd–C	88	19
Fluoro-, chloro-, bromo-, or iodonitrobenzene (all locations)	Ni	64–96	111
All bromonitrobenzenes	Ru–C	. . .	144
2-Bromonitrobenzene	Ru–Ca	92	145
3-Bromonitrobenzene	Ru–Ca	86	145
4-Bromonitrobenzene	Ni, Ru–Ca	. . ., 88	66, 145
2-Chloronitrobenzene	Ru–Ca	84	145
3-Chloronitrobenzene	. . ., Ru–Ca	84, 66	134, 145
4-Chloronitrobenzene	Ru–Ca	86	145
2-Iodonitrobenzene	Ru–Ca	89	145
4-Iodonitrobenzene	Ru–Ca	89	145
2,5-Dichloronitrobenzene	Ru–Ca	89	145
1-Fluoro-2-nitrofluorene	Ni	96	64
3-Fluoro-2-nitrofluorene	Ni	96.5	65
8-Fluoro-2-nitrofluorene	Ni	95	64
1,2,6-Tribromo-3-nitronaphthalene	Pd–C	46	178
D. With dehalogenation			
4-Chloro-2-nitroaniline	Pd–C	82–100	130
9-Bromo-3-nitrophenanthrene	Pd–C	87.5	131
2-Chloro-8-nitroanthraquinone	Pd–C	82–100	130



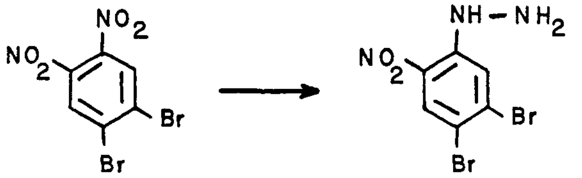
VI

VII

Fletcher and Namkung (63) confirmed that, in the main, carbonyls are unaffected by this procedure. However, an almost quantitative reduction of 2-nitrofluorenone to its amine was obtained with a side product of 3% 2-aminofluorenol.

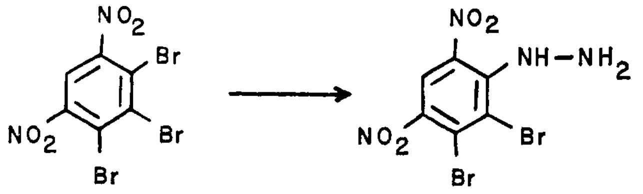
Nitrofluorenones (VI) can be selectively reduced to the corresponding nitrofluorenols (VII) *via* the hydrazone if no catalyst is used (38). It is also possible to reduce the double bond in cinnamic acid and obtain the phenylpropionic acid with hydrazine and Pd–C (140).

Unusual substitutions may occur. In a series of papers (72, 92) reports were made on the treatment of dinitro-, di- (VIII), and tri- (X) substituted halobenzenes with hydrazine *sans* catalyst. Representative products were obtained (IX, XI).



VIII

IX



X

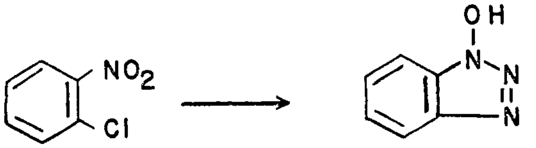
XI

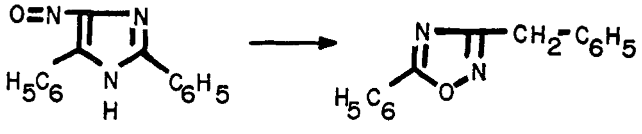
Under certain conditions, the formation of ring compounds would be expected, especially N-heterocyclic rings. The reaction of *o*-chloronitrobenzene (XII) and hydrazine to give 1-hydroxybenzotriazine (XIII) (90) is not surprising. More unusual is the formation of a pyrazolidone (XV) from the epoxide (XIV) (123). The formation of the nitrogen heterocyclic compound may go *via* a hydrazine–acid hydrazide (XVI).

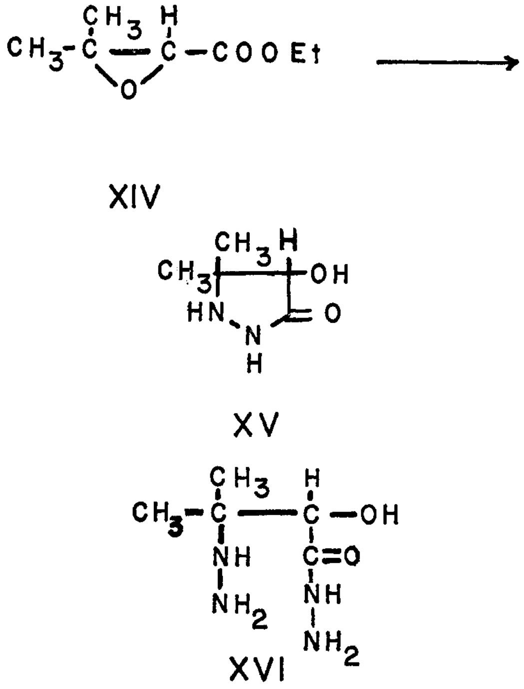
TABLE II

COMPLETE REDUCTION OF HETEROCYCLIC NITRO COMPOUNDS

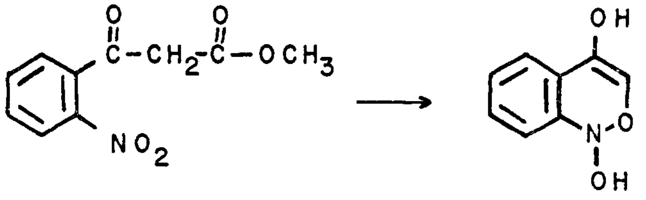
Compound	Catalyst	Yield, %	Ref.
5-Nitro-6-amino-2-methylpyridine	Pd–C	82	19
6-Nitroindole	Ni	75.6	27
Ethyl 6-nitroindole-3-carboxylate	Ni	68	28
6-Nitroindole-3-carboxylic acid	Ni	74	28
6-Nitroindole-3-carboxylic acid hydrazide	Ni	...	28
8-Nitroquinoline	Pd–C, Ni	65, 90–95	49, 63
6- or 7-nitro-3,4-benzocoumarin	Ni	94	138
4-Nitronicotinic acid 1-oxide	Ni	6.9	173
2-Chloro-5-nitro-4-amino-6-ethylpyrimidine (dehalogenation and reduction)	Pd–$SrCO_3$	...	154
5-Nitroindole	Ni	82	174
5-Nitro-2-methylindole	Ni	...	174
6-Nitro-2-methylindole	Ni	91	174
5-Nitro-2-methylindoline	Ni	...	174
Methyl 3-bromo-5-nitrothianaphthene-2-carboxylate (dehalogenation)	Ni	54	122
5-Nitro-2-morpholinomethylthianaphthene	Ni	90	114
5-Nitrofurfurylidene diacetate	...	...	54, 60
5-Nitrofurfural dimethyl acetal	...	...	36
4-Nitro-5-phenylpyrazole	...	...	137
6-Nitroquinoline	Ni	90–95	63
5-Nitrotryptophan	Pd–C	65	67


XII XIII

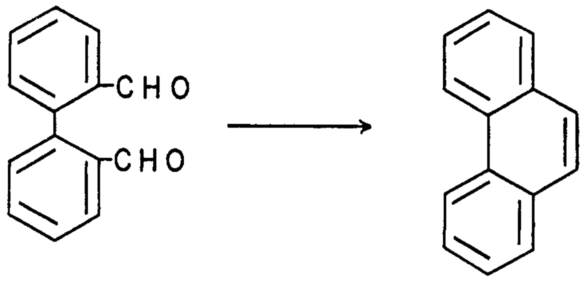

XVII XVIII

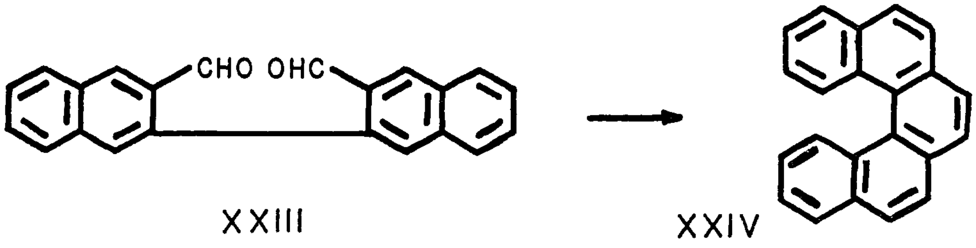

XIV XV XVI

It is more difficult to interpret the formation of a 1,2,4-oxadiazole (XVIII) from an imidazole (XVII) (157). The reduction of methyl *o*-nitrobenzoylacetate (XIX) with hydrazine catalyzed by Pd–C gave 1,2-dihydro-1,4-dihydroxy-2-oxaquinoline (XX) (42).

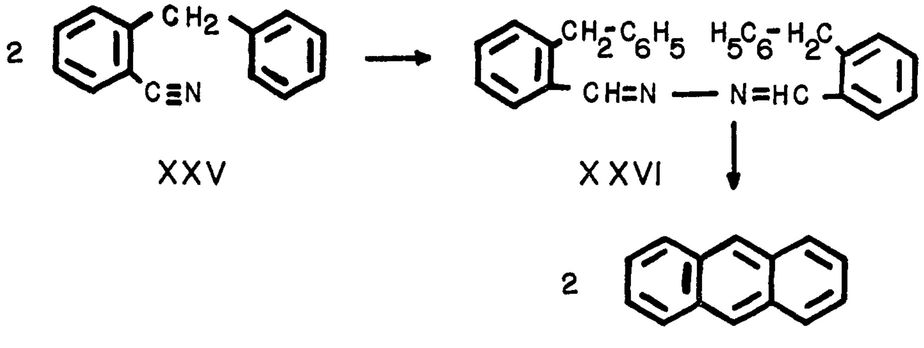

XIX XX

Polynuclear hydrocarbons have also been products of hydrazine reductions. Biphenyl-2,2′-dicarboxaldehyde (XXI) was reduced to phenanthrene (XXII) (17). The


XXI XXII



XXIII XXIV



XXV XXVI XXVII

corresponding 2,2′-binaphthyl-3,3′-dialdehyde (XXIII) on treatment with hydrazine gave on reductive cyclization no cyclic azine, but pentaphene (XXIV), a phenanthrene derivative in 40% yield (16). Pyrene can also be obtained from biphenyltetraaldehyde (151). A polynuclear aromatic hydrocarbon (XXVII) also was obtained by treating 2-cyanodiphenylmethane (XXV) with hydrazine (183).

4. Comparisons with Hydrogenation and Other Reduction Methods

In most cases the catalytic hydrazine reduction method gives yields equal to or better than direct catalytic hydrogenation or other reduction methods, and the catalytic hydrazine reduction can be carried out more conveniently in that no pressure apparatus is needed. A few comparisons will be made.

Nitromesitylene is reduced by hydrazine and nickel in 88% yield, and by hydrogenation over nickel in 57% yield. Better yields are obtained in the formation of *m*-aminostyrene from the nitro compound by reduction with stannous chloride (48%) than with hydrazine (12%) (8). Reduction of 2,2′-dinitrobiphenyl gives an 80% yield if tin and hydrochloric acid are employed, and 74–83% if hydrazine is used (157).

In indole chemistry, the 6-nitro derivative is reduced to the 6-aminoindole in yields of 13% with sodium hydrosulfite, 65% with hydrogenation, and 76.5% with hydrazine (27). Equal yields (69%) are obtained by hydrogenating or using catalytic hydrazine reduction methods on ethyl 6-nitroindole-3-carboxylate (28). A 5-nitrotryptophan is reduced in 71% yield by hydrogenation and in 65% yield by hydrazine (67).

B. REDUCTION TO COUPLED INTERMEDIATES

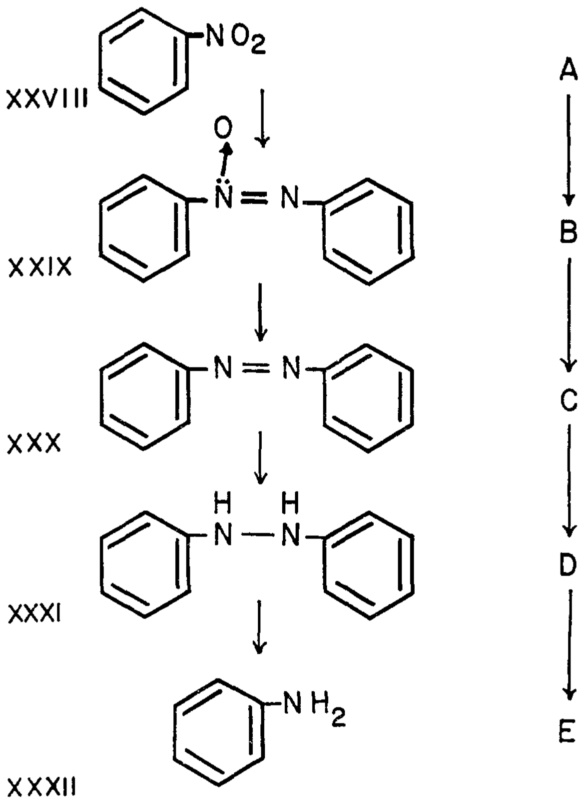
1. General

Classically, it has been known for some time that by varying the nature of the reducing agent it is possible to reduce nitrobenzene to any of the following coupled products: azoxybenzene, azobenzene, or hydrazobenzene. Any of these intermediates can now be obtained by the catalytic hydrazine reduction method.

Unsubstituted azoxybenzene (XXIX) can easily be isolated if solvent volumes are small. Catalysts can be Pd–C (19, 143), Pd–$CaCO_3$ (1%) (31), Ni (69, 82, 128, 165), or Cu (101). It appears that the rate of reduction of these intermediates is such that azobenzene (XXX), while it can be isolated, tends to go to hydrazobenzene (XXXI) (19, 31, 35, 44, 63, 82, 106, 127) in high yields regardless of the catalyst used; even Ru–C will catalyze this reaction (143). Azo dyes like methyl orange and methyl red are easily reduced to the hydrazo in the presence of Cu (106).

Substituted nitrobenzenes, or pyridines, also can be reduced to various intermediate states, and substituted azoxybenzenes, azobenzenes, and hydrazobenzenes can be isolated. For many pyridyl compounds, the catalytic hydrazine reduction method, using a nickel catalyst, is an excellent procedure for obtaining the hydrazo derivatives (165).

In certain cases. the product isolated seems to be related to the position of the substituted group in relation to the nitro; nitrotoluenes are an example. Busch and Schulz (31) using Pd–$CaCO_3$ (1%) reduced the



ortho derivative to azoxy, the *meta* to azo, and the *para* to a mixture of azo and hydrazo. Furst and Moore using Ni (69, 128) obtained azoxy from the *ortho*, *meta*, and *para* derivatives.

Without the use of a catalyst, Müller and Weisbrod (133) reduced 1-chloro-2,4-dinitronaphthalene to 4,4′-dinitro-2,2′-azonaphthalene.

Phenylhydroxylamine (82) was reduced to hydrazobenzene in 77% yield if nickel was used. Nitrosobenzene could be reduced to hydrazobenzene (82) or azoxybenzene (128).

All of the compounds mentioned in this section can be reduced to aromatic or heterocyclic amines by prolonging the reaction time or increasing the molar ratio of hydrazine to the original nitro reactant. Table III summarizes these reactions.

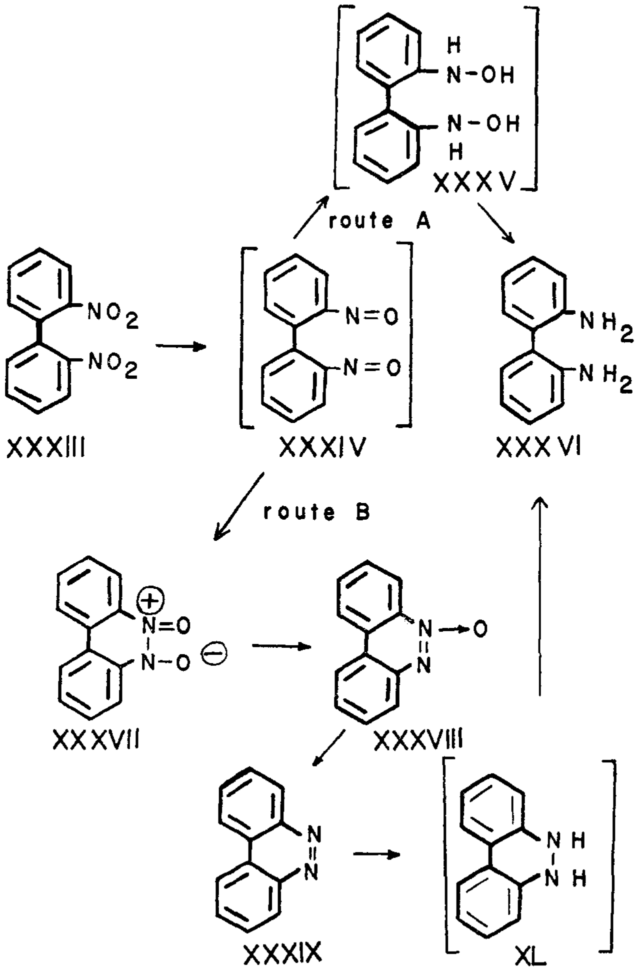
TABLE III

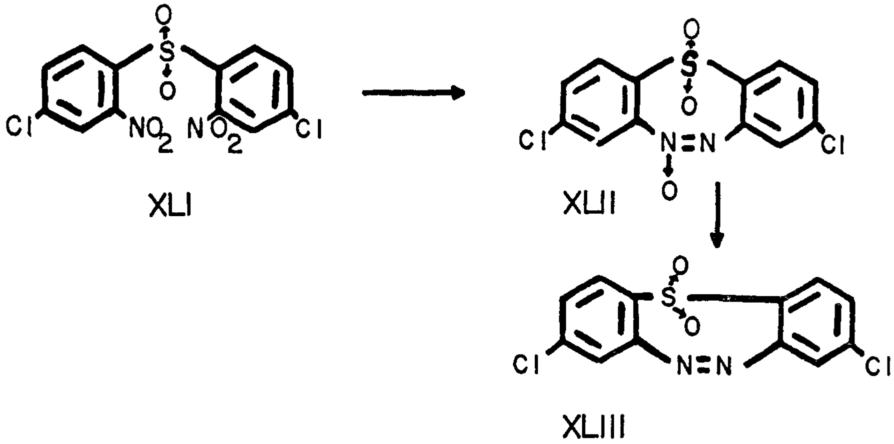
REDUCTION OF AROMATIC INTERMEDIATES TO AMINES

Compound	Catalyst	Yield, %	Ref.
Nitrosobenzene	Pd–C	93	19
	Ni	. .	69
Phenylhydroxylamine	Pd–C	89	19
4-Nitrosodimethylaniline	. .	Poor	155
Nitrosobenzene, substituted	Ni	. .	69
	Pd–C	80–90	143
Phenylhydroxylamine	Ni	77	82
Phenylazide	Pd–C	90	143

2. Reduction of 2,2′-Dinitrobiphenyl

The reduction of 2,2′-dinitrobiphenyl (XXXIII) indicates that almost every possible intermediate may be obtained. Moore and Furst (129) proposed two possible routes for the synthesis of 2,2′-diaminobiphenyl (XXXVI); the nature of the catalyst is important. When a Raney nickel catalyst low in aluminum is used, route A predominates and an almost quantitative yield of the diamine XXXVI is obtained. Other Raney nickel catalysts yield a series of intermediates most of which can be isolated. Benzo[*c*]cinnoline (XXXIX) is not easily reduced to the diamine, and thus the heterocyclic compound usually is the end product of the reduction (19). Lloyd and McDougall (116) confirmed that the diamine can be made; they obtained 74–85% yields by this method if starting quantities of less than 1 g. of the dinitro were used. Either nickel or Pd–C (10%) gave the same product. If larger batches of starting material were used, benzo[c]cinnoline (XXXIX) was also obtained. They found that benzo[*c*]cinnoline 6-oxide (XXXVIII) was the product when the dinitro compound was reduced with hydrogen gas using Pd as a catalyst. A comparison of the hydrazine and Raney nickel method with the tin and hydrochloride acid procedure gave comparable yields, 80%. Benzo[c]cinnoline (XXXIX) in 80% yield is also the end product when 2,2′-dinitrobiphenyl (XXXIII) is reduced in 5% alcoholic potassium hydroxide using Ru as a catalyst (147).





Szmant and Infante (166) reduced di(2-nitro-4-chlorophenyl) sulfone (XLI) with Raney nickel and hydrogen and obtained the corresponding diamine. Using hydrazine and Raney nickel they obtained derivatives of 1-thia-4,5-diazocyclohepta-2,4,6-triene (XLIII). The azoxy (XLII) derivative was reduced to the azo (XLIII) in 97% yields.

C. REDUCTIONS WITH RANEY NICKEL WITHOUT HYDRAZINE

It is possible that some of the reductions attributed to hydrazine may be those of the Raney nickel catalyst alone. It is also possible that those reactions taking place in the presence of nickel will go faster and more efficiently with the addition of hydrazine. Some success was achieved by this latter procedure (153). Karabinos and Ballun (93) refluxed some monosaccharides in aqueous ethanol in the presence of Raney nickel and reduced D-mannose to D-mannitol in 79% yields. Similarly, D-galactose was reduced to D-galactitol in yields of 74%. Ainsworth (4) cleaved acid hydrazides to amides by flooding the reaction mixture with Raney nickel. Cyclohexanecarboxamide was obtained in 70% yields. Primary amines treated with alcohols in the presence of Raney nickel were converted to secondary amines (5). Hinman (78) cleaved alkyl-substituted monoacylhydrazides and also obtained amides, but the reaction time was in hours and yields ranged from 5 to 60%.

Where hydrazine was used in conjunction with Raney nickel for cleaving nitrogen–nitrogen bonds including cyclic hydrazides (*i.e.*, maleic acid phenylhydrazide to maleamic acid anilide), the minimum yield was 50% in about 1 hr. (153).

D. NATURE OF CATALYSTS

For the reduction of aromatic nitro compounds, completely or partially, by the catalytic hydrazine reduction method, the classical hydrogenation catalysts, Ni, Pd, and Pt, are most commonly used. These are documented throughout this review.

Less common is the use of Ru (143). Iron is also being used (107).

In the case of hydrogenation of carbon–carbon double bonds by the intermediate diimide, oxidation conditions are used, and catalysts employed can be copper or iodine (see section VIIA).

Some catalysts may merely serve as a surface for hydrazine decomposition to yield hydrogen. This argument is presented by Stafford, Los, and Thomson (165) who merely used porous tile as the catalyst. More work needs to be done in this area.

E. NATURE OF SOLVENTS

The solvent generally used for the catalytic hydrazine reactions is ethanol or methanol. Dioxane (100) and xylene (19) have also been used. The only study reported to date showing the relationship of solvents to reaction products is the early work of Busch and Schulz (31), who reduced nitrobenzene in the presence of hydrazine, Pd–$CaCO_3$ (1%), and potassium hydroxide. Azoxybenzene was obtained in ethanol but azobenzene was obtained in methanol. Is this a temperature effect? High boiling solvents like ethylene glycol or its ethers can be used with or without catalysts for the reduction of nitro compounds to amines. This becomes essentially part of the modified Wolff–Kishner reduction (85, 176) and will be discussed in that section.

F. NATURE OF HYDRAZINES

Most of the work reported in the literature is concerned with catalyzed, unsubstituted hydrazine, either anhydrous or as the hydrate. Kuhn (108) successfully reduced hexyl nitrate and nitrobenzene using monomethylhydrazine and either platinum black or palladium. Both methane and ethane were identified in the reaction gases by infrared spectroscopy. Berlo and Furst (24) were unable to isolate 1-naphthylamine from a mixture of 1-nitronaphthalene, methanol, and UDMH (unsymmetrical dimethylhydrazine). In a parallel experiment, the naphthylamine was isolated (as the acetyl derivative) in 77% yield when hydrazine was used in place of UDMH. The same compound was obtained when Pd–C was used (140).

Ochiai (136) used phenylhydrazine with a catalyst to reduce 4-nitropyridine N-oxide to the hydroxylamine without cleaving the N→O bond.

G. MECHANISMS OF REDUCTION

Surprisingly little has been published on the mechanisms of the reduction of nitrobenzene either to aniline or to the intermediate coupled products by any reductive method. Most books on theoretical organic chemistry do not treat this topic. When any mention is made of these reductions, only the over-all statement is given: nitrobenzene under neutral or basic conditions can be reduced to the azoxy, azo, or hydrazo intermediate.

By the catalytic hydrazine reduction method, most of these coupled products can be isolated. In the very first step of the reduction of nitrobenzene, nitrosobenzene is postulated but has not been isolated. It is possible that once formed the nitrosobenzene is rapidly transformed to the phenylhydroxylamine, which has been isolated (19, 53, 128, 136). This occurs especially with substituted nitrobenzenes. The phenylhydroxylamine can then be further reduced to the aniline. To obtain the coupled intermediates, it is always assumed that either nitrosobenzene or phenylhydroxylamine is present along with some of the completely reduced product, aniline.

An acid-catalyzed mechanism may be logically invoked for the reduction of nitrobenzene to aniline. Hydrazine may enter both acid and basic catalysis as the hydrazide negative ion or hydrazinium positive ion, for hydrazine itself is more basic than aniline. It may, on the other hand, donate a proton to initiate the reduction of nitrobenzene.

The formation of nitrosobenzene (XLV) is not easily explained by the catalytic hydrazine reduction method, but nitrosobenzene itself is an unusual compound and the first step of its formation may be the *diazoxy*benzene (XLIV). This molecule has never been isolated by this or any other method. In the aromatic polycyclic system it does exist. What is the nature of the molecular species? Does it dissociate easily into nitrosobenzene?

The heat of dissociation can be calculated. Is it possible the extra resonance energy of benzo[*c*]cinnoline di-N-oxide (XXXVII) associated with the accepted structure of this molecule is responsible for its stability?

A good logical explanation of the step-by-step mechanism for the formation of nitrosobenzene and hydroxylamine is still forthcoming. A postulated mechanism for the formation of the coupled products can be worked out.

III. REDUCTION OF MISCELLANEOUS NITROGEN COMPOUNDS

A. REDUCTION OF NITRITE ESTERS, OXIMES, AND NITROSO COMPOUNDS

Miscellaneous nitrogen compounds, especially aliphatics, have had very little study. The nitrite and nitrate esters of C_4 and C_6 alcohols are smoothly reduced to alcohols in the presence of Pt or Pd (108, 126). Oximes are reduced either to the amine (73) or hydrazone (155), but no details are given.

N-Nitrosodiethylamine is reduced to diethylamine by Ni, but not Pd (79). Table IV summarizes the work in this field.

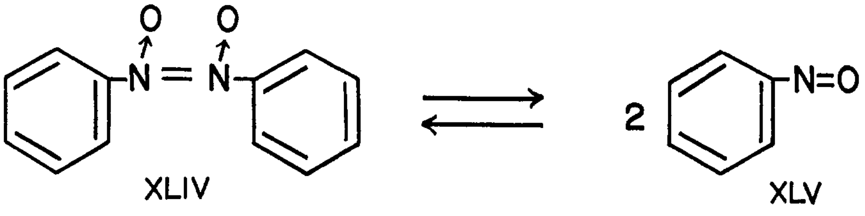
TABLE IV

REDUCTION OF MISCELLANEOUS NITROGEN COMPOUNDS

Compound	Product	Catalyst	Yield, %	Ref.
2-Methylcyclohexanone oxime	Amine	Ni	...	73
Acetone oxime	Hydrazone	...	...	155
Acetaldehyde oxime	Hydrazone	...	...	155
N-Nitrosodiphenylamine	Diphenylamine	Ni	...	143
n-Butyl nitrite	*n*-Butyl alcohol	NaOH	...	126
Hexyl nitrite	Hexanol	Pt or Pd	90+	108
Hexyl nitrate	Hexanol	Pt or Pd	90+	108

B. REDUCTION OF AROMATIC NITRILES

Aromatic nitrile compounds in the presence of nickel can be reduced to the anil (XLVI). These can then be hydrolyzed to the corresponding aldehydes in 50–60% yields (148). A side product is the reduced secondary amine (XLVII) (39, 67). This is not effective as a method for the formation of aliphatic aldehydes from aliphatic nitriles (149). In the aldehyde reaction, phenylhydrazine can substitute for hydrazine if Raney nickel is the catalyst (70).



Aromatic nitriles can also be reduced to azines (149) and hence to amines (82), or directly to amines (175). In one case the reduction product isolated was an amide (139).

$$\underset{\text{XLVI}}{C_6H_5\text{—}N\text{=}CH\text{—}C_6H_5} \rightarrow \underset{\text{XLVII}}{C_6H_5\text{—}NH\text{—}CH_2\text{—}C_6H_5}$$

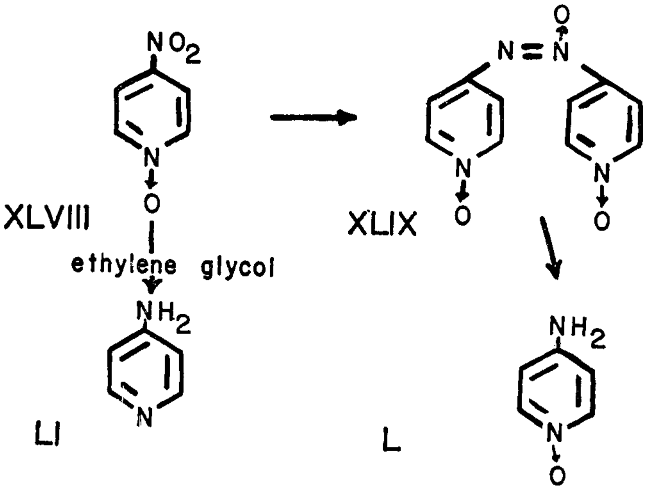
Indoleacetonitrile was reduced to tryptamine in 90% yields; phenylacetonitrile gave phenylethylamine in 59% yields when Raney nickel was used as a catalyst (175).

Polynuclear hydrocarbons in 90+% yields can also be obtained from the reduction of *o*-cyanodiphenylmethane (183) (see section IIA3).

C. REDUCTION OF N-OXIDES

Variable results were obtained upon treating heterocyclic nitrogen N-oxide compounds with hydrazine. Taylor and Driscoll (173) reduced 4-nitronicotinic acid 1-oxide using a Raney nickel catalyst. Both 4-aminonicotinic acid 1-oxide (6.9% yield) and 4-hydrazinonicotinic acid 1-oxide (22% yield) were obtained. Maffei and Pietra (121) reduced phenazine N-oxide nearly quantitatively to phenazine when a Pd–C catalyst was employed. Pietra (144, 145) also reduced the oxide of 2-chlorophenazine N-oxide using Ru–C without dehalogenation.

A study of the copper-catalyzed hydrazine reduction of 4-nitropyridine 1-oxide (XLVIII) was made by Kubota and Akita (101). The azoxy 1,1′-di-N-oxide (XLIX) derivative was first isolated then reduced to 4-aminopyridine 1-oxide (L). When high boiling ethylene glycol solvent was employed, only 4-aminopyridine (LI) was recovered after refluxing for 2 hr. (101). On treating 2-methyl-4-nitropyridine 1-oxide by the catalytic hydrazine reduction method, again using a copper catalyst, the azo 1,1′-di-N-oxide rather than the corresponding azoxy was obtained (101, 106).



IV. DEHALOGENATIONS

A. INTRODUCTION

Expected products from the treatment of an organic halo compound with hydrazine are the substituted hydrazine and the unsymmetrical disubstituted hydrazine (33). Active halogens are easily substituted, and the diacetophenonehydrazone in about 80% yield is recovered from the reaction mixture of hydrazine and phenacyl bromide (130).

Hydrazine can also be employed as a reducing agent for organo halides. Completely reduced, hydrolyzed, or side products are obtained from this reaction.

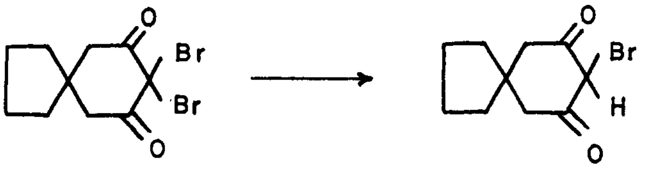
B. DEHALOGENATION OF ALIPHATIC COMPOUNDS

Aliphatic halo compounds are reduced or hydrolyzed in the presence of hydrazine without a catalyst. Iodoform was obtained from the reduction of carbon tetraiodide (179) by hydrazine in a liquid ammonia medium. The halogen is replaced by hydrogen on methane if more than one nitro group is also present (119). However, no reaction took place between hydrazine and 1-bromo-1,1-dinitroethane (80).

Halo-substituted active methylene compounds are readily reduced to the methylene compound itself. A large variety of α,α-dibromomalonic esters were reduced by hydrazine (79), as were the α,α-dibromo derivatives (71). The *mono*chloro- and *di*chloromalonamides were also completely reduced. The dibromomalonamide was converted to mesoxalamide hydrazone (81). The bromo- and chloroacetoacetates (118) as well as the halonitroacetates (120) were also dehalogenated (without nitro reduction).

α-Halo-substituted aliphatic acids and esters were dehalogenated (83), but the hydrogenated product was not obtained; the apparent hydrolysis compound, the α-hydroxy derivative, was isolated (22).

Aliphatic cyclic halo compounds were also dehalogenated. Cyclopentanespiro-4,4-dibromocyclohexane-3,5-dione (LII) was reduced to the monobromo compound (LIII) (117). Both N-bromosuccinimide and N-chlorosuccinimide were dehalogenated with explosive violence (80), as was the other Wohl–Ziegler reagent, N-chloroacetamide (79).



LII LIII

C. DEHALOGENATION OF AROMATIC COMPOUNDS (WITH AND WITHOUT NITRO GROUP)

Until recently the use of hydrazine as an agent for the complete reduction of aromatic halo compounds was too unpredictable to be employed as a preparative dehalogenation method (37).

Inconsistent results were obtained in dehalogenation with or without nitro reductions. Using nickel, no dechlorinations were noted on reducing nitrochlorophenyl sulfone (166). Leggetter and Brown (111), using nickel, also reduced a large series of aromatic nitro compounds without dehalogenation, whereas Müller and Weisbrod (133) obtained both dechlorination and intermediate reduction of 1-chloro-2,4-dinitronaphthalene. In the presence of Pd–$SrCO_3$, 2-chloro-4-amino-5-nitro-6-ethylpyrimidine was dehalogenated and reduced to 2,3-diamino-4-ethylpyrimidine (154). This reaction gives evidence that not all pyrimidine rings are cleaved by the catalytic hydrazine reduction method.

A series of the aromatic halonitro compounds have been reduced to the anilines without dehalogenation (see Table I, part C), whereas other nitrohalo compounds were reduced to the anilines with dehalogenation (see Table I, part D).

Evidence that the catalyst might be important in the dehalogenation reaction came from the following: Busch and Schmidt (30) dehalogenated a series of halobenzenes with hydrazine, employing Pd–$CaCO_3$ (1%) in methanolic potassium hydroxide. They obtained both benzene and biphenyl; dihalo compounds gave terphenyls. Os, Rh, and Ru were ineffective as catalysts (32). Pietra (144) found that upon reducing bromonitrobenzenes, bromoaniline was obtained if Ru–C was the catalyst, but only aniline was the product if Pd–C was used. Thus he concluded that Ru is not as effective as Pd as a catalyst for dehalogenations (143). Mosby (131), using Pd–C, was able to both dehalogenate and reduce halonitrophenanthrenes (131). He later presented a good laboratory procedure for dechlorination and debromination of aromatic and heterocyclic compounds using Pd–C (130). Tribromonitronaphthalene can also be converted by this procedure to naphthylamine (178).

On investigating the nature of the catalysts in the catalytic hydrazine reduction method, Furst and Berlo (68) found that Pd was a specific catalyst for the dehalogenation. Neither Ni nor Pt could replace Pd. [Defluorinations have not been investigated adequately as yet; some indications appear that defluorinations may not go readily (64, 68).]

D. MISCELLANEOUS REACTIONS OF HALOGENATED COMPOUNDS WITH HYDRAZINE

Halogenated polynitrobenzenes react in a variety of ways with hydrazine. No catalysts are necessary in this series. Nitro groups may act as activating groups and may enhance the replacement of a bromo by a hydrazine (91). The treatment of 1,2,3-tribromo-4,6-dinitrobenzene with hydrazine yields 2,3-dibromo-4,6-dinitrophenylhydrazine (72). On the other hand, a nitro rather than a bromo may be displaced by hydrazine; 3,4-dibromo-1,6-dinitrobenzene yielded 3,4-dibromo-6-nitrophenylhydrazine (72). In both of these cases cited, no reductions were noted. Chloro compounds act similarly to bromo compounds, but poor yields are obtained (132).

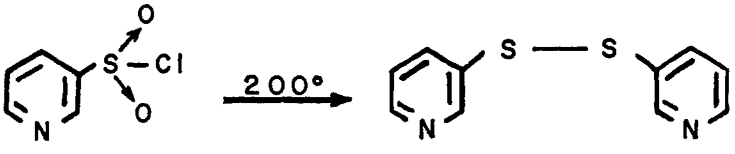
Side reactions are also encountered during dehalogenations of aromatic and heterocyclic compounds. Some halopolynitrobenzenes on treatment with hydrazines without catalyst reacted to give substituted 1-hydroxybenzotriazoles (90, 92).

The catalytic hydrazine reduction method may be used as an alternate to the Ullmann synthesis of biaryls (58). Yields of 75% of biphenyl and polyphenyls can be obtained during the treatment of halobenzenes in methanolic potassium hydroxide if Pd–$CaCO_3$ (1%) is the catalyst (30). Ueda (177) used this procedure to couple 2-, 5-, or 7-bromoquinoline. The corresponding 2,2′-, 5,5′-, or 7,7′-biquinolyl was obtained in yields of about 40%. This reaction has been extended to the pyridines (150).

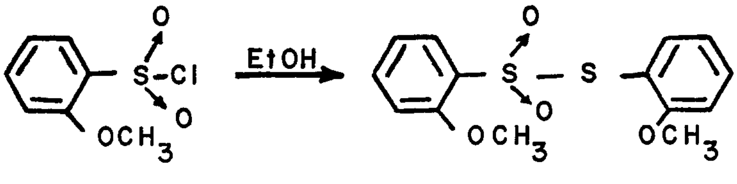
V. ACTION OF HYDRAZINE ON SULFUR COMPOUNDS

The product obtained from the treatment of a sulfur compound with hydrazine depends on the nature of the sulfur derivatives.

Most work has been on the organo sulfonyl chlorides, and the expected sulfonhydrazide is not always the product. Butanesulfonyl chloride yields dibutyl disulfide (103); similarly pyridinesulfonyl chloride (LIV) yields the corresponding dipyridyl disulfide (LV) in 70% yield (104). Some substituted benzenesulfonyl chlorides (LVI) will, at lower temperature in alcoholic solution, yield either the free acid or thiosulfonic acid, or a partially oxidized disulfide (LVII) (102). N,N-Dichlorobenzenesulfonamide was quantitatively dechlorinated



LIV LV



LVI LVII

(79) without modification of the sulfur linkage, whereas a di(2-nitro-4-chlorophenyl)sulfone was cyclized to 2-nitroso-2′-hydroxylamino-4,4′-dichlorophenyl sulfone, without dehalogenation; the sulfone group again remained unattacked.

The anilide of picolinic acid was converted to N^3-phenylpicolinamidazone with loss of hydrogen sulfide (164). Will the catalytic hydrazine reduction procedure make simple Raney nickel desulfurization methods more efficient? The conditions may be important, for diallyl disulfide was saturated to di-*n*-propyl disulfide without desulfurization using the diimide intermediate (167).

VI. Reduction of Oxygen Functional Groups

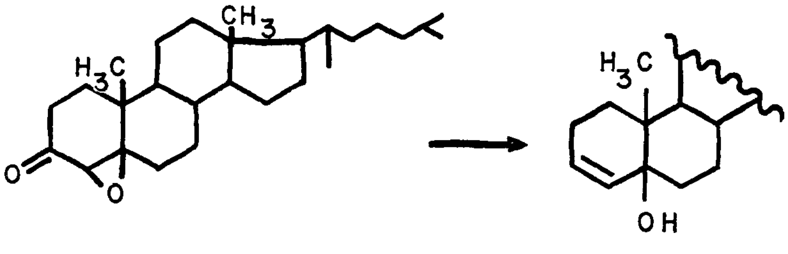
A. CARBONYL TO METHYLENE (WOLFF–KISHNER)

The Wolff–Kishner reduction has been adequately documented by Todd (176). To avoid sealed tube techniques, Huang-Minlon (85) used a high boiling solvent like diethylene glycol and made this a practical reaction at atmospheric pressure. It is not necessary to isolate the hydrazone first. A mixture of the aldehyde or ketone, hydrazine hydrate, potassium hydroxide, and ethylene glycol or diethylene glycol is heated to distil off the water. The temperature is then raised to 195° for 2 to 4 hr. The yields ranged from 60 to 90% (85, 176). During these investigations of the reduction of carbonyl compounds, Huang-Minlon reduced a number of nitro compounds (84). *p*-Nitrobenzaldehyde was reduced to *p*-toluidine. In the presence of potassium hydroxide, the yield was 71%; without the base, the yield fell to 41%. A series of nitro compounds were also reduced in yields approximating 70% (84). Included are *p*-nitrophenylacetic acid, *m*-nitrotoluene, and 4,4′-dinitrostilbene. Salzberg (158) using this method reduced methyl *m*-nitrobenzoate to *m*-toluidine in 25% yield. A nitrotropolone was reduced to an amino compound in 79% yield without carbonyl reduction (34).

A further modification of the Wolff–Kishner reduction utilizes dimethyl sulfoxide as the solvent and potassium *t*-butoxide as the base (43). Aldehyde or ketone hydrazone (pure) is added slowly over a period of 8 hr. to a solution of sublimed potassium *t*-butoxide in anhydrous dimethyl sulfoxide at 25°. Yields of 64 to 90% of the methylene compound were obtained with varying amounts of the azine as a by-product. Since this modification enables the reaction to be carried out at room temperature, it is of value when other functional groups are present which would react with potassium hydroxide in diethylene glycol at 160–200°. However, it is more time consuming than the Huang-Minlon procedure mentioned above, requiring anhydrous conditions and prior preparation of the pure hydrazone.

B. OTHER OXYGEN FUNCTIONAL GROUPS

Not all of the Huang-Minlon modifications of the Wolff–Kishner reduction result in the reduction of carbonyls to methylene groups. An α,β-epoxy ketone (LVIII) was reduced to an allylic alcohol (LIX) (182). Benzoquinones were reduced to corresponding dihydroxy compounds (6). Cumene hydroperoxide was reduced to acetophenone at 0° in the presence of hydrazine and ferric-EDTA complex (124). *o*-Nitrobenzonitrile was converted to *o*-aminobenzamide by the usual nickel–hydrazine reduction procedure (139). β-Naphthol was first made into the tosylate derivative and then converted to naphthalene (109, 156). Thus a phenol group can now effectively be replaced, although not directly, by a hydrogen without resorting to zinc dust procedures. More work needs to be done in this area.



LVIII LIX

VII. REDUCTION OF UNSATURATED COMPOUNDS

A. REDUCTION OF OLEFINIC COMPOUNDS

Two parallel but independent series of papers appeared in 1956 on the use of hydrazine for the reduction of multiple bonds. Pietra (140–142) reduced a series of unsaturated dicarboxylic acids by hydrazine and Pd–C. Succinic acid was obtained from maleic or fumaric acid, butyric from crotonic acid, and hydrocinnamic from cinnamic acid. Stilbene was reduced to diphenylethane. Aylward and Rao (11, 12) also used hydrazine for the saturation of unsaturated fatty acids. They reviewed the literature and tried to find the optimum conditions for the saturation of unsaturated fatty acids first reported by Falciola and Mannino in 1914 (57).

In summary articles, Aylward and Sawistowska (13–15) reported the effects of pH, temperature, solvents, length of carbon chain of the fatty acid, oxygen, and catalysts on the saturation reaction. Oxygen was found necessary, thus better yields up to 90% were obtained by agitation. Oxidizing agents like hydrogen peroxide and potassium iodate and dichromate also promoted the saturation reaction. An alkaline pH was essential, and the optimum temperature was 50°.

Metallic catalysts like copper would promote the oxidation of hydrazide, but had no effect on the reactivity of the double bonds. They repeated the conditions of Balcom and Furst (18) and found the hydrazine was decomposed at too rapid a rate, and poor saturation yields were obtained by this method. These results are at variance with those reported by Pietra (141, 142) whose work was not quoted.

Kinetic studies on C_{12} and C_{15} unsaturated acids (51) showed that individual double bonds were randomly reduced (52) without reference to the position of the double bonds. Nonconjugated double bonds react at the same rate anywhere along the chain; faster rates were found for terminal unsaturated groups and for conjugated acids (160). No isomerization was noted (159). From the results of the kinetic studies it was concluded that an oxidation product was the effective reducing agent (15), and hydrazine alone may not be the true reactant.

B. REDUCTION OF ACETYLENE COMPOUNDS

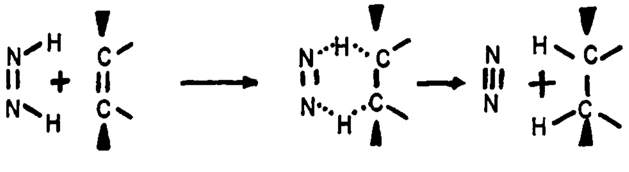
Only three reports include acetylene compounds. Phenyl-conjugated acetylenic acids (LX) were completely saturated by hydrazine with either PtO_2, Raney Ni, Ru–C, or Pd–C (146) to yield LXI.

$$\underset{\text{LX}}{C_6H_5—C\equiv C—COOH} \rightarrow \underset{\text{LXI}}{C_6H_5—(CH_2)_2—COOH}$$

Butyne-1,4-diol was saturated to butane-1,4-diol in 40% yields (40). When similar conditions were employed, phenylpropiolic acid was reduced to *cis*-cinnamic acid in 40% yield (87).

C. MECHANISM. THE DIIMIDE

A study of the saturation of ethylene bonds led a number of independent investigators to conclude that the actual reducing species is diimide (LXII) (40, 87, 167). Hydrazine alone is not effective as a saturating agent, though it may act as a source for hydrogen in the presence of the metal hydrogenation catalysts (156, 160).



LXII LXIII LXIV LXV LXVI

The postulation of the *diimide* mechanism is remarkable in that a net reduction reaction first requires an oxidation step. Thus hydrazine must be dehydrogenated to diimide prior to the saturation reaction. Oxidative conditions (dehydrogenation) are thus necessary, and when the reaction is carried out in the presence of air, hydrogen peroxide, cupric ion, ferricyanide, or iodine, the yield of the saturated product will be increased. Energetically, the ΔH of the formation of diimide, and its use as a saturating agent, is thermodynamically acceptable (40).

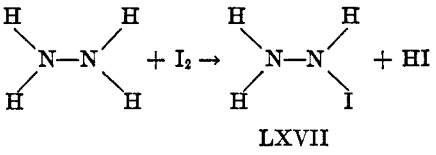
The stereochemistry of the reduction has also been postulated. Double bonds are reduced by a *cis* mechanism (169). It is possible that the reaction goes through a *cis* addition by means of a cyclic transition state (LXIV) (86, 87). Studies with deuteriodiimide seem to support this postulation (41).

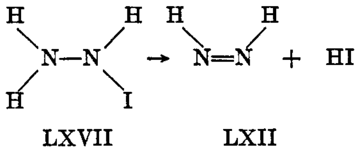
Diimide has been used to hydrogenate unsaturated dicarboxylic acids, and either *cis*- or *trans*-2-butenedicarboxylic acid (maleic or fumaric) can be reduced to succinic acid; *trans*-cinnamic acid is converted to hydrocinnamic acid, and β-phenylpropiolic acid is reduced to *trans*-cinnamic acid in 40% yield (87). Azobenzene is readily converted to hydrazobenzene and may be used as a test for diimide (40).

Not all hydrazine reductions involve a diimide intermediate. The reduction of nitrobenzene (18) probably does not involve a diimide mechanism (167), nor is dehydroxylation of naphthol dependent upon this intermediate (156).

The effectiveness of diimide as a reducing agent has been reported: symmetrical bonds, $C=C$, $S—S$, $N=N$, and $O=O$ are easily reduced; $C=O$, $C=N$, $C\equiv N$, $S=O$, $C\equiv N$, $S—C—S$, $O=N—O$, and other unsymmetrical polyfunctional bonds are reduced with difficulty (167). Diimides do not split sulfur–sulfur bonds (167).

There are a variety of procedures and precursors for the formation of diimide. Catalysts available include air, hydrogen peroxide, and copper, and recently iodine has been added and an iodohydrazine (LXVII) intermediate is postulated.





More unusual sources of diimide are decomposition of imide-containing molecules like anthracene-9,10-diimine (39), chloramine (161), the hydrazine of phenolphthalein (105), hydroxylamine-O-sulfonic acid (7), *p*-toluenesulfonic hydrazide (50), and azodicarboxylic acid (87, 168).

One drawback to the publication of Communications to the Editor without an immediate follow-up with completed papers giving experimental details is the impression left that some of the intermediates are stable, or have been isolated. The diimide is made *in situ*, it is not isolated, for it has only a transient half-life; it cannot be trapped by Diels-Alder reactions. Also, the azodicarboxylic acid is immediately and rapidly decomposed in water and also cannot be isolated (99). Experimental conditions thus become important, and the experimenter will be greatly aided if procedures are published soon after as complete papers.

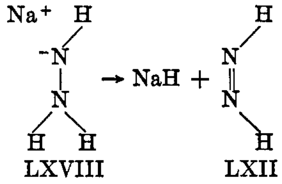
VIII. Reductions Using Sodium Hydrazide

A modified system has been recently introduced which employs sodium hydrazide and hydrazine in an organic solvent. Many reactions are done at temperatures of 0° or below under an atmosphere of nitrogen. Many of the catalytic hydrazine reactions are now being repeated with this new system.

Styrene can be reduced to ethylbenzene (98). The sodium salt and β-phenylethylhydrazine are side products. Unsaturated aromatic compounds with more than one ring, including quinaldine and polynuclear hydrocarbons, are reduced to the dihydro derivatives in yields above 85% (97). These reductions include stilbene to 1,2-diphenylethane in 92% yields, 1,4-diphenylbutadiene to 1,4-diphenylbutane in 67% yield (94), and phenanthrene and anthracene to the corresponding dihydro derivatives. A side product in the reduction of stilbene is 2-hydrazinobibenzyl (97).

Reductive dehalogenations in high yields have also been achieved (96); included in this series are the bromo derivatives of mesitylene, anisole, naphthalene, and chloroferrocene. A quantitative replacement of fluorine by hydrazine is noted in the formation of *p*-toluylhydrazine from *p*-fluorotoluene. The proposed mechanism goes through a benzotriazole step (95).

The mechanism of reduction proposed by Kauffmann (98) involves sodium hydrazide (LXVIII) itself. Evans (56) suggests that sodium hydrazide may dissociate to sodium hydride, and the resultant diimide may be the reactive species.



IX. Conclusion and Suggestions

The catalytic hydrazine reduction method may replace low pressure hydrogenation for most reactions. By this means it is possible to reduce nitrobenzene derivatives completely to the anilines or, in most cases, to intermediate coupled products. By varying conditions in some reactions, the phenylhydroxylamine may be the end product. Nitrosobenzene has not as yet been isolated by this procedure, but it is postulated as an intermediate for coupled products. Dehalogenation of active halogens goes smoothly for aliphatic compounds. Aromatic chloro, bromo, or iodo compounds can now be effectively dehalogenated too; the fluorines are still equivocal. By modifying the catalytic hydrazine reduction method, then invoking the diimide, intermediate aliphatic unsaturated compounds may be completely saturated. Most of these reduction reactions can be duplicated by using sodium hydrazide in hydrazine.

There is much work left to be done. To date there has been no systematic study of the reduction of aliphatic nitro compounds by hydrazine. More work needs to be done on the nature of the catalyst. Does the catalyst serve more than as a surface for the decomposition of hydrazine to form hydrogen *in situ*? Can other powdered metals be used, for example, aluminum? The nature of the solvent and its role in this reaction also needs investigation. This latter study may make a good undergraduate research problem.

Will the addition of hydrazine enhance the reactions that are commonly associated with Raney nickel alone, *i.e.*, in the splitting of acid hydrazides to amides, and catalytic desulfurizations? Can the catalytic hydrazine reaction serve to split benzyl ether, or benzyl sulfide groups? Lastly, a study of substituted hydrazines should be made. There are references that imply the phenylhydrazines may be useful. If so, monomethylhydrazine should also be used. What about the other substituted hydrazines that may not be ready sources of the diimide?

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