leum ether (5 ml) and placed on a neutral alumina column (10 g, Woelm, activity I) packed in petroleum ether. Elution with petroleum ether–benzene (1:1, 100 ml) gave a colorless oil (50 mg), which crystallized upon persistent rubbing. Recrystallization from methanol yielded fine needles of **7** (30 mg): mp 88–89°; ir $\lambda_{max}^{CCl_4}$ 6.23, 6.37, 6.80, 6.90, 7.09, 7.22, 7.33, 7.39, 7.52, 7.57, 7.68, 9.80, and 10.62 μ; mass spectrum *m/e* 328 (M^+), 313, 271, 265, 243, 228, and 201.

Anal. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83. Found: C, 80.27; H, 9.70.

Mesylation of Alcohol 5.—A solution of alcohol **5** (50 mg) in pyridine (10 ml) was cooled to 0–5° and treated with methanesulfonyl chloride (0.5 ml). After standing at room temperature, the reaction mixture was worked up in the normal way to afford a crystalline residue (30 mg), which was recrystallized from methanol to yield needles of **7**, mp 88–89°. The melting point was undepressed by admixture with **7** and the infrared spectra ($CHCl_3$) of the respective samples were identical. The two samples showed identical tlc and glpc behavior.

11,12-Dimethoxyabieta-8,11,13-triene (8).—A solution of **7** (25 mg) in ethyl acetate (10 ml) containing perchloric acid (60%, 1 drop) was hydrogenated in the presence of platinum oxide (5 mg) until the consumption of hydrogen ceased (1 mol equiv in 1 hr). The catalyst was removed by filtration and the filtrate was worked up in the normal way to yield an oil (23 mg). Although the oil appeared homogeneous by tlc (solvent: petroleum ether), glpc indicated a 60:40 mixture of two components. Alumina chromatography and preparative tlc (silica gel GF_{254}, 2 mm) failed to separate the mixture. The mixture was ultimately resolved by preparative glpc. Crystallization from methanol of the compound with longer retention time yielded **8** (3 mg) as fine needles, mp 87–88°. The identity of **8** with 11,12-dimethoxyabieta-8,11,13-triene prepared by the method of Wenkert and coworkers[17] was confirmed by comparison of infrared, nmr, and mass spectra, melting point, mixture melting point, and tlc and glpc behavior.

7-Aminotaxodione (11).—To a solution of taxodione (100 mg) in ethyl acetate (20 ml), concentrated ammonium hydroxide solution (5 drops) was added and the reaction mixture was stirred at room temperature for 30 min. Evaporation of the solvent yielded a purple crystalline residue (100 mg), which on crystallization from ether gave large plates of **11**: mp 208–210°; uv λ_{max}^{MeOH} 265 (ϵ 4200), 295 (ϵ 3800), and 485 mμ (ϵ 15,300); ir λ_{max}^{KBr} 2.99, 3.12, 5.85, 6.06, 6.34, 6.62, 7.15, 8.03, 9.35, 9.80, 10.36, and 11.05 μ; mass spectrum *m/e* 329 (M^+), 314, 301, 286, 260, 245, and 233.

Anal. Calcd for $C_{20}H_{27}O_3N$: C, 62.92; H, 8.26; N, 4.25. Found: C, 62.57; H, 8.44; N, 3.97.

Hydrogenation of Taxoquinone.—A suspension of taxoquinone (**13**, 100 mg) in glacial acetic acid (30 ml) was hydrogenated over platinum oxide (5 mg) at atmospheric pressure. The reduction was completed within 2 hr, after which the catalyst was removed by filtration and the filtrate was evaporated. The residue was dissolved in benzene and passed through a silica gel column (20 g) packed in benzene. Elution with benzene (100 ml) gave a crystalline product, mp 179–181°. The product was identical with an authentic sample of royleanone (**12**) by mixture melting point, tlc, and infrared spectral comparisons.

Registry No.—**1**, 19026-31-4; **2**, 21838-12-0; **3**, 21887-45-6; **4**, 21838-13-1; **5**, 21764-39-6; **6**, 19039-02-2; **7**, 21764-40-9; **8**, 7726-32-1; **11**, 21886-99-7; **13**, 21764-41-0; **14**, 21887-01-4; **15**, 21764-42-1.

Selective Reductions. XIV. The Fast Reaction of Aryl Bromides and Iodides with Lithium Aluminum Hydride in Tetrahydrofuran. A Simple, Convenient Procedure for the Hydrogenolysis of Aryl Bromides and Iodides

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Unactivated aromatic bromides are reduced quite rapidly and quantitatively to the corresponding hydrocarbons by lithium aluminum hydride in refluxing tetrahydrofuran. Iodides are reduced at a reasonable rate even at room temperature. The ease of reduction of the different halogens, as indicated by rate studies, follows the order I > Br > Cl > F. Iodo and bromo substituents can be selectively removed in the presence of chloro substituents. This provides a convenient synthetic procedure for debromination and deiodination of aryl halides where this is required in synthetic operations.

The inertness of nonactivated aromatic halides toward attack by nucleophilic reagents is generally recognized. However, Karabatsos and Shone recently reported that aromatic halides exhibit surprising reactivity toward lithium aluminum hydride in tetrahydrofuran.[2] Their results indicated that the reaction was less facile than dehalogenation of such halides with triphenylstannane.[3,4] Consequently, the latter substance was recommended as the reagent of choice.[2]

We had also been examining the reaction of lithium aluminum hydride with aromatic halides in tetrahydrofuran (THF). However, the rates that we observed are very much faster than those reported previously.[2] Indeed, they are considerably faster than the corresponding dehalogenations with triphenylstannane. Accordingly, we must question the conclusion that the latter substance should be considered as the preferred reagent for the hydrodehalogenation of unactivated aryl halogen.

Our interest in this problem arose in the course of a systematic comparison of the behavior of lithium aluminum hydride[5] and of aluminum hydride[6] toward representative organic compounds. We decided to extend these studies to organic halides. In the course of these studies, we noted that aromatic halides, such as bromobenzene and iodobenzene, are essentially inert toward aluminum hydride, but react relatively rapidly with lithium aluminum hydride. Moreover, the production of hydrocarbon is essentially quantitative.

$$\mathrm{ArX} \xrightarrow[\mathrm{THF}]{\mathrm{LiAlH_4}} \mathrm{ArH}\ (>90\%)$$

This was surprising in view of the commonly accepted position that aromatic halides are extremely

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[1] Graduate research assistant on a research grant, DA 31-124 ARO(D) 453, supported by the U. S. Army Research Office (Durham).

[2] G. J. Karabatsos and R. L. Shone, *J. Org. Chem.*, **33**, 619 (1968). See also J. E. Johnson, R. H. Blizzard, and H. W. Carhart, *J. Amer. Chem. Soc.*, **70**, 3664 (1948).

[3] L. A. Rothman and E. I. Becker, *J. Org. Chem.*, **25**, 2203 (1960).

[4] D. H. Lorenz, P. Shapiro, A. Stern, and E. I. Becker, *ibid.*, **28**, 2332 (1963).

[5] H. C. Brown, P. M. Weissman, and N. M. Yoon, *J. Amer. Chem. Soc.*, **88**, 1458 (1966).

[6] N. M. Yoon and H. C. Brown, *ibid.*, **90**, 2927 (1968).

resistant to hydrogenolysis with lithium aluminum hydride. Consequently, we undertook a systematic study of the approximate rates, stoichiometry, and products of the reaction between lithium aluminum hydride in THF with representative aryl halides.

In view of the considerable differences in the results and conclusions between the present study and that reported earlier,[2] it appears desirable to present in detail our data and procedures.

Results and Discussion

In all cases, lithium aluminum hydride was dissolved in THF to give clear solutions, 1.00 *M*.[7] For studying the major characteristics of the reaction, we used solutions which were usually 0.25 *M* in the aryl halide and 0.25 *M* in lithium aluminum hydride. The solutions were maintained at constant temperature and aliquots were removed at appropriate intervals of time and analyzed for residual "hydride" by hydrolysis. The solutions were also examined by glpc at appropriate intervals for residual halide and hydrocarbon.

Stoichiometry.—The reaction of lithium aluminum hydride with iodobenzene proceeded quite rapidly at 25° in the initial phases of the reaction. However, it rapidly decreased in rate and approached 50% reduction asymptotically (Figure 1). Further reduction was relatively slow.

From this result, we conclude that in the fast initial stage the reaction must utilize 2 mol of lithium aluminum hydride, as indicated by the equation

$$\mathrm{ArI} + 2\mathrm{LiAlH_4} \longrightarrow \mathrm{ArH} + \mathrm{LiAl_2H_7} + \mathrm{LiI}$$

Subsequent reduction by the species $LiAl_2H_7$ then takes place at a much slower rate.

The formation of $LiAl_2H_7$ and NaB_2H_7 in reactions of lithium aluminum hydride and sodium borohydride has been described previously.[8,9] Consequently, we did not attempt to confirm the formation of $LiAl_2H_7$. However, the results of this and of other experiments clearly indicate the desirability of utilizing at least 2 mol of lithium aluminum hydride per mol of aryl halide to be reduced.[10]

Effect of the Halogen.—A series of reductions was carried out utilizing the individual monohalobenzenes under identical conditions. The results (Figure 1) clearly reveal that the reactivity varies in the order $I > Br > Cl > F$.

This result indicates that the reaction mechanism does not involve a simple nucleophilic attack on carbon. Such S_N2 reactions in aromatic derivatives normally exhibit the order $F \gg Cl \sim Br < I$.[11]

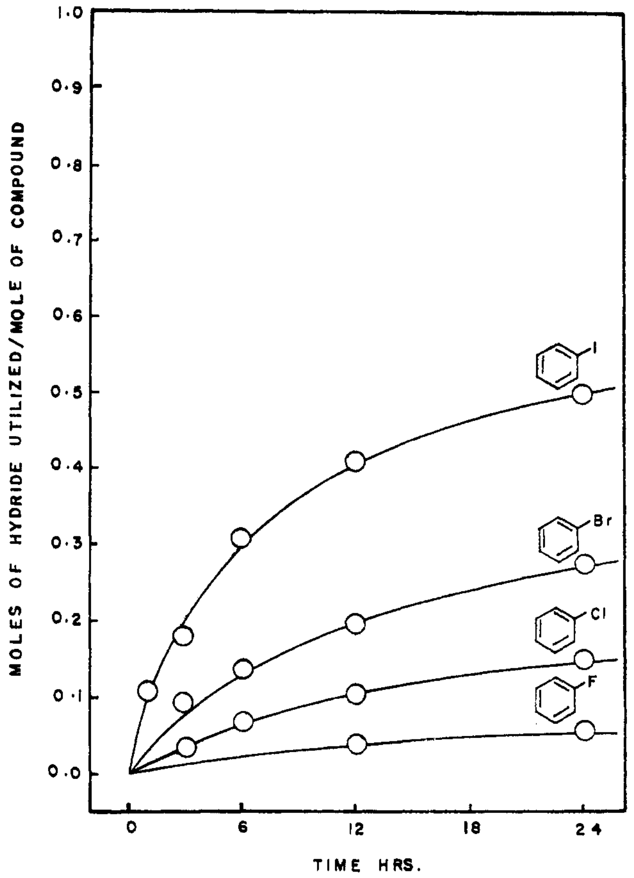

Figure 1.—Rates of reduction of the halobenzenes with lithium aluminum hydride in tetrahydrofuran at 25° (both reagents 0.25 *M*).

Effect of Structure.—Substituents in the aromatic ring exert a significant influence upon the reaction rate. Thus, electron-releasing substituents, such as *p*-methyl and *p*-methoxy, result in a decrease in rate, whereas electron-withdrawing substituents, such as *p*-bromo and *p*-chloro, bring about an increase in rate (Figure 2, Table I). On the other hand, a *p*-phenyl substituent has little effect on the rate.

Steric compression of the halogen substituent by an adjacent group apparently results in an enhanced rate. Thus, *o*-bromo-*t*-butylbenzene is reduced at a faster rate than is the *para* isomer. Similarly, the enhanced rate of 1-bromonaphthalene may arise from the steric interactions with the *peri* position.

Synthetic Applications.—The stoichiometry study previously discussed indicated that for optimum rate of reduction it was desirable to utilize at least 2 mol of lithium aluminum hydride per mol of aryl bromide. We adopted the use of a 4:1 molar ratio, utilizing solutions 0.25 *M* in halide and 1.00 *M* in lithium aluminum hydride. The greatly enhanced rate which results is indicated by Figure 3. An increase in temperature to 65° (refluxing THF) caused the reaction to be essentially complete in 6 hr (Figure 3). Accordingly, we adopted these conditions (1.0 *M* in lithium aluminum hydride, 0.25 *M* in the aromatic halide) for examining the synthetic applicability of the procedure. Room tempera-

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(7) In the earlier study,[2] slurries of "lithium aluminum hydride" in THF were used. Since lithium aluminum hydride is easily soluble in the solvent to give clear solutions at the concentrations utilized, the precise nature of these "slurries" must be considered questionable. This may be the basis for the apparent major differences in reactivity in the two studies. In a communication which has recently appeared, P. Olavi, I. Virtanen, and P. Jaakkola [*Tetrahedron Lett.*, 1223 (1969)] report that they achieved a relatively rapid hydrogenolysis of aryl chlorides with solutions of lithium aluminum hydride in tetrahydrofuran and report kinetic data for a number of such compounds. These results confirm the present conclusion that it must have been the use of slurries that was responsible for the slow reaction observed by previous workers.

(8) G. G. Evans, J. K. Kennedy, Jr., and F. P. Del Greco, *J. Inorg. Nucl. Chem.*, **4**, 40 (1957).

(9) H. C. Brown and P. A. Tierney, *J. Amer. Chem. Soc.*, **80**, 1552 (1958).

(10) Alternatively, it should be possible to utilize lithium hydride in the reaction mixture to regenerate lithium aluminum hydride.

$$\mathrm{LiAl_2H_7} + \mathrm{LiH} \longrightarrow 2\mathrm{LiAlH_4}$$

(11) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951).

Table I

Reaction of Lithium Aluminum Hydride with Representative Aryl Halides in Tetrahydrofuran[a,b]

Compd	Registry no.	$LiAlH_4$ concn, *M*	Temp, °C	Reduction, % 0.5 hr	1.0 hr	3.0 hr	6.0 hr	12 hr	24 hr
Fluorobenzene	462-06-6	0.25	25	0	0	0	0	4	6
Chlorobenzene	108-90-7	0.25	25	0	0	4	8	11	15
Bromobenzene	108-86-1	0.25	25	0	6	10	14	20	28
Bromobenzene[c]		1.00	25		20	31	52	70	95
Bromobenzene[c]		1.00	65	36	46	79	100		
Iodobenzene	591-50-4	0.25	25	6	11	18	31	41	50
1-Bromonaphthalene	90-11-9	0.25	25	2	4	10	16	24	34
4-Bromobiphenyl	92-66-0	0.25	25	0	2	8	14	20	28
o-Bromotoluene	95-46-5	0.25	25	0	4	8	12	14	21
p-Bromotoluene	106-38-7	0.25	25	0	6	8	12	14	20
o-Bromo-*t*-butylbenzene	7073-99-6	0.25	25	4	6	10	17	21	29
p-Bromo-*t*-butylbenzene	3972-65-4	0.25	25	0	4	8	8	12	15
p-Dibromobenzene	106-37-6	0.25	25	9	13	21	26	33	43
p-Bromoanisole	104-92-7	0.25	25	0	0	4	7	13	17
m-Chloroiodobenzene[d]	625-99-0	0.25	25	11	24	48		70	100

[a] In all cases, the initial concentration of the aryl halide was 0.25 *M*. [b] Except where otherwise indicated, the reactions were followed by the decrease in "hydride" concentration. [c] Followed by glpc determination of the decrease in concentration of bromobenzene and the increase in concentration of benzene. [d] The reaction mixture became turbid as the reaction proceeded. The data from hydride uptake were checked by glpc analysis for chlorobenzene. Good agreement was realized.

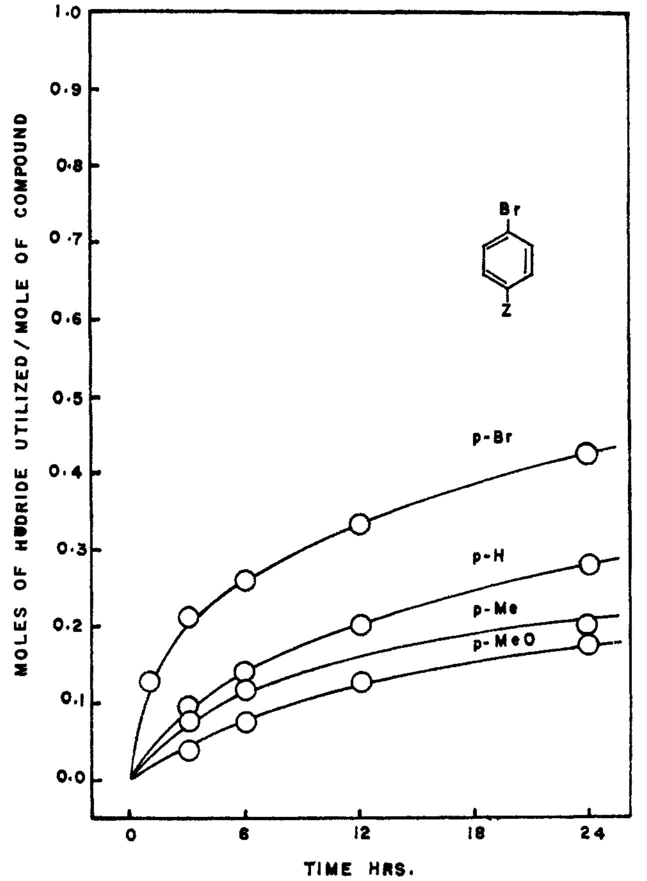


Figure 2.—Rates of reduction of substituted bromobenzenes with lithium aluminum hydride in tetrahydrofuran at 25° (both reagents 0.25 *M*).

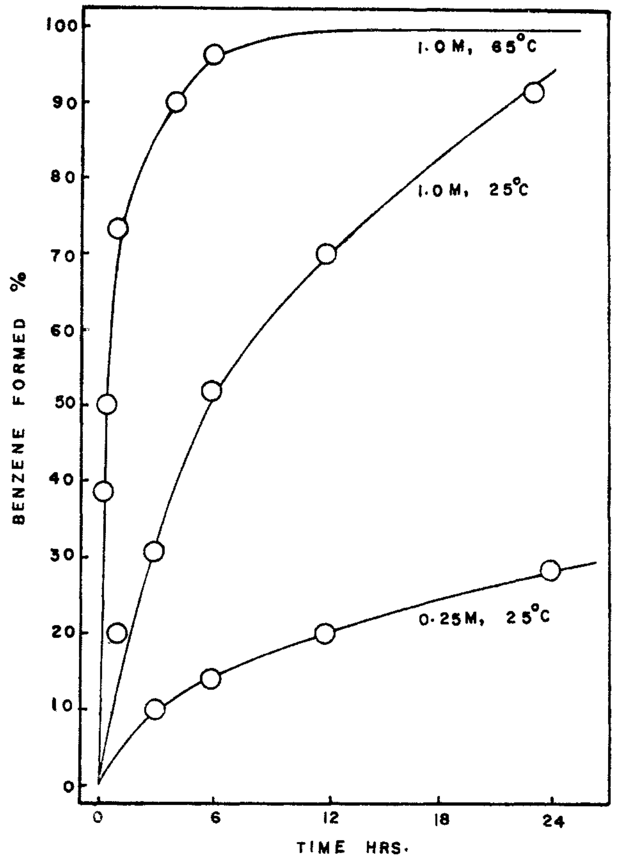


Figure 3.—Rates of reduction of bromobenzene (0.25 *M*) with lithium aluminum hydride in tetrahydrofuran.

ture was adequate for the reduction of aryl iodides; refluxing THF was used for the aryl bromides.

Iodobenzene was converted into benzene in 94% yield in 24 hr at room temperature.

Bromobenzene was converted into benzene in 97% yield in 6 hr in refluxing THF. Similarly, 1-bromonaphthalene was converted into naphthalene in 99% yield, and 4-bromobiphenyl was converted into the hydrocarbon in a yield of 94%.

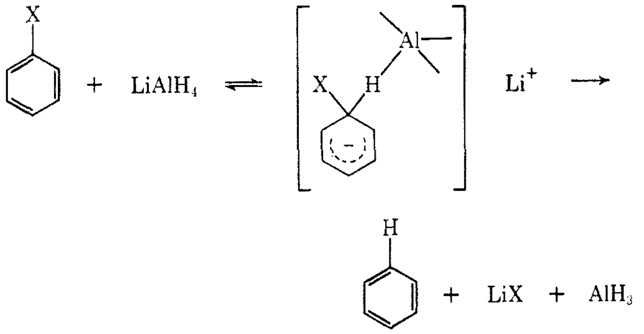
Finally, by utilizing a limited amount of lithium aluminum hydride, the iodine substituent in *m*-chloroiodobenzene was removed selectively at 25° to yield 94% of chlorobenzene.

Applicability.—Karabatsos and Shone concluded that hydrogenolysis of aryl halides with lithium aluminum hydride[2] was not competitive with hydrogenolysis by triphenylstannane.[3,4] However, their conclusion was based on the very slow rates they achieved in their reaction. For example, they report that the reduction of *p*-bromotoluene proceeds in refluxing tetrahydrofuran only to the extent of 7% in 24 hr. This compares to the 20% conversion that we realized for the same time period at 25° (Figure 2). The concentrations in the two experiments were comparable. The only way that we can account for the evident vast difference in rates is the authors' report that they added the aryl halide to a "slurry" of lithium aluminum hydride and the solvent. Since lithium aluminum hydride is easily soluble in the solvents used to concentrations far higher than the 0.25 *M* solutions that should have been formed, the quality of the hydride used is in question.

In our experiments, the relatively fast rate at 25° was further enhanced both by utilizing higher concentrations of lithium aluminum hydride and by raising the temperature to 65°. Under these conditions, essentially quantitative reductions of aryl bromides were achieved within 6 hr.

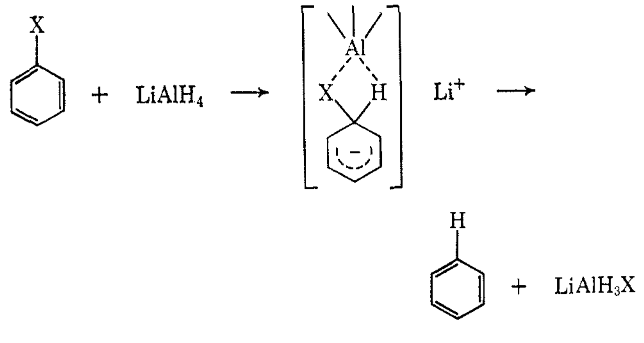
In contrast, the hydrogenolysis of iodobenzene with triphenylstannane requires a temperature of 95°, and a temperature of 154° is recommended for the hydrogenolysis of aryl bromides.[3] Consequently, it appears from the present results that hydrogenolysis of aryl halides by lithium aluminum hydride requires much milder conditions than the corresponding reactions utilizing triphenylstannane.

Mechanism.—Although we have not yet undertaken any detailed study of the mechanism, it may be pertinent to consider possible reaction paths. Nucleophilic substitution of aryl halides has been the subject of detailed study.[12] Such a mechanism would involve the following stages.



$$LiAlH_4 + AlH_3 \longrightarrow LiAl_2H_7$$

Alternatively, the reaction might involve a four-center mechanism.



$$LiAlH_4 + LiAlH_3X \longrightarrow LiAl_2H_7 + LiX$$

The rate-enhancing effect of electron-withdrawing substituents and the rate-retarding effect of electron-releasing substituents are in accord with these mechanisms. The rate-enhancing effect of a bulky alkyl group in the *ortho* position, as in *o*-bromo-*t*-butylbenzene, can be interpreted in terms of a decrease in steric strain as the bromo substituent is moved out of the plane of the aromatic ring, away from the bulky *t*-butyl group.

The reactivity order, I > Br > Cl > F, is different from that commonly observed in nucleophilic aromatic substitutions and indicates that bond breaking must be involved in the rate-determining stage.

Experimental Section

Materials.—Tetrahydrofuran was treated with small quantities of lithium aluminum hydride until hydrogen evolution ceased. Then the tetrahydrofuran was distilled at atmospheric pressure and kept under a nitrogen atmosphere. The lithium aluminum hydride was >95% pure material from the Ventron Corp. Most of the compounds used were commercial products of the highest purity. They were further purified by distillation, sublimation, or recrystallization when necessary. In all cases, physical constants agreed satisfactorily with constants in the literature.

Preparation of Lithium Aluminum Hydride Solution in Tetrahydrofuran and Standardization.—Standard solutions of lithium aluminum hydride in tetrahydrofuran were prepared in the following manner. In a typical experiment, 45 g of lithium aluminum hydride was added to 700 ml of THF (distilled over $LiAlH_4$) and the mixture was stirred for 3 hr under a dry nitrogen atmosphere. The resulting solution was then filtered under a slight positive nitrogen pressure through a 2-in. bed of tightly packed celite, prepared on a sintered-glass disk previously sealed into a large cylinder for enclosing the solution. The clear filtered solution was stored in a 1-l. flask with a rubber septum syringe inlet. The solution (*ca.* 1.5 *M* in lithium aluminum hydride) was standardized by removing a known aliquot with a hypodermic syringe, injecting it into a glycerol–water mixture, and measuring the hydrogen evolved.

Prepared in this manner and vigorously protected from atmospheric moisture, these solutions of lithium aluminum hydride appeared to be stable indefinitely.

Procedure for Rate and Stoichiometric Studies.—All reduction experiments were carried out under a dry nitrogen atmosphere. Hypodermic syringes were used to transfer solutions.

The reduction of bromobenzene is representative. The 100-ml reaction flask was dried in an oven and cooled down in a dry nitrogen atmosphere. The flask was equipped with a rubber syringe cap and a magnetic stirring bar, and a reflux condenser was connected to an inverted gas buret *via* a Dry Ice vapor trap. The reaction flask was immersed in a water bath at room temperature (*ca.* 25°), and 23.4 ml of tetrahydrofuran was introduced through a syringe into the reaction flask. Next, 6.6 ml (10 mmol) of 1.5 *M* lithium aluminum hydride solution was introduced into the reaction flask by another syringe. Then 10 ml of 1.0 *M* bromobenzene in THF (10 mmol) was introduced. The hydrogen evolved was measured. Simultaneously, a blank was run in which, instead of 10 ml of the aryl bromide solution, there was added 10 ml of tetrahydrofuran, all other conditions being the same.

At the end of 30 min, a 4.0-ml aliquot of the reaction mixture was removed with a hypodermic syringe and injected into a hydrolyzing mixture of 1:1 glycerine–water in tetrahydrofuran. The hydrogen evolved was measured with a gas buret. Immediately, 4.0 ml of the blank was also taken out and hydrolyzed, and the hydrogen evolved was measured. The difference between the blank value and the reaction mixture in millimoles gives the amount of hydride used by 1 mmol of the compound. The hydrogen evolution measurement and the hydrolysis of the reaction mixture were done at 0.5, 1, 3, 6, and 24 hr. The results are summarized in Table I.

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[12] J. Miller, "Aromatic Nucleophilic Substitution," Elsevier Publishing Co., New York, N. Y., 1968.

TABLE II

EFFECT OF TEMPERATURE ON THE RATE OF REDUCTION OF BROMOBENZENE WITH LITHIUM ALUMINUM HYDRIDE IN THF[a]

Reduction at 25°			Reduction at 65°		
Time, hr	Bromobenzene concn, %	Benzene concn, %	Time, hr	Bromobenzene concn, %	Benzene concn, %
1.0	80	20	0.25	64	39
3.0	69	31	0.50	54	50
6.0	48	52	1.0	21	73
12.0	30	70	4.0	5	90
24	5	93	6.0	0	97

[a] 0.25 *M* in bromide and 1.0 *M* in $LiAlH_4$.

TABLE III

PRODUCTS OF REDUCTION OF ARYL HALIDES WITH LITHIUM ALUMINUM HYDRIDE IN THF[a]

Compd	Time, hr	Temp, °C	Concn of $LiAlH_4$, *M*	Ratio $LiAlH_4$/ArX	Reaction products	Yield,[b] %
Bromobenzene	24	25	0.25	1.0	Benzene	20
					Bromobenzene	79
Bromobenzene	24	25	1.0	4.0	Benzene	92
Bromobenzene	6.0	65	1.0	4.0	Benzene	97
Iodobenzene	24.0	25	0.5	2.0	Benzene	83
					Iodobenzene	15
Iodobenzene	24.0	25	0.75	3.0	Benzene	94
1-Bromonaphthalene	6.0	65	1.0	4.0	Naphthalene	99 (79)
4-Bromobiphenyl	12.0	65	1.0	4.0	Biphenyl	94 (88)
m-Chloroiodobenzene	24.0	25	0.375	1.5	Chlorobenzene	95
					Benzene	traces
					m-Chloroiodobenzene	4.0
o-Bromo-*t*-butylbenzene	24.0	25	0.25	1.0	*t*-Butylbenzene	20
					o-Bromo-*t*-butyl benzene	83
p-Bromo-*t*-butylbenzene	24.0	25	0.25	1.0	*t*-Butylbenzene	5.0
					p-Bromo-*t*-butyl benzene	93.5

[a] Concentration of the aryl halide was 0.25 *M* in all cases. [b] All the yields reported were determined by glpc using ethylbenzene as internal standard. The numbers in parentheses indicate the yield isolated.

Product Analysis.—For analyzing the reduction products, separate reactions on a 5-mmol scale were carried out employing conditions identical with those in the previous experiment. The reaction mixture was analyzed both for the hydrocarbon and for the remaining halide by a temperature-programmed Varian Aerograph 1200 using ethylbenzene as the internal standard. The analysis of the reduction product of bromobenzene is representative. The experimental setup and conditions were the same as in the rate studies. Thus, 11.7 ml of tetrahydrofuran, 3.3 ml (5 mmol) of lithium aluminum hydride, and 5 mmol of bromobenzene in 5 ml of THF were introduced into the reaction flask in the order indicated. The reaction flask was immersed in a water bath (*ca.* 25°). The reaction mixture was 0.25 *M* in lithium aluminum hydride and 0.25 *M* in bromobenzene. The mixture was stirred well by a magnetic stirrer. After 24 hr, 5 mmol of ethylbenzene was added to the reaction mixture through a syringe. The flask was cooled in an ice bath and excess hydride was destroyed by adding slowly a 1:1 mixture of tetrahydrofuran and water using a microsyringe. The condenser was washed with ether and the washings were collected in the reaction flask so as to recover any volatile products on the condenser surface. Then the precipitate of aluminum hydroxide was coagulated into a pasty mass by adding 1–2 g of sodium hydroxide pellets, followed by 1 g of anhydrous sodium sulfate. The dry upper ethereal layer was then subjected to glpc analysis. In 24 hr, the presence of 20% of benzene and 79% of unreacted bromobenzene was indicated.

Effect of Temperature. Reduction of Bromobenzene with Lithium Aluminum Hydride at 25 and 65°.—These experiments utilized solutions 1.00 *M* in $LiAlH_4$ and 0.25 *M* in bromobenzene. A dry 100-ml flask fitted with a rubber syringe cap, magnetic stirring bar, nitrogen inlet, and reflux condenser was flushed with nitrogen. The reflux condenser was fitted with a drying tube to protect against moisture. Then 0.7 ml of THF was injected into the reaction flask with a hypodermic syringe, followed by 13.3 ml (20 mmol) of lithium aluminum hydride solution. The flask was heated carefully to reflux temperature. Then 5 mmol of bromobenzene in 5.0 ml of THF was introduced by a syringe, followed by 1.0 ml of 5.0 *M* ethylbenzene (5 mmol) to serve as an internal standard. The mixture was stirred, and, at appropriate intervals of time, 1.0 ml of the reaction mixture was withdrawn from the reaction mixture and transferred into a small vial cooled in ice. The excess of hydride was destroyed by carefully adding a 1:1 mixture of tetrahydrofuran and water through a microsyringe. A pinch of anhydrous sodium sulfate was added, followed by 1.0 ml of ether. The clear ethereal layer was analyzed by gas chromatography for the benzene formed and the unreacted bromobenzene. The glpc analysis showed that at 6 hr, the reduction was essentially complete; no bromobenzene was detected.

A similar study was made at 25°. The results for 25° and 65° are summarized in Table II. Results for other halides are summarized in Table III.

General Procedure for the Reduction of Aryl Bromides.—The following general procedure, illustrated for the reduction of 4-bromobiphenyl, is suggested for the reduction of aryl bromides. (Depending upon the other substituents present, the time required may require an increase or a decrease.)

The experimental set-up is the same as in the previous experiment. A typical reaction set-up was assembled, 40 mmol of lithium aluminum hydride solution in tetrahydrofuran was placed in the reaction flask, and the flask was carefully brought to reflux temperature. Then 10 mmol of 4-bromobiphenyl in 10 ml of tetrahydrofuran was added, with the aid of a hypodermic syringe, to the reaction mixture. The total volume was 40 ml (0.25 *M* in bromide and 1.0 *M* in $LiAlH_4$). The heating was stopped after 12 hr and the reaction flask was cooled in an ice bath. Excess hydride was destroyed by injecting slowly a 1:1 mixture of water and tetrahydrofuran, drop by drop. Then 3.0 ml of a saturated solution of sodium potassium tartrate was added to complex the aluminum salts. (Alternatively, one can add 3.0 g of sodium hydroxide pellets. This will coagulate all the aluminum salt and a clear organic layer is obtained.) The aqueous phase was extracted five times with 20-ml portions of ether. The combined extract was dried over anhydrous sodium sulfate. Evaporation of the solvents gave 1.36 g (88%) of pure biphenyl, mp 68.5–69.5°. The infrared and nmr spectra were identical with an authentic sample.

Similarly, 1-bromonaphthalene was converted into isolated naphthalene, mp 79–80°, in a yield of 79%.

Selective Reduction of *m*-Chloroiodobenzene to Chlorobenzene.—The experimental set-up was the same as in previous experiments. To the reaction flask was added 10.0 ml of tetrahydrofuran, followed by 5.0 ml (7.5 mmol) of lithium aluminum hydride solution in tetrahydrofuran. The flask was immersed in a water bath at 25°, and 5.0 mmol of *m*-chloroiodobenzene (5.0 ml of 1.0 *M* solution in THF) was introduced.

(The reaction mixture is 0.375 *M* in lithium aluminum hydride and 0.25 *M* in compound.) After 24 hr, 5.0 mmol of ethylbenzene was added as internal standard. After the destruction of the residual hydride as usual and work-up, gas chromatographic examination of the ethereal layer indicated a 95% yield of chlorobenzene, traces of benzene, and 4% of unreacted *m*-chloroiodobenzene. No iodobenzene was detected.

Registry No.—Lithium aluminum hydride, 16853-85-3; tetrahydrofuran, 109-99-9.

The Reduction of Organic Halogen Compounds by Sodium Borohydride[1]

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Treatment of organic halogen compounds and related derivatives with sodium borohydride in dimethyl sulfoxide or diglyme results in reduction of the carbon–halogen bond; the reactivity in dimethyl sulfoxide is somewhat greater than that in diglyme. The order of reactivity of simple haloalkanes and related derivatives is consistent with a typical S_N2 displacement by borohydride on carbon, but some more complex derivatives exhibit unusual reactivity. Thus, carbon tetrachloride reacts very rapidly in aqueous diglyme or dimethyl sulfoxide to produce chloroform and dichloromethane, whereas chloroform is unreactive under the same conditions. The behavior of *o*-nitroiodobenzene is similar; reduction to nitrobenzene is rapid and quantitative in aqueous solvents. Substitution of deuterium oxide for the water results in almost quantitative incorporation of deuterium in the *ortho* position. In addition to the synthetic utility with respect to organic substrate, the reaction can be used as a convenient method for preparing solutions of diborane.

The reduction of organic halogen compounds and related derivatives with complex metal hydrides is a fairly well-established reaction.[3-8] The stoichiometry for the two most common cases is shown below.

$$RX + BH_4^- \text{ (or } AlH_4^-\text{)} \longrightarrow RH + X^- + BH_3 \text{ (or } AlH_3\text{)}$$

Lithium aluminum hydride reductions are ordinarily performed in ether or tetrahydrofuran; evidence indicates that the mechanism involves a typical S_N2 displacement on carbon.[4-6] The stability of sodium borohydride in aqueous solvents permits a greater variety of reaction conditions than in the case of lithium aluminum hydride. Thus, it was observed that secondary and tertiary alkyl derivatives could be reduced by sodium borohydride in aqueous diglyme.[7] This reduction of secondary and tertiary derivatives under conditions leading to S_N1 behavior has been studied in some detail; however, the reduction of primary derivatives under the usual S_N2 conditions has received only limited attention.[9-11] We therefore undertook a study of this reaction; in addition to the more common primary and secondary alkyl derivatives, we have investigated in a preliminary manner the borohydride reduction of aromatic halides and polyhaloalkanes.

Results and Discussion

Because of the rate enhancements realized when performing nucleophilic substitution reactions in dimethyl sulfoxide (DMSO),[12] it was of considerable interest to study the behavior of sodium borohydride in this solvent. Sodium borohydride is quite soluble in DMSO, and at room temperature no noticeable reaction between the two is observed. It has been reported that sulfoxides undergo a slow reaction with solutions of diborane;[13] this presented no difficulty in the current investigation, since the fate of the diborane was of no particular interest. Several reductions were also performed in diglyme, and in aqueous solutions of diglyme and DMSO.

Reductions of Simple Monohaloalkanes in DMSO and Diglyme.—In Table I we have summarized the results of the reduction of a number of simple primary and secondary derivatives in DMSO. Excellent yields are realized for primary iodides, bromides, and tosylates, as well as for secondary iodides. Only the more reactive chlorides, such as the benzyl derivatives, can be reduced in good yield under such mild conditions. The relative reactivity, as evidenced by the rate of gas evolution and overall yield of product, is iodide > bromide > tosylate > chloride, and methyl > ethyl > propyl > isopropyl; this is consistent with an S_N2 mechanism. No alkene was found in the analysis of the above reactions. However, this does not rule out a small amount of elimination, followed by rapid hydroboration of the alkene produced.

Table II shows the results of some reductions in anhydrous diglyme. Clearly, the reaction is slower than in DMSO; only the methyl derivatives and primary iodides can be reduced in good yield in a reasonable time at a temperature below 50°.

Reduction of Benzylic Derivatives.—In Table III we have summarized the results of an investigation of the reduction of benzylic halides. In each case, the product is the corresponding toluene derivative; borohydride did not react with any of the *para* substituents under the reaction conditions used. Because of the greater reactivity of the *p*-methoxy and *p*-nitro derivatives, it was felt that the data for 1-hr reaction

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[1] Based in part on the M.S. thesis submitted to Virginia Polytechnic Institute by C. W. V. (1968).

[2] National Science Foundation Undergraduate Research Participant, Summer 1968.

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