yield of cyclopropane, a 0.2% yield of propylene, and a 4% yield of 1-propanol.

Preparation of 5-Hydroxypentyl Tosylate.—To 8.6 ml. (8.5 mmoles) of 0.987 *M* borane solution was added at 0°, 4.82 g., (20.1 mmoles) of 4-pentenyl tosylate. The solution was stirred 1 hr. at 0°, and then oxidized by adding 2.4 ml. of 3 *M* sodium hydroxide and 2.2 ml. (24 mmoles) of 33% hydrogen peroxide at 10–25°. The oxidized mixture was diluted with 15 ml. of ether, and the layers were separated. The aqueous layer was extracted twice with 10 ml. of ether. The organic layer was combined with the extracts, washed with 1 *M* sodium hydroxide, water, and saturated sodium chloride, and then dried over magnesium sulfate at 0°. The solvent was evaporated *in vacuo*, and the residue was stripped at 0.1 mm. to constant weight (4 hr. at 25°). There was obtained 4.78 g., a 92% yield, of 5-hydroxypentyl tosylate, a viscous, opaque oil.

Anal. Calcd. for $C_{13}H_{18}O_4S$: C, 55.8; H, 7.02; S, 12.4. Found: C, 55.3; H, 7.09; S, 12.1.

In another experiment 18.7 g. (77.9 mmoles) of 4-pentenyl tosylate was added at 0° to 59.0 ml. (85.0 mmoles) of 1.44 *M* disiamylborane solution. After stirring for 3 hr. at 0°, 25 ml. (275 mmoles) of 33% hydrogen peroxide and 23 ml. of 3 *M* sodium hydroxide were added simultaneously at 10–23°. The oxidized mixture was treated with 5 g. of potassium carbonate, and the layers were separated. The aqueous layer was saturated with potassium carbonate and extracted with ether. The combined organic phase was dried over magnesium sulfate at 0°. The solvent was evaporated *in vacuo* at room temperature, and the residue was stripped to constant weight at 0.1 mm. (7 hr. at 25°). There was obtained 20.5 g., a 102% yield, of crude 5-hydroxypentyl tosylate, a viscous, opaque oil.

Anal. Calcd. for $C_{13}H_{18}O_4S$: C, 55.8; H, 7.02; S, 12.4. Found: C, 57.4; H, 7.55; S, 11.9.

No further purification was attempted because the hydroxypentyl tosylate decomposed slowly at room temperature. The crude material (19.2 g.) was treated with 21 ml. of 2,6-lutidine and heated 7 hr. at 100–140°. There was collected 3.97 g., a 62% yield, of liquid, $n^{20}D$ 1.4223, which was shown by gas chromatography to be 99% pure tetrahydropyran.[23]

(23) D. D. Reynolds and W. O. Kenyon, *J. Am. Chem. Soc.*, **72**, 1593 (1950).

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

Hydroboration. XXII. The Reaction of Unsaturated Esters with Diborane and Disiamylborane[1]

BY HERBERT C. BROWN AND KESTUTIS A. KEBLYS[2]

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The treatment of several representative ω-unsaturated esters with excess diborane in tetrahydrofuran at 0° results in both addition to the carbon–carbon double bond and concurrent reduction of the ester group. Oxidation of the products with alkaline hydrogen peroxide yields mixtures of hydroxy esters and diols. Under standard conditions the extent of reduction of the ester grouping decreases with increasing number of carbon atoms between the ester grouping and the double bond: ethyl 3-butenoate > ethyl 4-pentenoate > ethyl 10-undecenoate. It is proposed that a major side reaction is reduction of the ester group intramolecularly by the monoalkylborane formed in the initial addition of borane to the double bond. The use of the theoretical quantity of diborane added to a concentrated solution of the unsaturated ester minimizes the side reaction and produces the organoborane in good yield. Oxidation produces the ω-hydroxy esters, accompanied by smaller quantities of the secondary isomers. The use of disiamylborane for the hydroboration circumvents the partial reduction of the ester group and essentially eliminates the formation of the secondary isomer. The ω-carboethoxyalkylboranes fail to undergo a base-catalyzed cyclization to cyclic ketones. The reactions of diborane and disiamylborane with ethyl acrylate are relatively complex, apparently the result of a strong directive influence of the carboethoxy group which directs the boron predominantly to the α-position of the ester, followed by a transfer of the boron to the neighboring oxygen of the carbonyl group.

The development of hydroboration, the reaction of olefins, dienes, and acetylenes with diborane and diborane derivatives, has opened up a new and convenient route to a variety of organoboranes.[3–6] Owing to their ability to undergo numerous chemical transformations, the organoboranes promise to become important intermediates in organic synthesis.[7] The extension of hydroboration to functional derivatives of olefins and acetylenes would not only provide access to new types of organoboranes, but would also extend significantly the synthetic usefulness of the hydroboration reaction.

In the preceding publication we examined the hydroboration of unsaturated alkyl chlorides and tosylates.[8] These derivatives represent substituents normally inert to diborane under hydroborating conditions.[9] Of far greater significance is the achievement of the hydroboration of unsaturated derivatives containing substituents capable of undergoing reduction by diborane. In the present paper we examine the practicality of achieving the selective hydroboration of unsaturated carboxylic esters, while avoiding or minimizing concurrent reduction of the ester grouping.

Apart from its more general implications, it is evident that such a study is of interest in demonstrating the possibility of synthesizing organoboranes containing carboethoxy substituents. It is evident that were the hydroboration step feasible, one would have readily available a wide range of carboethoxy derivatives containing a reactive center on which one could operate to introduce other substituents, such as the hydroxy group,[7] to convert into other organometallics, such as the mercury derivative,[10] or to join to other groupings *via* carbon–carbon bonds.[11]

Although esters are reduced by diborane,[9] the rate of reduction appears to be considerably slower than the

(1) Based upon a thesis submitted by K. A. Keblys in 1962 to the Faculty of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Research assistant on an XR Grant provided by the Purdue Research Foundation.

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

(4) H. C. Brown and G. Zweifel, *ibid.*, **83**, 1241 (1961).

(5) H. C. Brown and G. Zweifel, *ibid.*, **83**, 3834 (1961).

(6) G. Zweifel, K. Nagase, and H. C. Brown, *ibid.*, **84**, 183 (1962).

(7) H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962, pp. 59–80.

(8) H. C. Brown and K. A. Keblys, *J. Am. Chem. Soc.*, **86**, 1791 (1964).

(9) H. C. Brown and B. C. Subba Rao, *ibid.*, **82**, 681 (1960); research in progress with Dr. P. Heim.

(10) J. B. Honeycutt, Jr., and J. M. Riddle, *ibid.*, **82**, 3051 (1960).

(11) H. C. Brown, N. C. Hébert, and C. H. Snyder, *ibid.*, **83**, 1001 (1961); H. C. Brown and C. H. Snyder, *ibid.*, **83**, 1001 (1961); H. C. Brown, C. Verbrugge, and C. H. Snyder, *ibid.*, **83**, 1002 (1961).

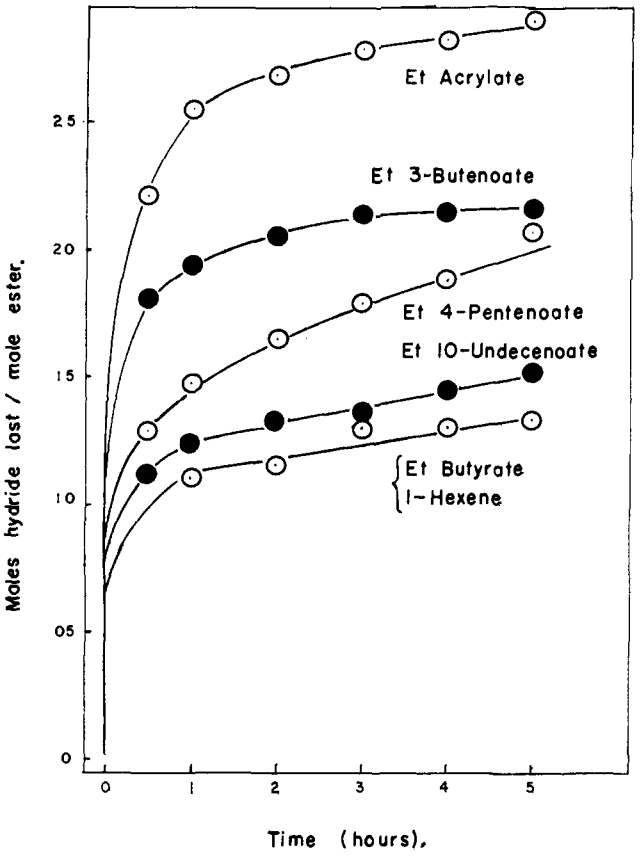


Fig. 1.—Relative rates of reaction of diborane with unsaturated esters at 0°.

rate of reaction of diborane with representative olefins.[12] For example, in a competitive experiment, cyclohexene was hydroborated successfully in the presence of ethyl benzoate.[12]

These results indicated that a selective hydroboration of unsaturated esters might be feasible. In fact, several hydroborations of unsaturated esters have been reported. Fore and Bickford treated methyl oleate with diborane and, after oxidation and saponification, obtained a mixture of 9- and 10-hydroxystearic acids in 40% yield.[13] Similarly, Dulou and Chrétien-Bessière treated methyl 10-undecenoate with the theoretical amount of diborane and, after oxidation, obtained methyl 11-hydroxyundecanoate in 25 to 50% yield.[14] However, when an excess of diborane was used, a mixture of the 11-hydroxyundecanoate and 1,11-undecanediol was obtained.[14]

In these two reported hydroboration reactions of unsaturated esters the two potential reaction sites, the olefin linkage and the ester group, are isolated from each other by at least seven methylene groups. Consequently, the available results provide no assurance that the hydroboration reaction will be applicable to a wide range of esters where the two reaction sites are much nearer to each other. It appeared desirable, therefore, to explore more fully the scope of this potentially promising application of the hydroboration reaction.

Consequently, a systematic study of the hydroboration of unsaturated esters of the type, $CH_2{=}CH{-}(CH_2)_nCO_2C_2H_5$ (where n = 0, 1, 2, and 8), was undertaken. The main objectives of this study were to determine the feasibility of a selective hydroboration, to estimate the directive influence of the carboethoxy group, and to explore possible synthetic applications of the organoboranes derived from unsaturated esters.

Results

Preliminary hydroboration experiments with ethyl 3-butenoate revealed that both the ester group and the olefin linkage were being attacked concurrently by the diborane utilized for the hydroboration. At 0°, ethyl 3-butenoate, treated with borane[15] in a 1:1 molar ratio, consumed 2.5 equivalents of hydride[16] in 4 min. and only 2.6 equivalents in 1.5 hr. Since only one equivalent of hydride is required to convert the olefin group completely into organoborane, it is obvious that a selective hydroboration had not been achieved. Moreover, the very rapid uptake of hydride in the initial phases of the reaction suggested that both the olefinic linkage and the ester group in ethyl 3-butenoate were reacting exceedingly rapidly with the reagent.

In view of these unexpected results, it appeared desirable to ascertain whether this very rapid reduction of the ester group required a special structural relationship between the ester grouping and the double bond. Consequently, we undertook an examination of the stoichiometry of the reaction between selected homologs of ethyl 3-butenoate and diborane.

Stoichiometry.—The four ethyl esters utilized, acrylate, 3-butenoate, 4-pentenoate, and 10-undecenoate, were dissolved in tetrahydrofuran and cooled to 0°. To 50 mmoles of each ester, in 25 ml. of solvent, was added, over 30 min., 50 mmoles of borane as a 1.0 M solution in tetrahydrofuran. The progress of the reaction was followed by a periodic analysis for residual hydride. In one reaction, the usual quantity of unsaturated ester was replaced by a mixture of 50 mmoles each of 1-hexene and ethyl n-butyrate. The results of these experiments are summarized in Table I.

TABLE I
STOICHIOMETRY OF THE REACTION BETWEEN UNSATURATED ETHYL ESTERS AND DIBORANE AT 0°

	Moles of hydride utilized per mole of ethyl ester				
Time,[a] hr.	Acrylate	3-Butenoate	4-Pentenoate	10-Undecenoate	1-Hexene, ethyl n-butyrate
0.5	2.22	1.82	1.29	1.14	1.13
1	2.56	1.94	1.48	1.24	1.11
2	2.70	2.06	1.65	1.32	1.18
3	2.80	2.15	1.80	1.37	1.30
4	2.83	2.16	1.89	1.46	1.31
5	2.89	2.17	2.08	1.53	1.34

[a] Includes 30 min. required to add the borane solution.

The hydride uptake pattern is shown in Fig. 1. In all cases a very rapid utilization of 1 to 2 moles of hydride was observed. Further utilization of hydride occurred at a much slower, measurable rate. The amount of hydride taken up per mole of ester at any time decreased in the order: acrylate > 3-butenoate > 4-pentenoate > 10-undecenoate > 1-hexene, n-butyrate.

(12) H. C. Brown and W. Korytnyk, *J. Am. Chem. Soc.*, **82**, 3866 (1960).

(13) S. A. Fore and W. G. Bickford, *J. Org. Chem.*, **24**, 920 (1959).

(14) R. Dulou and Y. Chrétien-Bessière, *Bull. soc. chim. France*, 1362 (1959).

(15) Diborane exists in tetrahydrofuran solution as the borane derivative: B. Rice and H. S. Uchida, *J. Phys. Chem.*, **59**, 650 (1955).

(16) It is convenient to discuss the stoichiometry of hydroboration reactions in terms of "hydride" utilization. Thus 1 mole of borane, BH_3, contains three "hydrides" and will either react with 3 moles of a simple olefin, or will liberate 3 moles of hydrogen on hydrolysis.

The hydroboration of the olefinic linkage requires 1 mole of hydride, while a complete reduction of the ester group to the alcohol stage requires 2. The reaction of diborane with simple terminal double bonds appears to be very fast and quantitative. Consequently, the amount of hydride consumed in excess of 1 mole should give an approximate measure of the extent to which the ester group has undergone reduction.

According to this interpretation, at least some reduction of the carboethoxy group had occurred in all of the unsaturated esters examined. After 4 hr. at 0°, the indicated amount of reduction for each system was: 1-hexene, *n*-butyrate, 16%; 10-undecenoate, 23%; 4-pentenoate, 45%; 3-butenoate, 58%; acrylate, 92%.

In order to confirm this interpretation of the stoichiometric results, the products of the reaction (after 5 hr.) were oxidized with alkaline hydrogen peroxide and examined by gas chromatography. The results are presented in Table II.

TABLE II

OXIDATION PRODUCTS OF THE ORGANOBORANES FROM UNSATURATED ESTERS AND EXCESS DIBORANE[a]

Unsaturated ethyl esters	Hydroxy esters		Diols	
	Isomer	Yield, %	Isomer	Yield, %
10-Undecenoate	10-OH	5	1,10-	..[b]
	11-OH	58	1,11-	10
	Total	63	Total	10
4-Pentenoate	4-OH	3	1,4-	7
	5-OH	41	1,5-	39
	Total	44	Total	46
3-Butenoate	3-OH	5	1,3-	5
	4-OH	27	1,4-	29
	Total	32	Total	34
Acrylate	2-OH	0	1,2-	30
	3-OH	0	1,3-	8
	Total	0	Total[c]	38

[a] 5 hr. at 0°. [b] No 1,10-undecanediol was detected by gas chromatography. It is possible that the peaks of 1,10-diol and 11-hydroxyundecanoate had not been resolved. [c] In addition to diols there was also found 15% of 1-propanol and 14% of 1-ethoxy-2-propanol.

All of the unsaturated esters, with the exception of ethyl acrylate, gave the expected mixture of hydroxy esters and diols. The ratios of diols to hydroxy esters were in reasonably good agreement with the extent of ester group reduction indicated by the data of the stoichiometry study. However, ethyl acrylate was exceptional in that no hydroxypropionates were detected. Instead, only the propanediols, 1-propanol, and 1-ethoxy-2-propanol were found in the reaction products.

In no case was there detected any hydroxyaldehyde, the result of a partial reduction of the ester group. Similarly, no ω-unsaturated alcohols were found. This argues against the possibility that the diborane might have reacted more rapidly with the ester group than with the olefinic linkage.

Selective Hydroboration.—The reaction conditions employed in the stoichiometric study were obviously not favorable for the selective hydroboration of the carbon–carbon double bond in an unsaturated ester. It appeared that a slow addition of the theoretical quantity of the borane solution to a concentrated solution of the unsaturated ester might achieve a more selective hydroboration of the olefinic center.

Consequently, 14 mmoles of borane (1.0 *M* solution in tetrahydrofuran) was added in 1 hr. at 0° to 40 mmoles of (undiluted) unsaturated ester. The solution was stirred for 2 hr. at 0°, followed by 2 hr. at 25°, and then oxidized with hydrogen peroxide, maintaining the pH at 7 to 8 by concurrent addition of aqueous alkali.[17] The products were analyzed by gas chromatography.

This procedure resulted in excellent selectivity in all cases except ethyl acrylate. The yields of hydroxy esters ranged from 78 to 92%. Only in the reactions of ethyl 3-butenoate and ethyl 4-pentenoate were small amounts of diols obtained. The hydroxyundecanoates were isolated in 71% yield.[18] The results of these selective hydroborations with diborane are summarized in Table III.

TABLE III

OXIDATION PRODUCTS OF THE ORGANOBORANES FROM THE SELECTIVE HYDROBORATION OF UNSATURATED ESTERS WITH DIBORANE

Unsaturated ethyl ester	Yield,[a] %			Ratio of isomers[c]
	Unsatd. ester[b]	Hydroxy ester	Diol	
10-Undecenoate	5	88	0	91:9
4-Pentenoate	7	92	Trace[d]	93:7
3-Butenoate	8	78	1[e]	81:19
Acrylate	27	0	2[f]	...

[a] Based on the amount of reacted starting ester. [b] Recovered. [c] Ratio of primary to secondary hydroxy esters. [d] 1,4-Pentanediol. [e] 1,4-Butanediol. [f] 1,2-Propanediol; in addition, 5% of ethyl propionate was found.

From the synthetic point of view, the selective reaction of unsaturated esters with diborane suffers from one significant disadvantage. Although the major product, the ω-hydroxy ester, is obtained in good yield, there is formed simultaneously a significant amount of the isomeric secondary derivative. Indeed, the product from ethyl 3-butenoate contains nearly 20% of the 3-hydroxy isomer. Fortunately, this is the worst case and the amount of the secondary isomer decreases with increasing distance of the double bond from the ester grouping. Nevertheless, a hydroboration procedure that would eliminate, or at least minimize, the formation of the secondary isomers is clearly desirable.

In the hydroboration of terminal olefins, the proportion of secondary organoboranes can be significantly reduced by employing disiamylborane,[19] a more selective hydroboration reagent.[4] Furthermore, disiamylborane does not reduce esters at 0°.[20] This reagent, therefore, appeared particularly suitable for the selective hydroboration of terminal unsaturated esters and for their conversion into pure ω-hydroxy esters.

Consequently, the reactions of ethyl acrylate, 3-butenoate, 4-pentenoate, and 10-undecenoate with disiamylborane were investigated. In each case 20 mmoles of unsaturated ester was added to 21 mmoles of disiamylborane in tetrahydrofuran at 0° and stirred for 1 hr. at room temperature. The reaction mixture, after oxidation with hydrogen peroxide in a controlled alkaline medium, was analyzed by gas chromatography.

(17) Addition of alkali, prior to treatment with hydrogen peroxide, causes considerable loss through saponification of the hydroxy esters.

(18) Dulou and Chrétien-Bessiére (ref. 14) obtained methyl 11-hydroxyundecanoate in 50% yield, with a somewhat different hydroboration procedure.

(19) Bis(3-methyl-2-butyl)borane.

(20) H. C. Brown and D. B. Bigley, *J. Am. Chem. Soc.*, **83**, 486 (1961).

The yields of ω-hydroxy esters ranged from 80 to 90%. Only small amounts, 1 to 2%, of the secondary hydroxy ester were found. However, the reaction with ethyl acrylate was again anomalous. Only a 9% yield of 3-hydroxypropionate was obtained. Instead, ethyl propionate, propionaldehyde, 1-ethoxy-2-propanol, and small amounts of 1-propanol and 1,2-propanediol were obtained.

The reactions of unsaturated esters with disiamylborane were repeated on a larger, preparative scale. The hydroxy esters were isolated in yields of 75 to 80%. The results are summarized in Table IV.

TABLE IV

OXIDATION PRODUCTS OF THE ORGANOBORANE FROM UNSATURATED ETHYL ESTERS AND DISIAMYLBORANE

Hydroxy ethyl esters	Yield, % Analysis[a]	Yield, % Isolated
3-Hydroxypropionate	9[b]	..
4-Hydroxybutyrate	88[c]	76
5-Hydroxyvalerate	92[d]	78
11-Hydroxyundecanoate	...	81[e]

[a] By gas chromatography. [b] The following products were also formed: 25% of ethyl propionate, 17% of propionaldehyde, 6% of 1-ethoxy-2-propanol, 1% of 1-propanol, and 1% of 1,2-propanediol. [c] Also 1 to 2% of the 3-hydroxy isomer. [d] Also 1% of the 4-hydroxy isomer. [e] Traces of the 10-hydroxy isomer indicated.

Attempted Cyclization of ω-Carboethoxyalkylboranes.—The γ-chloroalkylboranes readily undergo cyclization to cyclopropanes at 0° under the influence of alkali.[21] However, we were unable to achieve an analogous cyclization of the organoboranes from ethyl 3-butenoate or ethyl 4-pentenoate.

In spite of these unsuccessful attempts, it appeared possible that the cyclization reaction might proceed more readily if the ethoxy group in the organoborane were replaced by a better leaving group, such as chloride. Consequently, a cyclization of an organoborane derived from 3-butenoyl chloride was considered. Since no information was available on the hydroboration of unsaturated acyl halides, an investigation of the reaction of diborane with 3-butenoyl chloride was undertaken.

With excess diborane, 3-butenoyl chloride exhibited a hydride consumption pattern similar to that of the corresponding ethyl ester. One mole of acyl chloride consumed 2.0 moles of hydride in 30 min. and 2.2 moles in 5 hr. However, an attempt to achieve a selective hydroboration of 3-butenoyl chloride with a stoichiometric amount of borane was not successful, even under the optimum conditions which had proved satisfactory for the esters.

A selective hydroboration of 3-butenoyl chloride was achieved with disiamylborane. Ethanolysis and oxidation of the reaction mixture gave ethyl 4-hydroxybutyrate in 56% yield, establishing that the desired organoborane had been synthesized *in situ*. However, the attempted cyclization of this derivative, using N,N,N′,N′-tetramethylethylenediamine as a catalyst, failed to produce cyclobutanone.

Discussion

Hydroboration–Reduction of Unsaturated Esters.—Diborane reacts both with esters (1) and with olefins (2).

(21) M. F. Hawthorne and J. A. Dupont, *J. Am. Chem. Soc.*, **80**, 5830 (1958).

$$RCH{=}CH_2 + HB{<} \longrightarrow RCH_2CH_2B{<} \quad (1)$$

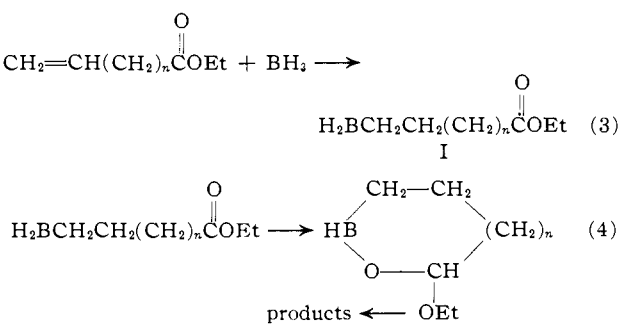
$$R\overset{O}{\overset{\|}{C}}OR' + 2HB{<} \longrightarrow RCH_2OB{<} + R'OB{<} \quad (2)$$

However, the reaction of diborane with esters is generally much slower than with olefins.[12] It would, therefore, be anticipated that in a system containing both the olefinic linkage and the ester group diborane would react preferentially with the olefinic linkage, even in the presence of excess reagent. In that event, there would occur a rapid loss of 1 equivalent of hydride, followed by a much slower loss of the remaining 2 equivalents of hydride. Such a pattern is indeed observed with the mixture of 1-hexene and ethyl *n*-butyrate. The analysis of the oxidation products confirms the conclusion that the initial rapid uptake of 1 mole of hydride involves preferential reaction with the carbon–carbon double bond.

However, in the case of systems which contain both reaction sites in the same molecule, a different reaction pattern is evident. As shown in Fig. 1, only ethyl 10-undecenoate exhibits a pattern similar to that observed in the 1-hexene, *n*-butyrate mixture. The other ω-unsaturated esters consume 1.3 to 2.6 moles of hydride before the hydride uptake levels off. The results reveal the following apparent order of ester group reactivities: acrylate > 3-butenoate > 4-pentenoate > 10-undecenoate > *n*-butyrate. This indicates that the presence of an olefinic linkage in the molecule, particularly in cases where the double bond is near the carboethoxy group, considerably enhances the reactivity of the ester group toward diborane.

Oxidation of the products produced in the reaction of unsaturated esters with excess diborane yields only a mixture of hydroxy esters and diols. The absence of unsaturated alcohols clearly indicates that diborane must react preferentially with the olefinic linkage, in spite of the apparent enhanced reactivity of the carboethoxy groups.

The results can be reasonably accounted for in terms of the following reaction sequence. The first step must be a rapid addition of borane to the olefinic linkage (3). There must follow a rapid intramolecular reaction of the borane intermediate with the ester grouping (4).

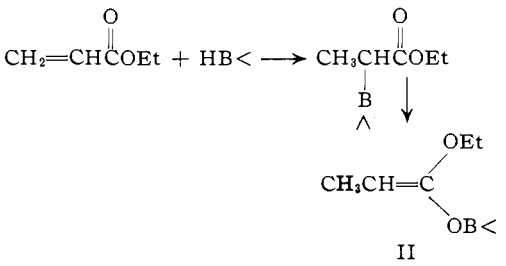


This intramolecular path, leading to the formation of cyclic intermediates, offers the most reasonable explanation for the greatly enhanced reactivity of carboethoxy groups observed in these unsaturated esters. It also accounts for the effect of the chain length on the apparent sensitivity of the ester grouping toward reduction. According to the proposed mechanism, the induced reduction of the ester grouping

should be greatest in those compounds which are capable of forming five- or six-membered cyclic intermediates. In compounds where the intramolecular reduction would require the formation of larger rings, the reactivity of the carboethoxy groups should approach that of monofunctional esters incapable of intramolecular reaction.

These conclusions are consistent with the experimental observations. For example, in the case of ethyl 10-undecenoate, where an intramolecular reduction would lead to a 13-membered cyclic intermediate, the reactivity of the carboethoxy group is almost the same as in ethyl *n*-butyrate. The ester group in ethyl 4-pentenoate, which requires a seven-membered cyclic intermediate, undergoes reduction to an extent somewhat greater than that of the ester group in 10-undecenoate, but significantly slower than that of the ester group in ethyl 3-butenoate, where formation of a six-membered cyclic intermediate is feasible.

The unusual reactivity of ethyl acrylate, as well as the unexpected reaction products such as ethyl propionate and 1-ethoxy-2-propanol, suggest that the hydroboration–reduction of this ester must proceed by a very different path. The first step might involve a 1,2-addition in which the powerful directive influence of the carboethoxy group would favor placing the boron atom predominantly in the α-position (5), followed by a rapid transfer of boron from carbon to the neighboring oxygen. This rearrangement would lead to an inter-



(5)

mediate, II, capable of forming ethyl propionate on hydrolysis, or of reacting further with the hydroborating agents. All of the products observed in the reaction can be explained by a series of addition–β-elimination steps. However, in view of the complexity of the reaction there appears to be little point in attempting to arrive at a complete understanding of the reaction mechanism at this time.

Selective Hydroborations.—Intermediate I, formed in the first step of the reaction between diborane and unsaturated esters (3), might either undergo an intramolecular reduction (4), or add to the olefinic linkage of another molecule of unsaturated ester (6). The

$$\mathrm{I} + CH_2{=}CH(CH_2)_nCO_2Et \longrightarrow HB[CH_3CH_2(CH_2)_nCO_2Et]_2 \quad (6)$$

relative rates of paths 4 and 6 would determine the extent of selective hydroboration. If a selective reaction with the olefinic linkage were desired, the rate of step 6 should be increased at the expense of step 4. Obviously, a high concentration of ester and a low concentration of borane should favor hydroboration over reduction.

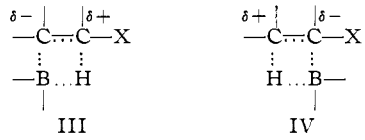
These requirements were met by adding slowly a dilute borane solution to the vigorously mixed, undiluted unsaturated esters. In all cases, with the exception of ethyl acrylate, excellent selectivity was achieved. The corresponding hydroxy esters were practically the sole products obtained after oxidation. These results demonstrate that it is possible to eliminate the intramolecular reduction step almost entirely by careful control of the experimental conditions.

Another approach to the selective hydroboration of unsaturated esters involves the use of monofunctional hydroborating reagents, such as disiamylborane, which exclude the possibility of a cyclic intramolecular reduction. Except for the special case of ethyl acrylate, the use of disiamylborane produces excellent yields of the corresponding organoboranes, and, after oxidation, excellent yields of the corresponding hydroxy esters. The absence of diols in the products demonstrates that the reagent has achieved essentially quantitative selectivity (7).

$$CH_2{=}CH(CH_2)_nCO_2Et + Sia_2BH \longrightarrow Sia_2BCH_2CH_2(CH_2)_nCO_2Et \xrightarrow[H_2O_2]{NaOH} HOCH_2CH_2(CH_2)_nCO_2Et \quad (7)$$

The successful selective reaction of ω-unsaturated esters with diborane and disiamylborane provides a convenient synthetic method for the preparation of organoboranes containing carboalkoxy groups and, through oxidation, the corresponding ω-hydroxy esters. The reaction with diborane produces, in addition to the ω-hydroxy esters, from 8 to 20% of the secondary isomers. On the other hand, the reaction of ω-unsaturated esters with disiamylborane gives almost exclusively the ω-hydroxy isomers. Consequently, for most synthetic applications, disiamylborane would appear to be the preferred reagent.

Directive Effects.—It has been suggested that the direction of addition of the boron–hydrogen moiety to substituted olefins is determined by both steric and electronic influences.[22] A four-center transition state has been proposed for the addition step.[23] Consequently, the direction of addition to an olefin carrying a substituent would be determined by the relative stability of the two possible transition states III and IV.



An electron-supplying substituent might be expected to stabilize transition state III. On the other hand, an electron-withdrawing substituent, such as carboethoxy, would be expected to favor transition state IV at the cost of III. In other words, substituents having strong −I effects should influence the addition reaction to place an increased proportion of the boron at the carbon atom of the double bond nearest the substituent.

The few available data on the addition of diborane to olefins containing polar substituents are in accord with this view. For example, the trifluoromethyl

(22) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 4708 (1960).
(23) H. C. Brown and B. C. Subba Rao, *ibid.*, **81**, 6434 (1959).

group directs 74% of the entering boron to the secondary position of 1,1,1-trifluoropropene.[24]

In view of its strong inductive effect, the carboethoxy group should exert a powerful influence on the direction of borane addition to the olefinic double bond. Indeed, in ethyl acrylate it was anticipated that most of the boron would appear at the α-position of the ester. Unfortunately, the complex nature of the reaction made it impossible to check this prediction.

It was possible, however, to observe the powerful directive influence of the carboethoxy group in the next higher member, ethyl 3-butenoate. In spite of the fact that the carboethoxy group is insulated from the double bond by a methylene group, there is observed 15 to 19% of the secondary derivative. With an additional methylene group separating the double bond from the substituent, the amount of the secondary isomer drops sharply, and approaches the 6 to 7% observed in simple 1-alkenes.[22]

The tendency of the carboethoxy group to influence the direction of hydroboration of the double bond appears to be greater than that of the phenyl group[22] and approximately the same as that of the chloromethyl group.[8]

The available data on the directive influence of various substituents on the direction of hydroboration of a terminal double bond are summarized in Table V.

TABLE V

DIRECTIVE EFFECTS IN HYDROBORATION EXHIBITED BY VARIOUS FUNCTIONAL SUBSTITUENTS IN THE SYSTEM Y—CH=CH$_2$

	Diborane		Disiamylborane	
Substituent Y	1°	2°	1°	2°
CH_3CH_2–[a]	94	6	..	..
C_6H_5–[a]	80	20	98	2
p-ClC_6H_4–[a]	65	35	..	..
p-$MeOC_6H_4$–[a]	91	9	98	2
$C_6H_5CH_2$–[a]	90	10	..	..
$EtOC(=O)CH_2$–	83	17	98	2
$EtOC(=O)CH_2CH_2$–	91	9	99	1
$ClCH_2$–[b]	60	40	97	3
$ClCH_2CH_2$–[b]	82	18	99	1
p-$MeC_6H_4SO_3CH_2$–[b]	55	45	95	5
Me_3Si–[c]	67	33	..	..
F_3C–[d]	26	74	..	..

[a] Ref. 4 and 22. [b] Ref. 8. [c] D. Seyferth, *J. Inorg. Nucl. Chem.*, **7**, 152 (1958). [d] Ref. 24.

Knowledge of the directive effect of representative substituents might make it possible to predict the approximate isomer distribution in the hydroboration of other unsaturated molecules containing functional substituents, and to utilize the directive effect to achieve useful results in planning a synthetic approach. Accordingly, we are undertaking a systematic study of the directive influence exerted by representative substituents.[25]

Experimental

Materials and General Procedures.—The materials used and general operating procedures have been described in the preceding publication.[5] Unsaturated esters were prepared from the corresponding acids (Columbia Organic Chemicals Co.) by sulfuric acid-catalyzed esterification. All esters used were 98 to 99% pure by gas chromatographic examination.

Gas Chromatography Analysis.—The Aerograph Model A90-S instrument (Wilkens Instrument and Research Co.) was used for all gas chromatography analysis. Hydroxybutyrates and -valerates were analyzed using a 2.5-ft. column packed with 4% d-sorbitol and 16% silicone 703 on regular firebrick, operated at 120–130° and 80–100 ml./min. flow of helium. Above this temperature and with other solid supports, extensive decomposition of 4-hydroxybutyrate and 4-hydroxyvalerate was observed. All other products were analyzed using standard columns packed with Carbowax 1540, Carbowax 20M, or Ucon Polar on Chromosorb-W. Aromatic hydrocarbons were normally used as internal standards.

The expected products of hydroboration were identified by comparing gas chromatography retention times with samples of known compounds. Other products were isolated by preparative gas chromatography and characterized by their infrared spectra.

Stoichiometry of the Reaction of Unsaturated Esters with Diborane.—The following procedure, given for the reaction of ethyl 3-butenoate, was used in all experiments of this series.

To 6.09 g. (53.3 mmoles) of ethyl 3-butenoate, dissolved in 25 ml. of tetrahydrofuran, was added at 0° in 27 min .50.0 ml. (53.3 mmoles) of 1.07 M borane solution. The solution was stirred 5 hr. at 0 ± 1°. Periodically, 10-ml. samples were withdrawn and injected into a mixture of ethylene glycol and diglyme to determine the amount of unreacted hydride. A blank run was carried out to determine the amount of hydride lost in handling.

After 5 hr., a 10-ml. sample of the reaction mixture was hydrolyzed with water and oxidized by adding simultaneously 1.2 ml. (7.9 mmoles) of 22% hydrogen peroxide and 5.8 ml. of 1 M sodium hydroxide. The oxidized solution was diluted with 20 ml. of ether, and the layers were separated. The aqueous layer was extracted with three 5-ml. portions of ether, then saturated with potassium carbonate, and extracted with 20 ml. of tetrahydrofuran.

The organic layer and ether extracts were dried over magnesium sulfate, concentrated to 4.1 ml., and analyzed by gas chromatography using a 1,4-butanediol solution as external standard. There was found 1.91 mmoles, a 29% yield, of 1,4-butanediol, and 0.34 mmole, a 5.3% yield, of 1,3-butanediol.

Gas chromatography analysis showed no 3-buten-1-ol present. Samples of extracts and aqueous phase gave no precipitate with 2,4-dinitrophenylhydrazine.

Selective Hydroboration of Unsaturated Esters with Diborane.—The procedure, given here for ethyl 4-pentenoate, was used in all experiments of this series.

To 4.97 g. (38.7 mmoles) of ethyl 4-pentenoate and 0.98 g. (7.3 mmoles) of t-butylbenzene (internal standard) was added in 64 min. at 0° 15.0 ml. (13.7 mmoles) of 0.910 M borane solution. After stirring for 2 hr. at 0° and 2 hr. at 25° the solution was hydrolyzed. No hydrogen was evolved. Next, 10.0 ml. (41 mmoles) of 13.4% hydrogen peroxide and 8.2 ml. of 1 M sodium hydroxide were added simultaneously at 10–22°. The isolation of the products from the oxidized mixture was identical with the procedure described above.

The ether solution and the tetrahydrofuran extracts were analyzed by gas chromatography. There was found 2.76 mmoles, 7%, of unreacted ethyl 4-pentenoate; 30.4 mmoles, an 85% yield, of ethyl 5-hydroxypentanoate; and 2.36 mmoles, a 6.6% yield, of ethyl 4-hydroxypentanoate. Only a trace of 1,4-pentanediol and no 1,5-pentanediol was found.

Selective Hydroboration of Unsaturated Esters with Disiamylborane.—The procedure, given here for ethyl 3-butenoate, was used in all other experiments of this series.

Disiamylborane solution was prepared *in situ* using 25.0 ml. (10.9 mmoles) of 0.436 M borane solution and 1.56 g. (22.2 mmoles) of 2-methyl-2-butene. To this solution 1.065 g. (9.33 mmoles) of ethyl 3-butenoate was added at 0°. After stirring for 30 min. at 0°, the solution was hydrolyzed with 1.0 ml. of water. There was evolved 0.6 mmole of hydrogen. Next, 39 mmoles of hydrogen peroxide and 4.0 ml. of 1 M sodium hydroxide were added simultaneously in 20 min. at 10–20°. The oxidized mixture was diluted with 20 ml. of ether, and the layers were separated. The aqueous layer was extracted with two 10-ml. portions of ether. The combined organic phase was washed with 10 ml. of saturated sodium sulfite, then dried over magnesium sulfate, and analyzed by gas chromatography. There were found 8.2 mmoles, an 88% yield, of ethyl 4-hydroxybutyrate and a small amount

(24) J. R. Phillips and F. G. A. Stone, *J. Chem. Soc.*, 94 (1962).

(25) Research in progress with Dr. O. J. Cope and Mr. R. M. Gallivan.

(1–2%) of ethyl 3-hydroxybutyrate. Only traces of diols were detected.

Ethyl 4-Hydroxybutyrate.—Disiamylborane solution was prepared *in situ* using 65.0 ml. (75.3 mmoles) of 1.16 *M* borane solution and 10.6 g. (151 mmoles) of 2-methyl-2-butene. To this solution was added 7.65 g. (67.0 mmoles) of ethyl 3-butenoate at 0°, stirring for 1 hr. at 0° and 30 min. at 25°. The solution was hydrolyzed with 3 ml. of water, then oxidized with 35 ml. of 1 *M* sodium hydroxide, added simultaneously at 20–26°. The oxidized mixture was diluted with 50 ml. of ether, and the layers were separated. The aqueous layer was extracted with 100 ml. of ether. The organic layer was combined with the extracts, washed with 15 ml. of 1% sodium carbonate, 15 ml. of saturated sodium sulfite, and 15 ml. of saturated sodium chloride, and then dried over magnesium sulfate. The solvent and most of the siamyl alcohol were evaporated *in vacuo* at room temperature. The residue was distilled rapidly at 0.1 mm. into an ice-cooled receiver. Redistillation of the flash distillate gave 6.7 g., a 76% yield, of ethyl 4-hydroxybutyrate, collected at 43–44° at 0.15 mm., $n^{20}D$ 1.4294. The product was 98% pure by gas chromatography.

Anal. Calcd. for $C_6H_{12}O_3$: C, 54.53; H, 9.15. Found: C, 54.32; H, 9.24.

The 3,5-dinitrobenzoate derivative of the product, recrystallized from ether–hexane, melted at 63.0–63.8° (reported[26] m.p. 62–63°).

Ethyl 5-Hydroxyvalerate.—By the procedure described above, ethyl 4-pentenoate (11.2 g., 87.2 mmoles) was treated with 96 mmoles of disiamylborane. Distillation gave 9.92 g., a 78% yield, of ethyl 5-hydroxyvalerate, collected at 64–65° at 0.1 mm., $n^{20}D$ 1.4342 (reported[27] b.p. 114° at 14 mm.).

Ethyl 11-Hydroxyundecanoate.—Similarly, ethyl 10-undecenoate (10.8 g., 51 mmoles) was treated with 57 mmoles of disiamylborane. Distillation gave 9.52 g., an 81% yield, of ethyl 11-hydroxyundecanoate, collected at 111.0–112.5° at 0.1 mm., $n^{20}D$ 1.4478.

(26) S. Okamura, M. Masumura, and T. Horie, *Yuki Gosei Kagaku Kyokai Shi*, **17**, 419 (1959); *Chem. Abstr.*, **53**, 17958*c* (1959).

(27) R. Robinson and L. H. Smith, *J. Chem. Soc.*, 371 (1937).

Anal. Calcd. for $C_{13}H_{26}O_3$: C, 67.78; H, 11.38. Found: C, 67.66; H, 11.68.

Reaction of 3-Butenoyl Chloride with Disiamylborane.—To disiamylborane, prepared *in situ* from 25.0 ml. (15.2 mmoles) of 0.608 *M* borane solution and 2.14 g. (30.3 mmoles) of 2-methyl-2-butene, was added at 0° 1.58 g. (15.1 mmoles) of 3-butenoyl chloride. The solution was stirred for 2 hr. at 0°, and then treated with 1.03 g. (15.2 mmoles) of sodium ethoxide and 5 ml. of ethanol. After stirring 10 min. at 0–10°, the solution was oxidized by a simultaneous addition of 55 mmoles of hydrogen peroxide and 7.5 ml. of 1 *M* sodium hydroxide. After standard work-up, the analysis by gas chromatography showed 8.4 mmoles, a 56% yield, of ethyl 4-hydroxybutyrate.

Attempted Cyclizations.—The organoborane, prepared *in situ* from 12.2 mmoles of ethyl 3-butenoate and 14 mmoles of disiamylborane in tetrahydrofuran, was treated with 0.97 g. of sodium ethoxide and 1.3 ml. of ethanol. The resulting solution was stirred for 7 hr. at 25°. No cyclobutanone was obtained. After oxidation, a 49% yield of ethyl 4-hydroxybutyrate was found. The experiment, was repeated, allowing the solution to reflux for 7 hr. at 65°. Again no cyclobutanone was detected. After oxidation, a 38% yield of ethyl 4-hydroxybutyrate was found. In another experiment, after addition of sodium ethoxide, the solvent was evaporated, and the residue heated *in vacuo* for 20 hr. at 100–200°. The distillate, collected in a Dry Ice-cooled trap, contained no cyclobutanone.

The organoborane, prepared *in situ* from 36.5 mmoles of ethyl 4-pentenoate and 14.2 mmoles of borane, was treated with 28.4 mmoles of sodium ethoxide. The resulting solution was stirred for 3 hr. at 23° and 4 hr. at 67°. Examination by gas chromatography showed no cyclopentanone. The solvent was then evaporated, and the residue heated *in vacuo* for 10 hr. at 150–170°. No cyclopentanone was found in the −80° traps.

The organoborane, prepared *in situ* from 27.6 mmoles of 3-butenoyl chloride and 30.5 mmoles of disiamylborane, was treated with 44 mmoles of tetramethylethylenediamine. The mixture was stirred 24 hr. at 25°, then heated 7 hr. at 67°. No cyclobutanone was detected.

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

Hydroboration. XXIII. Directive Effects in the Hydroboration of Representative Allyl Derivatives. The Elimination Reaction of β-Substituted Organoboranes

BY HERBERT C. BROWN AND O. J. COPE[1]

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The hydroboration of representative allyl derivatives was examined in order to observe the effect of the substituent on the direction of addition of diborane to the double bond. The per cent addition of the boron to the secondary carbon atom decreases with decreasing electronegativity of the substituent: allyl tosylate, 45%; chloride, 40%; acetate, 35%; benzoate, 25%; borate, 18%; phenyl ether, 32%; phenyl thioether, 22%; ethyl ether, 19%; alcohol, 24%. Whereas the secondary boron derivatives derived from allyl tosylate, chloride, benzoate, and acetate undergo a spontaneous elimination to propylene during the hydroboration of the allyl derivative, the borate, phenoxide, and ethoxide derivatives survive the hydroboration reaction at 0°. However, at elevated temperatures (refluxing tetrahydrofuran, 64°) the elimination reaction is essentially complete within 2 hr. in the case of these derivatives. A base-catalyzed elimination at room temperature was observed for the secondary hydroboration product of allyl phenyl ether. This controlled elimination reaction of β-substituted organoboranes should find useful application in organic synthesis. The hydroboration of representative allyl derivatives with disiamylborane greatly reduces the formation of the secondary isomer and permits conversion of the allyl compounds into desirable products in very high yield.

The present investigation is a logical extension of an earlier study of directive effects in the hydroboration[2] of simple olefins.[3] In the case of terminal olefins, the addition of boron takes place predominantly on the terminal carbon atom of the double bond. This was explained in terms of polarization of the double bond by the alkyl substituent, increasing the electron density at the terminal carbon atom and thereby favoring the attachment of the electrophilic boron atom at that position.[3]

The introduction of electron-withdrawing functional groups at the allyl position brings about a marked increase in the addition of boron to the secondary carbon atom of the double bond.[4] Thus, in the hydroboration of allyl tosylate and allyl chloride, 45 and 40%, respectively, of the boron adds to the nonterminal position.

(1) Postdoctorate research associate on Research Grant DA-ARO(D)-31-124-G106 supported by the U. S. Army Research Office (Durham).

(2) For a summary of the main characteristics of the hydroboration reaction and its application to organic synthesis, see H. C. Brown, "Hydroboration," W. A. Benjamin, Inc., New York, N. Y., 1962.

(3) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **82**, 4708 (1960).

(4) H. C. Brown and K. A. Keblys, *ibid.*, **86**, 1791 (1964).