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Hydroboration. XV. The Influence of Structure on the Relative Rates of Hydroboration of Representative Unsaturated Hydrocarbons with Diborane and with Bis-(3-methyl-2-butyl)-borane

BY HERBERT C. BROWN AND A. W. MOERIKOFER^{1,2}

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Some nineteen representative olefins were hydroborated competitively with diborane (in diglyme) at 0° in order to establish the influence of structure on relative reactivity. The main conclusion indicated by the results is that this reaction is relatively insensitive to the structure of the olefin—only a factor of 20 to 30 separates the most reactive of the olefins, 2-methyl-1-butene, from the least reactive, 2,4,4-trimethyl-2-pentene and 2,3-dimethyl-2-butene. Hydroboration with bis-(3-methyl-2-butyl)-borane is far more sensitive to the structure of the unsaturated reactant. In this case a factor of 10,000 separates 1-octene, the most reactive of the olefins examined, from cyclohexene, one of the least reactive. The factor would be very much larger had it been possible to extend the study to the highly inert structures, 2,4,4-trimethyl-2-pentene and 2,3-dimethyl-2-butene. Acetylenes, such as 1-hexyne and 3-hexyne, are more reactive than the most reactive of the olefins studied. Consequently, hydroboration can be achieved either with a relatively non-selective reagent, diborane, or with the highly selective reagent, bis-(3-methyl-2-butyl)-borane.

The hydroboration of olefins³ and acetylenes⁴ provides a convenient route to the organoboranes and to the various derivatives into which the organoboranes may be transformed.⁵ It is of obvious interest to possess an understanding of the influence of olefin structure on the relative rate of hydroboration.

The reaction of diborane in ether solvents is too fast to measure by the usual methods. Accordingly, we had recourse to a competition method, in which the reactivity of the olefin under study was compared with a standard olefin, either 1-hexene or cyclopentene.

Previous studies had shown that bis-(3-methyl-2-butyl)-borane, or disiamylborane,⁶ is a highly selective hydroborating agent.⁷ In the case of a number of less reactive olefins it proved possible to establish the kinetics of the reaction of these olefins with disiamylborane in tetrahydrofuran solution and to determine the rate constants for the reactions.⁸ In the present study the relative reactivities of more reactive structures were established by a competitive method.

Consequently, the present study makes available data on the relative reactivities of a wide range of unsaturated hydrocarbons toward a relatively non-selective hydroborating agent, diborane, and toward a highly selective reagent, disiamylborane.

Results and Discussion

Relative Reactivities with Diborane.—In the experiments two olefins were selected as standards—1-hexene, with an assigned reactivity of 100, and cyclopentene, with a reactivity of 72 (determined by comparison with 1-hexene). The procedure involved the placing of an equimolar mixture of the olefin under study and one of the standard olefins in a diglyme solution of sodium borohydride, using sufficient borohydride to achieve the hydroboration of one-half of the

total olefin present. Hydroboration was achieved by adding the calculated quantity of boron trifluoride in diglyme to the reaction mixture maintained at 0°. The residual olefin was then analyzed by gas chromatography. An internal standard was utilized to achieve higher precision.

TABLE I
COMPETITIVE HYDROBORATIONS OF SELECTED PAIRS OF OLEFINS
TO TEST EXPERIMENTAL PROCEDURE

Olefin pairs	Relative reactivity			
Cyclopentene	69	71	77	72
1-Hexene	100	100	100	100
Cyclohexene	29	30	31	30
1-Hexene	100	100	100	100
Cyclohexene	13	14	13	14
Cyclopentene	72	72	72	72

The reliability of the measurements was tested by running competitive hydroborations of the pairs 1-hexene and cyclopentene, 1-hexene and cyclohexene, cyclopentene and cyclohexene on four separate occasions. The results, summarized in Table I, reveal a satisfactory precision.

An attempt was made to explore the effect of temperature on the relative rate of hydroboration. However, the competitive hydroboration of a mixture of cyclopentene and cyclohexene at 0, 25 and 50° revealed no significant difference in the observed relative rates. Consequently, we were content to restrict ourselves to a competitive study at one temperature, 0°.

Although the experimental precision proved satisfactory, there is an obvious theoretical difficulty. The reaction of diborane with an olefin obviously involves a number of successive stages, $H_2BH_2BH_2$, $RHBH_2BH_2$, $RHBH_2BHR$, $R_2BH_2BH_2$, R_2BH_2BHR , $R_2BH_2BR_2$, each with its own rate constant. In a competitive reaction involving two different olefins, the number of possible intermediates involved increases markedly. Consequently, we could not hope to obtain precise values of relative rates independent of the reference olefin. We hoped merely to obtain empirical values which would reflect major structural effects and find utility in synthetic work. The results are summarized in Table II.

Although there are some discrepancies, presumably a consequence of the complex nature of the reactions involved, the results reveal reasonable agreement in the relative reactivities established by the use of either 1-hexene, or of cyclopentene, as the reference olefin.

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(2) Post-doctorate research assistant, 1960–1961, on a Research Award (585-C) provided by the Petroleum Research Fund of the American Chemical Society.

(3) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **78**, 5694 (1956); **81**, 6423, 6428 (1959).

(4) H. C. Brown and G. Zweifel, *ibid.*, **81**, 1512 (1959); **83**, 3834 (1961).

(5) For a recent summary, see H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

(6) This reagent is proving highly useful as a selective hydroborating and reducing agent. Consequently, it appears desirable to have a convenient term for common usage, and the common name, disiamylborane, has been proposed. ("Siamyl" is derived from the fact that the 3-methyl-2-butyl- grouping is the only possible *sec*-isoamyl structure.)

(7) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 3222, 3223 (1960); **83**, 1241 (1961).

(8) H. C. Brown and A. W. Moerikofer, *ibid.*, **83**, 3417 (1961).

TABLE II

RELATIVE REACTIVITY OF OLEFINS IN HYDROBORATION BY SODIUM BOROHYDRIDE-BORON TRIFLUORIDE IN DIGLYME AT 0°

Compound	Relative reactivity	
	1-Hexene	Cyclopentene
1-Pentene	98	99
1-Hexene	(100) ^a	100
1-Octene	102	98
3-Methyl-1-butene	75	91
3,3-Dimethyl-1-butene	28	54
2-Methyl-1-butene	121	121
2-Methyl-1-pentene	102	102
2,4,4-Trimethyl-1-pentene	44	41
Styrene	19	41
2-Pentene	34	37
Cyclopentene	72	(72) ^a
Cyclohexene	30	13
2-Methyl-2-butene	50	23
<i>trans</i> -4,4-Dimethyl-2-pentene	27	
2,4,4-Trimethyl-2-pentene		4
1-Methylcyclopentene	52	40
1-Methylcyclohexene		15
1,2-Dimethylcyclopentene		15
2,3-Dimethyl-2-butene		7

^a Assumed values.

Straight-chain olefins, such as 1-pentene, 1-hexene and 1-octene, exhibit essentially identical reactivities. Branching of the alkyl group attached to the double bond, as in 3-methyl-1-butene and 3,3-dimethyl-1-butene, result in a modest decrease in reactivity. Somewhat surprisingly, a methyl substituent on the double bond, as in 2-methyl-1-butene and 2-methyl-1-pentene, does not diminish the reactivity, but appears to bring about a slight increase. The effect of branching of the alkyl group in decreasing the rate is likewise evident in 2,4,4-trimethyl-1-pentene.

Conjugation of the phenyl group with the double bond, as in styrene, produces a decrease in rate.

Internal double bonds, as in 2-pentene, cyclopentene and cyclohexene, result in modest decreases in rate. The accumulation of additional alkyl groups on the double bond, as in 2-methyl-2-butene, 1-methylcyclopentene and 1-methylcyclohexene, has very little additional effect on the reactivity. Even the presence of two alkyl substituents, as in 1,2-dimethylcyclopentene and 2,3-dimethyl-2-butene, results in only modest decreases in reactivity.

As a matter of fact, the main result of this study is the conclusion that the hydroboration reaction with diborane is remarkably insensitive to major changes in the structure of the olefin. This is in accord with the accumulated evidence as to the wide generality of the hydroboration reaction⁵—up to the present time only two olefins, 3,20-bis-cycloethylenedioxy-5 β -pregn-9(11)-ene⁹ and test-9(11)-ene,¹⁰ have been reported to fail to undergo hydroboration under the usual mild conditions.

Relative Reactivities with Disiamylborane.—The reaction of disiamylborane (dimer) with olefins is second order, first order in the dimer and first order in the olefin.⁸ In the case of less reactive olefins, such as cyclopentene and cyclohexene, the reactivities can be established by a direct determination of the second-order rate constants. In this way, the rate constants for cyclopentene, $k_2 = 14 \times 10^{-4}$ l. mole⁻¹ sec.⁻¹, and cyclohexene, $k_2 = 0.13 \times 10^{-4}$ l. mole⁻¹ sec.⁻¹, establish cyclopentene to be more reactive than cyclohexene by a factor of 100. The much greater selectivity of disiamylborane is indicated by the fact that the relative reactivity of these two olefins toward diborane is much

smaller, involving a factor of approximately 3 (Table II).

Disiamylborane has only a single active hydroborating center. Consequently, the complexities involved in competitive reactions with the multifunctional diborane reagent are absent. The relative reactivities were therefore determined by adding one mole of disiamylborane to a mixture containing one mole each of two olefins of closely related reactivities. The residual olefins were determined by gas chromatography.

The entire series of relative reactivities was then translated into rate constants by utilizing the previously measured value for cycloheptene.

The results are summarized in Table III.

TABLE III

SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF REPRESENTATIVE OLEFINS, ACETYLENES AND DIENES WITH DISIAMYLBORANE (DIMER) IN TETRAHYDROFURAN AT 0°

Compound	Relative reactivity	Second-order rate constant, k_2 , 10^{-4} l. mole ⁻¹ sec. ⁻¹
1-Pentene	105	1070
1-Hexene	100	1020
1-Octene	108	1100
3-Methyl-1-butene	57	580
3,3-Dimethyl-1-butene	4.7	48
2-Methyl-1-pentene	4.9	50
2,4,4-Trimethyl-1-pentene	0.8	7.8
α -Methylstyrene	2.3	23
<i>cis</i> -2-Butene	2.3	23 ^a
<i>trans</i> -2-Butene	0.4	3.9 ^a
<i>cis</i> -2-Pentene	2	21 ^a
<i>trans</i> -2-Pentene	0.3	3.0 ^a
<i>cis</i> -3-Hexene	2	21 ^a
<i>trans</i> -3-Hexene	0.2	2.2 ^a
<i>cis</i> -4-Methyl-2-pentene	.5	4.8 ^a
<i>trans</i> -4-Methyl-2-pentene	.1	1.2 ^a
<i>cis</i> -4,4-Dimethyl-2-pentene	.08	0.78 ^a
<i>trans</i> -4,4-Dimethyl-2-pentene	.01	0.10 ^a
<i>cis</i> -2,4-Dimethyl-2-pentene	.1	1.1 ^a
<i>trans</i> -2,4-Dimethyl-2-pentene	.04	0.42 ^a
Cyclopentene	1.4	14 ^a
Cyclohexene	0.01	0.13 ^a
Cycloheptene	26	266 ^a
Cyclooctene	57	580
1,5-Hexadiene	176	1800
1-Hexyne	373	3800
3-Hexyne	225	2300

^a Rate constants by direct kinetic measurement (ref. 8).

The data reveal that the straight-chain 1-alkenes are indeed highly reactive toward disiamylborane. Thus, they react some 50 times faster than the corresponding *cis*-2-alkene and 300 times faster than the corresponding *trans* isomer. There appears to be no significant change in reactivity with increase in chain length.

A single branch in the alkyl group attached to the double bond, as in 3-methyl-1-butene, decreases the rate by a modest factor of 2. However, a double branch, as in 3,3-dimethyl-1-butene, brings about a further decrease by a factor of 10. It is evident that one could achieve the selective hydroboration of a straight-chain olefin, such as 1-hexene, in the presence of the branched-chain olefin, such as 3,3-dimethyl-1-butene.

In contrast to the results with diborane, the presence of a methyl substituent in the 2-position, as in 2-methyl-1-pentene, brings about a 20-fold decrease in rate over the parent olefin. Moreover, the results support the feasibility of the selective hydroboration of 4-methyl-1-pentene in the presence of 2-methyl-1-pentene.⁷ This observation is of special importance in view of the fact

(9) W. J. Wechter, *Chem. Ind.* (London), 294 (1959).(10) M. Nussim and F. Sondheimer, *ibid.*, 400 (1960).

that such isomeric mixtures are readily synthesized through the isomerization-displacement reactions of organoboranes.¹¹

Branching of the alkyl group, as in 2,4,4-trimethyl-1-pentene, reduces the rate considerably beyond that exhibited by 2-methyl-1-pentene.

Conjugation of the phenyl ring with the double bond appears to have little effect—the reactivity of α -methylstyrene is only moderately smaller (23/50) than that of 2-methyl-1-pentene.

The major differences in reactivity of *cis-trans* olefin pairs and of cyclopentene, cyclohexene and cycloheptene have been discussed previously.⁸ However, it is of interest to note that cyclooctene exhibits a reactivity more than twice that of the highly reactive cycloheptene molecule.

The reactivity of 1,5-hexadiene is normal, revealing only a statistical factor of approximately two, as compared to 1-hexene, presumably arising from the presence of two double bonds per molecule. Evidently, there is no important interaction of these isolated double bonds.

Finally, the high reactivity of the acetylenes is of considerable interest and importance. This observation suggests that it should be possible to achieve the selective hydroboration of an acetylenic structure in the presence of nearly any double bond, other than a simple, unhindered terminal double bond.

Conclusions.—It is evident from this study that diborane is a highly active hydroborating reagent which exhibits remarkably little discrimination between different olefin structures. Consequently, it is best utilized for hydroboration of molecules containing only a single center of unsaturation, except in cases where complete reaction of all unsaturated centers is desired.

On the other hand, disiamylborane is a highly selective hydroborating agent. It can be usefully employed to achieve hydroboration of a more reactive olefin in a mixture or of a more reactive center of unsaturation in a polyfunctional system.

Study of the reaction of highly hindered olefins with diborane has revealed that a number of monoalkyl- and dialkylboranes can be readily synthesized.^{12,13} This makes available a number of additional reagents whose utility for selective hydroborations are being currently explored.¹⁴

Experimental

Materials.—The olefins were predominantly Phillips Petroleum Company products, certified to be at least 99% pure. In a few cases olefins of certified purity from American Petroleum Institute Project No. 45 at Ohio State University were utilized.

The solvents and hydroboration reagents utilized were purified as described in earlier publications.

Competitive Hydroboration with Sodium Borohydride-Boron Trifluoride in Diglyme.—The following experiment with 1-hexene and cyclohexene is representative. A carefully dried 100-ml. three-necked flask was assembled with a condenser, thermometer, pressure-equilibrated funnel, a magnetic Teflon-covered stirring bar, and an injection port fitted with a rubber serum cap to allow introduction and removal of samples with a syringe. In cases where the olefins used were quite volatile (b.p. $\sim 60^\circ$), a Dry Ice cooled condenser was used to minimize losses. The flask was flushed with nitrogen. Then 15 ml. of a standard solution (0.833 *M*, 12.5 mmoles) of sodium borohydride in diglyme was injected, followed by 10 ml. each of standard solutions of 1-hexene and cyclohexene (5.0 *M*, 50 mmoles) and of cyclohexane (2.5 *M*, 25 mmoles), the latter to serve as an internal standard. The reaction flask was cooled to 0° with an ice-water-bath and then maintained at that temperature throughout the reaction. A minute aliquot of the reaction mixture was removed and analyzed by gas chromatography. Hydroboration was achieved by adding through the dropping funnel over a period of 30 min-

utes 10 ml. of a 1.67 *M* solution of boron trifluoride in diglyme.¹⁵

The reaction mixture was permitted to stand for 1 hour. Then a small sample of the reaction mixture was removed with a syringe and analyzed by gas chromatography, utilizing an adiponitrile column of 1 to 4 meters in length, depending on the separation to be achieved, and temperatures of 25 to 50° . The injection block temperature on the instrument (Perkin-Elmer 154 C Fractometer) was maintained at $100-150^\circ$ in order to avoid any thermal decomposition of the organoborane.

Any hydrogen evolved during the reaction was measured. After the reaction, the reaction mixture was treated with 2.0 ml. of 2 *M* hydrochloric acid and any hydrogen evolved was measured. In this way a complete material balance could be maintained of both the olefin and hydroborating agent utilized.

The ratios of the corresponding peaks, determined before and after hydroboration, allow the direct estimation of the amount of residual olefin. The relative reactivity was calculated from the expression of Ingold and Shaw¹⁶

$$\text{relative rate} = \frac{\log y_0 - \log y}{\log x_0 - \log x}$$

where x_0 , y_0 are the amounts of olefins in mmoles before hydroboration, and x and y are the amounts after.

For example, in the above experiment involving 1-hexene and cyclohexene, the reaction mixture contained initially 50 mmoles each of the two olefins. A total of 0.6 mmole of hydrogen was evolved during hydroboration. There was found in the reaction product 16.5 mmoles of 1-hexene and 35.7 mmoles of cyclohexene. This indicates that 33.5 mmoles of 1-hexene and 14.3 mmoles of 1-hexene had reacted, a total of 47.8 mmoles instead of the 49.4 (50.0 - 0.6) mmoles anticipated from the borohydride utilized. Introduction of these quantities into the above equation gives a relative reactivity of cyclohexene to 1-hexene of 30/100.

The reproducibility realized is indicated in Table I.

Competitive Hydroboration with Disiamylborane in Tetrahydrofuran.—A standard solution of disiamylborane in tetrahydrofuran was prepared in the following manner. In a 500-ml. three-necked flask was placed 670 mmoles of 2-methyl-2-butene (47.0 g., 3% excess) and 28.6 ml. of tetrahydrofuran. The flask was cooled to -20° . Then, through the pressure-equalized dropping funnel there was added over 1 hour 208 ml. of 1.56 *M* borane (BH_3) in tetrahydrofuran. The reaction mixture was maintained at 0° . After 4 hours only a small amount of residual 2-methyl-2-butene ($\sim 2\%$) was detected. Analysis of the reaction mixture with glycerol-water in diglyme indicated a concentration of active hydride of 0.9 *M*.

The following experiment is typical of the procedure followed.

Into a carefully dried 10-ml. volumetric flask were weighed 2.11 g. (25.0 mmoles) of 1-hexene and 1.75 g. (25.0 mmoles) of 3-methyl-1-butene. To the same flask was added 1.36 ml. (12.5 mmoles) of cyclohexane as the internal standard and the flask filled to the mark with tetrahydrofuran. The apparatus was identical with that used in the diborane experiments. The contents of the volumetric flask were introduced into the reaction vessel, and an additional 5.0 ml. of tetrahydrofuran was used to rinse the volumetric flask and added to the reaction vessel. The mixture was cooled to 0° and a minute sample withdrawn and analyzed by gas chromatography. Then 25.0 ml. of the standard solution of disiamylborane (22.5 mmoles) in tetrahydrofuran was added by means of a syringe over 10 to 15 minutes, maintaining the temperature at 0° . The total volume was 50 ml. and the concentration was 0.5 *M* in each of the two olefins and slightly lower in the reagent, disiamylborane.

The hydrogen evolved during the reaction was always quite small, 0.6 mmole or less. The temperature was maintained at 0° for an additional hour and then a sample was removed and analyzed by gas chromatography. Completeness of the reaction was tested at this point by addition of glycerol-water in diglyme to the reaction mixture. In all cases the reaction was complete, with no significant hydrogen evolved.

Analysis of the 1-hexene, 3-methyl-1-butene pair revealed the presence of 12.1 mmoles of 1-hexene and 16.5 mmoles of 3-methyl-1-butene. This indicates that 12.9 mmoles of 1-hexene and 8.5 mmoles of 3-methyl-1-butene had reacted, a total of 21.4 mmoles of olefin, as compared to 21.9 mmoles of available hydride (22.5 - 0.6). Substituting the results into the Ingold-Shaw expression results in a reactivity of 3-methyl-1-pentene to 1-hexene of 57/100.

The following pairs of olefins were examined: cycloheptene/cyclooctene, cyclooctene/2,4,4-trimethyl-1-pentene, 2,4,4-trimethyl-1-pentene/2-methyl-1-pentene, 2-methyl-1-pentene/1-octene, cyclooctene/ α -methylstyrene, 1-hexene/1-octene, 1-hexene/1-pentene, 1-hexene/3-methyl-1-butene, 1-hexene/3,3-dimethyl-1-butene, 1-hexene/1-hexyne, 1-hexene/3-hexyne, 1-hexene/1,5-hexadiene.

(15) This solution is readily prepared by adding freshly distilled boron trifluoride etherate to an appropriate quantity of diglyme and removing the ethyl ether under reduced pressure (ref. 7). Removal of the ether facilitates the gas chromatographic analysis.

(16) C. K. Ingold and F. R. Shaw, *J. Chem. Soc.*, 2918 (1927).

(11) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 1504 (1960);

H. C. Brown and M. V. Bhatt, *ibid.*, **82**, 2074 (1960).

(12) H. C. Brown and A. W. Moerikofer, *ibid.*, **84**, 1478 (1962).

(13) H. C. Brown and G. J. Klender, *Inorg. Chem.*, **1**, 204 (1962).

(14) Research in progress with G. Zweifel and N. R. Ayyangar.