

THE REDUCTION OF ORGANIC HALIDES AND DIAZONIUM
SALTS WITH SODIUM BOROHYDRIDE

by

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To my mother, whose sacrifices made this possible.

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INTRODUCTION

The subject of this dissertation is the investigation of the uses of sodium borohydride for reducing haloaromatic compounds, polyhalo alkyls and diazonium salts. The work is primarily concerned with the mechanistic study of each type reaction as well as developing it to be a synthetic tool for chemists.

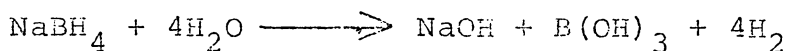
In the cases of the aryl halides and the polyhalogenated alkanes the reactions appear to occur via a displacement on-halogen by the hydride ion. For the diazonium salt reduction the reduction is a nucleophilic aromatic substitution.

Each of these three types of reactions appears to have considerable synthetic utility because of the selectivity of sodium borohydride.

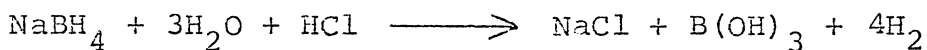
HISTORICAL

Sodium borohydride (SBH) has long been known as a reducing agent for the conversion of ketones to secondary alcohols and acid chlorides to primary alcohols. Lithium aluminum hydride has also been used for the same purpose with comparable yields², but sodium borohydride exhibits many properties which makes it a much more desirable material to use. These properties include ease of handling, stability and ability to be used in a wide range of solvents, such as water, alcohols, ethers, amines, dimethylformamide (DMF), and dimethylsulfoxide (DMSO). Sodium borohydride is a white crystalline, salt-like solid of remarkable stability - stable to 300°C in dry air (400°C in a vacuum). Above 300°C there is a slow evolution of hydrogen and traces of diborane. It ignites in a flame in air and burns quietly³. The density is 1.074 to 1.08 g/cc^{4,5}. One of its most useful properties is that it dissolves in cold water without extensive evolution of hydrogen. At higher temperatures the hydrolysis is more rapid, but the material is fairly stable in basic solution - no appreciable reaction with water at room temperature occurs above a pH of 11.5³. As sodium borohydride decomposes in water sodium hydroxide is formed, thus helping

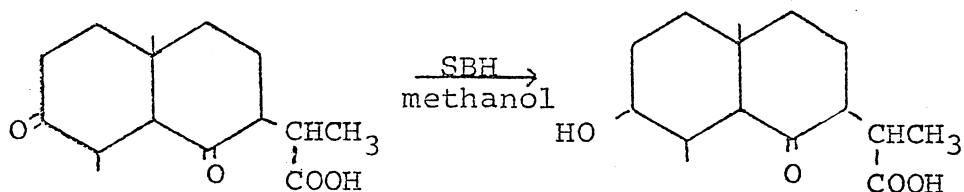
to stabilize it⁶.



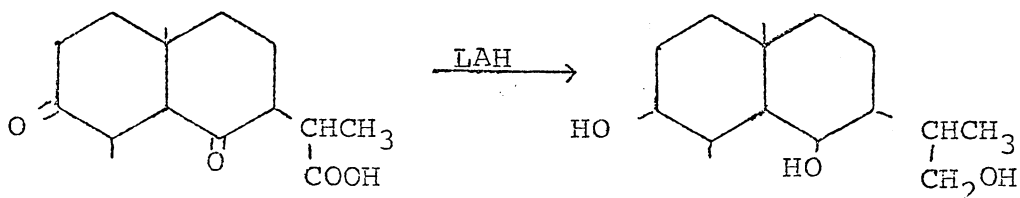
Sodium borohydride decomposes rapidly in acid solution as follows⁷:



Another advantage for sodium borohydride is its selectivity. A typical example of this selectivity is in the reduction of the substituted santonin with keto groups at the 3 and 5 positions. Using sodium borohydride only the keto group in the 3 position is reduced¹⁰.



When lithium aluminum hydride was used, both keto groups as well as the carboxylic acid were reduced.



From this example one can see the value of sodium borohydride in the syntheses of steroids. This usefulness has

Table I

Solubility of Sodium Borohydride^{3,6,8,9}

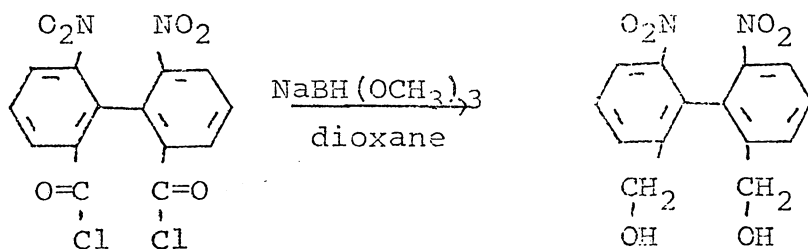
Solvent	Temperature °C	Solubility g/100g
water	20	55
methanol	25	25
ethanol	20	4
isopropanol	20	0.25
pyridine	25	3.1
diglyme	20	3.3
dimethylsulfoxide (DMSO)	25	5.8
dimethylformamide (DMF)	25	25.5

been shown in investigations by Norymberski and Woods^{11,12} where the fully saturated pregnane series undergoes selective reduction at the C-3 keto position, with keto groups in positions C-11, C-12, C-17, and C-20 not reacting except under more forcing conditions.

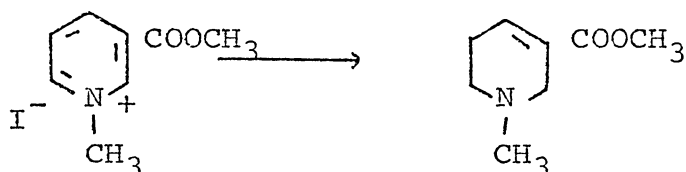
Sodium borohydride has the additional selectivity of normally not reducing such groups as carboxylic acids, lactones, esters, and amides, all of which are reduced by lithium aluminum hydride.

In order to effect the reduction of certain groups that are relatively unreactive toward sodium borohydride in alcoholic or aqueous solutions, Brown and Subba Rao¹³ employed a mixture of aluminum chloride and sodium borohydride in diglyme (dimethyl ether of diethylene glycol) to reduce carboxylic acids, esters and lactones. They also employed other polyvalent metal halides and sodium borohydride to accomplish these more difficult reductions. In their work it was shown that the reduction of the carboxylic acid and ester group can be accomplished in the presence of the nitro group.

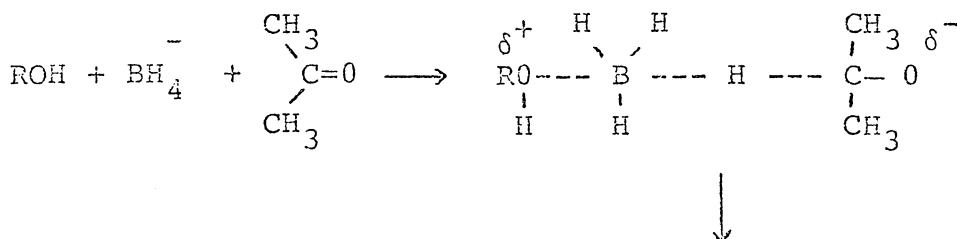
Instead of using a mixture of SBH and a polyvalent metal halide, Iffland and Siegel¹⁵ used sodium trimethoxyborohydride in dioxane to reduce the diacid chloride of 6,6'-dinitrodiphenic acid to the corresponding dialcohol in a 56% yield.

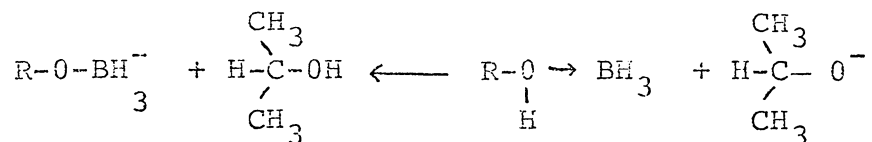


Another method for obtaining selectivity has been by varying the metal ion, that is, to use lithium or potassium borohydride instead of sodium borohydride^{14,16,17}. An example is the reduction of methyl nicotinate methiodide to arecoline, the principal alkaloid of the betel nut¹⁸.

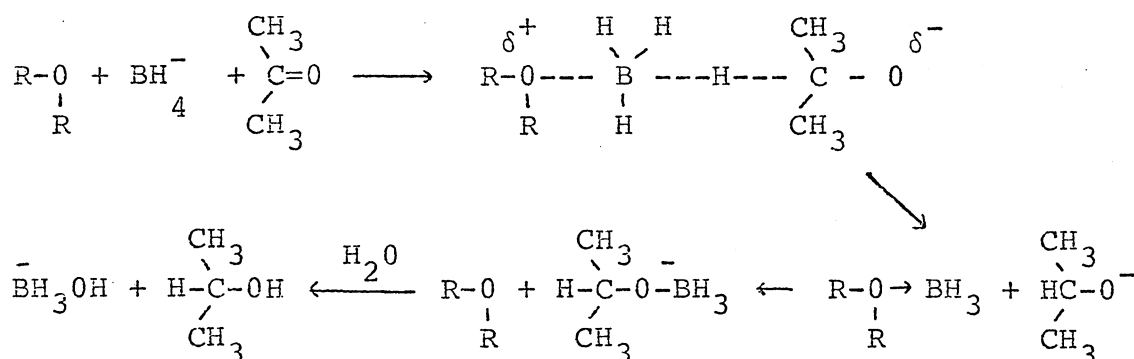


In these latter reductions the use of the aluminum chloride necessitated the use of a solvent without active hydrogens. Brown, Mead, and Subba Rao¹⁴ studied the properties of sodium borohydride in diglyme, and found a much slower rate for the reduction of acetone than when isopropanol was used as the solvent. They attributed the slow reaction in diglyme to the poor donor properties of the ether oxygen in the solvent as compared to the oxygen in the alcohol.



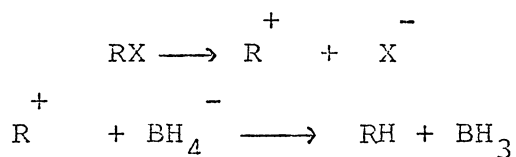


Also, in the diglyme there is no proton available for transfer, thus the product was not obtained until water was added.



These variations illustrate some of the ways sodium borohydride (or its derivatives) can be used to accomplish a reduction that would be very difficult and time-consuming following another pathway.

Until the 1960's it was generally accepted that sodium borohydride was inert towards the reduction of organic halides. In 1962 Brown and Bell¹⁹ reported that the solvolysis of readily ionizable secondary and tertiary organic halides in the presence of sodium borohydride resulted in an excellent yield of the corresponding hydrocarbon.



These reactions were carried out both in diglyme and in a mixture of diglyme and water, the better yields being obtained from the latter solvent mixture. In 1965 Brown and Bell²⁰ published the results shown in Table II for the reduction of alkyl halides with sodium borohydride (1.8 molar) in 80% diglyme - 20% water at 45°.

In 1969 Bell, Vanderslice and Spehar²¹; and Hutchin, et al.²² reported the successful reduction of primary, secondary, and tertiary alkyl halides in DMSO with yields of the hydrocarbon ranging from 42 - 99%. The relative reactivity as evidenced by the rate of gas evolution was iodide > bromide > tosylate > chloride, and methyl > ethyl > propyl > isopropyl; consistent with an Sn2 mechanism²¹. Attempted reduction of these same alkyl halides with lithium aluminum hydride yielded in some cases large amounts of olefin due to elimination³. Also, 1,2-dibromides are reduced to the hydrocarbons in good yields with SBH,²² whereas, lithium aluminum hydride affords only olefin²³.

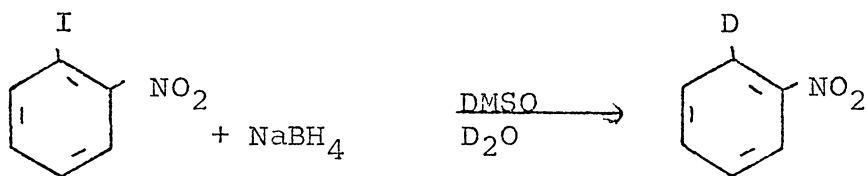
Bell, Vanderslice and Spehar also reported the reduction of two activated aryl halides: o-fluoroiodobenzene and o-nitroiodobenzene with sodium borohydride in 80%

Table II

Reduction of Alkyl Halides with Sodium Borohydride

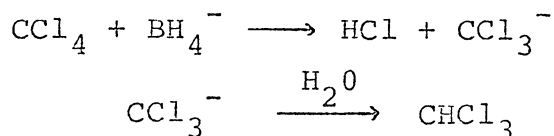
<u>Alkyl Halide</u>	<u>% Yield of Hydrocarbon</u>
benzhydryl chloride	73
benzhydryl bromide	87
p-chlorobenzhydryl chloride	62
p-methoxybenzhydryl chloride	97
triphenylmethyl chloride	97
diphenylmethylcarbonyl chloride	52
t-cumyl chloride	93
1-phenylallyl chloride	86

aqueous DMSO producing a 80% yield of fluorobenzene and a 90% yield of nitrobenzene. When the o-nitroiodobenzene was reduced in 80% DMSO and 20% D₂O, the product was o-deuterionitrobenzene.

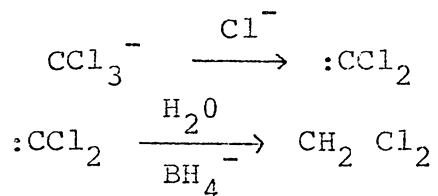


This deuterium incorporation showed that the proton (or deuterium) came from the water and not from the borohydride. This indicated the species $\left[\text{C}_6\text{H}_4\text{NO}_2^- \right]$ was an intermediate. This intermediate would appear to arise from a displacement on the halogen by the hydride ion²⁴ to generate a carbanion site on the benzene ring.

In the same paper it was reported that carbon tetrachloride reacted with sodium borohydride in 80% aqueous DMSO to yield 65 - 70% chloroform and 25 - 30% dichloromethane. Of significance is the fact that chloroform does not react under the same conditions, indicating the dichlorocarbene intermediate. Since S_N2 and S_N1 mechanisms must be eliminated for carbon tetrachloride, the on-halogen displacement by hydride was again postulated.



or



In summary, sodium borohydride which in 1960 was thought to be unreactive towards the reduction of organic halogen compounds has been shown to be reactive in three ways: 1) via an SN1 type displacement of the halide by the hydride ion, 2) via an SN2 mechanism and finally, 3) via the displacement on-halogen.

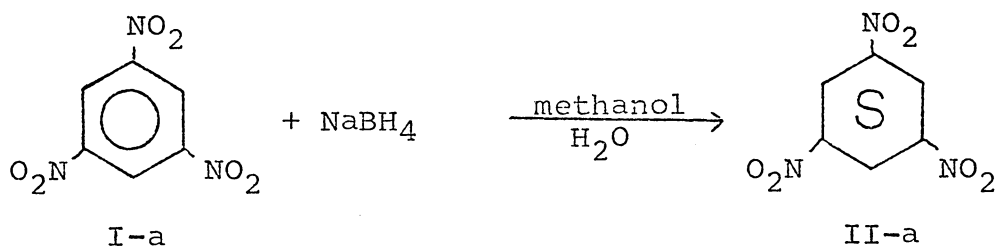
The reduction of halo-aromatic and polyhalo-organic compounds is the subject of this research.

Section A

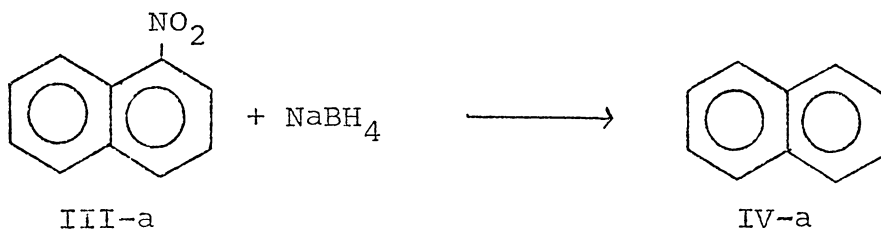
Reduction of Aryl Halides
with SBH in Aqueous DMSO

I. INTRODUCTION

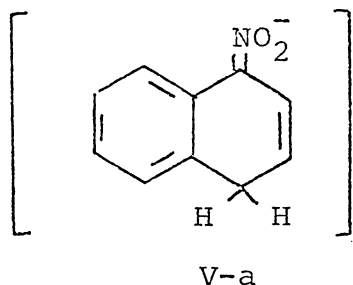
Most of the research involving the reactions of sodium borohydride with aromatic systems has been concerned primarily with the reduction of nitroaromatics. Severin and Schmitz²⁵ studied the reaction of 1,3,5-trinitrobenzene (I-a) with sodium borohydride in methanol and water. This reaction yielded 1,3,5-trinitrocyclohexane (II-a), i.e., the reduction of the aromatic ring.



Severin, Schmitz and Temme²⁶ investigated the reaction of α -nitronaphthalene (III-a) with borohydride and found that in this case the nitro group was lost with the product being naphthalene (IV-a).

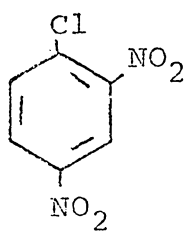


This reaction was postulated to occur by an addition-elimination mechanism with the hydride ion attacking the naphthalene system in the 4-position to form the intermediate (V-a) which loses a nitrous acid function to generate naphthalene.

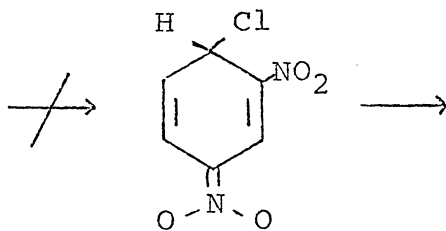


Recently Petersen and Letsinger²⁷ reported the conversion of α -nitronaphthalene to naphthalene in acetonitrile - water (95:5%) with sodium borohydride in the presence of ultraviolet light.

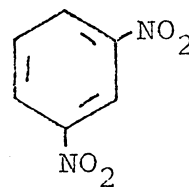
Severin and Adams^{28,29} reacted 2, 4 - dinitrochlorobenzene (VI-a) with sodium borohydride. With this compound there was a chance of forming the intermediate-complex (VII-a) resulting from attack of the hydride ion in the 1-position followed by loss of chloride ion to generate m-dinitrobenzene (VIII-a).



VI-a

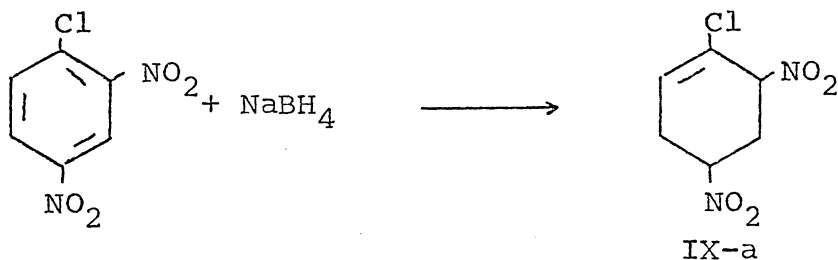


VII-a



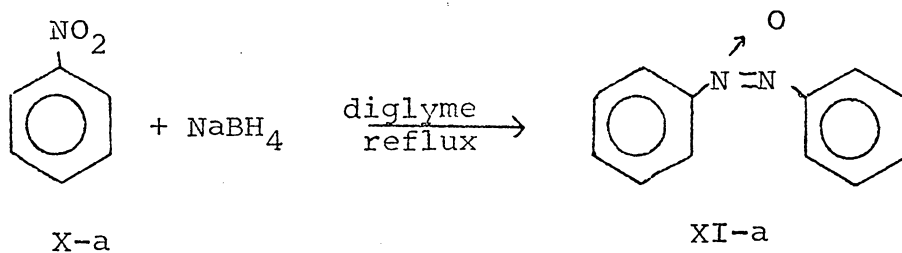
VIII-a

This reaction did not occur; instead, the aromatic ring was reduced to give 1-chloro 2,4-dinitrocyclohexene-6 (IX-a).

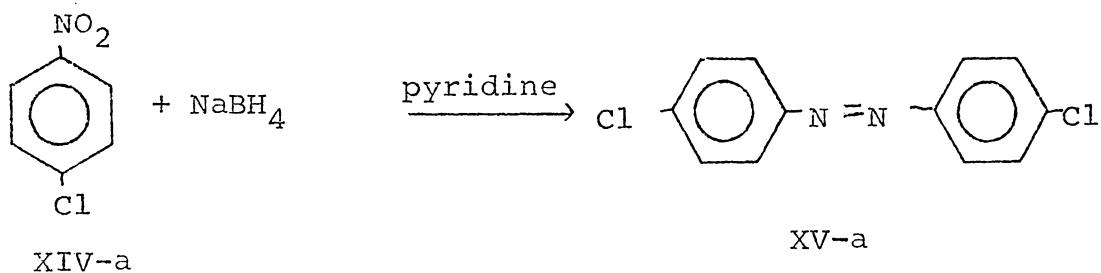
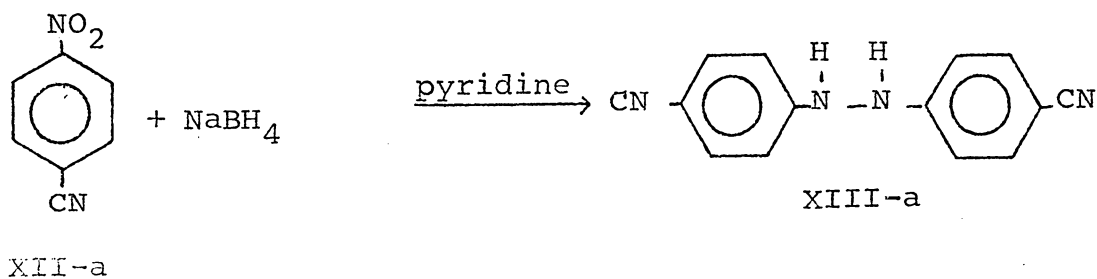


This same type product was obtained when the chlorine was replaced with $-\text{Br}$, $-\text{CH}_3$, $-\text{COOH}$, and $-\text{CH}=\text{CH}-\text{C}_6\text{H}_5$.

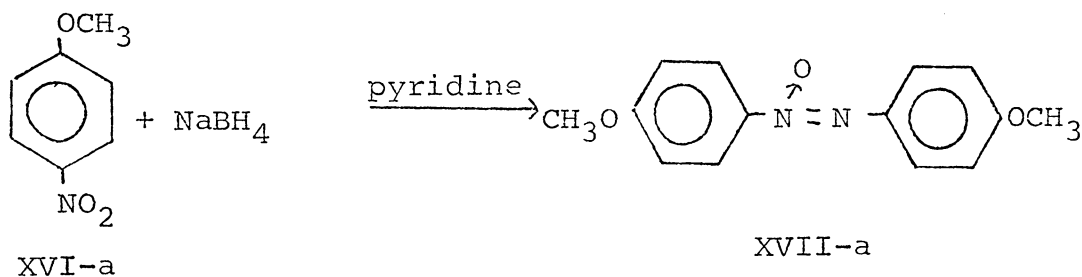
In the previous discussions the attempted reduction of the nitro group was unsuccessful. Either the aromatic system was reduced, or complete loss of the nitro group was encountered. Weill and Ponson³⁰ in 1956 reported the conversion of nitrobenzene (X-a) to azoxybenzene (XI-a) using sodium borohydride in refluxing diglyme.



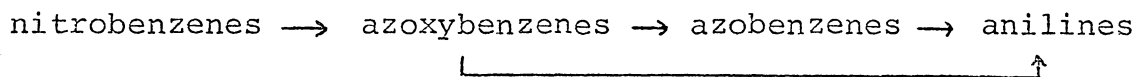
Further studies of the reactions of nitrobenzene and its derivatives with sodium borohydride in pyridine were carried out by Otani, Kikyama and Yamada³¹ who found that with this solvent the azo or hydrazo derivatives could be formed, the product depending on the substituents on the aromatic ring. Reduction of cyanonitrobenzene (XII-a) gave 4,4'-dicyanohydrazobenzene (XIII-a), and 4-chloronitrobenzene (XIV-a) was converted to 4,4'-dichloroazobenzene (XV-a).



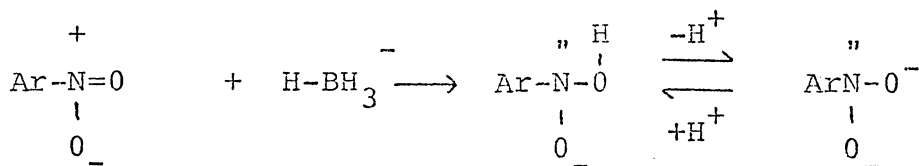
It was found that 4-nitroanisole (XVI-a) gave only the corresponding azoxy compound (XVII-a).



Hutchins, et al.³² studied the reduction of aromatic nitro compounds with sodium borohydride in DMSO and found that nitrobenzene and substituted nitrobenzenes can be reduced to the corresponding amine, to the azo, or to the azoxy derivative. They concluded that electron-withdrawing substituents facilitate both the initial production of the azoxy compounds and the further reduction to azobenzenes and anilines by the following steps:



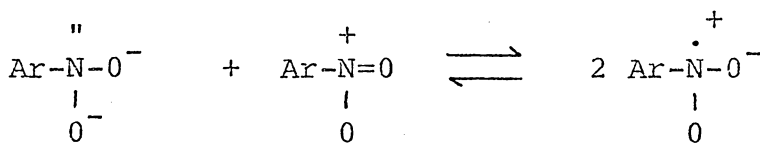
Recent work by Swanwick and Waters³³ indicates that the reduction of aromatic nitro compounds with sodium borohydride proceeds thru the anion-radicals, (ArNO₂^{•-})⁻. Evidence for this species is the existence of an esr signal corresponding to the radical-anion when various aromatic nitro compounds were reduced in aqueous - alcoholic - alkali solutions at room temperature. The proposed mechanism is as follows:



XVIII-a

XIX-a

XX-a

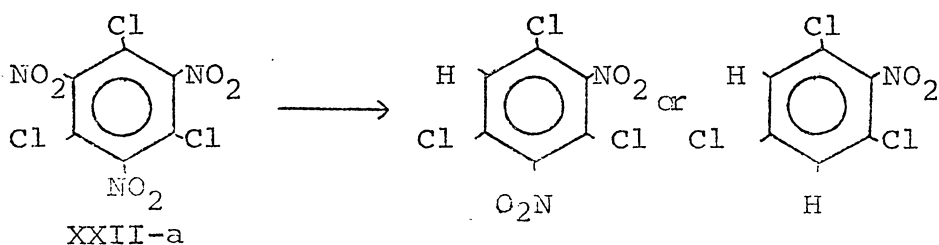


XX-a

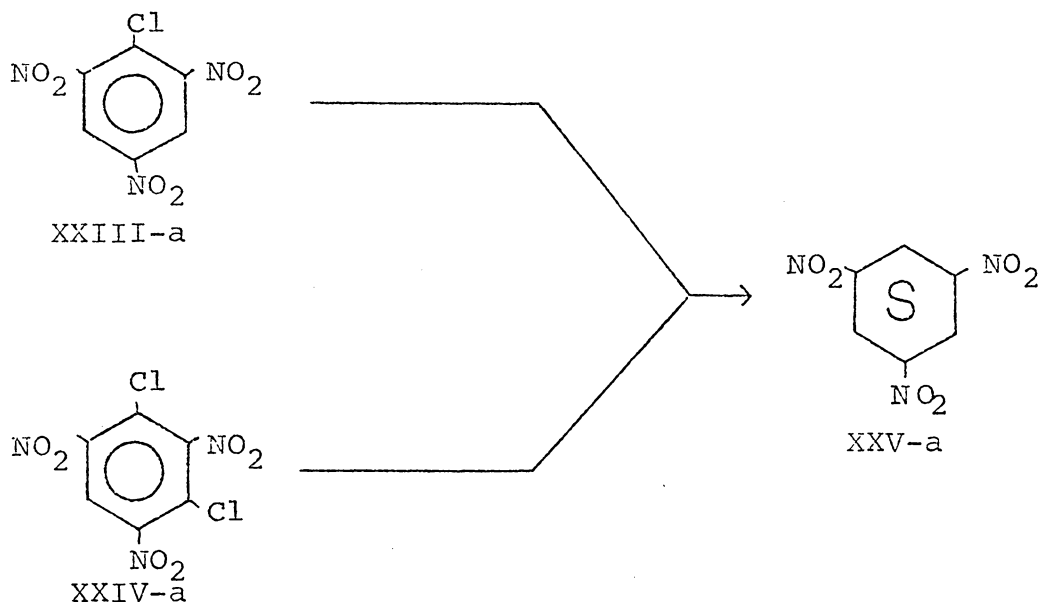
XVIII-a

XXI-a

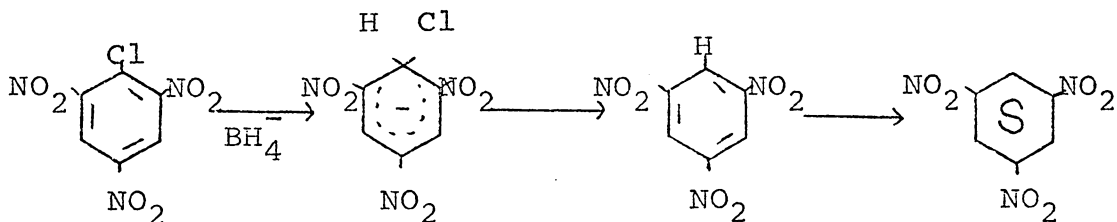
Until 1963 no one had been successful in replacing an aromatic halogen with a hydrogen using SBH. In that year Kaplan³⁵ was studying the reaction of 2,4,6-trinitro-1,3,5-trichlorobenzene (XXII-a) with SBH, and found one or two nitro groups could be replaced by hydrogen without destroying the aromatic system.



When picryl chloride (XXIII-a) and styphnyl chloride (XXIV-a) were reacted under the same conditions, only 1,3,5-trinitrocyclohexane (XXV-a) was obtained.



Kaplan proposed that the first step was the displacement of the chloride by hydride in an intermediate-complex mechanism followed by the reduction of the aromatic system.



One year later Egli³⁷ replaced aromatic halogens with hydrogens using aqueous SBH and a metal catalyst. The most successful catalyst was palladium on charcoal (Pd/C). He found that for ortho halobenzoic acids the ease of replacement was I>Br>Cl. The results are shown in Table I-a. The effect of the carboxylic acid position was also studied and it was found that the ortho halo acids reacted better than the meta or the para (see Table II-a). The study showed that the yield of dehalogenated product could be increased by increasing the amount of Pd/C used.

Table I-a

Reduction of Substituted Benzoic Acids
with SBH and Pd/C - with Heat

<u>Compound</u>	<u>Product</u>	<u>% Yield 10mg Pd/C</u>	<u>% Yield 100mg Pd/C</u>
o-iodobenzoic acid	benzoic acid	100	100
o-bromobenzoic acid	benzoic acid	20	100
o-chlorobenzoic acid	benzoic acid	7	100

Table II-a

Reduction of Substituted Benzoic Acidswith SBH and Pd/C - No Heating

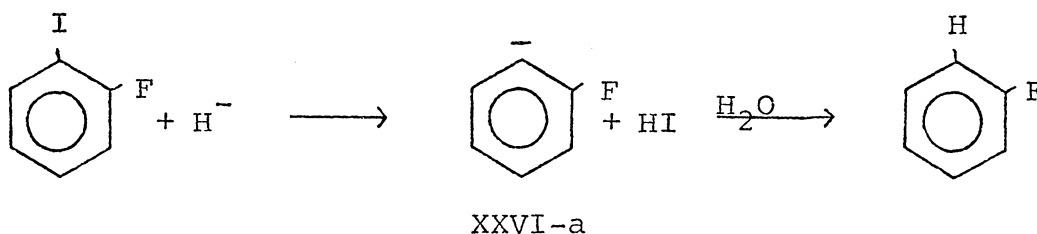
<u>Compound</u>	<u>Product</u>	<u>% Yield 100mg Pd/C</u>
o-bromobenzoic acid	benzoic acid	41
m-bromobenzoic acid	benzoic acid	29
p-bromobenzoic acid	benzoic acid	25

Table III-a

Reduction of Aryl Chlorides with SBH and Pd/C

<u>Compound</u>	<u>Product</u>	<u>% Yield</u>
chlorobenzene	benzene	99
4-chloroanisole	anisole	96
4-chloropyridine	pyridine	84
2-chloropyridine	pyridine	77
3-chloropyridine	pyridine	72
4-chloroaniline	aniline	70
4-chlorobenzonitrile	benzonitrile	44
4-chlorobenzoic acid	benzoic acid	38
3-chlorobenzoic acid	benzoic acid	37
2-chlorobenzoic acid	benzoic acid	35
4-chlorobenzene sulfonic acid	benzene sulfonic acid	33
4-chlorophenol	phenol	29

The work of Bell, Vanderslice and Spehar²¹ in which the two aryl iodides, o-iodonitrobenzene and o-iodofluorobenzene, were reduced to nitrobenzene and fluorobenzene, respectively, using sodium borohydride in aqueous DMSO, showed that the hydrogen which replaced the iodine did not come from the sodium borohydride, but rather from the water. This ruled out an intermediate-complex mechanism and indicated a displacement on the iodine by the hydride ion^{24,38,39} to produce a carbanionic species (XXVI-a), which then abstracts a proton from the water.



This mechanism indicates that the reaction will occur only when electron-withdrawing groups are on the ring to stabilize the negative charge. The groups and the effect of their position on the aromatic ring are the subjects of this thesis.

II. Experimental

A. General

All percent yields in this section are from gas chromatographic analysis using the internal standard method. This procedure involves the preparation of a standard solution which contains known amounts of a compound used as an internal standard along with the product to be analyzed. From the chromatogram of this solution the area of each component can be determined and a ratio of their relative molar thermal responses or the "Thermal Conductivity Correction Ratio" (T.C.C.R.) can be calculated using the following equation:

$$\text{T.C.C.R. (product)} = \frac{\text{area of product peak} \times \text{mmole of standard}}{\text{area of standard peak} \times \text{mmole of product}}$$

When a reduction was run, a known amount of an inert internal standard was added to the reaction mixture. Upon completion of the reaction the product as well as the internal standard (and any starting material that remained) was extracted with an organic solvent, usually diethyl ether. This organic layer was backwashed with water in order to remove residual DMSO, then dried over anhydrous magnesium sulfate. A sample was then taken and injected

into the gas chromatograph. The amount of product could then be determined from the areas under the peaks on the chromatogram by using a rearranged version of the T.C.C.R. equation.

$$\text{mmole of product} = \frac{\text{area of product} \times \text{mmole of standard}}{\text{area of standard} \times \text{T.C.C.R.}}$$

The percent yield was calculated by

$$\text{percent yield} = \frac{\text{mmole of product}}{\text{mmole of starting material}} \times 100$$

This internal standard method has the advantage of being independent of sample size and volume of solvent.

B. Chemicals

Sodium borohydride was obtained from Metal Hydrides, Inc. and was of 98% purity.

Dimethylsulfoxide was from Fisher Scientific and was purified by vacuum distillation from calcium hydride and stored over molecular sieve.

The chemicals that were reduced were reagent grade materials from Eastman Chemical Company, Fisher Chemicals, Aldrich Chemical Company, Columbia Chemical Company, and Pfaltz and Bauer.

C. Apparatus

Two gas chromatographs were used for the analyses. One was a Micro Tek DSS Series dual column, dual thermal

conductivity detection model equipped with a manual temperature programmer. The recorder was a Honeywell Model 143 x 58 Electronik having a one second full-scale deflection time and equipped with a Disk Chart Integrator. The other was a Perkin - Elmer Model 900 dual column unit which employed a Leeds and Northrup Speedomax G Model S60000 Series recorder also having a one second full-scale deflection time and a Disk Chart Integrator. This latter gas chromatograph was used with a thermal conductivity detector or with a flame ionization detector.

The reductions were run in a 100ml single-necked flask, with magnetic stirring. The flask was equipped with a screw-in thermometer well and an adaption for either a septum injection port or a gas take-off. This gas take-off was connected to a "cold-finger" condenser which was cooled by a mixture of dry-ice and acetone (-78°) in a dewar. The "cold-finger" was used to trap any product, starting material, internal standard, or solvent that was carried out of the reaction flask by the hydrogen gas that was produced during each reduction. The vent on the "cold-finger" was attached to a 500cc water-filled gas buret, which was used to measure the amount of hydrogen gas evolved.

All melting points were taken on a Thomas-Hoover Capillary Melting Point Apparatus. Infrared (ir) spectra were

obtained using either a Beckman IR5A or IR5 spectrophotometer. Nuclear magnetic resonance (nmr) spectra were obtained using a Varian A-60 unit. C, H and N analysis data were obtained with a Perkin-Elmer 240 Elemental Analyzer. Mass spectral data were obtained on a Hitachi Perkin-Elmer RMU-7 Mass Spectrometer.

D. Procedure

1. General

A 100ml single-necked flask equipped with an addition funnel, a magnetic stirrer, a thermometer and a gas take-off was charged with a solution of the alkyl halide and the internal standard in 6ml of DMSO. A solution of sodium borohydride in 10ml of DMSO and 4ml of water was placed in the funnel. About five drops of the SBH solution was added to the halide and the temperature was slowly increased until hydrogen gas evolution began or until 75° was reached. Any liquid or solid carried out of the reaction vessel was caught in a cold-finger trap located between the gas take-off and a gas buret used to determine the amount of gas evolved. The reaction mixture was brought to the temperature where the reaction began to occur and held there until the gas evolution stopped. The SBH solution was added at a rate so that the temperature could be held

at a minimum and still have a reaction occurring. The addition was normally completed in fifteen minutes, and the mixture was held at the reaction temperature (or at 75° if no hydrogen evolution occurred) for another forty-five minutes. For most reactions, the hydrogen evolution was essentially complete as soon as the last drop of SBH solution was added. After heating, the reaction mixture was cooled to room temperature or below and extracted three times with diethyl ether and the trap was washed out with 10ml of the ether and added to the extract. This combined ethereal extract was then washed with an equal volume of water in order to extract any DMSO. The ethereal layer was dried over anhydrous magnesium sulfate for gas chromatographic analysis by the internal standard method.

2. Aryl Iodides

Reduction of o-Iodonitrobenzene in Aqueous DMSO.- To a 100ml flask, with magnetic stirring, maintained at room temperature and connected to a cold-finger condenser at -78°, was added a solution of 10ml of DMSO, 4ml of water and 0.15g (3.9 mmole) of SBH. The temperature of this mixture rose slightly and was cooled again to room temperature (25°). Dropwise addition of a solution of 6ml of DMSO, 0.184g (2.0 mmole) of toluene (internal standard) and 0.50g (2.0 mmole) of o-iodonitrobenzene was begun and the tem-

perature was maintained at 30 - 35°. The addition was completed in 15 min and after 45 min 215cc of hydrogen gas had evolved. After 1 hr the reaction mixture was cooled and extracted by continuous liquid - liquid extraction for 6 hr with diethyl ether. The ether layer (50ml) was washed with a small amount of water (5ml) and dried over anhydrous magnesium sulfate. The ether layer was analyzed by G. C. Comparison of the peak areas of the toluene and nitrobenzene indicated a 100% yield of nitrobenzene.

This reaction was repeated with the toluene and nitrobenzene being extracted by shaking with six 5ml portions of diethyl ether, washing with 5ml of water, and drying with anhydrous magnesium sulfate. Again the yield of nitrobenzene was 100%.

Reduction of o-Fluoriodobenzene in Aqueous DMSO.-

The same general procedure was used as for the reduction of the o-iodonitrobenzene. The temperature for the reaction was 70 - 72°C and the internal standard was toluene. After 1 hr the reaction mixture was extracted, washed and dried. The G. C. analysis showed a 100% yield of fluorobenzene.

Reduction of o-Chloriodobenzene in Aqueous DMSO.-

The same procedure was used as for o-fluoriodobenzene and the yield of chlorobenzene by G. C. was 100%.

Reduction of o-Bromiodobenzene in Aqueous DMSO.-

Again the same procedure as for o-fluoriodobenzene was

employed. The yield of bromobenzene by G. C. was 100%. No benzene was present in the ether extract.

Reduction of o-Iodobenzotrifluoride in Aqueous DMSO.-

The o-iodobenzotrifluoride was reduced in the same manner as the o-iodonitrobenzene. However, the temperature at which the reaction occurred was 66°. When the mixture reached 66° the gas evolution was very vigorous. After 1 hr the reaction mixture was extracted with diethyl ether, washed with water and dried. The G. C. yield of benzotrifluoride was 100%.

Reduction of o-Diiodobenzene in Aqueous DMSO.- The same procedure was followed as for the reduction of o-fluoroiodobenzene. The reaction temperature was 75°C, and the G. C. analysis showed a 94% yield of iodobenzene and a 6% yield of benzene.

Reduction of Iodobenzene in Aqueous DMSO.- Iodobenzene was stirred with SBH for three hours at 80°C with toluene as the internal standard. After the extraction, washing and drying the G. C. analysis showed no trace of benzene, only iodobenzene.

Reduction of o-Diiodobenzene in Aqueous DMSO - excess SBH.- To a solution of 0.22g (6.0 mmole) of SBH in 14ml of DMSO and 6ml of water was added 0.66g (2.0 mmole) of o-diiodobenzene and 0.184g (2.0 mmole) of toluene (internal standard) in 2ml of DMSO. The mixture was stirred and

slowly heated to 45^o and held there for 50 min (total reaction time was 1 hr). After work-up, G. C. analysis showed a 16% yield of benzene and a 61% yield of iodobenzene.

Reduction of m-Chloriodobenzene in Aqueous DMSO.-

The m-chloriodobenzene was reduced by the same general procedure as used for the o-fluoriodobenzene. The yield of chlorobenzene was 21%.

Reduction of p-Chloriodobenzene in Aqueous DMSO.-

The same procedure as for m-chloriodobenzene was employed. The yield of chlorobenzene was slightly less than 1%.

Reduction of p-Iodonitrobenzene in Aqueous DMSO.- The

reduction of the p-iodonitrobenzene yielded 98% nitrobenzene using the same procedure as for the o-iodonitrobenzene, except the reaction temperature was 75^o.

Reduction of o-Iodobiphenyl in Aqueous DMSO.- Follow-

ing the same procedure as that used for the o-fluoriodobenzene, except the reaction time was extended to four hours, a 4% yield of biphenyl was obtained.

Reduction of o-Iodoanisole in Aqueous DMSO.- The

o-iodoanisole and SBH were stirred at 80 - 85^o for three hours with toluene as the internal standard. After work-up in the usual manner, the G. C. yield of anisole was 8%.

Reduction of p-Bromiodobenzene in Aqueous DMSO.- The

p-bromiodobenzene was reduced at a temperature of 77^o for

two hours. G. C. analysis indicated only a trace of bromobenzene with the starting material still present.

Reductions of o-Iodoaniline and m-Iodoaniline in Aqueous DMSO.- There was no trace of aniline after heating the o-iodoaniline at 75° for two and one-half hours or the m-iodoaniline at 75° for three hours.

Reduction of α -Iodonaphthalene in Aqueous DMSO.- The α -iodonaphthalene and SBH were heated to 75° and held there for one hour. After work-up in the usual manner, G. C. indicated only a trace of naphthalene.

Reduction of 2-Iodothiophene in Aqueous DMSO.- The 2-iodothiophene was added to a solution of SBH; vigorous gas evolution began. The temperature rose to a maximum of 42°. After work-up the G. C. yield of thiophene was 96%.

Reduction of 2-Iodothiophene in D₂O and DMSO with SBH.- The SBH (2.0 mmole) was dissolved in 12ml of dry DMSO and 4ml of D₂O: to this was added the 2-iodothiophene (2.0 mmole) in 2ml of dry DMSO. There was no appreciable gas evolution until the temperature reached 50° then 150cc of gas was evolved rapidly during approximately one minute, the gas evolution slowed and after 1 hr at 50°, 322cc of hydrogen has been collected. The reaction mixture was cooled and extracted with diethyl ether (50ml total volume). The extract was washed with 3ml of H₂O and dried over anhydrous magnesium sulfate. The ether was distilled

using a vigreux column and the concentrated extract was distilled under water aspirator vacuum into a receiver cooled in a dry-ice acetone mixture (-78°). The distillate was transferred to an nmr tube for analysis of deuterium incorporation in the 2-position. The nmr analysis showed 95% deuterium incorporation at the 2-position. Integration of the α -protons was 1290 units and for the β -protons 2450 units. The peaks were also photocopied, cut out and weighed. The ratio of the weights of the α to β protons was 1:2.

Reduction of 2-Iodothiophene in Aqueous DMSO with Sodium Borodeuteride (SBD) .- The SBD (3.9 mmole) was dissolved in 12ml of dry DMSO, the 2-iodothiophene (2.0 mmole) was dissolved in 3ml of dry DMSO and added to the SBD solution; then 4ml of distilled water were added and gas evolution began. The temperature was held at 45° for 1 hr. Total gas evolution was 215cc. The reaction mixture was extracted with 80ml of diethyl ether and washed twice with 5ml portions of water. After drying over anhydrous magnesium sulfate the extract was concentrated by distillation. Then five drops of CCl_4 were added to the concentrate and the mixture was heated until the ether no longer distilled. The thiophene- CCl_4 mixture was then distilled in a micro distillation apparatus and the distillate was transferred to an nmr tube. The nmr spectrum was identical to that of

thiophene. The integration was 33 units for the α -protons and 35 units for the β -protons.

3. Aryl Bromides

Reduction of o-Bromonitrobenzene in Aqueous DMSO.-

SBH (3.9 mmole) was dissolved in 12ml of DMSO and 4ml of water; to this was added a solution of o-bromonitrobenzene (2.0 mmole) and toluene (2.0 mmole) in 4ml of DMSO. The reaction mixture was magnetically stirred and heated to 75° and held there for one hour; gas evolution began. The total gas evolution was 360cc. The mixture was cooled to 25° and extracted with four 10ml portions of diethyl ether. The combined extracts were washed with 10ml of water and dried over anhydrous magnesium sulfate.

The G. C. analysis showed a 100% yield of nitrobenzene based on the internal standard, toluene.

Reduction of o-Bromofluorobenzene in Aqueous DMSO.-

The same procedure as for o-bromonitrobenzene was used and the yield of fluorobenzene was 25%.

Reduction of o-Bromochlorobenzene in Aqueous DMSO.-

The o-bromochlorobenzene and SBH in DMSO and water were heated to 85° and held there for four hours. After normal work-up the G. C. analysis showed 2% chlorobenzene and the starting material.

Reduction of o-Dibromobenzene in Aqueous DMSO.- The same procedure was used as that for o-bromonitrobenzene. There was no bromobenzene or benzene detected by G. C. from this reaction, only starting material.

Reduction of m-Bromobenzotrifluoride in Aqueous DMSO.- The same procedure was followed as that used for the reduction of o-bromonitrobenzene, except the reaction mixture was held at 75° for two hours. There was no benzotrifluoride in the ether extract, again only starting material remained.

Reduction of m-Bromochlorobenzene in Aqueous DMSO.- The m-bromochlorobenzene and SBH in aqueous DMSO were heated to 85° and stirred at that temperature for 4 hr. After the normal work-up the G. C. analysis indicated a 7% yield based on the internal standard, toluene.

Reduction of α -Bromonaphthalene in Aqueous DMSO.- The same procedure as that for the reduction of o-bromonitrobenzene was followed only the α -bromonaphthalene was held at 75° for 4 hr. G. C. analysis showed only a trace of naphthalene.

Reduction of 9-Bromoanthracene in Aqueous DMSO.- The halide and SBH in aqueous DMSO were stirred at 75° for twenty hours. There was obtained a 20% yield of anthracene.

Reduction of 2-Bromothiophene in Aqueous DMSO.- The 2-bromothiophene could not be reduced using the same procedure as for the reduction of o-bromonitrobenzene.

Reduction of 2-Bromopyridine in Aqueous DMSO.- The 2-bromopyridine was mixed with the SBH in aqueous DMSO, heated to 80° and stirred for ten hours. The analysis showed no peak at the retention time of pyridine.

4. Aryl Chlorides

Reduction of o-Chloronitrobenzene in Aqueous DMSO.- The o-chloronitrobenzene (2.0 mmole) in 4ml of DMSO was added to a solution of SBH (3.9 mmole) in 12ml of DMSO and 4ml of water at 75°. The reaction mixture immediately began to turn a brownish-red. After one hour of heating the mixture was cooled to 25° and extracted with six 10ml portions of diethyl ether. The combined layers were washed with 5ml of water and dried over anhydrous magnesium sulfate. G. C. analysis showed no nitrobenzene or starting material³².

Reduction of o-Chlorofluorobenzene in Aqueous DMSO.- SBH (3.9 mmole) was dissolved in 12ml of DMSO and 4ml of water; to this was added o-chlorofluorobenzene (2.0 mmole) and toluene (2.0 mmole) in 4ml of DMSO. The reaction mixture was heated to 77° and held there for one hour. The mixture was then cooled to 25°, extracted with diethyl

ether, washed with 3ml of water and dried over anhydrous magnesium sulfate. The G. C. analysis showed no traces of fluorobenzene, chlorobenzene or benzene. The o-chlorofluorobenzene was still present in a 1:1 molar ratio to the internal standard, toluene.

Reduction of o-Dichlorobenzene in Aqueous DMSO.- The same procedure as for o-chlorofluorobenzene was employed and the G. C. analysis showed only the starting material and the internal standard to be present; there was no chlorobenzene or benzene in the ether extract.

Reduction of 1,2,3-Trichlorobenzene in Aqueous DMSO.- Again the same procedure as for o-chlorofluorobenzene was used and the G. C. analysis showed no o-dichlorobenzene, m-dichlorobenzene, chlorobenzene, or benzene. Only starting material remained.

Reduction of α -Chloronaphthalene in Aqueous DMSO.- The α -chloronaphthalene and SBH in aqueous DMSO were stirred at 75^o for 4 hr. There was no naphthalene present in the extracted reaction mixture.

Reduction of 2-Chloropyridine in Aqueous DMSO.- The 2-chloropyridine in the DMSO-water solution of SBH was heated to 77^o and held there for three hours. Analysis by G. C., after the usual work-up, indicated a 0% yield of pyridine, only starting material remained.

Reduction of 2-Chloroquinoline in Aqueous DMSO.- A solution of 2-chloroquinoline (2.0 mmole) and toluene (2.0 mmole) in 2ml of DMSO was added to a solution of SBH (3.9 mmole) in 12ml of DMSO and 4ml of water. This reaction mixture was heated to 80° where gas evolution began. After 3.5 hr there had been 150cc of gas evolved and 250cc after ten hours of reaction. The mixture was cooled to room temperature and was extracted with five 10ml portions of diethyl ether. The ether layers were combined and washed with 10ml of water; after drying the ether extract was analyzed by G. C. The chromatogram had a peak at the retention time of quinoline. The yield of quinoline, based on the internal standard, was 64%.

Reduction of 2-Chloroquinoline in DMSO-D₂O.- SBH (10.0 mmole) was dissolved in 15ml of dry DMSO, to this was added 2-chloroquinoline (5.0 mmole) in 5 ml of dry DMSO followed by the addition of 6ml of D₂O. The mixture was heated to 80° and allowed to stir for twelve hours. After cooling the reaction to 25° and extracting with diethyl ether (50ml) the extract was washed with water (10ml), dried over anhydrous magnesium sulfate and concentrated to approximately 5ml. The product was obtained by micro vacuum distillation. The nmr showed no alpha proton signal.

Reduction of 2-Chloro-3-methylquinoxaline in Aqueous DMSO.- SBH (3.9 mmole) was dissolved in 12ml of DMSO and

4ml of water; to this was added 2-chloro-3-methylquinoxaline (2.0 mmole) and toluene (2.0 mmole) in 2ml of DMSO. The aromatic halide appeared to precipitate on addition, but as the temperature was increased it redissolved and gas began to evolve as the temperature reached 75°. The reaction mixture was stirred at this temperature for three hours, then cooled to 25° and extracted ten times with 10ml portions of diethyl ether. The extract was not washed due to the high solubility of 2-methylquinoxaline in water. The G. C. analysis showed a 90% yield of the dechlorinated product.

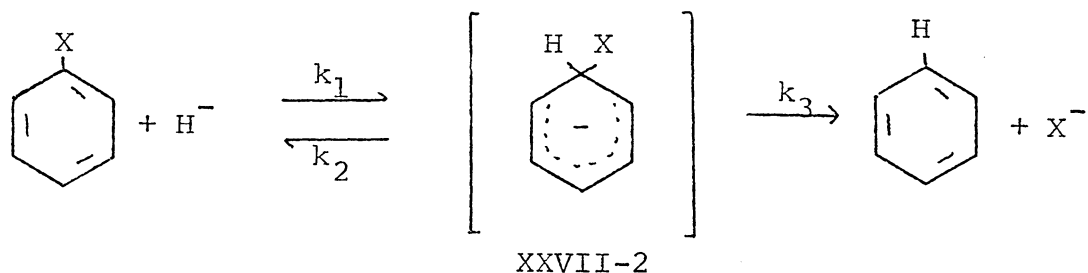
Reduction of 2-Chloro-3-methylquinoxaline in DMSO-

D₂O. - The same general procedure was followed as for the reduction of 2-chloroquinoline in DMSO-D₂O. The nmr spectrum of the product indicated a 20% incorporation of deuterium.

III. Discussion of Results

A. Mechanism

The reduction of an aryl halide with SBH at first glance would appear to be a simple displacement of the halide ion by the hydride ion in an intermediate-complex mechanism where $k_3 > k_2$ ⁴⁰⁻⁴⁴.

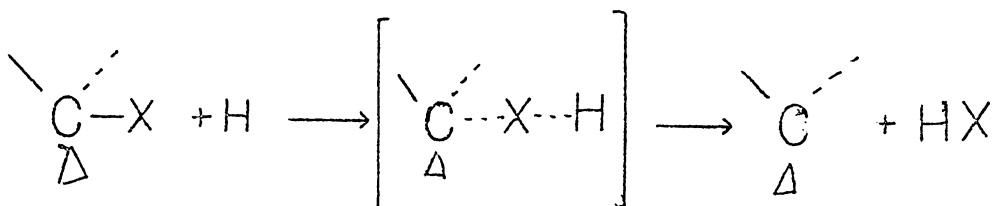


For the SN1 or SN2 displacements the order of reactivity is R-I > R-Br > R-Cl > R-F where the ease of breaking the carbon-halogen bond depends upon the relative bond strengths. The differences are quite large, for example, the alkyl bromides react 25 to 50 times faster than the alkyl chloride. In aromatic nucleophilic substitution, however, there is often very little difference in reactivity among the aryl halides and in most cases the aryl fluoride; the strongest bond is the most reactive. This indicates that the loss of halide, step k_3 , is the fast step and the rate of the reaction is determined by the

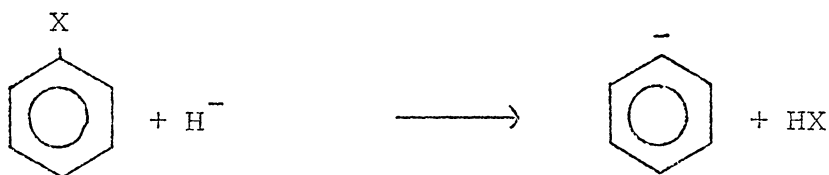
attack of the nucleophile in step k_1 . This attack is facilitated when the halide is strongly electron-withdrawing inductively, so that the carbon to which the halide is bonded will be more positive and the resulting intermediate (XXVII-a) will be stabilized.

In the reaction of SBH with the aryl halides this mechanism does not seem to fit since the aryl iodides are the most reactive and the fluorides are inert in all cases.

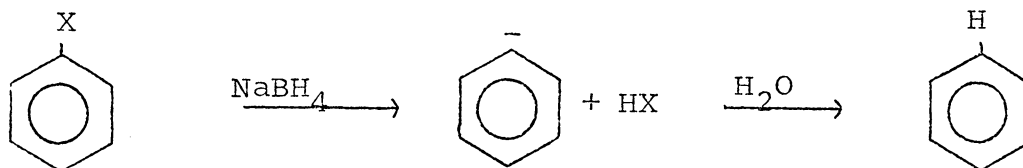
The other possibility for the aryl halide reduction is an "on-halogen" displacement^{24,38,39}. In this mechanism it is postulated that the halogen is lost to a nucleophile as X^+ , thus leaving a negative charge on the carbon.



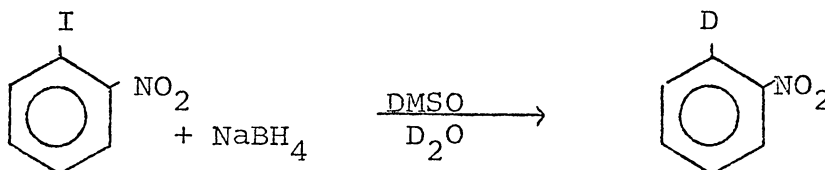
In the case of aryl halides the carbanionic site is on the aromatic ring.



If this is actually the case, the proton substituted on the ring would not be coming from the SBH but from the water. That is, as the carbanion is formed it is quenched by a proton from the water.



In an effort to substantiate the above hypothesis Bell and Vanderslice²¹ used deuterium oxide (D_2O) instead of water to quench the postulated carbanion formed when o-iodonitrobenzene was reacted with SBH in D_2O -DMSO. The nmr of the product, nitrobenzene, did indeed show that deuterium was incorporated in the ortho position at an 88% level.

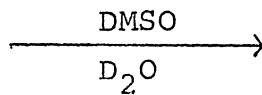
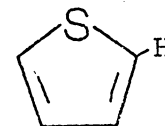
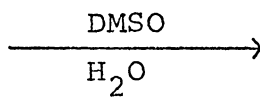
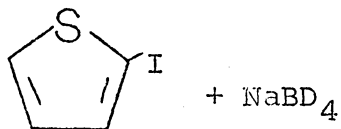
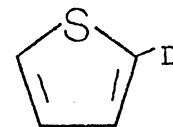
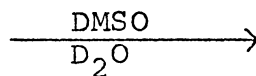
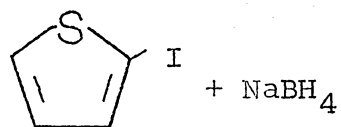


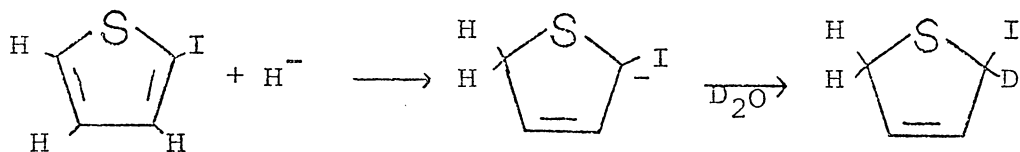
The analogous reaction run in diglyme gave o-deuterionitrobenzene in 98% purity.

The on-halogen displacement mechanism has also been substantiated by deuterium incorporation in the reduction of 2-iodothiophene with SBH in D_2O -DMSO (Fig. 1-a). There was also a possibility for an addition-elimination mechanism causing this deuterium to show up on the ring.

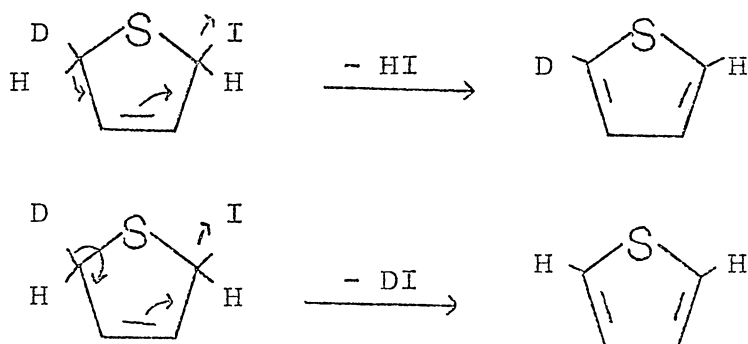
Figure 1-a

Deuterium Incorporation





In order to determine if the on-halogen displacement mechanism was valid or not, the reduction was run in sodium borodeuteride and water. If the reaction occurred by this addition-elimination route, there should be some deuterium incorporation in the alpha position. On a statistical basis this incorporation should be 50% at one alpha position since a deuterium would add to the molecule, but it can either remain or be lost in the elimination step.



The nmr spectrum of the product was identical to that of thiophene, thereby, ruling out this addition-elimination mechanism.

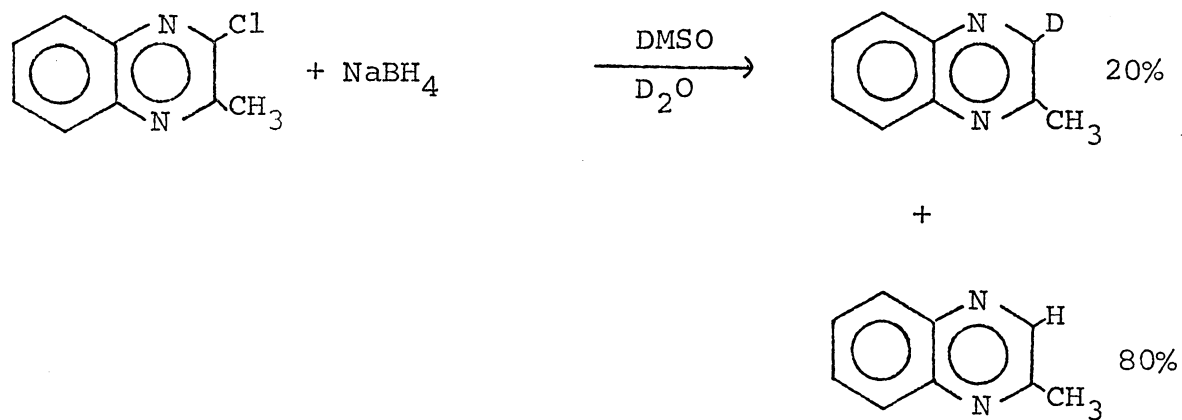
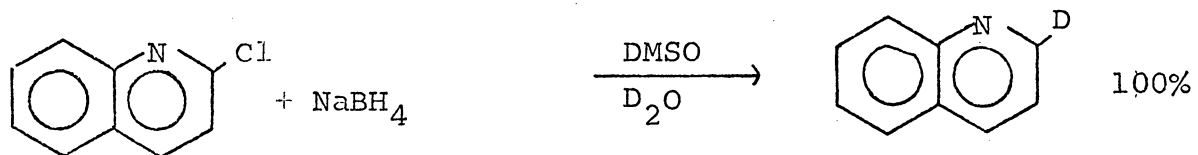
The reduction of 2-chloroquinoline yielded 64% quinoline, so this reaction was run in SBH and D_2O in order to determine if deuterium incorporation occurred. The signal for the 2-proton was completely absent in the nmr spectrum of the product. The reduction of 2-chloro-3-methylquinoxaline in SBH/ D_2O yielded 2-methylquinoxaline with a 20% incorporation of deuterium. However, in both cases deuterium incorporation into the SBH prior to reaction with the aromatic halide could also account for the presence of deuterium in the final product since these reactions were run under more forcing conditions than o-iodonitrobenzene (see Tables IV-a and VIII-a).

B. Effect of Substituent

A series of ortho substituted iodobenzenes was reduced with SBH in aqueous DMSO to determine the effect of the substituent in the replacement of the iodine (Table IV-a). The result was that any strong -I group tended to give a 100% replacement of iodine by hydrogen. The methoxy group yielded only 8% anisole. This low yield was attrib-

Figure 2-a

Deuterium Incorporation



uted to the electron-donating ability, by the resonance effect of this group, even though it has an electron-withdrawing inductive effect. This same reasoning was used to explain the low yields for the 2-iodobiphenyl and the 2-iodoaniline.

In order to see which ortho groups activate the halogen to the greatest extent towards this on-halogen displacement the halide was changed from iodide to bromide. The most activating substituent was the nitro group, followed by the fluoro, then chloro, and lastly no reaction for the ortho bromo.

The ortho substituted chlorobenzenes were unreactive towards this on-halogen displacement (Table VI-a).

The order $\text{NO}_2 > \text{F} > \text{Cl} > \text{Br}$ for enhancement of reactivity is consistent with the order of inductive electron-withdrawing abilities⁴⁵.

C. Effect of Substituent Location

Knowing the effects of different activating groups in the ortho position, it was next important to determine how these activating properties might be changed when the group was in the meta or para position. In order to do this the chloriodobenzene series was chosen. It was already known (Table IV-a) that o-chloriodobenzene could be reduced in a quantitative yield to chlorobenzene, but

Table IV--a

Ortho Substituted Iodobenzenes

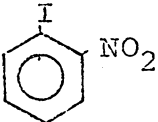
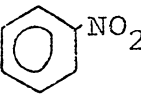
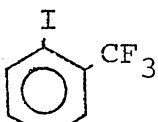

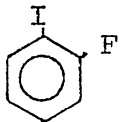
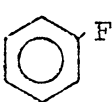
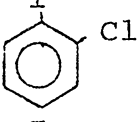
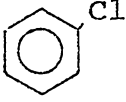
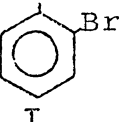
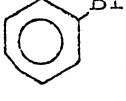
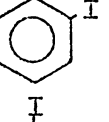
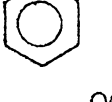
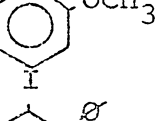
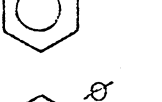
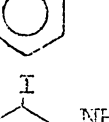
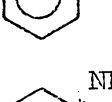


Starting Material	Temp °C	Time Hours	Product	Yield
	30	1		100%
	66	1		100%
	72	1		100%
	72	1		100%
	75	1		100%
	75	1		94%
	82	3		8%
	75	4		4%
	75	2.5		0%

Table V-a

Ortho Substituted Bromobenzenes

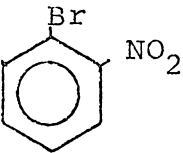
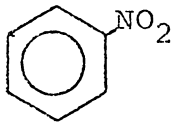
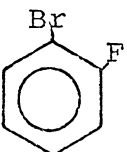
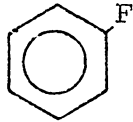
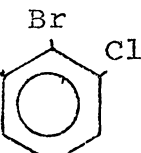
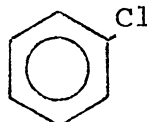
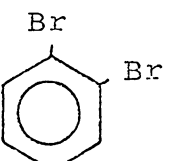
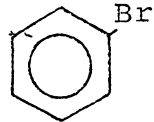
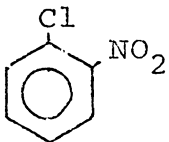
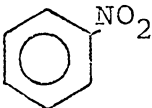
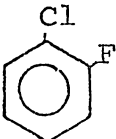
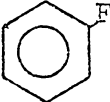
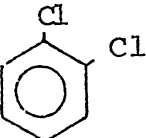
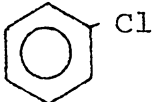
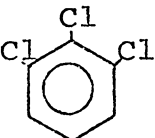
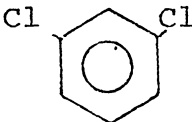
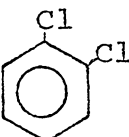
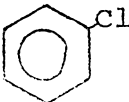
Starting Material	Temp °C	Time Hours	Product	Yield
	75	1		100%
	75	1		25%
	85	4		2%
	75	1		0%

Table VI-a

Ortho Substituted Chlorobenzenes

Starting Material	Temp °C	Time Hours	Product	Yield
	70	6		0%
	77	1		0%
	75	1		0%
	77	1		0%
				0%
				0%

when the m-chloriodobenzene was reduced under the same conditions only a 21% yield of chlorobenzene was obtained. When the chlorine was para to the iodine, there was only a trace of the reduction product (Table VII-a). These results are in agreement with the inductive electron-withdrawing ability of chlorine, that is, as the chlorine becomes further removed from the iodine, the -I effect drops off drastically⁴⁶. It should also be recalled that not only does the substituent serve to make the leaving halogen more positive, but it also helps to accommodate the negative charge that forms on the ring. This is best accomplished in both cases when there is a strong electron-withdrawing group adjacent to the carbon bearing the halogen to be replaced.

D. Aryl Halide Reductions of Systems

Other Than Benzene

The replacement of halogens by hydrogen was also accomplished on aromatic systems other than benzene. An aromatic ring system such as naphthalene or anthracene should be more susceptible to a displacement on-halogen since the additional aromatic ring tends to withdraw electrons⁴⁷. Also the greater the number of fused rings the more a negative charge may be stabilized by the electron-withdrawing character of the additional aromatic rings.⁴⁸

Table VII-a
Effect of Substituent Location

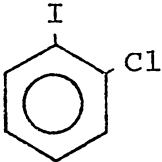
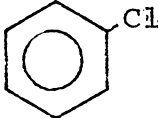
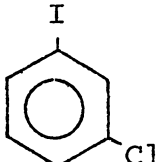
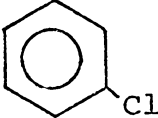
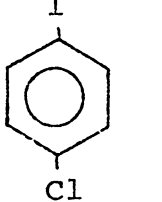
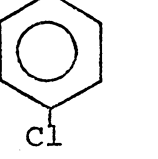
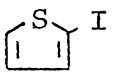

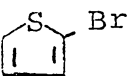

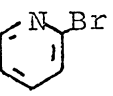

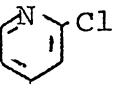

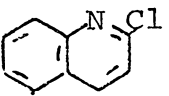
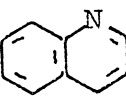
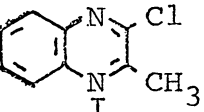
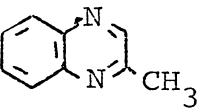
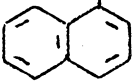
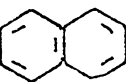
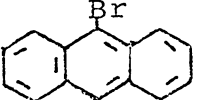
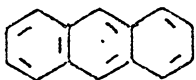
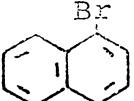
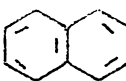
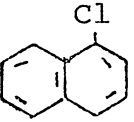
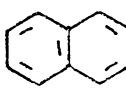
Starting Material	Temp °C	Time Hours	Product	Yield
	72	1		100%
	75	1		21%
	72	1		>1%

Table VIII-a

Reduction of Halogenated Heterocyclic Aromatic
Compounds with SBH

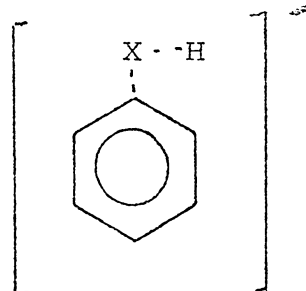
Starting Material	Temp °C	Time Hours	Product	Yield
	42	1		96%
	75	1		0%
	80	10		0%
	77	3		0%
	80	10		64%
	75	3		90%
	75	1		Trace
	75	20		12%
	75	4		Trace
	75	4		0%

The order of reactivity towards reduction with SBH in aqueous DMSO was bromoanthracene > bromonaphthalene > bromobenzene.

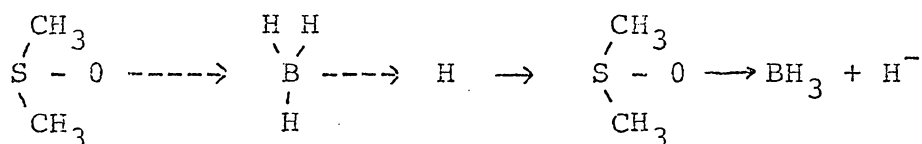
Samples of 2-bromopyridine and 2-bromothiophene were unreactive. As expected, 2-chloropyridine was also unreactive, but 2-chloroquinoline, a naphthalene analog, yielded 64% of the dehalogenated quinoline. When 2-chloro-3-methylquinoxaline was reduced, a 90% yield of 2-methylquinoxaline was obtained. A sample of 2-iodothiophene was found to be very reactive yielding 96% thiophene at a relatively low reaction temperature of 42°.

E. Solvent

According to the Hughes-Ingold Theory of solvent effects, the rate of solvolysis of electrically neutral molecules by either SN1 or SN2 mechanism would be expected to increase with the ion-solvating power of the medium, since the reaction by either mechanism, involves charge formation in the transition state⁴⁹. For the case of the on-halogen displacement the intermediate is



DMSO, being an electron-donating solvent, can coordinate with the cation and leave the anion relatively free to react⁵⁰, and can even accelerate the reaction of the borohydride anion by helping to free the hydride ion by coordinating with the borane.



The solvating power of DMSO is attributed to its high dielectric constant of 48 and its high dipole moment of 4.3 debye units (D)⁵¹ as well as its electron donating properties. By comparison, the dielectric constant of water is 80⁵² and its dipole moment is 1.8 D⁵³.

The importance of the dielectric constant is in reducing interactions between charges. That is, in a solution of DMSO (dielectric constant of 48) two oppositely charged ions separated by a given distance will have only 1/48 the attraction for each other that they would have in a vacuum. For comparison, the dielectric constants of some common organic solvents are as follows: diethyl ether - 4.34, methanol - 33.6, ethanol - 25.1, benzene - 2.28, and acetonitrile - 37.5⁵⁴.

The other factor that must be considered in the solvation of charged species is the dipole moment of the solvent

molecule. This is important because the solvent molecules tend to align themselves in a manner to surround a charged intermediate and hence stabilize it. The larger the dipole moment, the better the charged specie will be solvated. The dipole moment of DMSO is even higher than that of water (4.3D versus 1.8D).

DMSO is also aprotic which is a distinct advantage for the SBH system since SBH tends to decompose in protic solvents. The solubility of SBH in DMSO is 5.8g per 100g of solvent at 25°. Most of the organic compounds that were used in this study were soluble in DMSO at room temperature and all were soluble at the reaction temperature.

F. Conclusions

In this work it has been shown that SBH in aqueous DMSO can selectively reduce aryl halides in the presence of groups that are extremely reactive towards other reducing agents such as lithium aluminum hydride. Of particular interest is the removal of the halogen (Br or I) from the halonitrobenzenes without reducing the nitro group, and the reduction of one halogen on an aromatic ring without reducing another that is present. This procedure can be very useful in synthetic work since halogens can be introduced either directly in an electrophilic attack or indirectly via a Gatterman or Sandmeyer reaction.

These halogens may be introduced to direct an incoming group to a certain position and then to be removed by use of SBH to yield a desired compound, or the removal of an amino group may be accomplished by converting it to a halogen and replacing it with a proton. Also of great importance is that a deuterium can easily be introduced into a molecule using SBH and D_2O . This introduction of a deuterium atom can be very useful in determining reaction mechanisms or in nmr studies. The incorporation of a deuterium is usually very difficult to accomplish synthetically and these deuterio compounds are quite expensive.

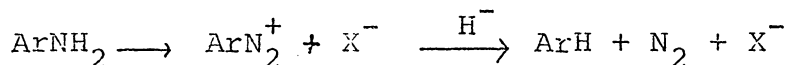
Section B

Reduction of Diazonium Salts

with SBH

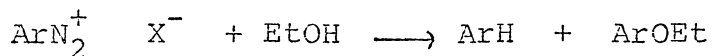
I. Introduction

The deamination of a primary aromatic amine is usually accomplished by the reduction of the diazonium salt of that amine.



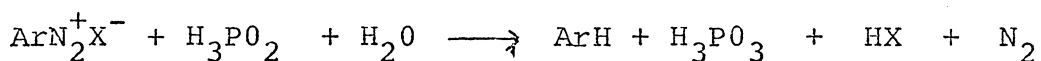
The success of this reduction is a function of the completeness of the diazotization as well as the reduction. Most primary aromatic amines are capable of being converted to the corresponding diazonium salts in yields that approach the theoretical maximum. The salt that forms is usually left in an acidic solution maintained at or near 0° because these salts are very unstable in their solid form or at elevated temperatures.

The classic method for the reduction of these diazonium salts was reported in 1864 by Griess⁵⁵. His method involved reducing the salt in ethanol. In some cases this procedure gave excellent yields, but it was later found that in other cases the aryl ethyl ether was the major product.



The primary product depended on a number of variables such as the acid used for the diazotization,⁵⁶ the substituents on the aromatic ring⁵⁷ and the temperature.⁵⁸

Another popular method that is often used for this reduction was discovered by Mai in 1902.⁵⁹ It involved treating the salt solution with 10% aqueous hypophosphorous acid. In most cases the yield of the deaminated product is directly related to the amount of hypophosphorous acid used, with up to 15 mmoles of this acid required to reduce one mmole of the diazonium salt. The usual ratio for yields in the 60-80% range is 5 mmoles of acid to one mmole of the salt.

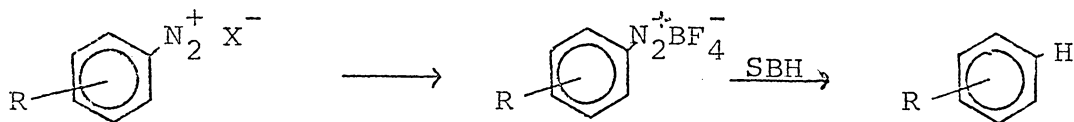


The reduction of diazonium salts can also be accomplished using alkaline formaldehyde.⁶⁰ This method is particularly effective in the cases where the ethyl alcohol method affords the ether product. Yields for this method are in the 60-80% range. A problem is that the salt tends to decompose more rapidly as the alkalinity of the solution is increased.

Other methods of less significance, but useful in isolated cases, involve stabilization of the salt with a substituted naphthalene sulfonic acid followed by treatment with zinc or copper;⁶¹ reduction with sodium stannite;⁶²

and conversion of the diazonium salt to the corresponding hydrazine and oxidizing it to the hydrocarbon.⁶³

More recent work on the reduction of these salts has involved converting them to their fluoroborates followed by reduction with SBH.^{64,65}



Hendrickson⁶⁴ accomplished this reduction in solutions of methanol or dimethylformamide (DMF). The yields ranged from 48% for the reduction of 2,4-dinitroaniline to 77% for anthranilic acid.

In 1949 W. G. Brown and S. G. Chaikin⁶⁶ attempted to reduce an aqueous solution of benzenediazonium chloride directly with SBH. They reported a rapid and strongly exothermic reaction with the isolation of benzene, aniline and phenylhydrazine in relatively small amounts. In this laboratory the direct reduction of aqueous solutions of diazonium salts with SBH was investigated with more satisfactory results than those reported by Brown and Chaikin.

II. Experimental

A. General

The amine to be reduced was purified and converted to the amine hydrochloride by stirring with hydrochloric acid. The amine hydrochloride in a two molar excess of hydrochloric acid was cooled to 0-5^o in a salt-ice water bath, and sodium nitrite was then added slowly, maintaining the temperature at 0-5^o. The excess hydrochloric acid was neutralized with small portions of a sodium carbonate solution. This solution was kept cool with pieces of cracked ice as it was slowly added to a cold aqueous solution (0^o) of SBH; gas was evolved vigorously. After the addition was completed, the mixture was allowed to come to room temperature and was stirred for one-half hour. The mixture was extracted with diethyl ether and the ether layer was backwashed with water and dried over anhydrous magnesium sulfate. Concentration of the ether layer yielded the deaminated product.

B. Procedure

The Reduction of the Diazonium Salt of o-Toluidine with SBH

The o-toluidine (0.02M) and the internal standard, benzotrifluoride, (0.02M) were cooled to 0-5^o; concentrated hydrochloric acid (5ml, 0.06M) was added followed by water (5ml) and ice (apx. 10g). A solution of sodium nitrite (0.02M) in 10ml of water was added slowly with stirring, care being taken to maintain the temperature of the reaction mixture at 0-5^o. When the addition was completed, the mixture was stirred for 15 min and the excess acid was neutralized with solid anhydrous sodium carbonate. A solution of SBH (0.04M) in 20ml of cold water was added slowly to the diazonium salt solution; gas evolution was vigorous (a dry ice-acetone trap was used to catch escaping liquid). A reddish organic layer formed on top of the aqueous layer. The layers were separated and the aqueous layer was extracted five times with 10ml portions of diethyl ether. The combined organic layer was washed with 10ml of water and dried over anhydrous magnesium sulfate. The G. C. analysis for toluene indicated a 70% yield based on the internal standard of benzotrifluoride.

The same reaction was run again only this time the neutralized diazonium salt solution was added to the SBH solution. The yield of toluene was 82%.

Reduction of the Diazonium Salt of p-Nitroaniline

with SBH.- Using the same procedure as that for the o-toluidine, a 37% yield of nitrobenzene was obtained.

The same reaction was run, but this time an aqueous solution of sodium hydroxide was used to neutralize the excess hydrochloric acid (half the base was added to the diazonium salt solution and the other half was added along with the SBH). The yield of nitrobenzene was 50%.

An 83% yield of nitrobenzene was obtained by adding a solution of the diazonium salt which had been partially neutralized with aqueous sodium carbonate to an alkaline solution of SBH (SBH in 10ml, of 5% N NaOH).

Reduction of the Diazonium Salt of o-Anisidine with

SBH.- The addition of SBH to the neutralized diazonium salt yielded 57% anisole, whereas, inverse addition gave 92% of the product.

Reduction of the Diazonium Salt of 2-Aminobiphenyl

with SBH.- The 2-aminobiphenyl (0.03M) was converted to the corresponding amine hydrochloric acid and heating the mixture until all of the amine had gone into solution. The reaction mixture was cooled in a salt-ice water bath and the amine hydrochloride crystallized from solution. A solution of sodium nitrite (0.03M) in 10ml of water was added slowly to the stirred reaction slurry; the diazonium formed as evidenced by the disappearance of the crystalline

material. The solution was a clear pale yellow. The solution of the diazonium salt was then neutralized with aqueous sodium carbonate. A solution of SBH (0.06M) in 25ml of 5% aqueous sodium hydroxide was added to the cold reaction mixture, gas evolution began immediately and a yellowish solid began to form on top of the water. After the addition was completed, the mixture was stirred for one-half hour, then extracted with five 20ml portions of diethyl ether. The combined ether layer was washed with 25ml of water and dried over anhydrous magnesium sulfate. The ether layer was reddish in color, so it was treated with Norit-A to remove the colored impurities. The ether layer was evaporated to yield 5.1g of a reddish-yellow solid; mp 55° . This solid was sublimed to yield 3.9g (80%) of biphenyl: mp $67.5-68.5^{\circ}$ (lit. mp $69-70^{\circ}$).

Reduction of the Diazonium Salt of 2-Iodoaniline with SBH. - The same procedure was used as for the reduction of o-toluidine. The yield of iodobenzene from the addition of SBH to the diazonium salt solution was 82%.

Reduction of the Diazonium Salt of 2-Bromoaniline with SBH - Isolation of a Liquid Product. - The diazonium salt of 2-bromoaniline was prepared using the same procedure as for o-toluidine. The excess acid was neutralized with sodium carbonate and the diazonium salt solution was added to a solution of SBH. The mixture was heated to 30° and

held there for one-half hour. The organic products were extracted from the aqueous layer with diethyl ether. The ether layer was backwashed and dried over anhydrous magnesium sulfate. This layer was then concentrated and bromobenzene was collected by distillation; the yield was 34%.

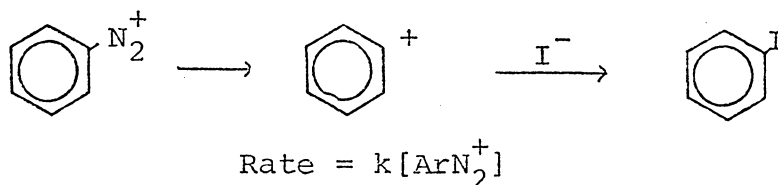
Reduction of the Diazonium Salt of o-Toluidine - Isolation of a Liquid Product.- This reaction was run in the same manner as the reduction of 2-bromoaniline. The yield of toluene by distillation was 52%.

Reduction of the Diazonium Salt of 2-Amino-4-methylpyrimidine with SBH - Isolation of a Liquid Product.- The same general procedure was used as for the 2-bromoaniline reduction. After extraction the ether layer was concentrated and a distillation was attempted. No 4-methylpyrimidine distilled and the material in the distillation flask decomposed.

III. Discussion of Results

A. Mechanism

The reduction of a diazonium salt with SBH appears analogous to the replacement of the diazonium grouping by the iodide ion.⁶⁸

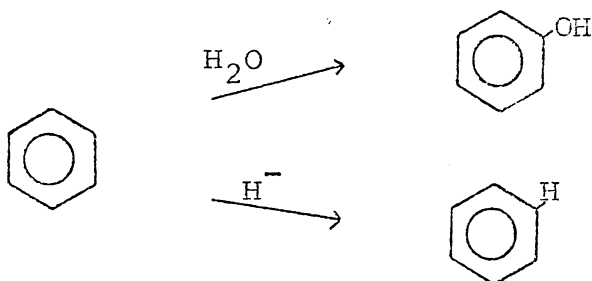


When the nucleophile is the bromide ion, there appears to be an $\text{S}_\text{N}2$ type mechanism in operation as well as the $\text{S}_\text{N}1$.⁶⁹ In this case the rate equation is

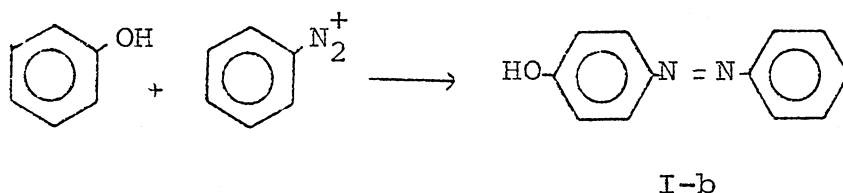
$$\text{rate} = k_1[\text{ArN}_2^+] + k_2[\text{ArN}_2^+][\text{Br}^-]$$

In the case of the SBH the reaction is quite exothermic, so the displacement by the hydride ion may initially have $\text{S}_\text{N}2$ character, but the heat of the reaction may cause more rapid decomposition of the diazonium salt leading to more of the "aromatic carbonium ion" which can be attacked by a water molecule or the hydride ion. It seems likely that as long as the reaction proceeds via an $\text{S}_\text{N}2$ route, the hydride ion is more likely to displace the nitrogen than is water since the diazonium salt is stable in water solu-

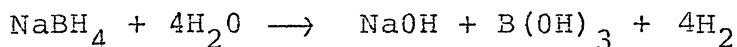
tion under the same conditions.



When water is the attacking species, phenol is the product, and this phenol can further reduce the yield of the reduction product by coupling with a molecule of the diazonium salt.



This type coupling is especially probable since the decomposition of the SBH in water makes the reaction medium alkaline. These coupling reactions are accelerated by basic conditions and occur even at ice-bath temperature.⁷⁰



The production of sodium hydroxide also brings about the possibility for attack by the hydroxide ion on the diazonium salt to yield the phenol product.⁷¹

The azo compounds (I-b) that are formed from the coupling reaction are highly colored and have been used as

dyes. Colored impurities were present in all cases when the diazonium salts were reacted with SBH, and especially when the reactions were scaled-up. In the case where iodide ion displaces nitrogen, formation of phenol is not a problem since the iodide ion is such a strong nucleophile. When this reaction was attempted with bromide or chloride ions, the major product was the phenol.⁷²

In Table I-b are the yields of reduction products obtained when the diazonium salt solution of the listed amine was neutralized and reacted with SBH by (1) adding the SBH solution to the diazonium salt (regular addition) and (2) adding the salt solution to the SBH (inverse addition). In general the better yield was obtained using the inverse addition method where the SBH is always in excess. The lower yield for the regular addition may be attributed to the attack of water on the "aromatic carbonium ion." In all cases where the reaction was run both ways the inverse addition method afforded the less colored product. From the data in Table I-b it can be seen that this reaction gives an excellent yield of deaminated material in each case. These yields were obtained using the internal standard method of G. C. analysis except in the case of the o-aminobiphenyl which was reduced to biphenyl. The product was isolated and sublimed to give an 80% yield.

Table I-b

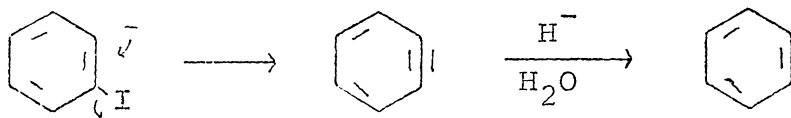
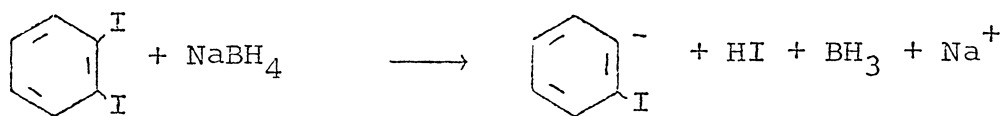
The Reduction of Diazonium Salts Using Sodium Borohydride

<u>Amine</u>	<u>Product</u>	<u>% Yield Regular Addition</u>	<u>% Yield Inverse Addition</u>
o-toluidine	toluene	70	82
p-nitroaniline	nitrobenzene	50	83
o-anisidine	anisole	57	92
o-aminobiphenyl	biphenyl	80	-
o-iodoaniline	iodobenzene	82	-

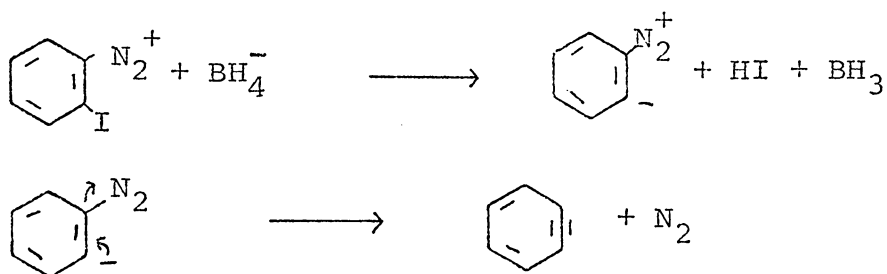
The reactions described previously were run on a 3 millimolar scale and attempts to run them on a larger scale led to a decrease in the yield of the desired product. Attempts to isolate a liquid product were very disappointing with the best yield being approximately 50%.

B. General

When o-diiodobenzene was reduced with SBH in aqueous DMSO (Chapter I). A 16% yield of benzene was obtained when the SBH was in a greater excess than normal (6.0 mmole versus 3.9 mmole). This was interesting since iodobenzene itself did not react to give benzene (starting material was recovered). This yield of benzene indicated the possibility for a benzyne type mechanism to explain the loss of both iodines.

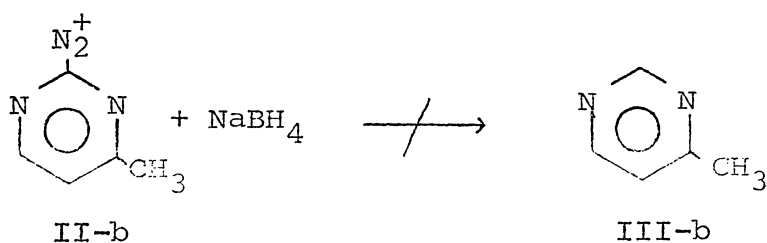


When the diazonium salt of o-iodoaniline was reacted with SBH, there was also a possibility for a benzyne if the borohydride were to react with the iodine, in an ortho-halogen displacement, before reacting with the diazonium salt group.



This was not the case, though, since the only product found was iodobenzene (82% yield). The diazonium salt portion was the more reactive in this aqueous medium.

An attempt was made to reduce the diazonium salt of 2-amino-4-methylpyrimidine (II-b), but no 4-methylpyrimidine (III-b) was isolated from the reaction.



C. Conclusions

The reduction of a diazonium salt with SBH in an aqueous medium appeared at first to be a useful synthetic method for the deamination of aromatic amines, but scale-ups of the reactions indicated that side reactions began to compete, thus reducing the yield of the desired product. Even though the attempts to run the reaction on a larger or preparative scale were not as successful, this work did show that the diazonium salts could be reduced directly by SBH to give reasonable yields of the reduction product, thus contradicting the report of Chaikin and Brown.⁶⁶

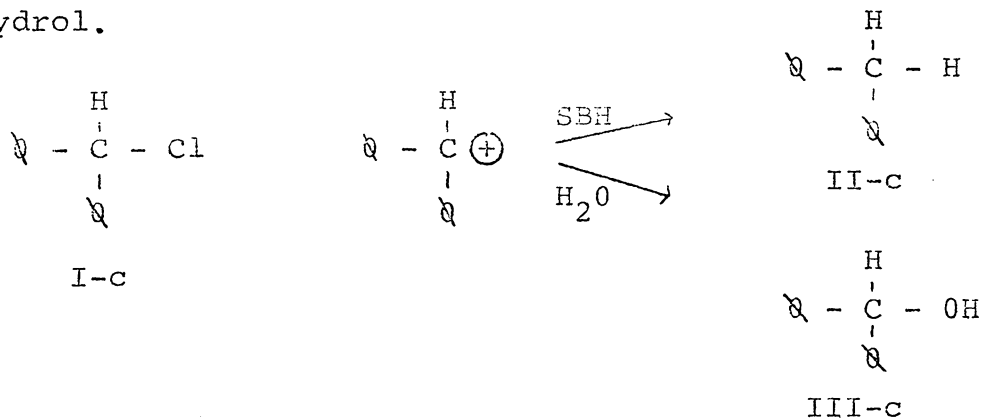
Section C

Reduction of Polyhalogenated Alkyl Compounds
with SBH in Aqueous DMSO

I. Introduction

In 1965 Bell and Brown^{19,20} reported the successful trapping of certain carbonium ions with sodium borohydride. These carbonium ions were generated under solvolytic conditions from reactive secondary and tertiary halides. In their work benzhydryl chloride (I-c) was shown to react quite slowly with SBH in anhydrous diglyme to produce only 6% diphenylmethane (II-c) in four hours at 45°.

When an 80% aqueous diglyme solution containing 1.8M SBH was used, the reaction proceeded approximately 60 times faster with a 72-75% yield of diphenylmethane. The remainder of product was benzhydrol (III-c) which resulted from attack of water on the carbonium ion. When benzhydryl chloride was placed in the same solvent system in the absence of SBH, the product consisted entirely of benzhydrol.



For the reduction of other carbonium ions the yields ranged from 60 to 90%.

Under the standard reaction conditions benzhydryl bromide gave an 87% yield of diphenylmethane as compared to 72-75% for the corresponding chloride. In 65% aqueous diglyme α -phenylethylbromide produced an 80% yield of ethylbenzene; the chloride yielded 39% of the same product.

In 1969 Bell, Vanderslice and Spehar,²¹ and Hutchins, et al.²² reported the successful reduction of primary, secondary and certain tertiary halides with SBH. These reactions were carried out in DMSO, diglyme or sulfolane. In these reactions Bell, et al. used the rate of gas evolution, as measured using a gas buret, to determine the relative reactivities. This analysis indicated the reactivities to be in the order iodide > bromide > tosylate > chloride and that the methyl > ethyl > propyl > isopropyl. These orders are consistent with an Sn2 mechanism. The results of the reductions carried out by these workers are in Table Ic. Table II-c shows the results of the reduction of some para-substituted benzyl halides in DMSO.

Trevoy and Brown⁷³ were successful in reducing some primary and secondary alkyl halides with a solution of lithium aluminum hydride in THF. The removal of one or more halides was accomplished in yields up to 78% for some selected compounds (see Table III-c). From the results of

Table I-c

The Reduction of Simple Monohaloalkanes and
Related Derivatives in DMSO

<u>Compound</u>	<u>Time, hr.</u>	<u>Temp, °C</u>	<u>Alkane %</u>
Methyl iodide	0.2	25	96
Methyl tosylate	0.3	25	90
Dimethyl sulfate	0.2	25	97
Ethyl iodide	1.5	25	96
Ethyl bromide	2.0	25	95
Ethyl tosylate	1.5	45	96
n-Propyl iodide	1.0	25	89
n-Propyl bromide	2.5	25	91
n-Propyl tosylate	1.0	45	90
n-Propyl chloride	8	35	16
n-Octyl chloride	4	45	42
β -Phenyl ethyl chloride	3	45	27
Isopropyl iodide	2.5	45	94
Isopropyl bromide	8	45	71
2-Iodoctane	2.0	45	85

Table II-c

The Reduction of para-Substituted Benzyl
Halides in DMSO

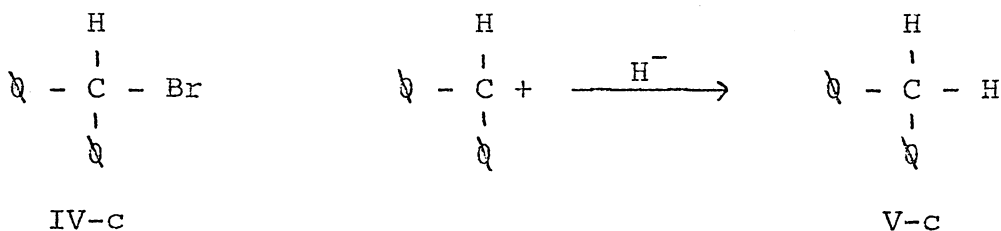
<u>Compound</u>	<u>4 hr.</u>	<u>1 hr.</u>	<u>0.1 hr.</u>
Benzyl chloride	86	49	10
Benzyl bromide		99	
p-Methoxybenzyl chloride		87	24
p-Methylbenzyl chloride		56	
p-Chlorobenzyl chloride		68	
p-Fluorobenzyl chloride		58	
p-Nitrobenzyl chloride		94	20
t-Cumyl chloride		1	

Table III-c

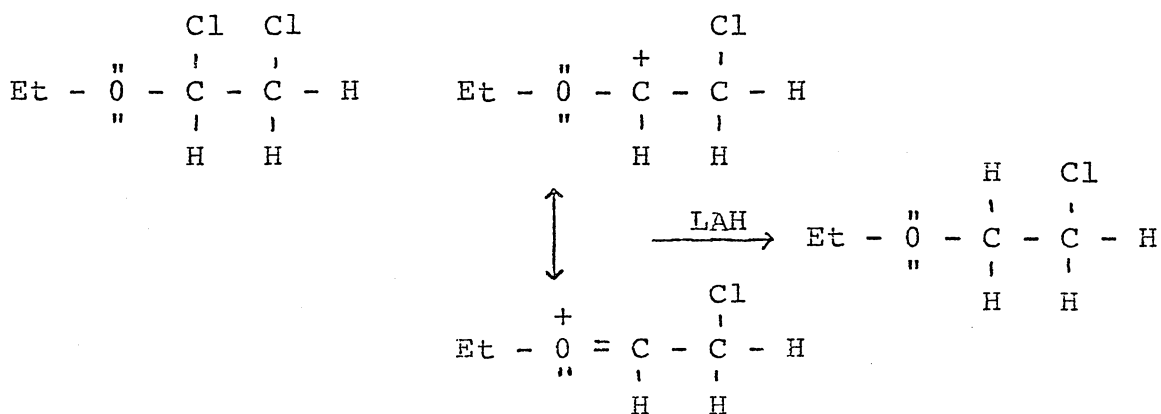
Reduction of Halides with Lithium
Aluminum Hydride in THF

<u>Compound</u>	<u>Temp.</u> <u>C</u>	<u>Time,</u> <u>hrs.</u>	<u>Product</u>	<u>%</u> <u>Yield</u>
Benzyl bromide	35	2	Toluene	78
Benzyl chloride	65	0.5	Toluene	72
1-Bromodecane	65	10	n-Decane	72
2-Bromooctane	65	10	n-Octane	30
Ethyl α , β -dichloro- ethyl ether	65	0.5	Ethyl β -chloro- ethyl ether	53
Diphenylbromomethane	65	0.5	Diphenylmethane	38
Styrene dibromide	65	0.5	Styrene	71
1,2-Dibromooctane	65	2	2-Bromooctane	26
			Octene	17

these investigators it appears that the primary halide is the more reactive specie. This would seem to imply an S_N2 mechanism, but in the case of the reduction of diphenylbromomethane (IV-c) there is a possibility that the product, diphenylmethane (V-c), resulted from the trapping of an intermediate carbonium ion as proposed by Bell and Brown.

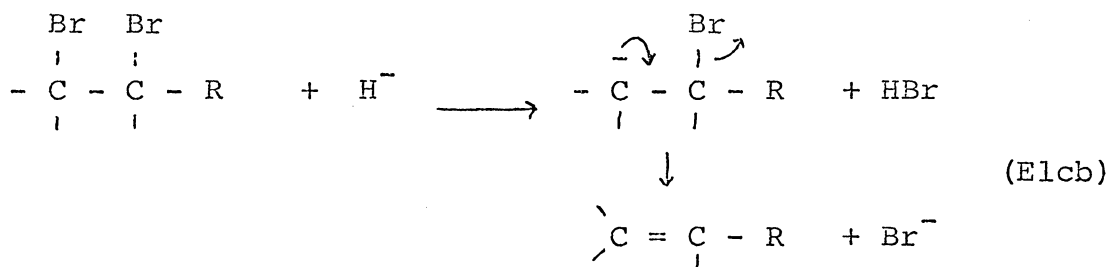


A carbonium ion mechanism may also explain why a secondary chloride was replaced rather than the primary when ethyl α , β -dichloroethyl ether was reduced with LAH.

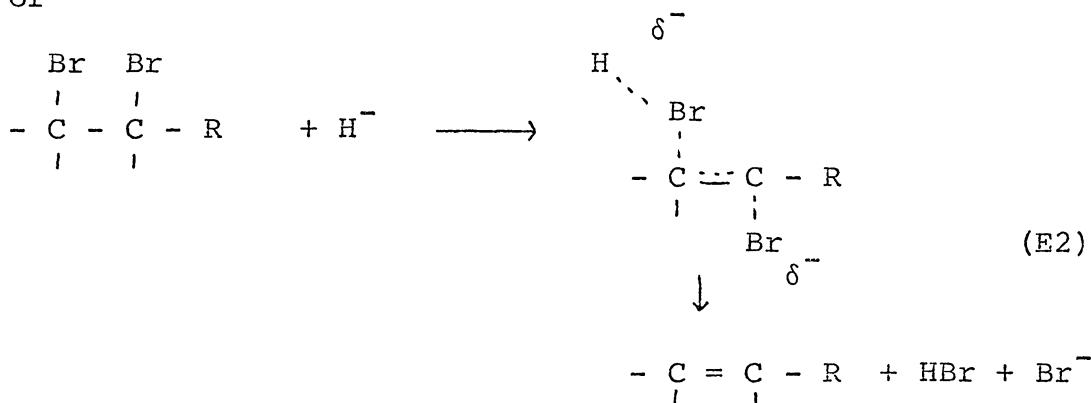


In the reaction of the 1,2-dibromooctane formation of 2-bromooctane would be predicted from an S_N2 displacement, but the other product, octene, is more difficult to explain. The most likely mechanism for the formation of the

olefin in light of more recent work by King and Pews²³ is a displacement, on-halogen, to generate a negative charge on the primary carbon, followed by a loss of the halide ion from the secondary carbon. This could either be viewed as a step-wise occurrence (Elcb) or a concerted mechanism (E2).

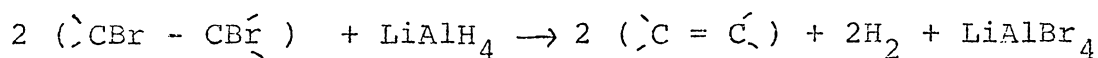


or



King and Pews were able to generate double bonds in a number of 1,2-dibromides using LAH in a variety of ethers. The main concern of these researchers was the generating of double bonds in steroid systems, so Table IV-c is a partial summation of simpler 1,2-dihalides that were reduced.

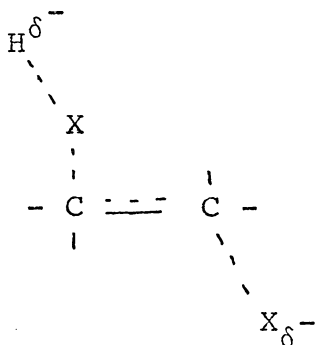
The reaction stoichiometry for the reduction of the 1,2-dihalides is as follows:



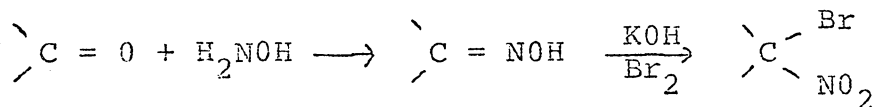
(work concerning the reaction of LAH with bromine indicates the inorganic products should be LiBr and LiAl_2Br_7 .⁷⁴)

In this work by King and Pews no success in the generation of double bonds using SBH or any of its derivatives under the most forcing conditions was reported.

As for the mechanism, the authors favored the E2. The E1cb was considered unsatisfactory because of an observed predominance of trans elimination (see Table IV-c).



Iffland and co-workers^{75,76} were interested in converting bromonitroalkanes to nitroalkanes. These starting materials were prepared by forming the oximes of ketones and reacting them with bromine in potassium hydroxide (hypobromite oxidation).



There had been previously two methods for replacing the bromine with a hydrogen. These were the reaction of the

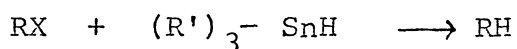
Table IV-c

Reduction of 1,2-Dihalides with LAH

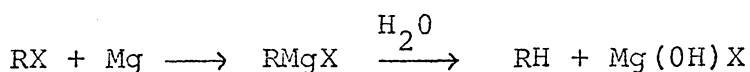
<u>Compound</u>	<u>Product</u>	<u>% Yield</u>
meso-Stilbene dibromide	trans-Stilbene	98
1,2,3,4-Tetrabromobutane	Butadiene	traces
Styrene dibromide	Styrene	71
trans-1,2-Dibromocyclohexane	Cyclohexene	77
cis-1,2-Dibromocyclohexane	Cyclohexene	26
1,2-Dibromooctane	Octene	17

bromonitroalkane 1) with ethanolic potassium hydroxide and 2) with methanol and potassium iodide. These investigators found, however, that an aqueous methanolic solution of sodium borohydride and the bromonitroalkane afforded a much greater yield of the desired product than either of the other two methods. A comparison is shown in Table V-c.

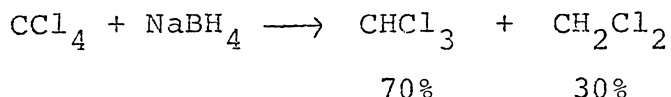
In recent years organotin hydrides have assumed increasing importance in the selective reductions of alkyl and aryl halides.⁷⁷



Also of importance in the conversion of alkyl or aryl halides to the corresponding hydrocarbon is the hydrolysis of the Grignard Reagent.



The main concern of the research reported in this section of the thesis is the type of reaction reported by Bell, Vanderslice and Spehar²¹ where carbon tetrachloride was reduced by SBH in aqueous DMSO to chloroform and methylene chloride in an approximate 2:1 ratio.



At first glance it would appear that the methylene chloride arises from a further reduction of the chloroform product,

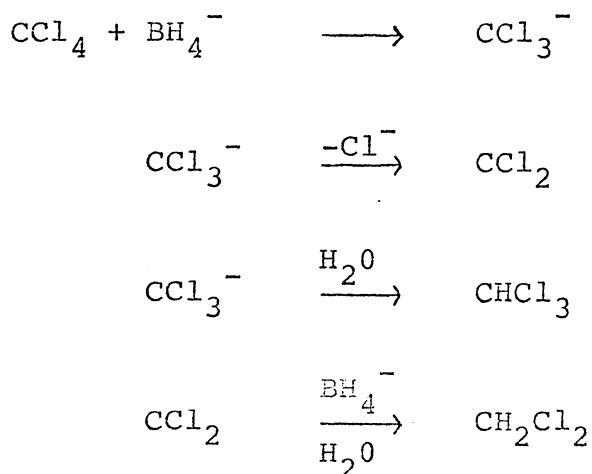
Table V-c

Yields of Nitrocycloalkanes from Bromonitrocycloalkanes

<u>Compound</u>	<u>C₂H₅OH- KOH %</u>	<u>CH₃OH- KI %</u>	<u>CH₃OH-H₂O NaBH₄ %</u>
Bromonitrocyclobutane	2	22	33
Bromonitrocyclopentane	32	22	76
Bromonitrocyclohexane	28	48	80
Bromonitrocycloheptane	--	2	76

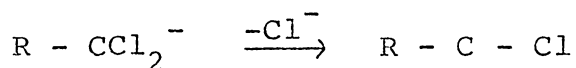
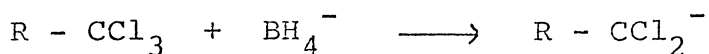
but when chloroform and SBH were stirred under the same conditions as the carbon tetrachloride, there was no reaction.

In determining a possible mechanism for the reaction it was concluded that there was no chance for either an S_N1 or S_N2 type displacement, consequently the mechanism was assigned as a displacement on-halogen to form a carbanion which could be quenched by a proton from the aqueous solvent to yield chloroform or the carbanion could lose a chloride ion to form the carbene. The carbene could then react with hydride ion or the aqueous solvent to produce methylene chloride.

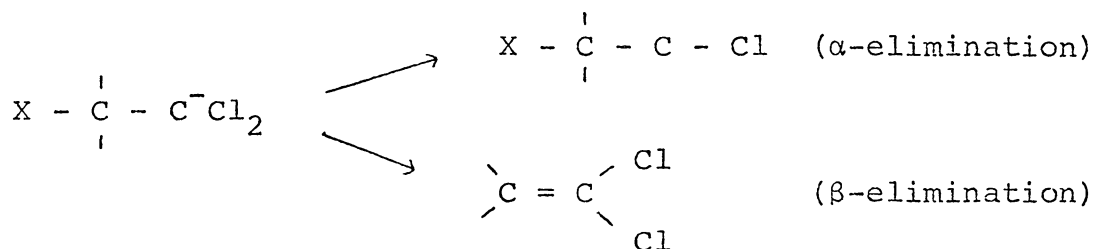
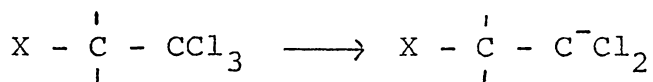


In order to study this proposed on-halogen displacement an in-depth investigation of the reaction of SBH with polychlorinated organic compounds was undertaken. One of the main points of interest was whether or not substituted

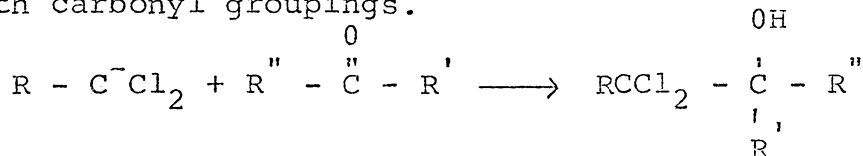
trichloromethanes would react with SBH under the same or similar conditions to generate a carbanion and if this carbanion would lose a chloride to form the carbene or merely be quenched by water.



The possibility of a β -elimination exists when a leaving group is on the β -carbon.



Also of interest was whether or not these carbanion intermediates would be reactive in condensation type reactions with carbonyl groupings.



These and other problems were explored by reacting a series of trichloromethanes and a few other interesting polyhaloalkanes with SBH in aqueous DMSO.

II. Experimental

A. General

The products from the reductions in this section are generally quite volatile, so they were in most cases trapped in a "cold-finger" condenser at -78° (dry ice-acetone). Because of their volatility and the evolution of hydrogen gas which made these products even more volatile a true yield was not always obtainable. The yields for the liquid products that are reported are based on gas chromatographic analyses. The solid products were isolated and weighed. Gaseous products were isolated using the "cold-finger" condenser and identified by gas chromatography or by infrared spectroscopy using a gas cell. In cases where a mixture of compounds was isolated and the components were volatile, the individual compounds were isolated by preparative gas chromatography and analyzed by infrared spectroscopy and/or mass spectrometry.

The gas chromatographic yields were obtained using the internal standard method which has previously been discussed (see experimental section A).

B. Chemicals

Sodium borohydride was obtained from Metal Hydrides,

Inc. and Fisher Scientific Company. The purity was listed as 98%.

Dimethylsulfoxide was from Fisher Scientific and was purified by vacuum distillation from calcium hydride and stored over molecular sieves.

Diglyme was from Columbia Organic Chemicals and was purified by vacuum distillation from lithium aluminum hydride (temperature kept well below 100°).

Preparation of Diethyldichloromethylphosphonate.-
Diethylphosphonate (0.14M) was stirred for three hours with diethyltrichloromethylphosphonate (0.07M) and triethylamine (0.07M), during which time heat was liberated. A solid residue of triethylamine hydrochloride was formed and filtered from the mixture.

The liquid material was vacuum distilled to give three fractions. The nmr spectrum of the fraction boiling at $96-98^{\circ}$ at 2mm pressure agreed with the spectrum postulated for diethyldichloromethylphosphonate.

Preparation of Diethyltrichloromethylphosphonate.--
Triethylphosphite (0.2M) and carbon tetrachloride (0.2M) were refluxed for 3 1/2 hours. The ethyl chloride which formed in the reaction was lost from the top of a reflux condenser fitted to the single-necked flask in which the reaction was carried out. The reaction mixture was cooled and vacuum distilled to yield a colorless liquid boiling

at 120-126^o (12-16mm). The G. C. analysis of the liquid indicated a 90% purity.

Preparation of p-Bitoluyl.- The Grignard Reagent of p-bromotoluene (1.17M) was formed in diethyl ether, then allowed to stir without heat under a nitrogen atmosphere for one hour. The solvent was then changed to benzene-ether (50:50). Next anhydrous cupric bromide (excess) was added in small portions; the reaction was exothermic. Solvent was removed by distillation until the reflux temperature reached 65^o (this temperature was attained from the exothermic reaction). After the cupric bromide ceased to cause visible reaction, the mixture was heated to reflux and held there for 1 1/2 hour. Metallic copper began to coat the flask. The reaction mixture was filtered hot. The filtrate was a clear yellowish solution. Ethanol was added to double the volume and the mixture was concentrated to remove the benzene. Upon cooling, white crystals formed from the concentrated ethanolic solution, mp 120-121^o (lit. mp 120-121^o),⁷⁸

The Free Radical Chlorination of p-Bitoluyl.- The bitoluyl (0.137M) was dissolved in benzene (300ml). Chlorine gas was bubbled through the solution as it was being irradiated with ultra-violet light. This procedure was continued during a 12 hour period. The mixture was cooled and ethanol was added, the product precipitated and

was recrystallized from ethanol. The crystals melted at 126-128°. The product was identified by nmr as α , α -dichloro-p-bitoluy1.

The free radical chlorination was attempted using nitrobenzene, carbon tetrachloride and chlorobenzene as solvents. The reaction was also run in the presence of triphenylphosphate, an iron scavenger, and phosphorus trichloride, an oxygen scavenger, with the same dichlorinated product being isolated.⁷⁹

Preparation of Perchloro-p-xylene.- $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ - Hexachloro-p-xylene (20g.) was dissolved in freshly distilled sulfuryl chloride (250ml). In a 2 liter, 3-necked, round bottom flask, equipped with a mechanical stirrer and reflex condenser, was placed 2.5g of anhydrous aluminum chloride, 5g of sulfur monochloride and 750ml of the freshly distilled sulfuryl chloride. The hexachloro-p-xylene was added through an addition funnel over a 30-minute period. The flask was then placed in an oil bath and the reaction mixture was concentrated to a volume of 50ml. The residue (50ml) was refluxed overnight (12 hrs.). By morning the mixture had concentrated to 25ml, so more sulfuryl chloride was added to make a total volume of 100ml. This mixture was refluxed for one hour and was cooled to room temperature. The sulfuryl chloride was removed at reduced pressure; a solid remained. To the

solid residue was added 1000ml of water, followed by portions of solid sodium bicarbonate to neutralize any excess acid. This mixture was heated for one hour and was then made acidic with concentrated hydrochloric acid, cooled and filtered. A yellowish crystalline material was collected (14.6g). The solid was dissolved in petroleum ether and this solution was dried over anhydrous magnesium sulfate. The ether solution was placed in a refrigerator and yellow-green needles formed, mp 147-148^o (lit. mp 153-154^o). Anal. (Found: C, 21.236; H, 0.103. Calculated for C₈H₁₀: C, 21.324; H, 0.000)

The liquid from which the perchloro-p-xylene was collected was concentrated and cooled to yield clear cubes of $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha', 2, 5$ -octachloro-p-xylene, mp 198-200^o (lit. mp 202-204^o). Anal. (Found: C, 25.205; H, 0.471. Calculated for C₈H₂Cl₈: C, 25.17; H, 0.53)^{80,81}

Preparation of Perchloro-p-xylylene.- Perchloro-p-xylene (0.001M) was dissolved in glacial acetic acid (20ml) and water (1ml), potassium iodide (0.004M) was added and the mixture was heated to 100^o. The reaction was kept under a nitrogen atmosphere by bubbling nitrogen through the mixture as it was stirred for 54 hours. The heat was removed and the mixture continued to stir for 48 hours and was then poured into 200ml of water. Solid sodium bisulfite was added to destroy the iodine. The mixture was then

heated for one hour on a steam cone, and then cooled and extracted with diethyl ether. The ether layer was washed with a sodium bicarbonate solution and dried over anhydrous magnesium sulfate. The solution was concentrated to dryness by evaporation. A solid yellowish material remained. After recrystallization crystals of the perchloro-p-xylylene were obtained, mp 166-169° (lit. mp 168-169°).⁸²

Preparation of 1,1,1-Trichloromethyl-1-methylcyclohexa-2,5-dien-4-one.- A solution of freshly distilled p-cresol (0.010M) in carbon disulfide (10ml) was added dropwise to a stirred suspension of anhydrous aluminum chloride (0.126m) in carbon disulfide (50ml). Next was added carbon tetrachloride (0.10M). The mixture turned to a dark maroon and was heated to reflux; hydrogen chloride gas was evolved and was trapped in water. After two hours the carbon disulfide was removed using a water aspirator. The product was collected by steam distillation.⁸³

C. Apparatus

The instruments used for detection and analyses have already been discussed in another part of this work.

The reductions in general were run in a 100ml single-necked flask. This flask was equipped with a gas take-off opening and a screw-in thermometer well and was magnetically stirred. The gas take-off was connected to a "cold-

"finger" condenser which was kept in a dewar containing a mixture of dry ice and acetone to maintain a temperature of -78° . The exit of the "cold-finger" was connected to a gas buret which was used to measure hydrogen evolution, a monitor of the reaction progress. The single-necked flask was equipped with an addition funnel for introduction of the material to be reduced.

D. Procedure

1. General

A magnetically stirred 100ml single-necked flask equipped with a thermometer and connected to a "cold-finger" condenser was charged with a solution of sodium borohydride in a mixture of DMSO (16ml) and water (4ml). Since this mixing was exothermic, the vessel was cooled to approximately 25° in an ice water bath. The halide to be reduced was then added drop-wise through an addition funnel and the gas evolution was monitored by use of a gas buret connected to the "cold-finger." If the reaction did not occur at 25° , the temperature was increased until hydrogen gas evolution or until the distillation temperature of the most volatile material in the reaction vessel was approached. After the addition was completed, the mixture was stirred at the reaction temperature for one hour. The reaction mixture was then cooled to 25° and extracted with

diethyl ether. The trap was washed out with diethyl ether and the ether layers were combined. The ether layer was then washed with an equal volume of water and dried over anhydrous magnesium sulfate for analysis by gas chromatography.

2. Polyhaloalkanes

Reduction of 1,1,1-Trichloro-2,2,2-trifluoroethane in Aqueous DMSO.- Sodium borohydride (0.004M) was dissolved in DMSO (15ml) and water (6ml) and cooled to 5-10⁰. To this was added drop-wise to the trichlorotrifluoroethane (0.001M) in DMSO (5ml). The reaction was exothermic and the temperature was held between 15-20⁰ for 1/2 hour. Hydrogen evolution was vigorous.

The reaction mixture was then warmed to 40-50⁰ in order to distill any products or starting material into the dry ice-acetone trap. This trap was connected to another dry ice-acetone trap. The trap containing the reaction products was then slowly warmed in order to collect dry products.

The material in the trap was analyzed by G. C. (20% Apiezon L on 60/80 Gaschrom R). There were three peaks. The last peak to elute had the same retention time as that of the starting material. The other two peaks were collected on small sections of trapping columns and were

analyzed by mass spectrometry.

The first peak which was approximately five times as large as the second peak was found to be 1-chloro-2,2,2,-trifluoroethane, and the second peak was 1,1-dichloro-2,2,2-trifluoroethane. An infrared spectrum of each was obtained using a gas cell.

Reduction of Bromotrichloromethane in Aqueous DMSO.-

The SBH (0.004M) was dissolved in DMSO (15 ml) and water (6 ml). The bromotrichloromethane (0.002M) was dissolved in DMSO (5 ml) and added drop-wise to the SBH solution. The temperature was maintained between 15 to 20° during the addition (the temperature was increased with each drop - very exothermic). After the addition was completed the mixture was stirred at 20° for 15 to 20 minutes. The reaction mixture was extracted with diethyl ether and back-washed with water. The ether layer was dried over anhydrous magnesium sulfate. The analysis by G. C. indicated only two products, dichloromethane and chloroform in an approximate 2 to 1 ratio, respectively.

Reduction of Bromodichloromethane in Aqueous DMSO.-

The bromodichloromethane (0.002M) in DMSO (5ml) was added to a solution of SBH (0.004M) in DMSO (15ml) and water (4ml). Gas evolution began as the temperature reached 25°, within 1/2 hour the gas evolution had subsided. The reaction mixture was extracted with diethyl ether which was

washed and dried. The G. C. analysis indicated the only product to be dichloromethane.

Reduction of Benzotrichloride in Aqueous DMSO.- The SBH (0.004M) was dissolved in DMSO (10ml) and water (4ml). To this was added benzotrichloride (0.002M) and the internal standard benzotrifluoride (0.002M), in DMSO (5ml). The reaction mixture was heated and another 0.004 mmoles of SBH was added along with 3ml of water. Gas evolution began as the temperature of the reaction mixture reached 60°. The mixture was stirred for one hour at 65°, cooled to room temperature and extracted with diethyl ether. The ether layer was washed with water and dried over anhydrous magnesium sulfate.

The G. C. analysis showed a 90% yield of benzal chloride, based on the internal standard.

Reduction of Benzalchloride in Aqueous DMSO.- The SBH (0.004M) was dissolved in DMSO (7ml) and water (4ml). To this was added a solution of benzal chloride (0.002M) and benzotrifluoride (0.002M) (internal standard) in DMSO (8ml). The mixture was heated to 65° and held there for two hours. The mixture was then cooled, extracted with diethyl ether, washed with water and dried over anhydrous magnesium sulfate. G. C. analysis showed all of the starting material was still present without a trace of benzyl chloride or toluene.

Reduction of 1,1-Dichloro-2,2,2-trifluoroethane in Aqueous DMSO.- This reduction was carried out in the same manner as the reduction of 1,1,1-trichloro-2,2,2-trifluoroethane, except the reaction time was increased from 1/2 hour to 1 1/2 hours.

G. C. analysis indicated approximately a 5% conversion of 1,1-dichloro-2,2,2-trifluoroethane to 1-chloro-2,2,2-trifluoroethane, the other 95% being starting material.

Reduction of 1,1,1-Trichloroethane in Aqueous DMSO.- SBH (0.005M) was dissolved in DMSO (7ml) and water (5ml), to this was added the 1,1,1-trichloroethane (0.002M) in DMSO (8ml). The reaction mixture was heated to 40° and held there for five hours. After extraction with diethyl ether the G. C. analysis indicated only starting material to be present.

Reduction of Chloroform in Aqueous DMSO.- Chloroform was treated in the same manner as the 1,1,1-trichloroethane. The G. C. analysis of this reaction indicated only starting material.

Reduction of Hexachloroethane in Aqueous DMSO.- The SBH (0.004M) was dissolved in DMSO (7ml) and water (4ml), to this was added a mixture of hexachloroethane (0.002M) and the internal standard toluene (0.002M) in DMSO (8ml). Gas evolution began immediately at a cooled temperature of 25°. The total reaction time was 1/2 hour.

After work-up with diethyl ether, the G. C. analysis indicated a 90% yield of tetrachloroethene.

Reduction of $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ -Hexachloro-p-xylene in Aqueous DMSO.- The SBH (0.012M) was dissolved in DMSO (10ml) and water (8ml) and stirred until solution was attained. The hexachloroxylene (0.005M) was added and gas evolution began. A white solid began to precipitate. After the addition was completed the solid was filtered from the solution. The white precipitate was then washed with large amounts of water and acetone.

The carbon-hydrogen analysis was C, 40.09%, H, 1.56%. The infrared was run on a KBr pellet.

Reduction of Perchloro-p-xylene in Aqueous Diglyme.- The halide was dissolved in 10ml of diglyme at 60°, to this was added drop-wise a solution of SBH in 6ml of diglyme and 5ml of water. Gas was evolved with each drop. All of the SBH appeared to be used up as soon as the addition was completed; the reaction mixture was stirred at 60° for one hour. After two recrystallizations, yellowish crystals were obtained that melted at 164-167° (lit. mp 168-168.5° for perchloro-p-xylene). Anal. (Found: C, 25.348; H, 0.335. Calculated for C₈Cl₈: C, 25.305; H, 0.000)

Reduction of 1,1,2-Trichloroethane in Aqueous DMSO.- The SBH (0.05M) was dissolved in DMSO (40ml) and water (10ml), to this was added the halide (0.015M) in DMSO

(10ml). The reaction was vigorous and the volatile product was collected in a dry ice-acetone trap during one-half hour of stirring at 20-35°. The reaction product in the trap contained some water, so the material was distilled away from the water into another dry ice-acetone trap. Some of the product was placed in an nmr tube; this sample showed a singlet at 5.2 ppm. The ir of this sample between salt plates was identical to Sadtler's spectrum for 1,1-dichloroethene. No yield data was obtained due to the volatility of the sample (37° at 760 mm).

Reduction of 1,1-Dichloroethane in Aqueous DMSO.-

There was no reaction of 1,1-dichloroethane with SBH in aqueous DMSO, as evidenced by G. C. analysis.

Reduction of 1,2-Dichloroethane in Aqueous DMSO.- The

1,2-dichloroethane also was not reduced in the aqueous DMSO.

Reduction of Tetrachloroethene in Aqueous DMSO.-

Tetrachloroethene failed to react with SBH in aqueous DMSO at 40° for two hours. The G. C. analysis showed only the tetrachloroethene.

Reduction of Trichloroethene in Aqueous DMSO.- The

trichloroethene did not react with the SBH in aqueous DMSO. The G. C. analysis indicated only starting material.

Reduction of Diethyltrichloromethylphosphonate in Aqueous DMSO.- The diethyltrichloromethylphosphonate

(0.005M) was dissolved in DMSO (10ml) and added drop-wise to a solution of SBH (0.015M) in DMSO (32ml) and water (8ml). Gas evolution was vigorous. After the addition was completed the mixture was stirred for 1/2 hour and then extracted with diethyl ether.

The G. C. of the ether extract showed two products, diethyldichloromethylphosphonate and diethylchloromethylphosphonate (analyses by mass spec. and nmr of the samples collected by preparative G. C.).

Reduction of Pentachloroethane in Aqueous DMSO.- The SBH (0.005M) was dissolved in DMSO (7ml) and water (4ml) and the solution was cooled to 15°. To this was added the pentachloroethane in DMSO (8ml), at all times keeping the temperature below 20°. After 1/2 hour the reaction mixture was extracted with diethyl ether (50ml). The ether layer was washed with water (50ml) and dried over anhydrous magnesium sulfate. The G. C. analysis indicated the two major products to be 1,1,2,2-tetrachloroethane (25%), and 1,1,2-trichloroethane (20%).

Reduction of 1,1,2,2-Tetrachloroethane in Aqueous DMSO.- The tetrachloroethane (0.002M) and toluene (0.002M) in DMSO (8ml) were added to a stirred solution of SBH (0.005M) in DMSO (7ml) and water (4ml) at 25°. The mixture was held at 25-30° for three hours with a slow steady gas evolution occurring. The product was extracted with

diethyl ether and washed and dried in the usual manner for G. C. analysis.

The only product was trichloroethene in a 90% yield based on the internal standard.

Reduction of 1,1,2,2-Tetrachloroethane in Non-aqueous DMSO.- The SBH (0.005M) was dissolved in dry DMSO (10ml) and cooled to 25°. The tetrachloroethane (0.002M) in dry DMSO (5ml) was added and the mixture was stirred for three hours at 25°; very little gas was evolved. The temperature was increased to 40° and more gas began to evolve, but still a very slow reaction rate as compared to the previous reaction. To the mixture was added water (4ml) and a violent gas evolution occurred; the temperature jumped. After work-up in the normal manner the G. C. indicated the following relative yields of products: 1,2-dichloroethane, 10%; 1,1,2-trichloroethane, 25%; trichloroethene, 65%.

Reduction of 1,1-Diphenyl-2,2,2-trichloroethane in Aqueous DMSO.- SBH (0.005M) was dissolved in DMSO (15ml) and water (8ml), to this was added a solution of the halide (0.002M) in DMSO (10ml). The temperature was increased to 68° before gas evolution began. The reaction was vigorous and the mixture was held at 70° for 2 1/2 hours. The mixture was cooled and extracted with diethyl ether. The ether layer was washed with water and dried with anhydrous magnesium sulfate. The ether layer was

concentrated and the product was collected by vacuum distillation at 120-130° at 3mm: the distillate crystallized as a white solid, mp 78-80°. The nmr was a singlet at 7 ppm and the ir was identical to Sadtler's spectrum of 1,1-dichlorodiphenylethene. The yield was 90%.

Reduction of $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ -Hexachloro-m-xylene in Aqueous DMSO.- SBH (0.012M) was dissolved in DMSO (15ml) and water (8ml). This mixture was cooled to 25° and the hexachloroxylene (0.005M) was added in DMSO (10ml). The mixture was heated to 55° and gas evolution began. The temperature rose to as high as 70° but was cooled to 65° and held there with stirring for 1 1/2 hours.

The reaction mixture was cooled and extracted with diethyl ether. The ether layer was washed with water, dried over anhydrous magnesium sulfate and concentrated. The yield was 1.05g, 88%, of $\alpha, \alpha, \alpha', \alpha'$ -tetrachloro-m-xylene (identified by nmr and ir).

Reduction of $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha', 2, 5$ -Octachloro-p-xylene in Aqueous Diglyme.- This reduction was attempted in aqueous and anhydrous DMSO, but the halide was insoluble in both mediums.

The halide (0.002M) was dissolved, with difficulty, in diglyme (6ml) and water (5ml) and was added drop-wise to the halide solution (this was done to keep the halide from precipitating from solution). As the SBH was added

a white solid began to precipitate. When the addition was completed, the mixture was allowed to stir for 15 minutes. The solid was filtered from the solution and washed with water and pet ether. The pet ether was concentrated and clear cubes formed. The melting point of the cubes was the same as for the starting material as was the ir. The solid was also identified as starting material.

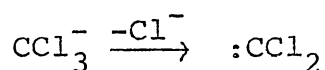
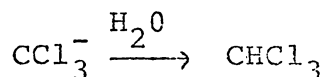
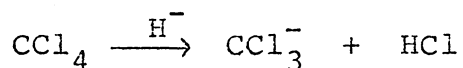
Reduction of $\alpha, \alpha, \alpha', \alpha', 2, 3, 5, 6$ -Octachloro-p-xylene in Aqueous Diglyme.- This octachloro-p-xylene did not react and only starting material was recovered.

Reduction of 1,1,1-trichloromethyl-1-methylcyclohexa-2,5-dien-4-one.- The 1,1,1-trichloromethyl-1-methylcyclohexa-2,5-dien-4-one (0.01M) was dissolved in DMSO (20ml) and heated to 70°, to this was added a solution of SBH (0.02M) in DMSO (15ml) and water (10ml). The addition was drop-wise and took approximately fifteen minutes. The solution turned brown but cleared after the addition was completed. The solution was stirred at 75° for four hours, cooled to room temperature and extracted with diethyl ether. The ether layer was washed and dried over anhydrous magnesium sulfate. The ether was stripped and white needles remained. The products were identified by nmr as the epimers that resulted from the reduction of the carbonyl group.

III. Discussion of Results

A. Mechanism

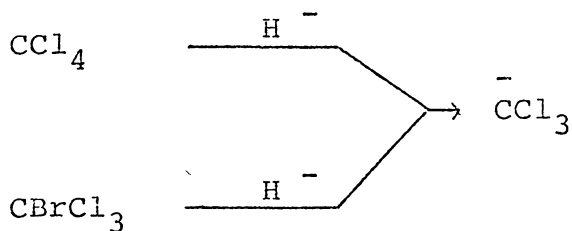
In work done by Bell, Vanderslice and Spehar²¹ it was postulated that the reduction of carbon tetrachloride with SBH in aqueous DMSO proceeded through a carbanionic intermediate which could be quenched by water or could lose a chloride ion to generate dichlorocarbene.



The carbene mechanism was introduced to explain the presence of dichloromethane when it was found that chloroform was inert toward SBH in this solvent system. The ratio of chloroform to dichloromethane in this reaction was 2 to 1, respectively. This indicated that competing reactions were occurring where the attack of water on the carbanion was slightly favored kinetically over the loss of the chloride ion to generate dichlorocarbene.

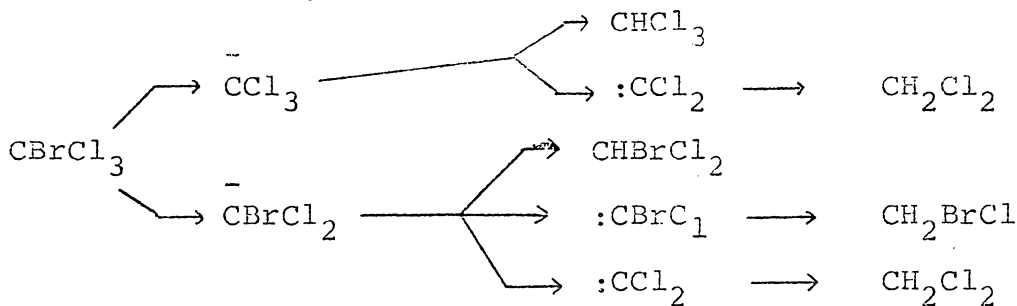
According to this postulation bromotrichloromethane should give the same ratio of chloroform to dichloromethane

since the bromonium ion (Br^+) loss should be favored over the loss of the chloronium ion (Cl^+) in the generation of the carbanion. The trichloromethyl carbanion should, therefore, be the reactive intermediate in the case of carbon tetrachloride or bromotrichloromethane.



When CBrCl_3 was reacted with SBH, the ratio of chloroform to dichloromethane was found to be 1 to 2, respectively.

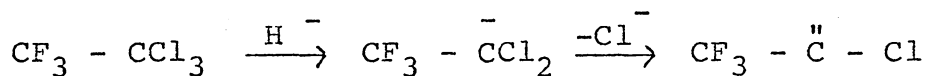
This reversal of yields indicated either the proposed mechanism for the reduction of carbon tetrachloride might be incorrect or the hydride ion was not selective in displacing on the bromine, thereby, producing the bromodichloromethyl carbanion which could be quenched to give bromodichloromethane.



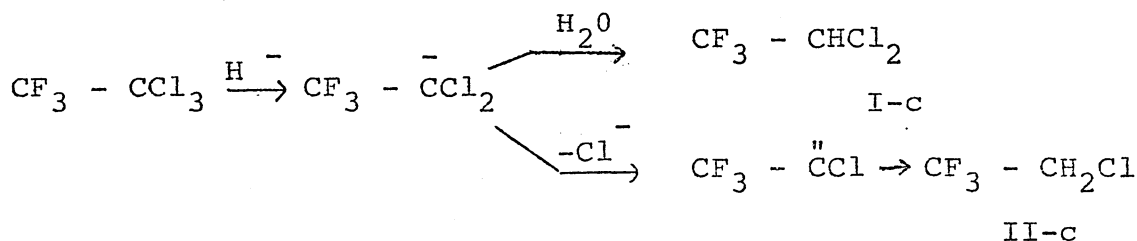
There was no bromodichloromethane present in the reaction mixture, so a sample of bromodichloromethane was

mixed with SBH in aqueous DMSO to see if it would react even though it was known that chloroform would not. The result was that, indeed, the bromodichloromethane did reduce and only to dichloromethane (no bromochloromethane was present by G. C. analysis). Therefore, the possibility of the carbene intermediate still existed.

It was thought that 1,1,1-trichloro-2,2,2-trifluoroethane would be more suitable for forming a carbene than carbon tetrachloride owing to the electron-withdrawing properties of the trifluoromethyl group.



A major product from this reduction should therefore be 1-chloro-2,2,2-trifluoroethane (II-c). When the reaction was run, the ratio of the product expected from the quench of the carbene (II-c) to the product from the quench of the carbanion (I-c) was 5 to 1, respectively.

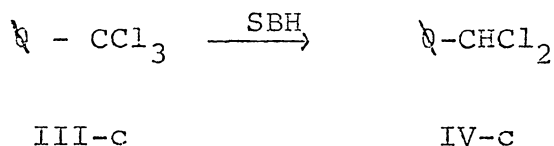


At this stage an unanswered question was whether or not the product from the carbanion quench (I-c) would react with SBH under the same conditions to yield the product

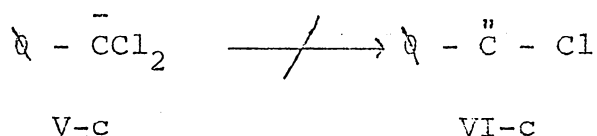
postulated to result from the reaction of the carbene intermediate (II-c). To test this a sample of the 1,1-dichloro-2,2,2-trifluoroethane (I-c) was allowed to react with SBH under the same conditions as employed with trichlorotrifluoroethane. There was no apparent reaction under these conditions (25° for 1/2 hr.), so the vessel was heated to double the temperature (50°) and held there for another hour. This resulted in only a 5% conversion of I-c to II-c. The amount of II-c was not nearly enough to explain the 5 to 1 ratio of II-c to I-c from the reduction of the trichlorotrifluoroethane, hence the carbene is indicated.

Attempts were made to trap this postulated carbene intermediate with cyclohexene and α -methylstyrene but no reaction would occur without water being present and when water was added the carbene addition product was not isolated.

When benzotrichloride (III-c) was reduced with SBH in aqueous DMSO, the only product was benzal chloride (IV-c) in a 90% yield.

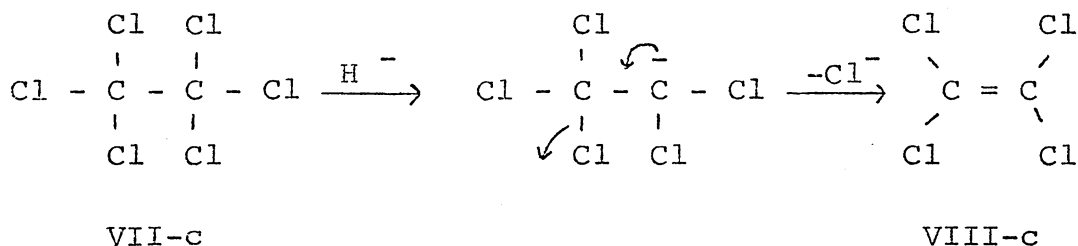


There was no benzyl chloride or toluene present (G. C. analysis). The absence of benzyl chloride suggested a carbene was not being formed in this case.



The absence of a product resulting from a carbene intermediate seemed to reflect the instability of this particular carbene (VI-c).

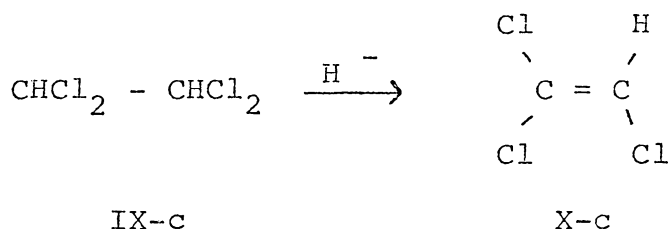
Another compound of interest in the study of the mechanism for the reduction of polyhaloalkanes with SBH was hexachloroethane (VII-c). With this compound after the carbanion forms there is a possibility for β -elimination to generate tetrachloroethene (VIII-c).



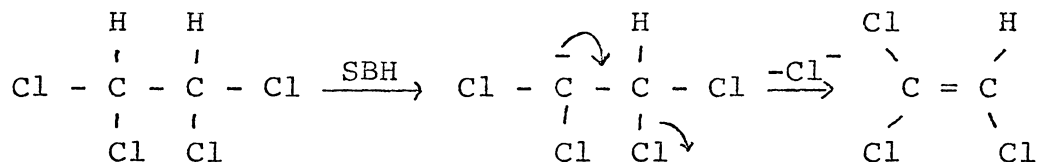
Tetrachloroethene (VIII-c) was the product in a 90% yield. The reasoning for the β -elimination in this case, but not in the case of the trifluorotrchloroethane is that chloride ion is a much better leaving group than fluoride⁸⁴ and the β -elimination route is favored over the α -elimination in this case.

When 1,1,2,2,-tetrachloroethane (IX-c) was reacted under the same conditions, the product was a 90% yield of

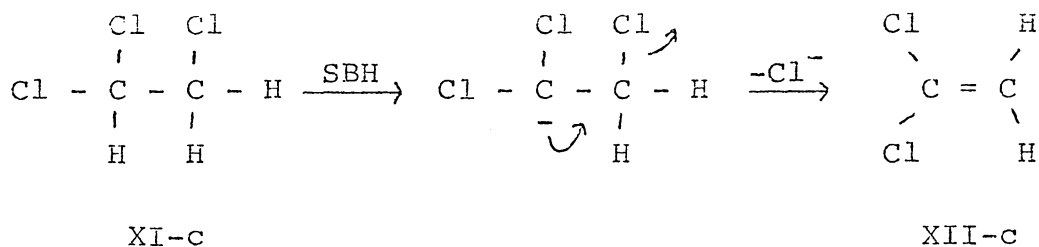
trichloroethene (X-c).



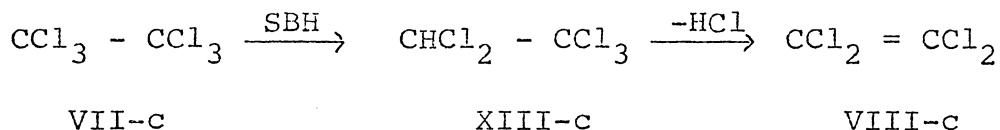
In this case it appeared that the SBH was probably acting as a strong base to abstract one of the acidic protons and this was being followed by a β -elimination of a chloride ion.



This type mechanism was substantiated when a sample of 1,1,2-trichloroethane (XI-c) was treated in the same manner. The product was 1,1-dichloroethene (XII-c) which would correspond to the loss of the more acidic proton from the carbon with the two chlorines followed by the β -elimination of chloride ion.



These two base-induced HCl eliminations introduced the possibility that the hexachloroethane (VII-c) might be reacting with SBH to form pentachloroethane (XIII-c) which could then eliminate HCl to produce the same product, tetrachloroethene (VIII-c).

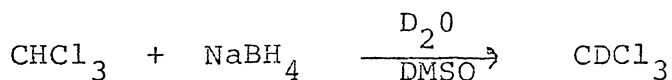


When a sample of pentachloroethane (XIII-c) was reacted under the same conditions, there was obtained a mixture of products with the major products being 1,1,2,2-tetrachloroethane (IX-c) and 1,1,2-trichloroethane (XI-c) both of which could react with excess SBH to give two more products (XII-c and X-c). There was a small amount of tetrachloroethene (VIII-c) present, but the 90% yield of tetrachloroethene from hexachloroethane seemed to eliminate the possibility of the reduction to pentachloroethane followed by an elimination of HCl.

Two trichloromethyl compounds, chloroform and methyl chloroform, were found to be unreactive towards SBH in aqueous DMSO. This seems to indicate that displacement on-chlorine does not occur unless three electron-withdrawing groups are present to stabilize the carbanion.

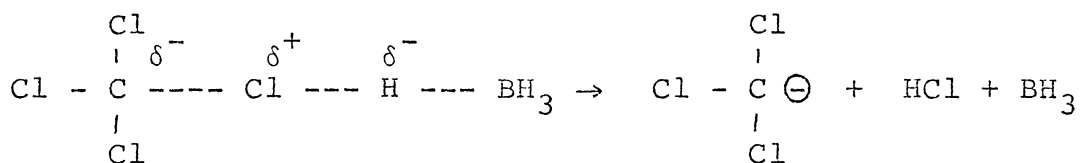
Even though chloroform did not react to give dichloromethane it was found that when deuterium oxide was used

instead of water, there was an exchange of deuterium for the hydrogen in the chloroform.²¹



This indicated that the trichloromethyl carbanion was forming and was being quenched by the deuterium oxide. This carbanion did not go on to the carbene as it did in the case of carbon tetrachloride. The explanation for the carbanion going on to the carbene in one case and not the other was due to the way the carbanion was formed.

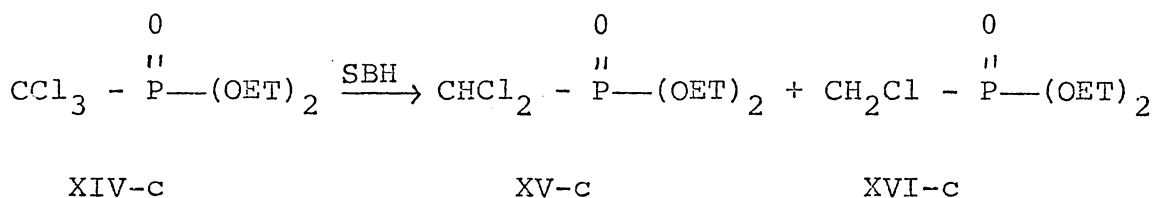
In the case of the chloroform there was merely a loss of a proton and a gain of a deuteron with no reaction involving the sodium borohydride (this is evidenced by no gas evolution). In the case of the carbon tetrachloride there was a displacement on-halogen which formed a molecule of hydrogen chloride in the immediate presence of a borane molecule, both in close proximity to the trichloromethyl carbanion. The reaction of these two species should be very exothermic and, therefore, impart a tremendous amount of energy to the adjacent trichloromethyl carbanion which



could cause it to lose a chloride ion, thusly generating

dichlorocarbene. The stability of the trichloromethyl carbanion has been shown by Winston and co-workers.^{85,86,87}

A trichloromethyl compound that was found to be very reactive toward this type reduction was diethyltrichloromethylphosphonate (XIV-c) which yielded two products, diethyldichloromethylphosphonate (XV-c) and diethylchloromethylphosphonate (XVI-c).



At present it has not been determined whether or not XV-c will react with SBH to yield XVI-c.

The stability of anions on the carbon adjacent to the phosphorus in phosphonate esters has been demonstrated by Corey and Kwiatkowski,⁸⁸ and their work indicates that XV-c might be converted to XVI-c via a carbanionic route. The possibility of XVI-c being formed by way of a carbene intermediate is still also a possibility.

When $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ -hexachloro-p-xylene (XVIII-c) was reacted with SBH in DMSO and water, the product was a white polymeric material which was insoluble in all common solvents that were tested. The carbon and hydrogen analysis was consistent with the molecular formula $\text{C}_8\text{H}_4\text{Cl}_4$. This was indicative of a chlorinated poly-p-xylylene (XVIII-c).

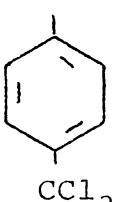
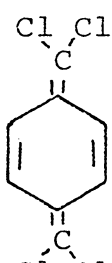
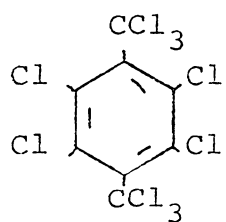
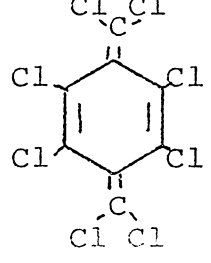
Table I-c

Reduction of Trichloromethyl Compounds with NaBH_4

Compound	Products	
H-CCl_3	No Reaction	
$\text{CH}_3\text{-CCl}_3$	No Reaction	
Cl-CCl_3	CHCl_3 CH_2Cl_2 major minor	
$\text{CF}_3\text{-CCl}_3$	$\text{CF}_3\text{-CHCl}_2$ $\text{CF}_3\text{-CH}_2\text{Cl}$ minor major	
$\text{C}_6\text{H}_5\text{-CCl}_3$	$\text{C}_6\text{H}_5\text{-CHCl}_2$	
$\text{CCl}_3\text{-CCl}_3$	$\text{Cl}_2\text{C=CCl}_2$	
$\text{CHCl}_2\text{-CCl}_3$	$\text{CHCl}_2\text{-CHCl}_2 + \text{CH}_2\text{Cl-CHCl}_2 + \text{others}$	
$\begin{array}{c} \text{O} \\ \parallel \\ \text{CCl}_3\text{-P-OC}_2\text{H}_5 \\ \\ \text{OC}_2\text{H}_5 \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CHCl}_2\text{-P-OC}_2\text{H}_5 \\ \\ \text{OC}_2\text{H}_5 \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_2\text{Cl-P-OC}_2\text{H}_5 \\ \\ \text{OC}_2\text{H}_5 \end{array}$

Table II-c

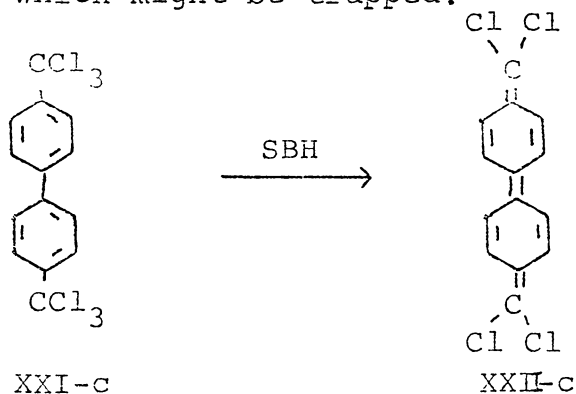
Generation of Double Bonds with NaBH_4

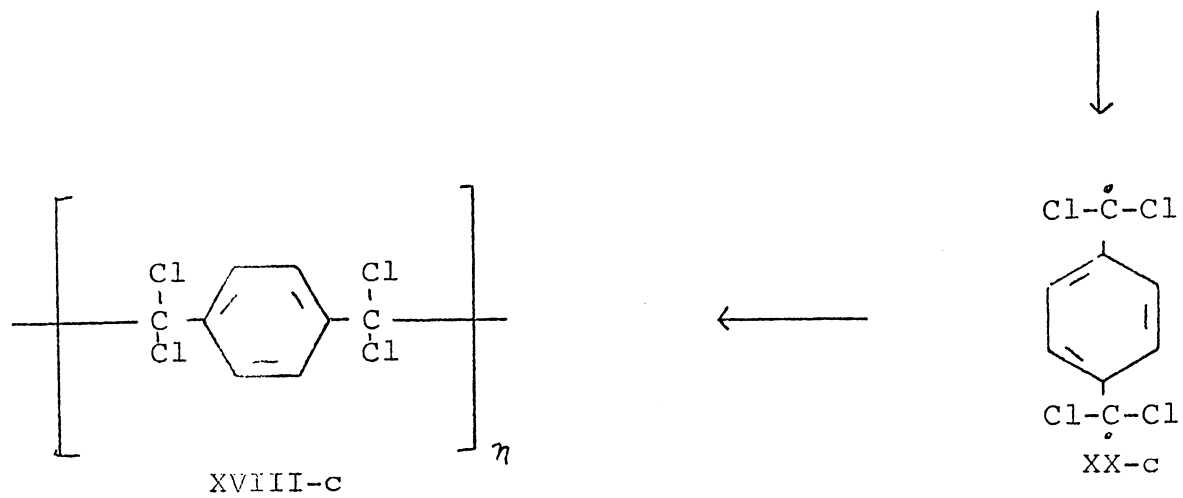
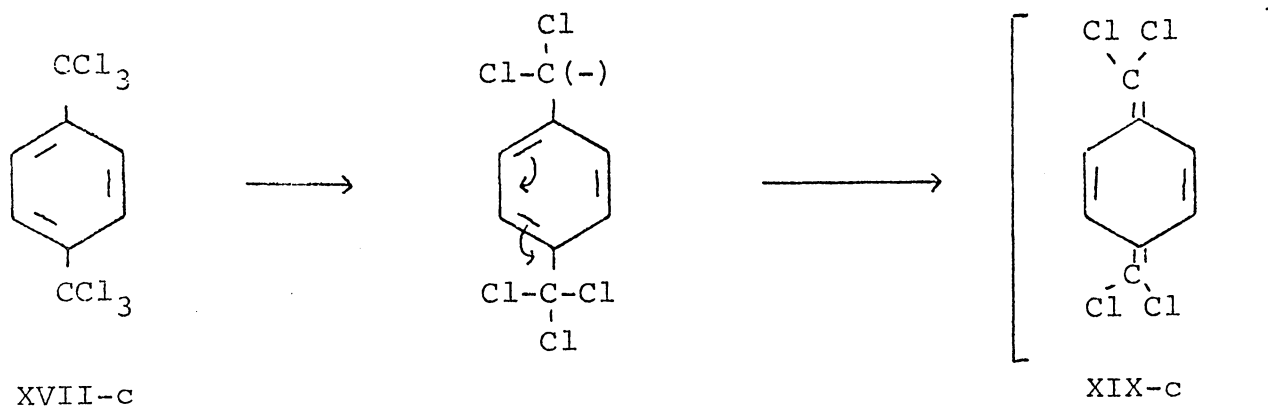
Compound	Product
$\text{CCl}_3\text{-CCl}_3$	$\text{CCl}_2=\text{CCl}_2$
$\text{CHCl}_2\text{-CHCl}_2$	$\text{CHCl}=\text{CHCl}$
$\text{CH}_2\text{Cl-CHCl}_2$	$\text{CH}_2=\text{CCl}_2$
CCl_3  CCl_3	
 CCl_3	

This type product seemed to point to the intermediacy of $\alpha, \alpha, \alpha', \alpha'$ -tetrachloro-p-xylylene (XIX-c) which could come about in the manner shown in Figure 1-c. This assignment was consistent with the carbon-hydrogen analysis and the ir of the material.

Work at Union Carbide on poly-p-xylylenes showed that they formed via the diradical (XX-c) shown in Figure 1-c.⁸⁹ An electron spin resonance (esr) spectrum was run on the polymer in order to detect any trapped end groups. There was a signal for the polymer, thus indicating the polymerization probably proceeded through the diradical.

Attempts at trapping the tetrachloro-p-xylylene (XIX-c) were unsuccessful. It was thought that this quinoid type intermediate would be stabilized if two rings were present instead of one.⁹⁰ This led to the attempted synthesis of $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ -hexachloro-p-bitoluyll (XXI-c) which could eliminate a Cl^+ and Cl^- through the aromatic systems to yield XXII-c which might be trapped.



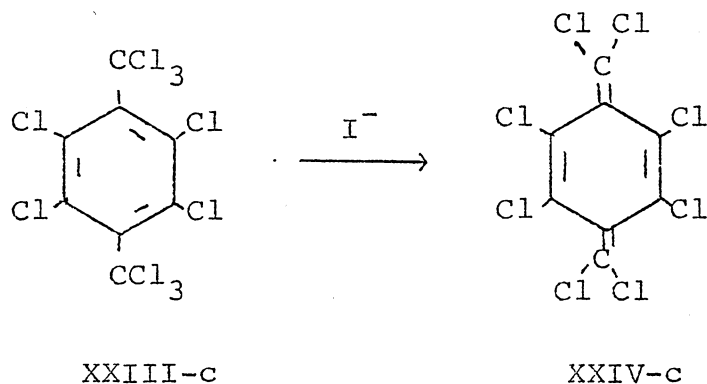


Reduction of $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ -Hexachloro-p-xylene

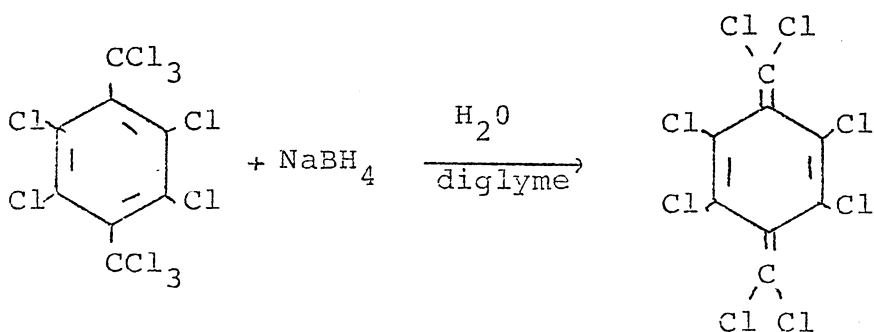
Figure 1-c

The synthesis of (XXI-c) was not successful. (p-bitoluyyl) resisted free radical chloronation).

The trapping of perchloro-p-xylylene (XXIV-c) has been reported by Ballester, et al.^{91,92} from the reaction of potassium iodide and perchloro-p-xylylene (XXIII-c) in acetic acid.



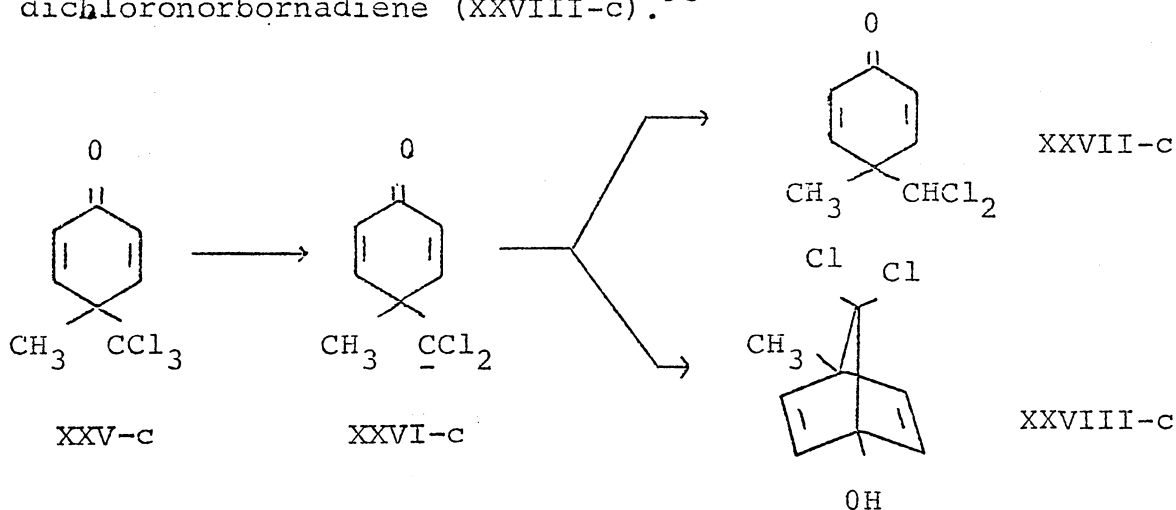
In the present study perchloro-p-xylylene (XXIII-c) was prepared⁸⁰ and reacted with SBH in aqueous diglyme and the product was the same as that from the reaction reported by Ballester, thus



substantiating the mechanism set forth in Figure 1-c from the reaction of the $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ -hexachloro-p-xylylene with SBH; i.e., the displacement on-halogen by the hydride ion

followed by an elimination of chloride ion through the aromatic system.

A sample of 4-methyl-4-trichloromethyl-2,5-cyclohexadienone (XXV-c) was prepared⁸³ and reacted with SBH in aqueous DMSO. It was thought that the carbanion (XXVI-c) might form and then either be reduced to the dichloromethyl compound (XXVI-c) or undergo an intramolecular condensation with the carbonyl to form 1-hydroxy-4-methyl-7,7-dichloronorbornadiene (XXVIII-c).⁹³



The result was that this trichloromethyl group was less reactive than the carbonyl group, with the result being a reduction of the ketone to a mixture of the two possible epimeric alcohols.

B. Solvent

The solvent system used in these reductions was either DMSO/water or diglyme/water. The DMSO/water system gave only limited trouble in that a few organic compounds were

not soluble. When solubility was a problem, the system was changed to diglyme/water and in some cases compounds were run in both systems with the results being comparable. When perchloro-p-xylene (XXIII-c) was found to be relatively insoluble in DMSO, the reduction was run in aqueous diglyme. To insure that this switching of solvent systems was not changing the mechanism of the reaction, the $\alpha, \alpha, \alpha, \alpha', \alpha', \alpha'$ -hexachloro-p-xylene (XVII-c) which had polymerized in aqueous DMSO was run in the diglyme/water system. The same polymeric product was isolated. In the case of the reduction of polyhalogenated alkyl compounds the solvent has to be able to stabilize charged intermediates just as in the aryl halide reductions. DMSO and diglyme are both excellent solvents for these type reactions (see Chapter I of this dissertation).

C. Conclusions

The reduction of polyhalogenated alkyl compounds with SBH in either aqueous DMSO or aqueous diglyme appears to proceed via a displacement on-halogen by the hydride ion (or the complexed hydride) to generate a carbanion. This carbanion could then be quenched by water or go on to the carbene, which then could react with a hydride ion and water to yield a compound where, in effect, two halogen atoms have been replaced with hydrogen atoms. In the cases

where there was a possibility for a β -elimination or an elimination through an aromatic system this route seemed to be more favorable than the α -elimination. This β -elimination led to the generation of double bonds and in two cases to the formation of p-xylyenes. In these reactions it was also observed that in some cases SBH could act as a base in bringing about the elimination of HCl in compounds with an acidic proton on a carbon atom adjacent to a carbon bonded to a chlorine.

APPENDIX

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The Reduction of Halogenated Organic
Compounds with Sodium Borohydride

by

Terry L. St.Clair

Abstract

Sodium borohydride in aqueous dimethylsulfoxide has been shown to be a good reducing agent for converting certain activated aromatic halo-compounds to their corresponding dehalogenated products. The order for ease of removal of the halogen is I>Br>Cl. The activating groups are those that are strongly electron-withdrawing. The reactivity for activating aryl halides substituted with groups such as -NO₂, -CF₃, -F, -Cl, -Br, and -I is in the order ortho > meta > para, thus indicating that the activating effect has its origins in inductive rather than resonance effects.

The removal of halogen appears to be occurring via a displacement on-halogen. This has been demonstrated in certain cases by using deuterium oxide instead of water in the reaction. When this is done, the halogen is replaced by deuterium instead of hydrogen. This indicates that the halogen leaves without its bonding electrons, thus leaving a carbanionic site on the aromatic ring. The carbanion is subsequently quenched by a proton from the water.

This reaction has also been shown to be applicable to aromatic systems other than benzene.

On-halogen type displacement by the hydride ion also occurs on certain polyhalogenated alkanes with the formation of a quasi-carbanionic intermediate which can be quenched by a proton from water, undergo alpha elimination, or undergo beta elimination. The alpha elimination occurs when a good leaving group is not present on the beta carbon. Attempts at trapping the carbene type intermediate from alpha eliminations were unsuccessful, evidently because of the presence of the water in the reaction medium. In two cases eliminations have occurred through a benzene system to generate para-xylylenes.

Diazonium salts were also shown to undergo direct reduction with sodium borohydride, thus providing a new route for the deamination of aromatic amines.