of the product was essentially the same as that of the analytical sample prepared by two recrystallizations from 95% ethanol (7.6 ml. per g.). The pure acid was dried at 26° and 0.3 mm. over calcium chloride for 3 hr. It showed an indefinite melting point as low as 146° with loss of water.

Anal. Calcd. for $C_{19}H_{30}BO_2N$: C, 72.38; H, 9.59; N, 4.44. Found: C, 72.52; H, 9.40; N, 4.49.

o-(Dicyclohexylaminomethyl)-benzeneboronic Acid Hydrochloride.—A solution of 60 mg. of pure acid in 30 ml. of dry ether was saturated with dry hydrogen chloride. The white powder was removed by filtration, washed copiously with ether, and dried at 25° and 0.1 mm. pressure over calcium chloride for 66 hr. The yield of amine salt was 60 mg. or 89.5%. The hydrochloride showed an indefinite melting point above 134° with loss of water.

The analytical data indicated that the hydrochloride contained excess hydrogen chloride. The results were consistent for a mixture of 98% hydrochloride and 2% hydrogen chloride (2% excess HCl requires C, 63.7; H, 8.77; and Cl, 11.84).

Anal. Calcd. for $C_{19}H_{31}BClO_2N$: C, 64.88; H, 8.88; Cl, 10.08. Found: C, 63.80; H, 8.81; Cl, 11.98.

1,2,3,6-Tetrahydro-4,5,7,8-dibenzo-2,1,3-boradiazapentalene (IX).—A solution of 6.58 g. of recrystallized *o*-phenylenediamine (61.0 millimoles) in 50 ml. of benzene was warmed and stirred under nitrogen. A solution, prepared by dissolving 3.58 g. of *o*-(bromomethyl)-benzeneboronic anhydride (6.06 millimoles) in 100 ml. of hot benzene and cooling, was added to the flask over a period of 20 minutes at slightly below reflux temperature. A precipitate appeared immediately and increased in amount. The addition funnel was rinsed with 5 ml. of benzene and the liquid was added to the flask. After 50 min. of stirring, the heating mantle was removed from the flask and the flask was cooled in an ice-bath. To the crude mixture, consisting of a brown solution over a yellow precipitate, was added 4.0 g. of sodium hydroxide dissolved in 30 ml. of water.

The alkaline slurry was stirred 3 min. and then rinsed into a separatory funnel with 50 ml. of water. The aqueous layer was withdrawn and the interfacial material was left with the organic layer. The organic layer was extracted twice with solutions consisting of 0.4 g. of sodium hydroxide, 25 ml. of water and a little sodium chloride, and the extracts were combined with the first water phase. The combined water layers were washed twice with 25 ml. of benzene. The caustic layer was allowed to stand about 1 hr. in the cold.

The caustic extract was neutralized in the cold with concentrated hydrochloric acid to a *p*H of 7.1 as measured by a *p*H meter. The brown solids which separated were collected. The apparent *p*H of the yellow filtrate was 6.5, and no more precipitate appeared at lower *p*H.

The aminoboronic acid was air-dried overnight and then extracted into boiling toluene for about 5 hr., or until no more colored material was being extracted. The dark red solution was concentrated under nitrogen and allowed to cool. The orange crystals (m.p. 215–229°) were removed by filtration, rinsed with cold toluene, and dried briefly in vacuum at room temperature. The yield was 512 mg. or 13.7%. The infrared spectrum was not greatly different from that of the pure product.

The crude boradiazapentalene was recrystallized from benzene to yield silvery-white flakes, very prone to acquire a static charge. The melting point was raised to 239–242°, and the recovery was 85%. The recrystallized boradiazapentalene sublimed readily at 150° and 0.4 mm. pressure. The analytical sample so obtained was very light and fluffy, statically charged, and thus hard to handle. The pure 1,2,3,6-tetrahydro-4,5,7,8-dibenzo-2,1,3-boradiazapentalene melts at 245° with dec.

Anal. Calcd. for $C_{18}H_{11}BN_2$: C, 75.77; H, 5.38; B, 5.25. N, 13.60. Found: C, 75.78; H, 5.29; B, 5.24; N, 13.36;

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY]

Hydroboration. IV. A Study of the Relative Reactivities of Representative Functional Groups toward Diborane

BY HERBERT C. BROWN AND W. KORYTNYK[1]

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The relative rates of reduction of a number of representative classes of organic compounds by diborane were established by competition experiments. The results indicate the rates of reaction to decrease in the order: carboxylic acids > olefins > ketones > nitriles > epoxides > esters. Of interest in synthetic chemistry is the marked ease of reduction of the carboxylic acid group, which permits its selective reduction in the presence of the ketone group, and the inertness of the epoxide ring, which permits the complete reduction of a ketone group, or the hydroboration of the carbon–carbon double bond, without significant attack on the epoxide grouping.

Diborane is a powerful reducing agent, capable of reducing many functional groups under exceedingly mild conditions.[2,3] Study of the reaction of typical organic molecules with an excess of diborane gave a rough indication of the relative ease of reduction by this reagent of representative functional groups.[3]

It was observed that aldehydes, ketones, epoxides, nitriles, lactones and azo compounds are reduced rapidly by the reagent, whereas esters react slowly, and acid chlorides and nitro compounds are relatively inert toward the reagent under the experimental conditions. Although the data permitted a rough estimate of the relative reactivities of these groups, it appeared desirable to obtain more quantitative data. It appeared that such data could be obtained by running competitive reductions in which the two components competed for a limited quantity of diborane. Accordingly, we undertook an investigation of such competitive reductions, utilizing vapor phase chromatography (V.P.C.) for analysis of the reaction mixtures.

Results

After preliminary exploration of various procedures, it was decided to examine the reductions in tetrahydrofuran as solvent, utilizing diborane generated externally. The high solubility of diborane in this solvent offered obvious advantages for quantitative work.

In these experiments the reactants were to compete for a limited amount of diborane. Consequently, it appeared desirable to establish the pre-

(1) American Cyanamid Co. Post-doctorate Fellow at Purdue University, 1958–1959.

(2) H. C. Brown, H. I. Schlesinger and A. B. Burg, THIS JOURNAL, **61**, 673 (1939).

(3) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1135 (1957); H. C. Brown and B. C. Subba Rao, THIS JOURNAL, **82**, 681 (1960).

cise stoichiometry of the reaction of diborane with several representative groups of interest to this study.

Stoichiometry.—Diborane, 2.9 mmoles, generated from sodium borohydride and boron trifluoride etherate, was passed into a solution of 25.0 mmoles of cyclohexanone in tetrahydrofuran over a period of one hour. An aliquot removed showed a hydride/boron ratio of 0.72; after a second hour at room temperature, the ratio was 0.49. At −78°, an identical experiment yielded the ratio 1.04 after the addition of diborane and a ratio of 1.12 after one additional hour.

It therefore appears that this ketone reacts rapidly in the ratio 2-cyclohexanone/BH_3, with further reaction being negligible at −78°, and proceeding slowly at room temperature (1).

$$2R_2CO + BH_3 \longrightarrow (R_2CHO)_2BH \quad (1)$$

In the same manner it was established that at room temperature, in the presence of excess benzonitrile, 1.2 mmoles of hydride per borane group remain, and this decreases to 0.7 in 18 hours. Consequently, the reaction must proceed as indicated by equation 2.

$$RCN + BH_3 \longrightarrow [RCH_2NBH] \quad (2)$$

Hydrolysis of the initial reaction product produces only benzylamine, with no aldehyde detectable. It is probable that the reaction product above is the N,N′,N″-tribenzylborazene, although we did not attempt to isolate it.

Treatment of 6 moles of carboxylic acid with one mole of diborane results in the liberation of six moles of hydrogen and no reduction of the acid. Treatment of six moles of acid with two moles of diborane results in the complete utilization of the "hydride," with the formation of three moles of acid and three moles of alcohol. Finally, utilization of three moles of diborane results in the complete utilization of the "hydride" introduced and the formation of six moles of alcohol.

Consequently, in this reaction the first step is the formation of the triacylborane (3), with the reaction proceeding further in the ratio 1RCO_2H/BH_3 (4).

$$3RCO_2H + BH_3 \longrightarrow (RCO_2)_3B + 3H_2 \quad (3)$$

$$RCO_2H + BH_3 \longrightarrow [RCH_2OBO] + H_2 \quad (4)$$

The latter product is presumably the boroxene, although here also we have been content with hydrolyzing it and identifying the alcohol produced in the reaction.

Competition Experiments.—In the competition experiments, equimolar amounts of the two compounds (8 to 15 mmoles of each) were dissolved in 10 to 15 ml. of tetrahydrofuran and sufficient diborane was introduced over a period of one hour at room temperature to achieve approximately 50% reduction. Water was added to hydrolyze the reaction products, the organic layer separated, and the aqueous layer extracted with ether. The ether layer was dried, the ether removed at room temperature, and the products analyzed by V.P.C.

In the cases where an olefin was involved, the organoborane was converted by oxidation with alkaline hydrogen peroxide into the corresponding alcohol prior to analysis.

In a number of cases it was not practical to determine all four components of the reaction mixture. In these experiments the fourth component was estimated by difference.

The competitive reduction of a mixture of *p*-chloroacetophenone and caproic acid resulted in the preferential reduction of caproic acid. On the other hand, in a mixture of *p*-chloroacetophenone and ethyl benzoate the ketone is reduced to the practical exclusion of the ester. Similarly, in a mixture of *p*-chloroacetophenone and benzonitrile, the ketone is preferentially reduced. Finally, cyclopentanone is reduced in preference to the epoxide, cyclohexene oxide.

The ease of reduction of carboxylic acids by this reagent is remarkable. As was pointed out, caproic acid is reduced in preference to *p*-chloroacetophenone. The acid is also reduced completely in the presence of an ester, ethyl benzoate, a nitrile, benzonitrile, and an oxide, cyclohexene oxide.

The nitrile group is also readily reduced by diborane, although less readily than the ketone or carboxylic acid groupings. Thus benzonitrile is selectively reduced by the reagent in the presence of the ester, ethyl benzoate.

The epoxide grouping is relatively inert toward the reagent, as indicated by the selective reduction of cyclopentanone, and of caproic acid, in the presence of cyclohexene oxide. Only the ester grouping proved less reactive, with the oxide being reduced preferentially in the presence of ethyl benzoate.

The reaction of diborane with olefins is very fast.[4] Accordingly, it was of interest to explore the competitive reaction of diborane with a typical olefin, such as cyclohexene, in the presence of molecules containing representative functional groups.

In the presence of ethyl benzoate, cyclohexene reacted to the total exclusion of the ester. Similarly, cyclopentene reacted without any observable reduction of cyclohexene oxide. In a competition between cyclohexene and benzonitrile, the olefin reacted preferentially, but the reaction was accompanied by a significant reduction of the nitrile. Even in the case of a competition between a ketone (cyclopentanone) and the olefin (cyclohexene), the olefin reacts preferentially. Only in the case of caproic acid does the rate of reaction of the diborane with the functional group approach its rate of addition to the double bond.

The experimental data are summarized in Table I.

Discussion

The reactivity of any functional group can be modified greatly by the organic structure to which it is attached. For example, aldehyde groups are generally quite reactive toward diborane, considerably more so than ketone groups.[5] However, the presence of the three chlorine substituents in chloral renders the aldehyde group exceedingly inert toward diborane.[2] Similarly, we have observed that the reactivity of various olefin double

(4) H. C. Brown and B. C. Subba Rao, *J. Org. Chem.*, **22**, 1136 (1957); H. C. Brown and B. C. Subba Rao, THIS JOURNAL, **81**, 6428 (1959).

(5) Unpublished studies of Dr. W. Korytnyk.

TABLE I

COMPETITIVE EXPERIMENTS FOR THE REACTION OF DIBORANE WITH REPRESENTATIVE COMPOUNDS IN TETRAHYDROFURAN SOLUTION AT 25°

Expt.	Compounds used	Mmoles	Diborane, mmoles	Reaction products	Mole %
1	*p*-Chloroacetophenone	15.0		*p*-Chloroacetophenone	43
			7.8	1-*p*-Chlorophenylethanol	7
	Caproic acid	15.0		Caproic acid	10
				1-Hexanol	40
2	*p*-Chloroacetophenone	12.1		*p*-Chloroacetophenone	0
			3.6	1-*p*-Chlorophenylethanol	50
	Ethyl benzoate	12.1		Ethyl benzoate	48
				Benzyl alcohol	2
3	*p*-Chloroacetophenone	8.3		*p*-Chloroacetophenone	0
			2.2	1-*p*-Chlorophenylethanol	50
	Benzonitrile	8.3		Benzonitrile	47
				Benzylamine	3[b]
4	Cyclopentanone	8.8		Cyclopentanone	26
			1.1	Cyclopentanol	24
	Cyclohexene oxide	8.8		Cyclohexene oxide	50
				Cyclohexanol	0
5	Caproic acid	10.0		Caproic acid	0
			6.0	1-Hexanol	50
	Ethyl benzoate	10.0		Ethyl benzoate	50
				Benzyl alcohol	0
6	Caproic acid	8.9		Caproic acid	20
			4.4	1-Hexanol	30
	Benzonitrile	8.8		Benzonitrile	50
				Benzylamine	0[b]
7	Caproic acid	10.0		Caproic acid	
			5.0	1-Hexanol	Present[c]
	Cyclohexene oxide	10.0		Cyclohexene oxide	
				Cyclohexanol	0
8	Benzonitrile	9.9		Benzonitrile	5
			6.0	Benzylamine	45[b]
	Ethyl benzoate	10.0		Ethyl benzoate	50
				Benzyl alcohol	0
9	Benzonitrile	11.2		Benzonitrile	25
			3.8	Benzylamine	25[b]
	Cyclohexene oxide	10.0		Cyclohexene oxide	40
				Cyclohexanol	10
10	Cyclohexene oxide	10.0		Cyclohexene oxide	16
			4.2	Cyclohexanol	34
	Ethyl benzoate	10.0		Ethyl benzoate	48
				Benzyl alcohol	2
11	Cyclohexene	10.1		Cyclohexene	5[a]
			4.4	Cyclohexanol[d]	45
	Cyclopentanone	10.1		Cyclopentanone	20
				Cyclopentanol	30
12	Cyclohexene	9.9		Cyclohexene	[a]
			5.0	Cyclohexanol[d]	57
	Caproic acid	10.0		Caproic acid	[b]
				1-Hexanol	43
13	Cyclohexene	10.1		Cyclohexene	7[a]
			1.8	Cyclohexanol[d]	43
	Ethyl benzoate	10.0		Ethyl benzoate	50
				Benzyl alcohol	0
14	Cyclohexene	10.1		Cyclohexene	22[a]
			1.7	Cyclohexanol[d]	28
	Benzonitrile	10.0		Benzonitrile	39
				Benzylamine	11[b]
15	Cyclopentene	10.0		Cyclopentene	15[a]
			1.7	Cyclopentanol[d]	35
	Cyclohexene oxide	10.0		Cyclohexene oxide	50
				Cyclohexanol	0

[a] Could not be determined directly because of short retention time; estimated by difference. [b] Could not be determined directly because of high retention time; estimated by difference. [c] See discussion in Experimental part. [d] After oxidation of the reaction product with alkaline hydrogen peroxide.

bonds may be greatly influenced by the parent structure.[6]

It is therefore important to recognize that the relative reactivities established by the present study must be considered approximate values for simple, representative groups, with the understanding that these relative reactivities may be greatly altered and even inverted by major modifications in the molecular structure.

With this caution in mind, it is appropriate to examine the summary of the experimental results in Table II.

The results clearly indicate that the reactivity of these groups toward diborane decreases in the order: carboxylic acids > olefins > ketones > nitriles > epoxides > esters > acid chlorides.[3] This is quite different from the order of reactivity exhibited by these groups toward sodium or lithium borohydride. This difference in behavior has been attributed to the fact that diborane is a Lewis acid, whereas sodium borohydride is a base.[3]

In view of the differences in their mode of attack on functional groups, it is not unexpected that these two different reagents should exhibit such markedly different orders of reactivity. The synthetic chemist can make valuable application of these differences in reactivities to achieve the reduction of a particular group in the presence of another, or to reverse the process almost at will.

Finally, the great ease of reduction of the carboxylic acid group by diborane, which permits its selective reduction in the presence of the ketone, ester, nitrile or epoxide groupings, should be of considerable value in synthetic work. Moreover, the relative inertness of the epoxide ring, which permits the complete reduction of the ketone group by diborane, or the hydroboration of the carbon–carbon double bond, without significant attack on the epoxide grouping, should greatly facilitate synthetic work in these derivatives.

Experimental Part

Materials.—The tetrahydrofuran was purified by keeping over potassium hydroxide pellets for several days, followed by a distillation over a small quantity of lithium aluminum hydride. The solvent was stored over calcium hydride.

The various organic compounds were all commercially available products whose purities were checked by V.P.C. to be 98% or better. Sodium borohydride (98%) from Metal Hydrides Inc., and freshly distilled boron trifluoride etherate from Distillation Products were utilized for the generation of diborane.

Competition Experiments.—The procedure was similar to that previously utilized to study the reaction of diborane with olefins, with some minor modifications. A glass stopcock was placed between the generator and the reaction vessel. The top part of the reaction vessel was enlarged to hold 30–40 ml. of liquid, and was provided with an oblique side-arm fitted with a rubber serum bottle cap to facilitate sampling with a hypodermic syringe. The outgoing gases were passed through a capillary tube dipping into mercury. Above the mercury was placed 5 cc. of acetone to absorb any diborane which escaped from the reaction vessel.

All apparatus and equipment (including the hypodermic syringes) were dried in an oven and fully protected from moisture prior to use. Measured quantities of the two components were placed in tetrahydrofuran solution in the reaction flask, the system flushed with nitrogen, and a deficiency of diborane, generated by adding sodium borohydride in

(6) Unpublished studies of Dr. A. Moerikofer.

TABLE II

RELATIVE RATES OF REACTION OF REPRESENTATIVE GROUPS WITH DIBORANE

	Ketone	Carboxylic acid	Ester	Nitrile	Epoxide	Olefin
Ketone[a]	.....	Slower (1)	Faster (2)	Faster (3)	Faster (4)	Slower (11)
Carboxylic acid	Faster (1)	.....	Faster (5)	Faster (6)	Faster (7)	Similar (12)
Ester	Slower (2)	Slower (5)	.....	Slower (8)	Slower (10)	Slower (13)
Nitrile	Slower (3)	Slower (6)	Faster (8)	.....	Faster (9)	Slower (14)
Epoxide	Slower (4)	Slower (7)	Faster (10)	Slower (9)	.....	Slower (15)
Olefin	Faster (11)	Similar (12)	Faster (13)	Faster (14)	Faster (15)	.....

[a] The compound in the vertical column reacts (faster, slower, or at a rate similar to) to compound indicated in the horizontal list. The number in parentheses refers to the relevant experiment in Table I.

diglyme to a solution of boron trifluoride etherate in diglyme, was added to the reaction mixture over a period of one hour.

Water was added to hydrolyze the reaction mixture, and the aqueous layer extracted several times with ether. The extract was dried, the ether removed at room temperature and the product analyzed by V.P.C. In cases where an olefin was one of the reactants, the hydrolyzed reaction mixture was treated with alkaline hydrogen peroxide in the usual manner, with subsequent ether extraction.

An Aerograph gas chromatograph (Wilkens Instrument and Research, Inc.) was used for the analyses. In each case, the retention time for each component of the reaction mixture was determined and columns and conditions utilized which would give adequate separation of each component.

For example, in the competitive reduction of caproic acid and *p*-chloroacetophenone, it was observed that on a 5-ft. silicone column, 50 p.s.i. of helium, 128°, the retention times and yields were: caproic acid, 2.5 min., 3.0 mmoles; 1-hexanol, 1.0 min., 12.0 mmoles; *p*-chloroacetophenone, 5.5 min., 12.9 mmoles; 1-*p*-chlorophenylethanol, 8.0 min., 2.1 mmoles.

The analytical procedures were tested with a number of representative synthetic mixtures. Each component in these mixtures was reproduced to within ±2%.

In the case of competitive experiment 7, between caproic acid and cyclohexene oxide, we encountered difficulties with the analysis. 1-Hexanol was present, but not in sufficient amount to account for all of the caproic acid. No cyclohexanol was present, indicating that cyclohexene oxide was not reduced. However, we did not observe the cyclohexene oxide peak. Instead, there was observed a prominent peak with a much longer retention time. Caproic acid itself does not react with cyclohexene oxide under the conditions of the experiment. Consequently, it appears that some intermediate formed in the reduction of the acid must react rapidly with the epoxide to give a condensation product with the longer retention time. This product was not examined further.

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LAFAYETTE, IND.

[CONTRIBUTION FROM THE ROHM & HAAS CO., REDSTONE ARSENAL RESEARCH DIVISION]

The Reactions of Certain Oxidized Nitrogen Compounds with Perchloryl Fluoride[1]

BY JEREMIAH P. FREEMAN

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The reactions of some oximes, hydroxamic acids and nitro compounds, in the form of their anions, with perchloryl fluoride have been examined. Simple ketoximes were converted to ketones, but negatively-substituted oximes were converted either to α-fluoronitro compounds or cleaved in the manner of the second-order Beckmann reaction. No ordinary Beckmann reaction was observed. Benzhydroxamic acid was similarly cleaved. The nitro compounds examined were cleanly converted to the corresponding α-fluoro derivatives. Some comments on the mechanism of these reactions are included.

The unique fluorinating power of perchloryl fluoride as evidenced by its action on active methylene anions[2] suggested its use for preparing fluoro derivatives of some oxidized nitrogen compounds.

Oximes.—Since it was anticipated that Beckmann rearrangements might constitute a major side reaction of oximes with perchloryl fluoride, the first oxime studied was dimethyl oximinomalonate (I), an oxime which possesses poor migrating groups. Treatment of the potassium derivative of I with perchloryl fluoride at 0–10° in dimethylformamide solution produced dimethyl fluoronitromalonate (II) in 40–70% yield. Potassium chlorate and chloride precipitated as the reaction proceeded. Some chloronitro ester was also produced. This side reaction was hardly observed in small

$$\underset{\text{I}}{HON{=}C(CO_2CH_3)_2} + FClO_3 \longrightarrow \underset{\text{II}}{\begin{matrix} O_2N \\ F \end{matrix}\!\!>\!C(CO_2CH_3)_2}$$

scale preparations, but became highly competitive as scale-up proceeded; in the larger reactions the concentration of chloride ions produced by the oxidation step builds up, and that ion is able to compete with perchloryl fluoride. In this important regard this reaction differs from the active methylene fluorinations where foreign anions are not competitive.[2] This oxidative halogenation bears some similarity to that involved in the conversion of oximes to *gem*-bromonitro compounds, although in that case two separable steps are involved.[3]

Other negatively-substituted oximes also were examined. No pure compound could be isolated from the reactions with sodio ethyl oximinoaceto-

(1) This research was carried out under Army Ordnance Research Contract No. DA-01-021-ORD-5135. It was presented in part at the 135th Meeting of the American Chemical Society, Boston, Mass., April, 1959.

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