mmol) in 7 mL of CH_2Cl_2 was added **5** (65 mg, 0.2 mmol). The reaction mixture changed from black to deep red in color after 24 h. The solvent was removed, and the residue was triturated with MeOH and filtered. The crude rust-colored **22** (140 mg, 99%) melted at 199–215 °C. Purification was effected by dissolving **22** in DMF and then adding H_2O until turbidity resulted. Filtration gave **22**, mp 244–253 °C. Anal. Calcd for $C_{42}H_{24}Cl_2N_2O_5$: C, 71.29; H, 3.42; N, 2.96. Found: C, 71.82; H, 3.90; N, 3.78.

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Supplementary Material Available: Atomic coordinates and all relevant details of X-ray crystallography of compounds **7b,c** and **21** (37 pages). Ordering information is given on any current masthead page.

Sodium Perborate: A Mild and Convenient Reagent for Efficiently Oxidizing Organoboranes

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Sodium perborate, a readily available and inexpensive reagent, efficiently oxidizes organoboranes. The reagent permits the oxidation of a wide variety of functionally substituted organoboranes. In nearly every instance, the product yields exceed those obtained using standard oxidation procedures.

Organoboranes have proven to be versatile intermediates in a number of synthetic sequences. The utility of the borane reagents is centered on the stereodefined nature of their reactions and on the fact that they can be prepared containing a wide variety of important functional groups, e.g. carboxylic acid esters, nitriles, etc.[1] Interestingly, nearly every synthesis involving organoborane reagents includes an oxidation reaction to remove organoborane byproducts or to generate the target molecule.[2] Currently, the most effective method for oxidizing organoboranes involves heating the boron reagent with 30% hydrogen peroxide and 3 N sodium hydroxide at 50 °C.[3] The harsh nature of this standard oxidation reaction is often incompatible with the functional groups present in the target molecules.

In an attempt to minimize side reactions of functionally substituted organoboranes, researchers have resorted to modifying the standard oxidation procedure. Successful methods include the simultaneous addition of the base and peroxide[4] and the use of milder bases.[5,6] Other modifications include the use of oxidizing reagents other than hydrogen peroxide; these reagents are often expensive,[7] inconvenient to handle,[8,9] difficult to prepare,[10] or are themselves reactive toward certain functional substituents.[7-11]

Scheme I

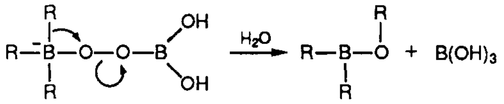

Table I. Comparison of the Efficiencies of the Sodium Perborate and Hydrogen Peroxide Oxidation Procedures

		yield, %	
organoborane	product	sodium perborate	hydrogen peroxide
tri-*n*-hexylborane	1-hexanol	94	94
tris(2-methylpentyl)-borane	2-methyl-1-pentanol	99	98
tris(1-ethylbutyl)-borane	3-hexanol	99	98
tricyclohexylborane	cyclohexanol	98	98
trinorbornylborane	*exo*-norborneol	98	98

[a] Yields determined via GLC analysis. [b] Conversion based on tri-*n*-hexylborane. [c] Oxidation was performed using 1 equiv of NaOH with heating to 50 °C for 30 min.

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[6] Brown, H. C.; Knights, E.; Coleman, R. A. *J. Am. Chem. Soc.* **1969**, *91*, 2144.

[7] (a) Kabalka, G. W.; Hedgecock, H. C. *J. Org. Chem.* **1975**, *40*, 1776. (b) Soderquist, J. A.; Najafi, M. R. *J. Org. Chem.* **1986**, *51*, 1330. (c) Soderquist, J. A.; Anderson, C. L. *Tetrahedron Lett.* **1986**, *27*, 3961.

[8] Brown, H. C.; Midland, M. M.; Kabalka, G. W. *Tetrahedron* **1986**, *42*, 5523.

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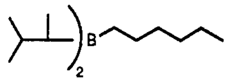
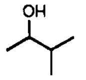
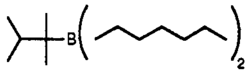
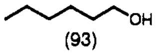
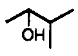
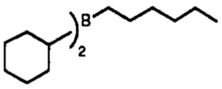
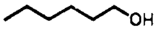
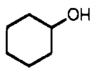
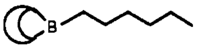
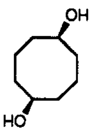
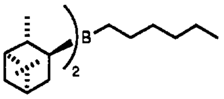
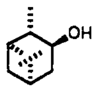
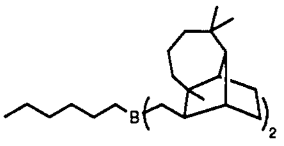
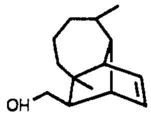
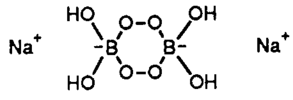
0022-3263/89/1954-5930$01.50/0

Table II. Oxidation of Mixed Organoboranes with $NaBO_3 \cdot 4H_2O$

organoboranes	ref	products (yield,[a] %)	
	1a	 (98)	 (98)
	1a	 (93)	 (97)
	1a	 (99)	 (99)
	1a	 (99)	 (98)
	1a	 (99)	 (84) (96)[b]
	15	 (98)	 (82)[c]

[a] By GLC analysis. [b] One equivalent of NaOH. [c] Isolated yield.

Sodium perborate (1) is an inexpensive, stable, and easily handled oxidant which has an excellent shelf life. The reagent has been shown to be a mild oxidizing agent,[12] yet the application of this reagent to organoboron compounds has been limited to the oxidation of alkenylboronic acids.[13]



1

We recently discovered that sodium perborate efficiently oxidizes trialkylboranes to the corresponding alcohols.[14] This newly developed oxidation procedure has been applied to a variety of borane reagents commonly utilized in organic syntheses, and the results are summarized herein.

Results and Discussion

Oxidations of organoboranes contained in THF are conveniently carried out at room temperature with sodium perborate in water. Only 1 equiv of the oxidizing agent is needed for every boron–carbon bond. Since the reagent is mildly basic (pH ~ 9.5), the addition of external base is not required in most cases. The rate of the oxidation reaction is temperature dependent. The data indicate that the second and third alkyl groups are removed more slowly than the first, requiring either slightly higher temperatures or longer reaction times. The rate of oxidation can also be enhanced by the addition of 1 equiv of sodium hydroxide. These results are summarized in Figure 1.

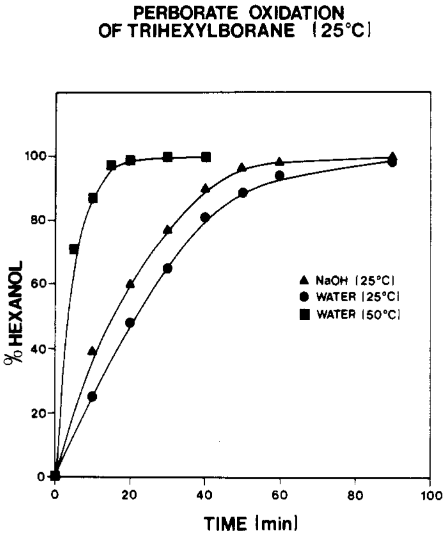


Figure 1. A comparison of the rates of oxidation of tri-*n*-hexylborane with sodium perborate under various conditions.

As the oxidation proceeds, the crystalline sodium perborate is consumed and sodium borate precipitates out. Although the oxidation mechanism is unclear, sodium perborate does not appear to be merely a mixture of hydrogen peroxide and sodium borate.[13] Presumably, the mild nature of this oxidant is a result of having borate as a leaving group as compared to hydroxide, which is formed in hydrogen peroxide oxidations (Scheme I).

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(13) (a) Matteson, D. S.; Moody, R. J. *J. Org. Chem.* **1980**, *45*, 1091. (b) Matteson, D. S.; Moody, R. J. *J. Organomet. Chem.* **1978**, *152*, 265. (c) Matteson, D. S.; Moody, R. J.; Jesthi, P. K. *J. Am. Chem. Soc.* **1975**, *97*, 5608.

(14) Kabalka, G. W.; Shoup, T. M.; Goudgaon, N. M. *Tetrahedron Lett.* **1989**, *30*, 1483.

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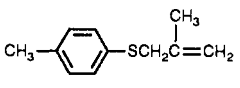
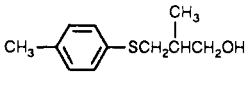
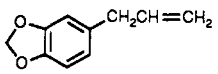
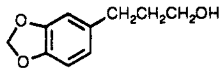
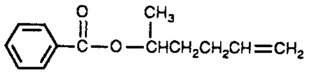
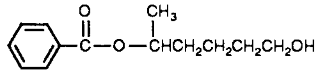
Table III. Comparison of the Sodium Perborate and Hydrogen Peroxide Oxidation Procedures for a Series of Functionally Substituted Organoboranes[a]

alkene	product[b]	yield,[c] % NaBO$_3$	yield,[c] % H$_2$O$_2$/OH
		92 (81)	85
		81 (84)	77
		84 (80)	86
ClCH$_2$C(CH$_3$)=CH$_2$	ClCH$_2$CH(CH$_3$)CH$_2$OH	86 (75)	60

[a] The organoboranes were formed via the hydroboration of the alkenes listed in the table. [b] Only the major product is indicated. [c] By GLC analysis, values in parentheses are isolated yields.

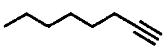
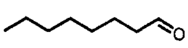
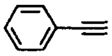
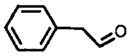
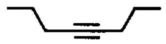
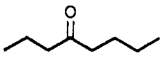
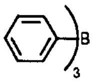
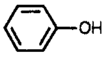
Sodium perborate permits an essentially quantitative conversion of an organoborane to corresponding alcohol. In all cases the yields of alcohols were as good or better than the results in which the standard oxidation procedure was employed. The results of a comparative study are summarized in Table I. The utility of sodium perborate as an oxidant for typical mixed hydroboration products used in synthesis is shown in Table II.

The oxidation appears to be somewhat sensitive to steric interactions. Trinorbonylborane is readily oxidized at room temperature to the corresponding alcohol whereas the more hindered tris(1-ethylbutyl)borane requires higher temperatures (50 °C) as well as the addition of 1 equiv of sodium hydroxide. Sodium hydroxide also enhances the rate of the perborate oxidation of organoboranes complexed to dimethyl sulfide which result from hydroborations using borane–dimethyl sulfide. Presumably, the sodium hydroxide increases the concentration of the perborate anion, which compensates for the strong borane–dimethyl sulfide complexation.

Since sodium perborate is a mild oxidant, a comparative study was performed in which a series of functionally substituted alkenes were hydroborated and oxidized using both the sodium perborate procedure and the standard procedure.[3] The results are presented in Table III. Only the major product is reported in Table III; isomeric alcohols are also formed due to the mesomeric and inductive effects of the functional substituent during hydroboration.[16] The product yields are comparable to those obtained using trimethylamine *N*-oxide (a relatively expensive reagent) and often exceed those obtained using the standard oxidation procedure because the strong base used in the peroxide method often leads to side reactions such as elimination and cyclization.[17]

We next examined the use sodium perborate for the oxidation of vinylboranes. Under identical conditions with those used for oxidation of saturated organoboranes, vinylboranes were oxidized to the corresponding carbonyl derivatives. In most cases, the product yields exceed those obtained using the standard oxidation procedure (Table IV). Alkyl groups are oxidized perferentially to vinyl groups. However, selectivity is not adequate to generate the boronic acid efficiently. For example, addition of only 2 equiv of sodium perborate to dicyclohexyl-1-octenylborane resulted in the formation of 1.5 equiv of cyclohexanol and 0.5 equiv of octanal.

Table IV. Comparison of Sodium Perborate and Hydrogen Peroxide Oxidation Procedures for Vinylboranes

reagent[a]	product	yield,[b] % NaBO$_3$	yield,[b] % H$_2$O$_2$/OH$^-$
		94 (79)	95
		94 (87)	96
		100 (86)	100
		87	85

[a] The vinylboranes were formed via the hydroboration of the alkynes using disiamylborane. [b] By GLC analysis, values in parentheses are isolated yields.

Conclusions

The use of sodium perborate as an oxidizing agent for organoboranes is a viable alternative to the standard peroxide/base oxidation procedure. The reagent is inexpensive, more stable, and far safer to handle than hydrogen peroxide. Furthermore, product yields are as good as or better than those obtained in the peroxide procedure. The oxidations proceed at room temperature for most organoboranes; highly hindered boranes and those complexed with dimethyl sulfide may require heating (50 °C) and the use of 1 equiv of sodium hydroxide.

Experimental Section

Proton NMR spectra were recorded on a FX90 Q spectrometer. All chemical shifts are reported in parts per million downfield from tetramethylsilane.

All melting points and boiling points are uncorrected. The gas chromatography analyses were performed on a Varian 3700 Model. The following columns were used: 5% SE-30 on Chromosorb W, 10 ft × 0.25 in.; 10% Carbowax 20M on Chromosorb W, 10 ft × 0.25 in. Commercially available samples of 1-hexene, cyclohexene, norbornene, 2-methyl-2-butene, 2-methyl-1-pentene, and 3-hexene were distilled over lithium aluminum hydride. Safrole, 3-chloro-2-methylpropene, 3-(*p*-tolylthio)-2-methyl-1-propene, and 5-benzoxy-1-hexene were passed through neutral alumina and distilled over calcium hydride. All alkynes were distilled over calcium hydride.

Oxidations. General Procedures. A. Sodium Perborate. The organoborane[3] (10 mmol) dissolved in 10 mL of THF was

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(16) Brown, H. C.; Gallivan, R. M. *J. Am. Chem. Soc.* **1968**, *90*, 2906.
(17) Brown, H. C.; Rhodes, S. P. *J. Am. Chem. Soc.* **1968**, *90*, 2149.

contained in a dry, nitrogen-flushed, 25-mL three-necked flask equipped with a nitrogen inlet tube, a gas outlet tube connected to a mercury bubbler, a thermometer, and a magnetic stirring bar and maintained under a positive pressure of N_2. Water (10 mL) and sodium perborate (4.6 g, 30 mmol) were added sequentially to the flask, and the mixture was maintained at room temperature (water bath) for 2 h with vigorous stirring. The two phases were separated, and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic phase was washed with saturated NaCl solution (10 mL) and dried ($MgSO_4$), and the product was analyzed by GLC and isolated by distillation.

B. Hydrogen Peroxide. The organoborane (3.0 mmol), dissolved in 3 mL of tetrahydrofuran, was contained in a dry, nitrogen-flushed, 25-mL three-necked flask, equipped with a nitrogen inlet tube, a gas outlet tube connected to a mercury bubbler, a thermometer, and a magnetic stirring bar and maintained under a positive pressure of N_2. Aqueous sodium hydroxide (3.0 mmol, 1.0 mL of 3 N solution) was added followed by the slow addition of hydrogen peroxide (1.0 mL of a 30% aqueous solution). The reaction mixture was heated to 50 °C for 1 h to ensure completion of the oxidation. The mixture was saturated with potassium carbonate, the two phases were separated, and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic phase was washed with saturated NaCl (10 mL) and dried ($MgSO_4$), and the product was analyzed by GLC.

Hydroboration: Alkenes. The hydroborations were carraied out using standard procedures.[3] The alkene (30 mmol) was added to a dry, nitrogen-flushed, 25-mL three-necked flask, equipped with a nitrogen inlet tube, a gas outlet tube connected to a mercury bubbler, a thermometer, and a magnetic stirring bar and maintained under a positive pressure of N_2. The flask was cooled to 0 °C (ice bath), and hydroboration was initiated by dropwise addition of a 1.0 M solution of borane–THF (10 mL, 10 mmol). The mixture was stirred at room temperature for 2 h.

Alkynes. Borane–THF (10 mL, 10 mmol) was placed, via syringe, into a N_2-flushed 25-mL flask, and the solution was cooled to −10 °C (ice–salt bath). 2-Methyl-2-butene (5.5 mL, 22 mmol) was then added, and the mixture was stirred at 0 °C for 2 h to yield a 1.0 M solution of disiamylborane. The alkyne (10 mmol) was added to the disiamylborane while the temperature was maintained below 5 °C. The mixture was stirred at 0 °C for 15 min and then at room temperature for 1 h to complete the hydroboration.

3-(*p*-Tolylthio)-2-methyl-1-propanol. 3-(*p*-Tolylthio)-2-methylpropene (5.34 g, 30 mmol) was hydroborated with 10.0 mmol of BH_3–THF at 0 °C for 15 min, and then the mixture was stirred at room temperature for 2 h. Oxidation was performed by stirring the resultant organoborane at 25 °C with sodium perborate (4.6 g, 30 mmol) and water (10 mL) for 2 h. GLC analysis (SE-30) indicated a 92% yield of 3-(*p*-tolylthio)-2-methyl-1-propanol. Distillation afforded 4.7 g (81%) of the alcohol: bp 130–132 °C (0.2 mmHg) [lit.[7] bp 112–113 °C (0.13 mmHg)]; ^1H NMR ($CDCl_3$) δ 1.0 (d, J = 7 Hz, 3 H, CH_3), 1.9 (broad m, 1 H, CH), 2.3 (s, 3 H, $ArCH_3$), 2.9 (m, 2 H, SCH_2), 3.0 (s, 1 H, OH), 3.6 (d, J = 6 Hz, 2 H, CH_2O), 7.3 (m, 4 H, ArH).

3-(3,4-(Methylenedioxy)phenyl)-1-propanol. Safrole (4.86 g, 30 mmol) was hydroborated with 10 mmol of BH_3–THF at 0 °C for 15 min, and then the mixture was stirred at room temperature for 2 h. The resultant organoborane was oxidized by sodium perborate (4.6 g, 30 mmol) and water (10 mL) at 25 °C for 2 h. GLC analysis (SE-30) indicated a 86% yield of 3-(3,4-(methylenedioxy)phenyl)-1-propanol; 12% of the secondary isomer was also present. Distillation afforded 4.5 g (84%) of a mixture of isomers: bp 130–132 °C (0.3 mmHg) [lit.[7] bp 124–128 °C (2 mmHg)]; ^1H NMR ($CDCl_3$) δ 1.8 (m, 2 H, CH_2), 2.7 (t, J = 7 Hz, 2 H, $ArCH_2$), 3.0 (s, 1 H, OH), 3.7 (t, J = 6.5 Hz, 3 H, CH_2O), 6.0 (s, 2 H, OCH_2O), 6.8 (s, 3 H, ArH).

5-Benzoxy-1-hexanol. 5-Benzoxy-1-hexene (6.12 g, 30 mmol) was hydroborated with 10 mmol of BH_3–THF at 0 °C for 15 min, and then the mixture was stirred at room temperature for 2 h. The resultant organoborane was oxidized by sodium perborate (4.6 g, 30 mmol) and water (10 mL) at 25 °C for 2 h. GLC analysis (SE-30) indicated a 86% yield of 5-benzoxy-1-hexanol. The product was isolated by distillation, 5.3 g (80%) of the alcohol: bp 140–142 °C (0.3 mmHg) [lit.[7] bp 121–125 °C (0.05 mmHg)]; ^1H NMR ($CDCl_3$) δ 1.5 (m, 9 H, alkyl), 3.3 (s, 1 H, OH), 3.7 (t, J = 6.5 Hz, 2 H, CH_2O), 5.2 (m, 1 H, OCH), 7.6 (m, 3 H, ArH), 8.2 (m, 2 H, ArH).

3-Chloro-2-methyl-1-propanol. 3-Chloro-2-methylpropene (2.72 g, 30 mmol) was hydroborated with 10 mmol of BH_3–THF at 0 °C for 15 min, and then the mixture was stirred at room temperature for 2 h. The resultant organoborane was oxidized by sodium perborate (4.6 g, 30 mmol) and water (10 mL) at 25 °C for 2 h. GLC analysis (SE-30) indicated a 86% yield of 3-chloro-2-methyl-1-propanol. The product was isolated by distillation, 2.4 g (75%) of the alcohol: bp 72–74 °C (15 mmHg) [lit.[7] bp 65–66 °C (10 mmHg)]; ^1H NMR ($CDCl_3$) δ 0.9 (d, J = 7 Hz, 3 H, CH_3), 1.9 (m, 1 H, CH), 3.5 (d, J = 6 Hz, 2 H, CH_2Cl), 3.6 (d, J = 5.5 Hz, 2 H, OCH_2), 4.6 (s, 1 H, OH).

4-Octanone. 3-Octyne (1.1 g, 10 mmol) was hydroborated with 20 mmol of disiamylborane at 0 °C for 15 min and then the mixture was stirred at room temperature for 1 h. The resultant organoborane was oxidized by sodium perborate (4.6 g, 30 mmol) and water (10 mL) at 25 °C for 2 h. GLC analysis (SE-30) indicated a 100% yield of 4-octanone. Distillation afforded 1.1 g (86%) of **5**: bp 75–77 °C (40 mmHg) [lit.[18] bp 163 °C (760 mmHg)]; ^1H NMR ($CDCl_3$) δ 1.0 (t, J = 7 Hz, 6 H, CH_3), 1.5 (m, 6 H, CH_2), 2.5 (t, J = 7 Hz, 4 H, $2CH_2CO$).

Octanal. 1-Octyne (1.1 g, 10 mmol) was hydroborated with 20 mmol of disiamylborane at 0 °C for 15 min, and then the mixture was stirred at room temperature for 1 h. The resultant organoborane was oxidized by sodium perborate (4.6 g, 30 mmol) and water (10 mL) at 25 °C for 2 h. GLC analysis (SE-30) indicated a 92% yield of octanal. Distillation afforded 1.0 g (79%) of octanal: bp 85–87 °C (45 mmHg) [lit.[1b] bp 83–85 °C (33 mmHg)]; ^1H NMR ($CDCl_3$) δ 1.0 (t, J = 7 Hz, 3 H, CH_3), 1.5 (m, 10 H, CH_2), 2.5 (m, 4 H, $2CH_2CO$) 9.7 (s, 1 H, CHO).

Phenylacetadehyde. Phenylacetylene (1.0 g, 10 mmol) was hydroborated with 20 mmol of disiamylborane at 0 °C for 15 min, and then the mixture was stirred at room temperature for 1 h. The resultant organoborane was oxidized by sodium perborate (4.6 g, 30 mmol) and water (10 mL) at 25 °C for 2 h. GLC analysis (SE-30) indicated a 94% yield of phenylacetaldehyde. Distillation afforded 1.0 g (87%) of phenylacetaldehyde: bp 76–78 °C (8 mmHg) [lit.[18] bp 88 °C (18 mmHg)]; ^1H NMR ($CDCl_3$) δ 2.8 (d, J = 7 Hz, 2 H, CH_2CO), 7.1 (s, 5 H, ArH), 9.8 (s, 1 H, CHO).

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