Hydroboration. XXIV. Directive Effects in the Hydroboration of Some Substituted Styrenes[1]

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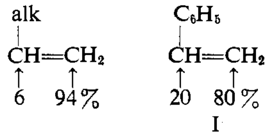
Abstract: In order to establish the role of electronic effects in influencing the direction of addition of the boron–hydrogen moiety to the carbon–carbon double bond, a number of substituted styrenes (styrene, *o*-, *m*-, and *p*-methoxy-, *o*-, *m*-, and *p*-chloro-, *o*-, *m*-, and *p*-trifluoromethyl-, and *m*- and *p*-nitrostyrene) were hydroborated under standard conditions (diglyme solution, 20°). The alcohols produced in the oxidation of the organoboranes were analyzed by glpc to establish the isomeric distribution in the hydroboration reaction. Styrene itself gives 19% addition of boron to the α position, 81% to the β. The *o*- and *p*-methoxy groups decrease the amount of α addition to 14 and 7%, respectively, whereas in the *meta* position this substituent has a negligible effect, 19% α. The *o*-, *m*-, and *p*-chloro substituents increase the amount of boron in the α position to 26% for *o*-, 30% for *m*-, and 27% for *p*-. The *o*-, *m*-, and *p*-trifluoromethyl derivatives exhibit an even greater directive effect: *o*-, 38% α; *m*-, 32% α; *p*-, 34% α. Finally, *m*-nitrostyrene directs 37% of the boron to the α position of the side chain. Hydroboration of *p*-nitrostyrene gave complex results which did not permit any definite conclusions as to the isomer distribution realized. Finally, it was observed that those organoboranes capable of yielding relatively stable carbanions underwent rapid hydrolysis under the usual oxidation procedure, forming the corresponding substituted ethylbenzenes. In such cases, by subjecting the organoborane to alkaline hydrolysis prior to oxidation it is possible to destroy selectively the α isomer and to realize the formation of the isomerically pure β alcohol after oxidation.

The hydroboration of a 1-alkene by diborane (or sodium borohydride plus boron trifluoride) proceeds to place 94% of the boron at the terminal position, 6% at the secondary.[3] On the other hand, styrene reacts to give 20% of the boron on the α position[3,4] (I).



$$\overset{\text{alk}}{\mathrm{CH}}{=}\mathrm{CH_2} \quad (6 \uparrow\ \ 94\% \uparrow) \qquad \overset{\mathrm{C_6H_5}}{\mathrm{CH}}{=}\mathrm{CH_2} \quad (20 \uparrow\ \ 80\% \uparrow)$$

I

It was previously noted that a *p*-methoxy substituent in styrene decreased the α addition from the 20% observed in styrene to 9%, whereas a *p*-chloro substituent increased it to 35%. Obviously the direction of hydroboration is sensitive to the electronic characteristics of the substituent. In the hope of realizing a better understanding of this electronic influence, we undertook a study of the hydroboration of styrene, *o*-, *m*-, and *p*-methoxy-, *o*-, *m*-, and *p*-chloro-, *o*-, *m*-, and *p*-trifluoromethyl-, and *m*- and *p*-nitrostyrene under standard conditions.

Results

The procedure adopted was similar to that utilized in the earlier study.[3] A solution of sodium borohydride and the styrene in diglyme at 20° was treated with the theoretical quantity of boron trifluoride etherate to achieve hydroboration. The product was oxidized by alkaline hydrogen peroxide.[5] The alcohol product was isolated and analyzed by glpc.

In our earlier study of *p*-methoxystyrene and *p*-chlorostyrene we had available only the α alcohols. Consequently, the analysis reported involved the assumption that the thermal conductivities of the substituted α- and β-phenylethyl alcohols were the same. In the present more extensive study, nearly all of the isomeric alcohols were synthesized, isolated, and utilized for standardization of the analytical procedure. We also improved the glpc procedure to give symmetrical, well-resolved peaks. Consequently, we believe the present results are more precise.

It has been reported that the hydroboration of styrene produces a 12:88 distribution of the α and β alcohols,[6] rather than the 20:80 distribution reported earlier.[3] Moreover, our preliminary results indicated the formation of 27% of the α isomer in the hydroboration of *p*-chlorostyrene, instead of the 35% noted earlier.[3] Consequently, we undertook to test the reproducibility of the procedure and to examine the possible influence of variations in the hydride/styrene ratios on the observed isomer distributions. The results are reported in Table I.

Since the results revealed no significant change in the distribution of the boron with these variations in the amount of hydride used, we adopted the use of a slight excess, 10%, of sodium borohydride for the standard hydroborating procedure.

In a number of cases an internal standard was added to the ether extract prior to the glpc analysis. In other cases the products were compared with external standards. Yields of recovered alcohols of between 87 to 93% were indicated. Consequently, we have assumed that all yields are in this range and have normalized the analytical results to obtain the reported distributions.

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[1] Based upon a thesis submitted by R. L. Sharp in 1966 to the faculty of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] Graduate research assistant on a research grant (5ROI-GM-10937) supported by the National Institutes of Health.

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

[4] The use of a more hindered hydroborating agent, disiamylborane, directs the entering boron atom to the terminal position in 98 to 99% distribution: H. C. Brown and G. Zweifel, *ibid.*, **83**, 1241 (1961).

[5] Numerous studies in this laboratory have shown that this oxidation is essentially quantitative, proceeding to replace each boron–carbon bond by a hydroxyl group. These experiments will soon be reported in a manuscript under preparation with B. C. Subba Rao, C. H. Snyder, and G. Zweifel.

[6] D. J. Pasto and C. C. Cumbo, *J. Am. Chem. Soc.*, **86**, 4343 (1964). Recently, it has been reported that styrene yields (25°) 16% 1-phenyl- and 69% 2-phenylethanol, which normalizes to a 19:81 distribution: D. J. Pasto, C. C. Cumbo, and P. Balasubramaniyan, *ibid.*, **88**, 2187 (1966).

Styrene was hydroborated five successive times using this standard procedure. The results indicated 19% α and 81% β, in excellent agreement with the 20:80 distribution reported earlier.[3]

Table I. Effect of the Olefin/Hydride on the Isomer Distribution Realized during the Hydroboration–Oxidation of Styrene and *p*-Chlorostyrene

Ratio olefin: hydride	Styrene,[a] % α	α-Chlorostyrene,[a] % α
50:40	17.3	25.4
50:50	17.7	24.4
50:60	17.2	25.2
50:70	17.3	25.8
Mean	17.4 ± 0.2	25.1 ± 0.4

[a] These values are the normalized values for the α and β alcohols obtained. They differ slightly from the values reported in Table II which are corrected for a small amount of hydrolysis of the α-boron derivative during the oxidation stage. See later discussion.

We observed the formation of minor amounts of ethylbenzene and its derivatives in the hydroboration–oxidation of styrene, and its methoxy and chloro derivatives. However, in the cases of *o*- and *p*-trifluoromethylstyrene and *m*-nitrostyrene major quantities of the corresponding ethylbenzenes appeared in the product, accompanied by a decrease in the yield of the α alcohol. Moreover, a transient reddish orange color, suggestive of the formation of a carbanionic intermediate, was observed in these oxidations.

In one experiment the hydroboration product of *p*-trifluoromethylstyrene was treated with the usual quantity of base and the reaction mixture maintained at 20°. Only small quantities of the ethylbenzene were produced in 1 hr. However, at 50° the concentration of the ethylbenzene increased rapidly to a constant value in a few minutes and did not change significantly in the next hour. Oxidation produced the β alcohol with only traces of the α. Since the oxidation reaction is a strongly exothermic reaction, with the temperature normally rising rapidly to the neighborhood of 50°, it is evident that in these cases hydrolysis of the α-boron derivative is competing with its oxidation.

Accordingly, in estimating the boron distribution between the α and β positions, we added to the α alcohol the observed yield of the ethylbenzene derivative.

Finally, hydroboration of *p*-nitrostyrene gave results which did not permit any definite conclusions concerning the directive influence of the *p*-nitro substituent. The data indicate that the reaction in this case is quite complicated, with competing reactions taking place. Thus, treatment of *p*-nitrostyrene with the usual 10 to 20% excess of hydroborating agent does not result in the usual full utilization of the olefin. Moreover, hydrogen is slowly eliminated throughout the hydroboration. These observations suggest that the rate of the hydroboration reaction is relatively slow and that the initial reaction product is capable of reacting competitively with the hydroborating agent to liberate hydrogen, possibly through the relatively acidic hydrogen in the α position. Accordingly, we deferred further study of this complex system.

The experimental results are summarized in Table II.

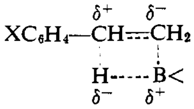
Table II. Directive Effects in the Hydroboration of Substituted Styrenes

X in XC_6H_4-$CH{=}CH_2$	Product yields, % α-ol			Boron distribution, %	
	α-ol	β-ol	XC_6H_4-C_2H_5	α[a]	β
o-CH_3O	12.0	86.0	1.6	14	86
m-CH_3O	17.8	80.8	1.4	19	81
p-CH_3O	5.4	93.3	1.2	7	93
H	17.9	80.8	1.3	19	81
o-Cl	23.1	74.2	2.7	26	74
m-Cl	27.6	70.1	2.2	30	70
p-Cl	24.9	73.4	1.7	27	73
o-CF_3	12.7	61.8	25.5	38	62
m-CF_3	29.9	67.7	2.4	32	68
p-CF_3	11.9	65.8	22.2	34	66
m-NO_2	14.6	63.0	22.4	37	63

[a] Based on assumption that the ethylbenzene product arises from the alkaline hydrolysis of the α-boron derivative.

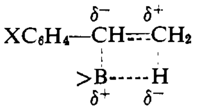
Discussion

All of the available evidence indicates that the addition of the boron–hydrogen moiety to olefins involves a four-centered transition state.[3,7] It follows that the effect of the substituent on the direction of the addition will be determined by its influence in stabilizing the two possible transition states, II and III.



$$\begin{array}{lcc} & \delta^+ & \delta^- \\ \mathrm{XC_6H_4{-}} & \mathrm{CH}\cdots & \mathrm{CH_2} \\ & \vdots & \vdots \\ & \mathrm{H}\cdots\cdots & \mathrm{B}< \\ & \delta^- & \delta^+ \end{array}$$

II



$$\begin{array}{lcc} & \delta^- & \delta^+ \\ \mathrm{XC_6H_4{-}} & \mathrm{CH}\cdots & \mathrm{CH_2} \\ & \vdots & \vdots \\ & >\mathrm{B}\cdots\cdots & \mathrm{H} \\ & \delta^+ & \delta^- \end{array}$$

III

A group with a powerful electron-withdrawing effect should favor transition state III relatively, resulting in increased α addition of boron. On the contrary, a group with a powerful electron-supplying effect would be expected to favor transition state II, causing decreased addition of boron to the α position.

Thus, the marked effect of the *p*-methoxy group in decreasing the amount of α addition, 7%, over that observed in styrene itself, 19%, is in accord with the usual observation that the +R influence of the *p*-methoxy substituent far outweighs its −I effect. Similarly, the distribution observed in *m*-methoxystyrene, 19% α, is in agreement with the usual observation that the *m*-methoxy substituent has no significant electron-supplying or electron-withdrawing effect. Finally, in the *ortho* position, the larger −I effect of the substituent tends to reduce the net electron supply, resulting in an intermediate value, 14% α.

It is of interest that the effects of the methoxy substituents in this hydroboration reaction parallels qualitatively their effects on the rates of solvolysis of the corresponding *t*-cumyl chlorides.[8]

In the case of the chlorine substituent, the −I effect far outweighs its +R influence. Consequently, the effect of the substituent is to stabilize transition state III, resulting in an increase in the boron appearing in the α position: *p*-chloro, 27% α; *m*-chloro, 30% α; *o*-chloro, 26% α. Presumably, the smaller yield of α in the *para* derivative as compared to *meta* is the combined result of a small resonance contribution in the *para* and a larger inductive effect in the *meta*. We might have anticipated a larger inductive effect for *o*-chloro,

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(7) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 2544 (1961).

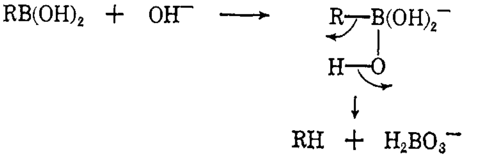
(8) H. C. Brown and T. Okamoto, *ibid.*, **79**, 1910 (1957).

leading to a modest increase in the α product. However, the observed yield, 26%, reveals not an increase, but a slight decrease over the 27% observed for the *para* isomer. Possibly a small steric effect is responsible.

The influence of the trifluoromethyl substituent is even more powerful: *p*- 34% α; *m*-, 32% α; *o*-, 38% α. However, the largest effect is exhibited by *m*-nitro: 37% α.

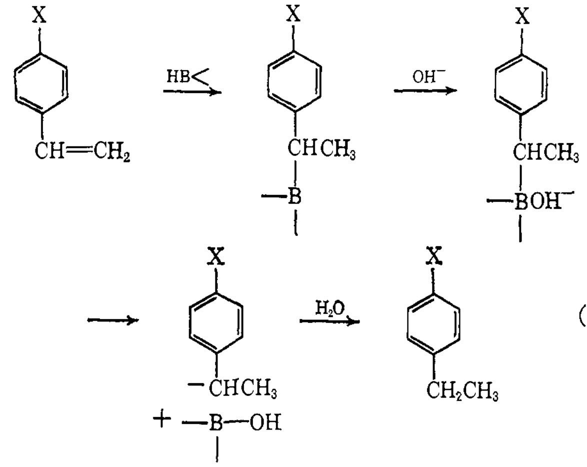
Again, it is of interest to point out that the effect of these substituents in influencing the direction of the hydroboration reaction parallels qualitatively their σ^+ values.[9] Indeed, a plot of log (k_β/k_α) against σ^+ reveals a reasonably good linear relationship (Figure 1).[10] Consequently, the results indicate that the hydroboration reaction involves an electrophilic attack by borane (and subsequent intermediates) on the styrene system.

It may be appropriate to comment on the unexpected large formation of substituted ethylbenzenes during the hydroboration–oxidation of *o*- and *p*-trifluoromethyl- and *m*-nitrostyrene. It has been observed previously that organoboranes of the benzylic type are susceptible to hydrolysis under the influence of alkali under remarkably mild conditions.[11] It was suggested that the mechanism (1) involved is of the SEi type in order to account for the high degree of stereoselectivity (retention) observed.



$$RB(OH)_2 + OH^- \longrightarrow R\!-\!B(OH)_2^- \,(\text{H–O}) \longrightarrow RH + H_2BO_3^- \qquad (1)$$

It is possible that the base-catalyzed deboronation observed during the oxidation of the organoboranes from *o*- and *p*-trifluoromethylstyrene may involve an intermediate which possesses more carbanionic character than that proposed by Weinheimer and Marsico. Certainly, the transient reddish orange color observed during the hydrolysis–oxidation stage may be indicative of the formation of a carbanionic intermediate. On this basis the mechanism would be that represented by (2).



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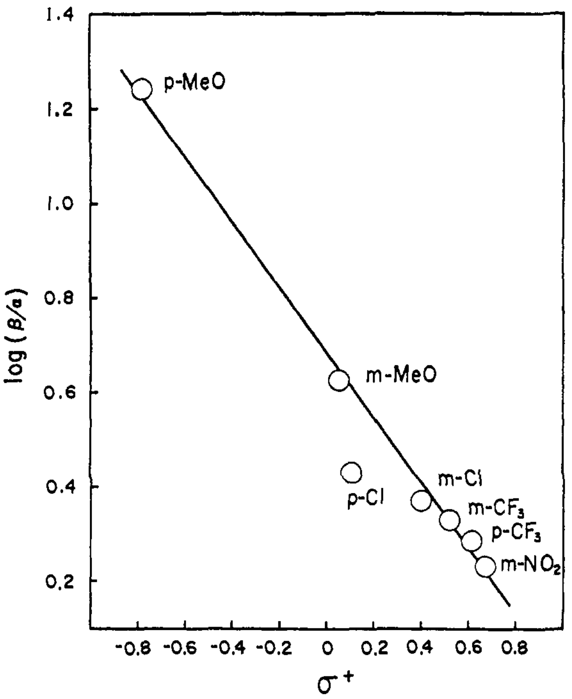
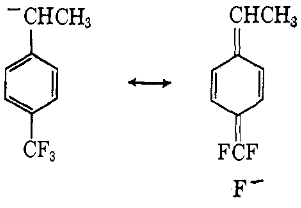


Figure 1. Linear free energy relationship between the ratios of β to α products in the hydroboration of substituted styrenes and the σ^+ constants.

The marked difference in the amount of hydrolysis product found in the standard oxidation procedure, 25.5% *o*- and 22.2% *p*-, as compared to 2.4% *m*-trifluoromethylethylbenzene, is surprising at first sight. This suggests that resonance contributions from mechanisms such as eq 3 (structure IV) may be quite important in stabilizing the carbanionic intermediate.[12,13]



(3)

IV

In the case of these substituted styrenes, the formation of two isomers in comparable amounts can be a difficulty in utilizing the hydroboration reaction for synthetic purposes. Fortunately, it is possible to circumvent the formation of the α isomer by utilizing disiamylborane for such hydroborations.[4] Alternatively, the α isomer can be selectively hydrolyzed prior to the oxidation.

Actually, we were interested in exploring these directive effects in the styrene derivatives primarily as a prelude to our related study of the hydroboration of related vinyl derivatives, RCH=CHX.[1,6] In these cases we also observe large directive effects of the substituent, X, but the interpretation is complicated by the necessity to consider both the electronic and the steric influences of the substituent in accounting for the results. However, we may point out that in these compounds we observe very similar, albeit greatly

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[9] H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958).

[10] The authors are indebted to Professor D. J. Pasto of Notre Dame University for pointing out the good fit realized in such a plot.

[11] A. J. Weinheimer and W. E. Marsico, *J. Org. Chem.*, **27**, 1926 (1962). Base-catalyzed deboronations in which heteroatoms are bonded to the carbon-bearing boron have been observed or postulated in a number of instances: H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 3834 (1961); D. J. Pasto and J. L. Miesel, *ibid.*, **85**, 2118 (1963); D. J. Pasto and C. C. Cumbo, *ibid.*, **86**, 4343 (1964).

[12] J. D. Roberts, R. C. Webb, and E. A. McElhill, *ibid.*, **72**, 408 (1950).

[13] R. G. Jones, *ibid.*, **69**, 2346 (1947).

Table III. Physical Properties of Substituted Styrenes

	Observed constants		Reported constants		
	Bp, °C (mm)	n^{20}D	Bp, °C (mm)	$n^{t,\,°C}$D	Ref
o-Trifluoromethylstyrene	49.5 (13)	1.4703	61 (40)	1.4677^{25}	*a*
m-Trifluoromethylstyrene	61–62 (23)	1.4658	64.5 (40)	1.4632^{25}	*a*
p-Trifluoromethylstyrene	69.4 (27)	1.4670	65.8 (40)	1.4648^{25}	*a*
o-Methoxystyrene	84.0 (9.5)	1.5622	61–62 (3)	1.5608^{20}	*b*
m-Methoxystyrene	71–72 (5)	1.5559[c]	89 (14)	1.5540^{20}	*d*
p-Methoxystyrene	90.0 (12)	1.5594	92–93 (13)	1.5608^{20}	*d*
o-Chlorostyrene	*e*	1.5650	58–59 (7)	1.5641^{20}	*f*
m-Chlorostyrene	*e*	1.5632	57.5 (10)	1.5630^{20}	*f*
p-Chlorostyrene	79.0 (32)	1.5651	60–62 (6.5)	1.5650^{20}	*f*
m-Nitrostyrene	*g*	1.5836	. . .	1.5838^{20}	*h*
p-Nitrostyrene	20.1–20.9[i]	. . .	19.5–20.5[i]	. . .	*h*

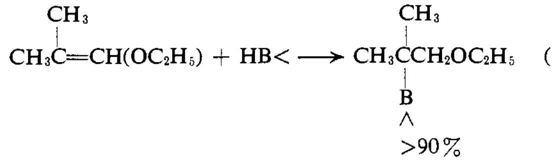
[a] A. B. Conciatori and J. Kraus, *J. Am. Chem. Soc.*, **72,** 2283 (1950). [b] C. S. Marvel and D. W. Heim, *ibid.*, **70,** 1895 (1948). [c] At 21°. [d] R. L. Frank, C. E. Adams, R.E. Allen, R. Gander, and P. U. Smith, *J. Am. Chem. Soc.*, **68,** 1365 (1946). [e] Monomer Polymer Co., purified by gas chromatography. [f] C. Walling and K. B. Wolfstirn, *J. Am. Chem. Soc.*, **69,** 852 (1947). [g] Aldrich Chemical Co. [h] E. L. Eliel, A. H. Goldkamp, L. E. Carosino, and M. Eberhardt, *J. Org. Chem.*, **26,** 5188 (1961). [i] Melting point.

Table IV. Physical Properties of Starting Materials and Intermediates for the Preparation of Substituted Styrenes

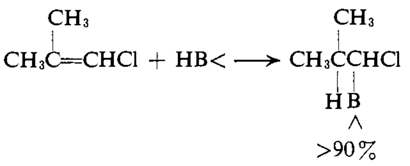
	Observed constants		Reported constants		
Compound	Bp, °C (mm)	n^{20}D	Bp, °C (mm)	$n^{t,\,°C}$D	Ref
o-Bromobenzotrifluoride[a]	. . .	1.4827	67–69 (28)	1.481^{27}	*b*
m-Bromobenzotrifluoride[a]	. . .	1.4727	155 (740)	1.4712	*b*
p-Bromobenzotrifluoride[a]	. . .	1.4731	154–155	1.4705^{25}	*c*
α-(*o*-Trifluoromethylphenyl)ethanol	82 (10)	1.4646	82 (10)	1.4623^{25}	*d*
α-(*m*-Trifluoromethylphenyl)ethanol	70–71 (1)	1.4583	101 (17)	1.4585	*d*
α-(*p*-Trifluoromethylphenyl)ethanol	94 (9)	1.4595	92.5 (10)	1.4578^{25}	*d*
o-Methoxyacetophenone[e]	118 (10.5)	1.5412	126 (4)	$1.5390^{20.5}$	*f*
m-Methoxyacetophenone[e]	125 (15)	1.5400	152 (38)	$1.5430^{15.4}$	*f*
α-(*o*-Methoxyphenyl)ethanol	86–87 (1)	1.5355	124 (13)	1.5390	*g*
α-(*m*-Methoxyphenyl)ethanol	127 (8)	1.5338	133 (14.5)	1.5343	*h*
p-Bromochlorobenzene	65.3–67.2[i]	. . .	67[i]	. . .	*j*
α-(*p*-Chlorophenyl)ethanol	102–104 (3)	1.5416	85 (1)	1.5420	*k*

[a] Pierce Chemical Co. [b] Corning Glass Works, U. S. Patent 2,494,817 (1950). [c] P. Tarrant and M. R. Lilyquist, *J. Am. Chem. Soc.*, **75,** 3034 (1953). [d] A. B. Conciatori, Ph.D. Thesis, University of Cincinnati, 1949. [e] Aldrich Chemical Co. [f] "Dictionary of Organic Compounds," Vol. III, Oxford University Press, New York, N. Y., 1965, p 1639. [g] D. E. Pearson and W. E. Cole, *J. Org. Chem.*, **20,** 488 (1955). [h] E. Stedman, *J. Chem. Soc.*, 611 (1929). [i] Melting point. [j] Footnote *f*, Vol. I, p 428. [k] C. G. Overberger, *et al.*, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p 200.

magnified directive influences, which possess promising possibilities for synthetic applications (eq 4 and 5).



$$CH_3\overset{CH_3}{\overset{|}{C}}{=}CH(OC_2H_5) + HB< \longrightarrow CH_3\overset{CH_3}{\underset{\substack{|\\B\\\wedge\\>90\%}}{C}}CH_2OC_2H_5 \quad (4)$$



$$CH_3\overset{CH_3}{\overset{|}{C}}{=}CHCl + HB< \longrightarrow CH_3\overset{CH_3}{\underset{\substack{|\\H}}{C}}\underset{\substack{|\\B\\\wedge\\>90\%}}{C}HCl \quad (5)$$

These results will be reported shortly.

Experimental Section

Materials. Tetrahydrofuran and diglyme were purified by distillation from lithium aluminum hydride, the distillation being under vacuum for diglyme. Ethyl ether (Mallinkrodt Chemical Company) and sodium borohydride (Metal Hydrides Inc.) were used without further purification. Boron trifluoride etherate was purified by distillation under vacuum from calcium hydride.

The source of the substituted styrenes used, their specific purities, and refractive indices are summarized in Table III.

In the great majority of cases, the alcohol products were identified by comparison of gas chromatographic retention times with authentic samples of the two isomeric alcohols. In a few instances we were content to identify only one of the two peaks. The ethylbenzene derivatives were produced by hydrogenation of the corresponding styrene derivatives utilizing the Brown procedure.[14] Table IV lists the physical properties of starting materials and intermediates used in the preparation of the substituted styrenes.

Hydroboration Procedure. In a dry, three-necked flask, equipped with a condenser, a thermometer, and a pressure-equilibrated dropping funnel were placed 50 mmoles of the olefin and 28 ml of a 0.5 *M* solution of sodium borohydride in diglyme. The flask was immersed in a water bath at 20°. Boron trifluoride etherate, 18.8 mmoles, diluted with 5.0 ml of diglyme was added over a period of 20 min to the well-stirred reaction mixture. After an additional hour at 20°, the flask was immersed in an ice bath; 5 ml of water was added to destroy residual hydride, and the reaction mixture was oxidized by adding 5.3 ml of 3 *N* sodium hydroxide and then slowly adding 5.3 ml of 30% hydrogen peroxide. Care was taken to maintain the solution slightly alkaline (pH 8). After stirring for 1 hr, the solution was poured into water, and the alcohols formed were extracted with ether (three 50-ml portions). The combined ether extracts were washed with a small quantity of saturated sodium bicarbonate solution; the ether layer was separated and dried over anhydrous magnesium sulfate.

The solution was analyzed by gas chromatography (F & M Model 500 chromatograph with a Brown 1-mv recorder fitted with a disk integrator), comparing the peaks with those of authentic samples. These samples were: (1) commercial products, (2) synthesized *via* the Grignard reaction, (3) synthesized by reduction of the ketones. Since all are known, well-characterized compounds, details of their preparation and purification are not included. The thesis should be consulted for such details.

In a representative number of cases the material balance of the reaction was determined by adding a suitable standard to the ether extracts. In other cases the ether extracts were compared with external standard solutions of the products. Yields of 87 to 93% were indicated. In a number of cases we prepared synthetic mixtures and established that we could reproduce their composition to ±1%.

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(14) H. C. Brown and C. A. Brown, *J. Am. Chem. Soc.*, **84,** 2827 (1962).