Table I. The Controlled Reaction of Organoboranes with Oxygen to Form Alcohol

Olefin in R_3B[a]	Time, min[b]	Yield, %[c]	Isomer[d]
1-Butene	5	94	95% p, 5% s
1-Octene	5	96	95% p, 5% s
Isobutene	75	98	100% p
2-Methyl-1-pentene	75	96	
2,4,4-Trimethyl-1-pentene	75	96 (88)	
2-Butene	5	95	
Cyclopentene	5	95	
Cyclohexene	6	98 (80)	
Norbornene	6	91	14% endo[e]
1-Methylcyclopentene	7.5	99	19% cis[e]

[a] 10 mmol of R_3B. [b] Time for absorption of 1.5 mol of O_2/mol of R_3B. [c] By glpc (isolated yield in parentheses). [d] p, primary; s, secondary. [e] Oxidation with alkaline hydrogen peroxide gives 99.5% exo isomer and 100% trans isomer.[5]

anol is representative. A dry 200-ml flask equipped with a septum inlet and a magnetic stirrer with Teflon collar was flushed with nitrogen. The flask was charged with 50 ml of dry THF and 16.9 g of 2,4,4-trimethyl-1-pentene (150 mmol) and cooled to 0°. Hydroboration was achieved by the dropwise addition of 18 ml of a 2.68 *M* solution of borane in THF (150 mmol of hydride) at 0° followed by stirring at room temperature for 1 hr. The solution was cooled to 0° and the flask attached to the automatic oxygenator previously flushed with oxygen (inject 15 ml of 30% hydrogen peroxide into generator with an empty 100-ml flask in place of the reaction flask). The system was further flushed by injecting 2 ml of 30% hydrogen peroxide once the flask was in place. The stirrer was started and oxygen absorption (with the flask immersed in an ice bath) was followed by reading the buret filled with freshly standardized 30% hydrogen peroxide (a more dilute solution, 3%, was used for glpc reactions on a 10-mmol scale). After the theoretical absorption of oxygen, the flask was removed and 18 ml of 3 *N* sodium hydroxide added dropwise at 0° (exothermic reaction). The solution was stirred for 5 min, the aqueous layer was saturated (K_2CO_3), separated, and washed with diethyl ether, and the combined extracts were dried (K_2CO_3). Distillation gave 17.2 g (88%) of 2,4,4-trimethyl-1-pentanol, bp 169–170°, $n^{20}D$ 1.4263.

The controlled oxidation of organoboranes is a very clean reaction. Only minor amounts of carbonyl and hydrocarbon products were detected. All organoboranes reacted quite rapidly in the initial stages, but varied considerably in the time required to achieve the desired uptake of oxygen (1.5 mol of O_2/mol of R_3B). The reaction involving organoboranes containing secondary alkyl groups, such as tri-*sec*-butylborane, proved exceptionally fast, but could be made to proceed at a convenient rate by not displacing all of the nitrogen atmosphere. The reactions involving straight-chain primary groups, such as tri-*n*-butylborane, are slower, but even so are complete in approximately 5 min. On the other hand, organoboranes containing primary alkyl groups with a β-methyl substituent are considerably slower, the quantitative uptake of oxygen requiring 75 min for triisobutylborane and similar derivatives. We account for the essentially quantitative yields realized on the basis that the mild reaction conditions used avoid decomposition of intermediate peroxides.

The first carbon–boron bond is oxidized very rapidly by a radical-chain process (eq 1–3).[2a] This initial oxidation produces a peroxide, which may either react with a second mole of oxygen (eq 5) or may undergo an intermolecular redox reaction[9] (eq 6). The borinate

$$RO_2BR_2 + O_2 \longrightarrow (RO_2)_2BR \quad (5)$$

$$RO_2BR_2 + R_3B \longrightarrow 2ROBR_2 \quad (6)$$

ester produced may then react with oxygen (eq 7). In

$$ROBR_2 + O_2 \longrightarrow ROB(O_2R)R \quad (7)$$

any event, irrespective of the precise components present in the reaction mixture, addition of sodium hydroxide then causes the remaining carbon–boron bonds to be oxidized by the remaining peroxide linkage. This may involve either a rearrangement with displacement of the alkyl group from boron to oxygen[10] (eq 8), or by

$$HO^- + R_2BOOR \longrightarrow HOB^-(OOR)R_2 \longrightarrow HOB(OR)R + {}^-OR \quad (8)$$

hydrolysis of the alkyl peroxide followed by base-catalyzed oxidation, as with hydrogen peroxide,[5] of the carbon–boron bond by the peroxide anion.

In contrast to oxidation by alkaline hydrogen peroxide, a portion of the present reaction proceeds through alkyl radicals (eq 1). This results in some loss of the stereospecificity of the hydroboration reaction, as reported for norbornene and 1-methylcyclopentene (Table I).

These results reveal that the reaction of organoboranes with oxygen may be controlled under remarkably mild conditions to give nearly quantitative conversion to alcohol. The discovery that organoboranes may undergo such clean free-radical reactions, readily controlled for preparative requirements, opens a new area of synthetic and theoretical interest. We are continuing to explore this area.

(9) S. B. Mirviss, *J. Org. Chem.*, 32, 1713 (1967).
(10) M. H. Abraham and A. G. Davies, *J. Chem. Soc.*, 429 (1959).
(11) National Science Foundation Predoctoral Fellow.
(12) Postdoctorate research associate on Grant No. 10937 from the National Institutes of Health.

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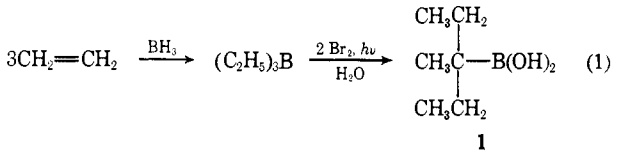
The Light-Induced Reaction of Bromine with Trialkylboranes in the Presence of Water. A Remarkably Simple Procedure for the Union of Two or Three Alkyl Groups to Produce Highly Substituted Alcohols

Sir:

Trialkylboranes undergo a rapid reaction with bromine in the presence of light to produce the corresponding α-bromoorganoboranes and hydrogen bromide. If water is present, the hydrogen bromide is absorbed and protonolysis of the α-bromo intermediate[1] is avoided. Instead, a facile rearrangement of alkyl groups from boron to carbon occurs (eq 1, 2).

(1) C. F. Lane and H. C. Brown, *J. Amer. Chem. Soc.*, 92, 7212 (1970).



(1)

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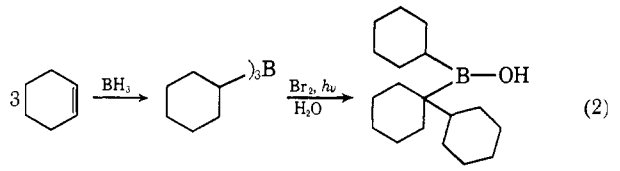

(2)

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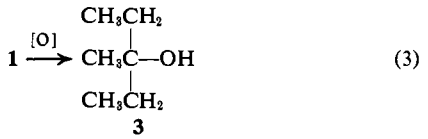
Alkaline hydrogen peroxide oxidation of these rearranged organoboranes gives the corresponding alcohols (eq 3, 4). Consequently, this development



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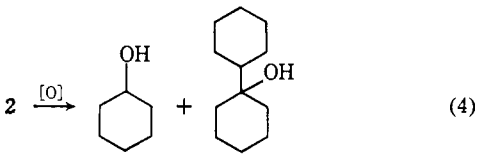

(4)

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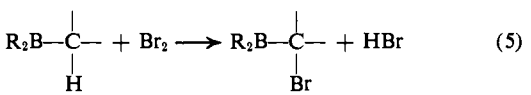
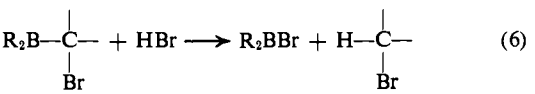
provides a new, remarkably simple procedure for the union of two or three alkyl groups to produce highly substituted alcohols.

We previously reported that the dark reaction of bromine with trialkylboranes to produce alkyl bromides appears to involve two distinct stages.[1] In the first stage there is a free-radical substitution in the α position to produce the α-bromoorganoborane and hydrogen bromide (eq 5). In the second stage the hydrogen



(5)

bromide ruptures the carbon–boron bond to produce the corresponding alkyl bromide (eq 6).



(6)

It was apparent that if the initial α bromination proceeded through a free-radical chain reaction, as originally proposed,[1] then the bromination stage should be greatly facilitated by light. Moreover, it appeared possible that by carrying out the photochemical bromination in the presence of a water phase the latter should rapidly absorb the hydrogen bromide and circumvent the protonolysis stage.

Accordingly, triethylborane (10 mmol) in 20 ml of methylene chloride was added to 10 ml of water. Then 10 mmol of bromine in 10 ml of methylene chloride was added to the reaction mixture illuminated with a 150-W incandescent light bulb.[2] Decolorization of the bromine was very fast, taking less than 5 min at 25°.[3]

(2) We later discovered that the normal lighting in the laboratory was adequate to achieve a convenient velocity for the bromination reaction.

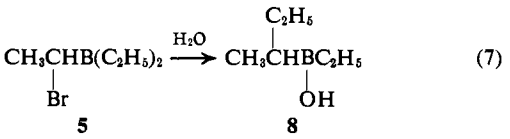
(3) This is an enormous rate enhancement over that observed for the dark reaction which required up to 24 hr for complete reaction.[1]

To our surprise, oxidation of the reaction mixture with alkaline hydrogen peroxide produced 4.4 mmol of 3-methyl-3-pentanol (**3**), a yield of 88% based on bromine. Use of 20 mmol of bromine produced 8.5 mmol of **3**, a yield of 85% based either on bromine or triethylborane.

Similarly, tri-*n*-butylborane was converted into 5-*n*-propyl-5-nonanol in a yield of 76%.

Repetition of the above bromination (10 mmol of bromine) of triethylborane (10 mmol) in the absence of the water phase also results in a rapid decolorization of the bromine (approximately 5 min). Immediate analysis by glpc indicated the presence of only a small amount of ethyl bromide. Addition of water to the reaction mixture followed by oxidation with alkaline hydrogen peroxide gave 5.2 mmol of 2-butanol, 1.8 mmol of 3-methyl-2-pentanol, and a trace amount of 3-methyl-3-pentanol (**3**).

These results are readily understood in terms of an approximately statistical bromination of the triethylborane almost exclusively in the α position[4] to give in decreasing amounts: **5** > **6** ≫ **7**.[5] The addition of water induces a rearrangement, so that oxidation produces the three alcohols (eq 7–9).



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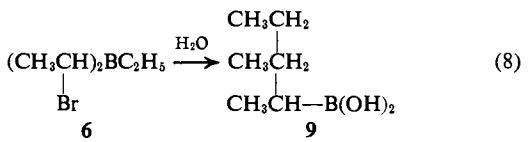

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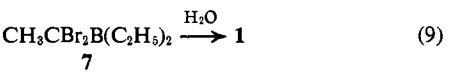

(9)

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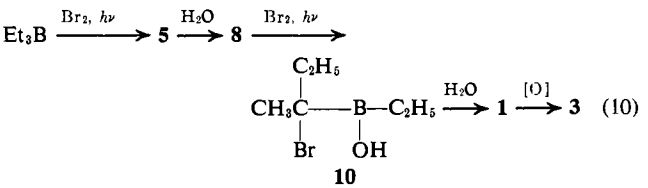
The much simpler product realized by brominating triethylborane (and similar trialkylboranes containing primary alkyl groups) in the presence of water is evidently the result of a rapid rearrangement of the initial bromination product **5** into the borinic acid **8**. The tertiary α hydrogen of the *sec*-butyl group undergoes preferential bromination (**10**). This rearranges to **1** which is oxidized to product **3** (eq 10).



(10)

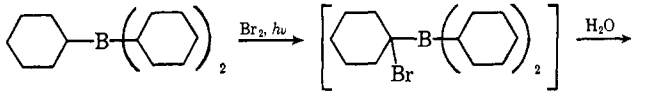
10

According to this mechanism, the bromination of trialkylboranes containing secondary alkyl groups should be particularly facile and simple. Indeed, treatment of tricyclohexylborane with an equimolar quantity of bromine by the standard procedure, fol-

(4) The remarkably active nature of the α position of these trialkylboranes toward photochemical bromination is indicated by the results realized in brominations utilizing cyclohexane as solvent. Even though the cyclohexane was present in large excess, only traces of cyclohexyl bromide could be detected. Essentially all of the bromine reacted with the organoborane in the α position to produce the product.

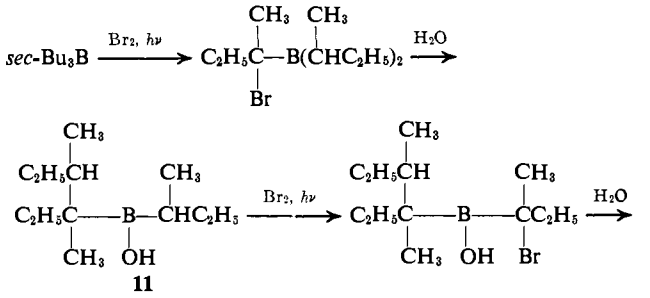
(5) The use of 20 mmol of bromine under these conditions gives **6** > **5** ≫ **7**. Oxidation produces 2.2 mmol of 2-butanol and 4.5 mmol of 3-methyl-2-pentanol.

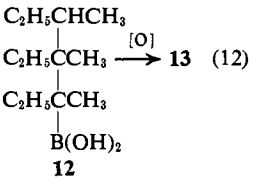
lowed by oxidation, gave an 89% yield of 1-cyclohexylcyclohexanol (**4**) (eq 11).



$$\mathbf{2} \xrightarrow{[O]} \mathbf{4} \qquad (11)$$

Similarly, tri-*sec*-butylborane is readily converted by an equimolar amount of bromine into 3,4-dimethyl-3-hexanol from oxidation of **11** in a yield of 86%. Use of 2 mol equiv of bromine produces 4-ethyl-





$$\xrightarrow{[O]} \mathbf{13} \qquad (12)$$

3,4,5-trimethyl-3-heptanol (**13**) (from oxidation of **12**) (eq 12). The results are summarized in Table I.

Table I. Dimerization and Trimerization of Olefins into Alcohols *via* Hydroboration–Bromination–Oxidation

Organoborane[a]	Bromine, mmol	Product	Yield[b] mmol	Yield[b] %
Triethylborane	10	3-Methyl-3-pentanol[d]	4.4	88[c]
Triethylborane	20	3-Methyl-3-pentanol[d]	8.5	85
Tri-*n*-butylborane	20	5-Propyl-5-nonanol[d]	7.6	76
Tri-*sec*-butylborane	10	3,4-Dimethyl-3-hexanol[d]	8.6	86
Tri-*sec*-butylborane	20	3,4-Dimethyl-3-hexanol[d]	4.4	44
		4-Ethyl-3,4,5-trimethyl-3-heptanol[e]	4.6	46
Tricyclohexylborane	10	1-Cyclohexylcyclohexanol[d]	8.9	89

[a] All reactions involve bromination of 10 mmol of R_3B in methylene chloride in the presence of a water phase. [b] By glpc analysis based on the maximum production of 1 mol of alcohol from 1 mol of R_3B, except where otherwise indicated. [c] Based on bromine used. [d] Structure assigned by comparison with an authentic sample. [e] Exhibited analytical data and spectra in accordance with assigned structure.

The lower yield realized in the case of **13** is evidently the result of a relatively sluggish migration of the bulky alkyl group in the last stage[6,7] (eq 12). Displacement of the α-bromo substituent by base appears to occur competitively. However, even yields of 50% must be considered quite satisfactory for the preparation of such highly branched structures.

Consequently, this new synthesis of carbon structures *via* α bromination of organoboranes appears to provide a convenient means of combining three molecules of a terminal olefin and either two or three molecules of an internal olefin to produce highly substituted tertiary alcohols.

(6) Removal of the water layer, followed by titration of the hydrogen bromide present, indicated that 90–94% of the calculated quantity of acid was present in all previous cases. Consequently, in these cases the alkyl transfers must have occurred prior to the treatment with sodium hydroxide and hydrogen peroxide. In the synthesis of **13**, only 28 mmol of acid was present in the aqueous phase. Only after sodium hydroxide was added did the last 10 mmol of acid appear. Consequently, in this case we believe that the transfer of the bulky alkyl group requires the base.[7]

(7) A similar reluctance to migrate has been observed for the bulky thexyl group in the carbonylation of organoboranes; see H. C. Brown and E. Negishi, *J. Amer. Chem. Soc.*, **89**, 5285 (1967).

(8) Graduate research assistant on Grant No. GM 10937 from the National Institutes of Health.

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Site-Selective Geminal Alkylation of Ketones. Reduction–Alkylation of *n*-Butylthiomethylene Derivatives

Sir:

The α alkylation of ketones is often beset by undesired side reactions including aldol condensation, uncontrollable polyalkylation, and, with unsymmetrical ketones, isomer formation.[1] A number of synthetic methods—the use of blocking groups,[1c,2] enolate trapping followed by separation and regeneration,[1b,3] and reduction–alkylation[1c,4]—have been employed in order to avoid these difficulties. At present, however, there exists no general means for achieving selective geminal alkylation of an α,α,α'-trisubstituted acetone. We have found that the corresponding *n*-butylthiomethylene derivatives of such ketones[2] undergo a "double reduction" with lithium–ammonia solutions[5] affording a methyl-substituted enolate anion at the original methylene position which can be alkylated *in situ*.[6] This facile reduction–alkylation operation permits the direct introduction of one methyl group and a second, variable substituent at the ketone flank which condenses with ethyl formate. This communication presents a preliminary survey of the scope of this new alkylation reaction.[7]

(1) For discussion and examples, see (a) J.-M. Conia, *Rec. Chem. Progr.*, **24**, 43 (1963); (b) H. O. House, *ibid.*, **28**, 99 (1967); (c) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, pp 184–204.

(2) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615, 1620 (1962).

(3) (a) G. Stork and P. F. Hudrlik, *J. Amer. Chem. Soc.*, **90**, 4462, 4464 (1968); (b) H. O. House, L. J. Czaba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).

(4) (a) G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Amer. Chem. Soc.*, **87**, 275 (1965); (b) M. Larcheveque, *Ann. Chim. (Paris)*, **5**, 129 (1970).

(5) For similar double reductions of (a) β-alkoxy α,β-unsaturated esters, see R. M. Coates and J. E. Shaw, *J. Org. Chem.*, **35**, 2597, 2601 (1970); (b) β-alkoxy α,β-unsaturated acids, see J. E. Shaw and K. K. Knutson, *ibid.*, in press; and (c) β-ethoxy-2-cyclohexenone, see D. S. Watt, J. M. McKenna, and T. A. Spencer, *ibid.*, **32**, 2674 (1967).

(6) Ireland and Marshall[2] reported that sodium–ethanol–ammonia reduction of the *n*-butylthiomethylene derivative of 9-methyl-*cis,trans*-Δ^6-octalone-1 afforded the 2-methyl octalol in 31–37% yield. This conversion can be interpreted as involving initial double conjugate reduction followed by ketone reduction. It should be noted, however, that alkyl vinyl sulfides themselves undergo reductive cleavage in sodium–ammonia: L. Brandsma, *Recl. Trav. Chim. Pays-Bas.*, **89**, 593 (1970).

(7) This transformation could also be achieved by conversion to the α-alkylidene ketone through aldol condensation, followed by reduction–alkylation. Although this tandem operation has not to our knowledge