g, 44.8% (8 mm), mp 94–95°[10] alone and when mixed with an authentic sample] and 5.7 g of material, bp 108–125° (20 mm), which appeared to consist of propiophenone and its self-condensed products.

Registry No.—Phenyllithium, 591-51-5; propiophenone, 93-55-0; propiophenone 2,4-dinitrophenylhydrazone, 3375-37-9; diphenylethylcarbinol, 5180-33-6; *n*-butyrophenone, 495-40-9; diphenyl-*n*-propylcarbinol, 5331-17-9; *n*-propyllithium, 2417-93-8; di-*n*-propylphenylcarbinol, 4436-96-8; methyl iodide, 74-88-4; *n*-butyl bromide, 109-65-9; phenyl bromide, 108-86-1.

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Action of Grignard Reagents on the Esters of Propiolic Acid

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When methyl propiolate (1) was treated with an excess of ethylmagnesium bromide, no ethane was evolved and the expected tertiary alcohol, diethylethinylcarbinol, was obtained in only 10% yield. The primary reaction product proved to be an unsaturated 3,4-epoxy ester (2) whose formation required two alkyl groups, *, from the Grignard reagent and a third, x, from a second mole of the original ester. Catalytic hydrogenation yielded the saturated analog (5) which upon mild hydrolysis underwent simultaneous loss of carbon dioxide and fissure of the epoxide ring to form an identifiable ethyl ketone (8). Several combinations of Grignards and esters were employed to show in each case analogous reaction products. A mechanism to account for the products obtained is presented.

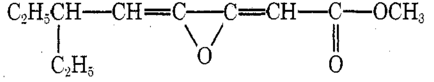
The investigation presented in this paper originated from the observation that methyl propiolate (1), HC≡C-COOCH$_3$, on treatment with methylmagnesium iodide in the Zerevitinov machine yielded no methane but did undergo a vigorous reaction which consumed 3 mol of Grignard reagent. The failure to form methane was particularly puzzling since the acidity of the acetylenic hydrogen is increased by its conjugation with the carbomethoxy group to such an extent that it not only forms a silver and copper salt, but also undergoes Claisen condensation with ethyl oxalate and Michael condensation with ethyl fumarate.[1]

Addition of Grignard reagents of higher molecular weight such as phenyl-, naphthyl-, or triphenylvinylmagnesium bromide[2] and the reagent prepared by the action of phenylmagnesium bromide on α-bromo-β-phenylbenzalacetophenone[3] produced immediate and vigorous reaction, but decomposition of the reaction mixtures yielded only heavy, intractable oils. Gilman and Robinson[4] reported similar difficulties when they added phenylmagnesium bromide to the ethyl ester of acetylenedicarboxylic acid.

The action of lighter Grignards such as methyl- and ethylmagnesium bromide on methyl propiolate yielded distillable oils from which definite compounds could be obtained by fractionation under vacuum. Thus, when methyl propiolate (1) was added to an excess of ethylmagnesium bromide, two pure liquids were isolated from the reaction mixture.

The first, a colorless, low-boiling oil, was identified as diethylethinylcarbinol through the formation of a silver salt and by catalytic hydrogenation to the known triethylcarbinol. The acetylenic alcohol was present only to the extent of 8–10% and its formation may be regarded as a secondary reaction in which the Grignard reagent undergoes the expected 1,2 addition to the ester carbonyl.

The primary reaction product 2, a pale yellow oil, was shown by analytical methods to be dimolecular product of empirical formula C$_{11}$H$_{16}$O$_3$, containing one methoxy group. All tests for the functional groups -HC=O, >C=O, and HC≡C- were negative, but catalytic hydrogenation consumed 2 mol of hydrogen, indicating the presence of two double bonds or one triple bond of the type RC≡CR.



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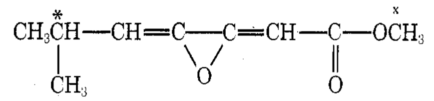

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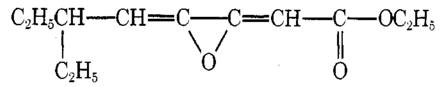

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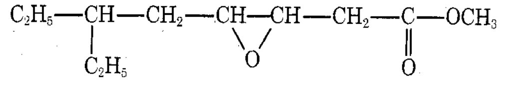
The reduction product 5, a colorless oil of empirical formula C$_{11}$H$_{20}$O$_3$, distilled without decomposition under vacuum. Because of its greater physical and chemical stability it was selected to elucidate the ultimate structure of 2. The reduction product 5 contained one methoxyl group, formed a crystalline amide, C$_{10}$H$_{19}$O$_2$N, with concentrated ammonia, and gave no test for aldehydic or ketonic carbonyl groups. In the Zerevitinov machine no gas was evolved but 2 mol of Grignard was consumed.



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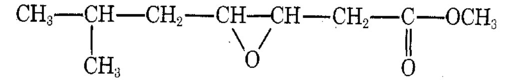

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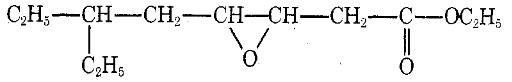

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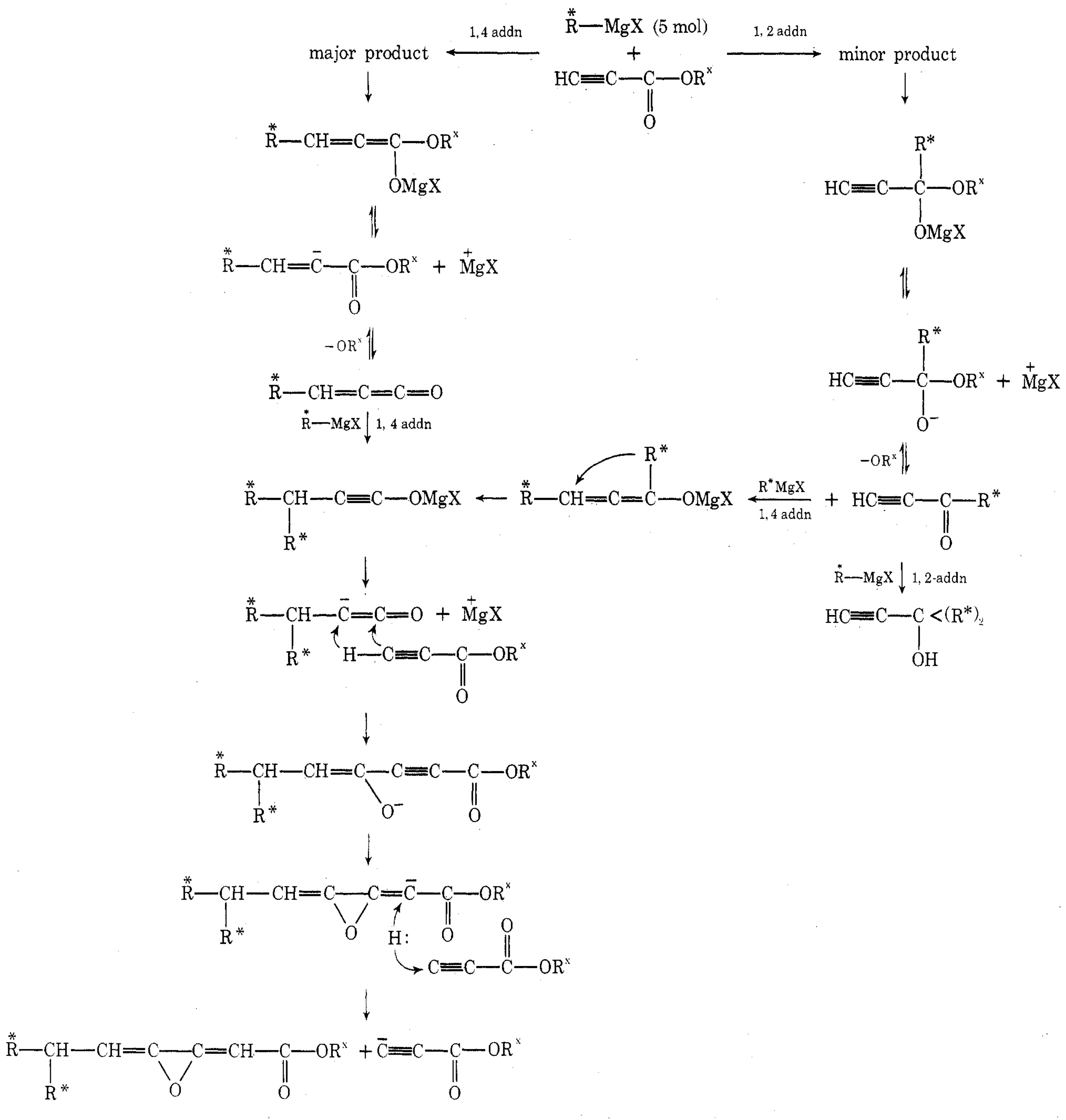
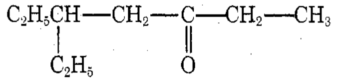
Scheme I



The above facts indicate strongly that two of the three oxygens were present in the form of the original ester group, which accordingly must be involved in the dimerization. The third oxygen was best represented by some form of ether linkage. On treatment with warm, 3% methyl alcoholic potassium hydroxide the ester linkage was readily saponified, but the saponification was accompanied by a simultaneous loss of carbon dioxide by the acid and fissure of the ether linkage to form a ketone, a reaction characteristic of epoxy esters. The presence of the 3,4-epoxy ring was confirmed by infrared spectra (Experimental Section). The ketone 8 was shown to be 5-ethyl-3-heptanone by comparing its semicarbazone with an authentic sample synthesized previously.[5] The formation of an ethyl ketone leads further support to the final structure as a 3,4- rather than a 2,3-epoxy ester.

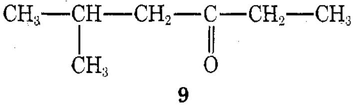
Important information on the course of the reaction and the structures of the major reaction products was obtained by using several combinations of alkyl groups in the esters and Grignard reagents employed. Thus a methyl ester and an ethyl Grignard yielded **2**, two methyls yielded **3**, and two ethyls produced **4**. The above structures indicate that the two alkyls introduced at point ∗ originate from the Grignard employed while the third, x, is from the original ester.

Catalytic hydrogenation of **2**, **3**, and **4** yields the saturated epoxy esters **5**, **6**, and **7**, which in turn can be saponified to yield one of two ethyl ketones, **8** or **9**, formed through a



$\underset{C_2H_5}{\underset{|}{C_2H_5CH}}-CH_2-\underset{O}{\underset{\|}{C}}-CH_2-CH_3$

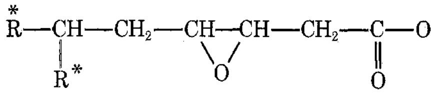
8



$CH_3-\underset{CH_3}{\underset{|}{CH}}-CH_2-\underset{O}{\underset{\|}{C}}-CH_2-CH_3$

9

simultaneous decarboxylation of the acid and fissure of the epoxide ring. A mechanism for arriving at the general formula **10** for the epoxy esters is presented in Scheme I.



$$\overset{*}{R}-\underset{\underset{R^*}{|}}{CH}-CH_2-\underset{\diagdown O \diagup}{CH-CH}-CH_2-\underset{\underset{O}{\|}}{C}-O\overset{x}{R},$$

10

The 1,4 addition of the Grignard to the conjugated system in propiolic esters is not surprising. There is no hindrance at all in the 4 position and covering up the acetylenic hydrogen, HC≡C–, would account for the lack of gas (methane or ethane) in the Grignard reaction. Formation of a carbanion and loss of the ester alkoxyl would yield an allene–ketene system which could react either 1,2 or 1,4 with the Grignard reagent. Again the 1,4 addition is preferred, this time because the requirement of two Grignard alkyls on carbon 4 is met and because allenes readily rearrange to alkynes as shown. Note also that this same intermediate containing the two required alkyl groups can also be obtained from the minor reaction products by 1,4 addition of the Grignard to the ethinyl ketone followed by a 1,3 shift of the alkyl group to give the more stable alkyne.

At this point dimerization with 1 mol of the original ester would satisfy the analytical data found for the unsaturated epoxy esters. Addition of the ester to the carbanion is illustrated followed by cyclization to form the 3,4-epoxy ester. The two double bonds are conjugated and the carbanion produced can be satisfied by the acetylenic hydrogen from yet another mole of ester. This would also account for the fact that some unchanged ester may be found at the end of the reaction, even in the presence of a large excess of Grignard reagent.

Experimental Section

Propiolic Acid. The acid was prepared by treating dibromosuccinic acid[6] (500 g) dissolved in 1200 ml of hot, 95% ethanol with a solution of 550 g of KOH in 2000 ml of 95% ethanol,[7] a modification of the original procedure of Perkin and Simonsen.[8] The purified product boiled at 62° (20 mm) with a yield of 15–18 g per 100 g of dibromosuccinic acid used.

Esterification of Propiolic Acid.[9] Direct esterification of propiolic acid by the acid-catalyzed reaction between organic acid and alcohol was complicated by the reactivity of the triple bond which resulted in very low yields (below 40%). Satisfactory yields of 55–65% could be obtained, however, by treating equal weights of propiolic acid and concentrated H_2SO_4 with a large excess of the required alcohol under refluxing conditions for 1 hr. Thus, 129 g of propiolic acid added to a mixture of 129 g of concentrated H_2SO_4 in 500 ml of absolute methanol yielded 85 g (56%) of methyl propiolate (**1**), bp 100–102°.

Grignard Reaction. The usual precautions for preparing Grignard reagents were employed including an atmosphere of dry nitrogen to prevent oxidation, 5.0 mol of Grignard per mole of ester in order to ensure an excess of Grignard, and an ice bath to cool the strongly exothermic reaction with the ester. The dried ($MgSO_4$) ether extracts, highly colored owing to polymerization, were concentrated via a long fractionating column to prevent loss of the volatile acetylenic tertiary alcohols. Heating was discontinued when the temperature reacted 65°. The residue weighed 70–80 g and still contained some ether.

This crude reaction product was next subjected to slow sublimation in an all-glass apparatus connected through a series of traps to a source of high vacuum (10^{-4} mm or better). A simple system employed a 250-ml round-bottom short-necked flask for the sublimation and two or more 500-ml two-neck round-bottom short-necked flasks for the receiving traps. The former was heated with a water bath and the latter could be cooled successively with Dry Ice in acetone. The flasks were connected through their 24/40 ₮ joints by inverted U tubes constructed of 30-mm Pyrex tubing. After several sublimations the residue contained about 15 g of black tar and the sublimate about 50 g of a pale yellow oil. Refractionation of the sublimate under vacuum at 2 mm with Mini-Lab equipment yielded 8–10 g of the acetylenic alcohol and 20–25 g of the glycidic ester plus a small amount of tar.

Catalytic Hydrogenation. General Procedure. The unsaturated materials (2.0–15.0 g) (ethinyl carbinols or unsaturated epoxy esters) were dissolved in 20–50 ml of absolute methanol containing 0.05–0.15 g of platinum oxide (Adams catalyst) and reduced (20–30 min) in a Parr low-pressure hydrogenator pressurized to 30 psi. The reaction mixture was filtered to remove the catalyst, poured into ice water to remove the methanol, extracted with ether, washed (H_2O), dried (Na_2SO_4), and repeatedly fractionated to produce colorless oils suitable for analysis.

Saponification of the 3,4-Epoxy Esters. General Procedure. The saturated 3,4-epoxy esters (5.0–10.0 g) were added to 150 ml of absolute methanol containing 6.0 g of KOH. Saponification was complete after 40 min of refluxing and a quantitative yield of K_2CO_3, formed by the loss of CO_2 from the acid, usually precipitated in the form of small white needles. The reaction mixture was poured into ice water, extracted with ether, washed (H_2O), and dried (Na_2SO_4) in the usual manner to yield the ethyl ketones as colorless oils which were carefully fractionated.

Characterization of Grignard Reaction Products. Methyl 3,4-epoxy-6-ethyl-2,4-octadienoate (**2**): bp 75–76° (2 mm); ir (CCl_4) 1740 (ester CO), 1590 (conjugated C=C), 1225 (epoxy CO), 1140, 1035 (ester CO), 870 cm^{-1} (epoxy CO).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.34; H, 8.16; OCH_3, 15.8; mol wt, 196. Found: C, 67.30; H, 8.40; OCH_3, 16.7; mol wt, 192 (benzene).

Methyl 3,4-epoxy-6-ethyloctanoate (**5**): bp 76–78° (2 mm), 125–127° (26 mm), 133–135° (38 mm); $n^{20}D$ 1.4413; $d^{20}{}_4$ 0.956; ir (CCl_4) 1740 (ester CO), 1225 (epoxy CO), 1140, 1035 (ester CO), 830 cm^{-1} (epoxy CO).

Anal. Calcd for $C_{11}H_{20}O_3$: C, 66.00; H, 10.00; OCH_3, 15.5; MD, 54.1. Found: C, 66.20; H, 10.20; OCH_3, 14.5; MD, 54.27.

Amide of **5** above, mp 152.5–153.0°.

Anal. Calcd for $C_{10}H_{19}O_2N$: C, 64.84; H, 10.34. Found: C, 64.70; H, 10.20.

5-Ethyl-3-heptanone (**8**): bp 70–72° (17 mm), 171–173° (1 atm); $n^{20}D$ 1.4240 (synthetic sample, 1.4237).

Semicarbazone of **8** above, mp 133–134°; it was identical with a synthetic sample[5] by mixture melting point.

Anal. Calcd for $C_{10}H_{21}ON_3$: C, 60.30; H, 10.60. Found: C, 60.30; H, 10.80.

Methyl 3,4-epoxy-6-methyl-2,4-heptadienoate (**3**): bp 61–63° (2 mm), 116–118° (40 mm); ir (CCl_4) 1740 (ester CO), 1610 (conjugated C=C), 1225 (epoxy CO), 1145, 1015 (ester CO), 860 cm^{-1} (epoxy CO).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.22; H, 7.14; OCH_3, 18.4; mol wt, 168. Found: C, 64.08; H, 7.28; OCH_3, 17.9; mol wt, 164 (benzene).

Methyl 3,4-epoxy-6-methylheptanoate (**6**): bp 65° (2 mm), 116–118° (40 mm); $n^{20}D$ 1.4341; $d^{20}{}_4$ 0.947; ir (CCl_4) 1740 (ester CO), 1230 (epoxy CO), 1145, 1030 (ester CO), 843 cm^{-1} (epoxy CO).

Anal. Calcd for $C_9H_{16}O_3$: C, 62.78; H, 9.30; OCH_3, 18.0 MD, 44.86. Found: C, 63.20; H, 9.60; OCH_3, 17.6; MD, 46.30.

5-Methyl-3-hexanone (**9**), bp 135–137° (1 atm).

Semicarbazone of **9** above, mp 149–150°; it was identical with a synthetic sample[5] by mixture melting point.

Ethyl 3,4-epoxy-6-ethyl-2,4-octadienoate (**4**): bp 75–76° (2 mm); ir (CCl_4) 1740 (ester CO), 1580 (conjugated C=C), 1230 (epoxy CO), 860 cm^{-1} (epoxy CO).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.60; H, 8.60; OC_2H_5, 21.2. Found: C, 68.80; H, 8.80; OC_2H_5, 19.0.

Ethyl 3,4-epoxy-6-ethyloctanoate (**7**): bp 76–78° (2 mm); ir (CCl_4) 1740 (ester CO), 1225 (epoxy CO), 1140, 1030 (ester CO), 825 cm^{-1} (epoxy CO).

Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.30; H, 10.40. Found: C, 67.10; H, 10.70.

The infrared spectra were obtained with a Perkin-Elmer Model 700 spectrophotometer. Samples were prepared by dissolving 100 μl in 3 ml CCl_4.

Acknowledgments. We are grateful to the National Science Foundation (Grant GY-9326) for support of this work, and to Janet Graham and Douglas Weber for technical assistance.

Registry No.—**1**, 922-67-8; **1** free acid, 471-25-0; **2**, 55058-94-1; **3**, 55058-95-2; **4**, 55058-96-3; **5**, 55058-97-4; **5** amide, 55058-98-5; **6**, 55058-99-6; **7**, 55059-00-2; **8**, 6137-18-4; **8** semicarbazone, 55059-01-3; **9**, 623-56-3; ethyl bromide, 74-96-4; dibromosuccinic acid, 526-78-3.

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(7) A 165-g portion of KOH pellets will dissolve rapidly in 600 ml of ethanol if the alcohol is placed in a glass tube (2.5 ft × 55 mm) and the alkali suspended in the upper third of the liquid. The time of solution is reduced from 6 hr (in a beaker or erlenmeyer) to 30 min in the glass tube.
(8) W. H. Perkin and J. L. Simonsen, *J. Chem. Soc.*, **91**, 833 (1907).
(9) Propiolic acid has a corrosive, blistering action on the skin. The esters are powerful lachrymators. It is essential to carry out all reactions in the hood with good ventilation and to protect the eyes and hands.

A Mild and Convenient Oxidation Procedure for the Conversion of Organoboranes to the Corresponding Alcohols[1]

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Organoboranes are oxidized efficiently by trimethylamine *N*-oxide dihydrate. The reagent is exceptionally mild, permitting the oxidation of a wide variety of functionally substituted organoboranes. In every instance the yields of product alcohol are as good as or better than the yields obtained using the standard oxidation procedure.

The oxidation of organoboranes has been utilized extensively as a convenient preparation of alcohols (eq 1).[2] In

$$R_3B \xrightarrow{\text{oxidn}} 3ROH \qquad (1)$$

fact, the hydroboration–oxidation sequence is the most efficient route for the anti-Markovnikov hydration of alkenes (eq 2).

$$RCH{=}CH_2 \xrightarrow{BH_3} \xrightarrow{\text{oxidn}} RCH_2CH_2OH \qquad (2)$$

The oxidation of organoboranes has become an increasingly important reaction as the role of organoboranes in organic synthesis has expanded.[3] One of the key features of the organoboranes is that they can be prepared containing a wide variety of functional substituents. These substituents are sometimes sensitive to the oxidation reagents, hydrogen peroxide and sodium hydroxide.[4] The presence of the strong base and oxidant can lead to undesirable side reactions.

In an attempt to minimize side reactions of functionally substituted organoboranes, researchers have resorted to modifying the standard oxidation procedure. Two modifications have been successful: the simultaneous addition of the base and peroxide[5] and the use of milder bases.[6,7] In addition alternate oxidation procedures have been explored. The alternate procedures generally utilize reagents which are inconvenient to handle, difficult to obtain, or are themselves reactive toward certain functional substituents.[8-10]

One reagent has been studied that appeared to offer promise as a mild oxidizing agent, trimethylamine *N*-oxide[11,12] (eq 3). However, anhydrous amine oxides are inconvenient to prepare and the reported procedure utilizes hydrocarbon solvents, whereas most organoboranes are formed in ethereal solvents.

$$R_3B + \overset{-}{O}{-}\overset{+}{N}R_3 \longrightarrow R_2B{-}OR + {:}NR_3 \qquad (3)$$

We now wish to report that the commercially available, easily handled, trimethylamine *N*-oxide dihydrate is an efficient reagent for organoborane oxidations. In addition the reagent will tolerate a wide variety of functional substituents and the reactions may be performed in any of the common organic solvents.

Results and Discussion

Temperature and Solvent Effects. Oxidations of organoboranes with trimethylamine *N*-oxide dihydrate (TAO) can be carried out in either hydrocarbon or ethereal solvents. The rate of the oxidations appears to be insensitive to the solvent utilized. This is presumably a consequence of the low solubility of TAO in all of the solvents used in the study.

Table I
Comparison of the Efficiencies of the Trimethylamine *N*-Oxide Dihydrate and Hydrogen Peroxide Oxidation Procedures[a,b]

Organoborane[c]	Registry no.	Product	Registry no.	Yield, %[d]	
				Amine oxide	Hydrogen peroxide
Tri-*n*-hexylborane	1188-92-7	1-Hexanol[e]	111-27-3	95	95
Tri-*n*-octylborane	3248-78-0	1-Octanol[e]	111-87-5	95	95
Tri-*sec*-butylborane	1113-78-6	2-Butanol	78-92-2	94	94
Tricyclohexylborane	1088-01-3	Cyclohexanol	108-93-0	94	92
Trinorbornylborane	14289-75-9	*exo*-Norborneol	497-37-0	100	100

[a] The amine oxide procedure was carried out by refluxing 3 equiv of trimethylamine *N*-oxide with the organoborane (1 *M* in diglyme) for 2 hr. [b] The peroxide oxidations were carried out by adding 3 equiv of hydrogen peroxide (30% aqueous solution) and 1 equiv of sodium hydroxide (3 *N*) to the organoborane (1 *M* in tetrahydrofuran) and heating to 60° for 1 hr.[4] [c] The organoborane was prepared via the hydroboration of the corresponding alkene using the standard procedures outlined in ref 4. [d] Yields determined via GLC analysis. [e] Conversion based only on tri-*n*-hexylborane and tri-*n*-octylborane.