Borane:1,4-Oxathiane - A New Convenient Hydroborating Agent

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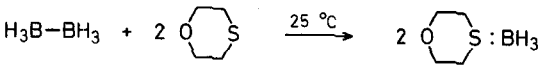
Borane:1,4-oxathiane (**2**), readily synthesized by passing gaseous diborane directly into 1,4-oxathiane (**1**), at 25 °C to saturation, is a stable liquid at 25 °C, which crystallizes on cooling to 0 °C, m.p. 11–15 °C. The neat reagent is 8.0 molar in borane. It hydroborates alkenes rapidly to form the corresponding trialkylboranes in excellent yields. The reaction product can be oxidized with alkaline hydrogen peroxide to provide alcohols in essentially quantitative yield. Alternatively, reagent **2** can be selectively oxidized with aqueous sodium hypochlorite to the sulfoxide, without oxidizing the organoborane[2]. The sulfoxide is highly soluble in water and is readily extracted into the aqueous phase. The residual organoborane in the organic phase can then be recovered, dried, and utilized for the many transformations that organoboranes undergo[3].



1 **2**

The applicability of borane:tetrahydrofuran[4] and borane:dimethyl sulfide[5] as valuable hydroborating agents is well recognized. Thus, these two reagents hydroborate essentially all alkenes rapidly and quantitatively to yield a wide variety of fully or partially substituted organoboranes. While the application of the commercially available dilute (1 molar) solution of borane in tetrahydrofuran[6] essentially limits its applicability to tetrahydrofuran as solvent, borane:dimethyl sulfide (10 molar in borane) can be utilized in a wide variety of solvents[5]. Moreover, borane:dimethyl sulfide is stable at room temperature for long periods of time, whereas, borane:tetrahydrofuran undergoes significant cleavage of tetrahydrofuran at room temperature, with loss of hydride[7].

These advantages of borane:dimethyl sulfide are sometimes negated by the properties of the ligand, dimethyl sulfide, present in the reaction mixture. It is insoluble in water and cannot, therefore, be removed from the reaction products by washing with water. It is highly volatile and odoriferous, and often draws complaints and criticisms from users of borane:dimethyl sulfide or their neighbors. (On the other hand, it can be considered an excellent warning agent of poor experimental techniques[8].)

The readily available 1,4-oxathiane (**1**) possesses a lower vapor pressure and a less obnoxious odor than dimethyl sulfide. It has the additional advantage that it is moderately soluble in water (0.3 molar). Consequently, it can be washed out with water from solutions in diethyl ether, dichloromethane, and pentane. In addition, selective oxidation of **1** in the presence of the organoborane with aqueous sodium hypochlorite yields the sulfoxide, which is highly soluble in water and is readily washed away from the organoborane[2]. Accordingly, we have now synthesized borane:1,4-oxathiane (**2**) and examined its hydroboration characteristics.

The ^{11}B-N.M.R. spectrum of **2** exhibits only one absorption at $\delta = -23.0$ ppm (relative to boron trifluoride etherate), supporting

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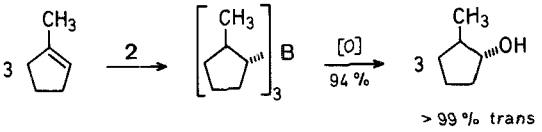
formation of the borane:1,4-oxathiane complex by coordination of borane with the sulfur atom (borane:dimethyl sulfide $\delta = -20.3$ ppm; borane:tetrahydrofuran $\delta = +1.0$ ppm). The neat reagent is stable at 25 °C for long periods of time, without exhibiting detectable change in the hydride content or in the ^{11}B-N.M.R. spectrum. It is miscible with the standard solvents utilized for hydroboration, tetrahydrofuran, diethyl ether, dichloromethane, and partially soluble in pentane.

1-Hexene was selected as a test case and its hydroboration was examined in these four solvents. Following completion of the hydroboration, the products were oxidized by alkaline hydrogen peroxide and the alcohols formed determined by G.L.C. The results of this study are summarized in Table 1. It is evident that in all four solvents the hydroboration proceeds smoothly with the usual distribution of 93–94% of the boron at the terminal position and 6–7% at the internal position[4].

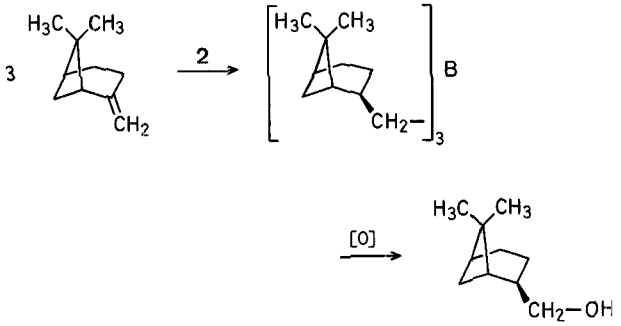
To examine more fully the applicability of **2** as a useful hydroborating agent, a selection of representative alkenes were treated in tetrahydrofuran with **2** in the usual 3:1 mol ratio under the conditions indicated. The results of this study are summarized in Table 2. The data indicate that the hydroboration proceeds smoothly. Oxidation of the organoborane produced in the hydroboration stage affords excellent yields of the corresponding alcohols.

Just as in the case of borane:dimethyl sulfide, the reaction of **2** with most of the alkenes examined is so fast at 25 °C that the rate of hydroboration could not be followed. However, the reaction with cyclohexene is relatively slow. Consequently, the rate of hydroboration with **2** and with borane:dimethyl sulfide was followed to compare the relative reactivities of the two reagents. The results reveal that **2** reacts at a significantly faster rate than borane:dimethyl sulfide.

The hydroboration-oxidation reaction with **2** exhibits the same high regio- and stereoselectivity of the earlier reagents.



The synthetic utility of this new reagent for hydroboration-oxidation is indicated by the following representative procedure for the conversion of (−)-β-pinene to (−)-*cis*-myrtanol.



Finally, the possibility of removing the 1,4-oxathiane as the sulfoxide with the recovery of the organoborane is illustrated by the procedure for the preparation and isolation of tri-*n*-octylborane.

Table 1. Hydroboration-Oxidation of 1-Hexene with Borane: 1,4-Oxathiane (**2**) – A Solvent Study[a]

Solvent	1-Hexanol[b] [%]	2-Hexanol[b] [%]	Total Yield[c] [%]
Tetrahydrofuran	94	6.0	99.3
Diethyl ether[d]	93.5	6.5	94.0
Pentane[d]	93.0	7.0	100
Dichloromethane[d]	93.0	7.0	100

[a] All reactions involved the addition of 1-hexene (15 mmol) to **2** (5 mmol) in sufficient solvent to make the reaction mixture 0.75 molar in borane. After 5 min at room temperature, the reaction mixture was oxidized with alkaline hydrogen peroxide.
[b] Relative amounts by G.L.C. analysis.
[c] Total yield by G.L.C. using 10% SE-30 on Chrom W (60/80), 6′ × 0.25″ column and *n*-tetradecane as the internal standard.
[d] Ethanol (3.0 ml) was added prior to oxidation.

Table 2. Hydroboration-Oxidation of Representative Alkenes with Borane: 1,4-Oxathiane (**2**) in Tetrahydrofuran[a]

Alkene	Time [min]	Alcohol Products	Relative amounts[b] [%]	Total Yield[c] [%]
1-Hexene	5[d]	1-Hexanol	94.0	99.3
		2-Hexanol	6.0	
1-Octene	5[d]	1-Octanol	93.4	93.9 (84)[e]
		2-Octanol	6.6	
Styrene	5[d]	2-Phenylethanol	84.6	96.0
		1-Phenylethanol	15.4	
2-Methyl-1-pentene	5[d]	2-Methyl-1-pentanol	100	95.0
Cyclopentene	5[d]	Cyclopentanol	100	95.0 (86)[h]
Cyclohexene	60+15[f]	Cyclohexanol	100	98.0
1-Methylcyclopentene	60+15[f]	*trans*-2-Methylcyclopentanol	>99[g]	94.0

[a] All reactions involved the addition of alkene (15 mmol) to **2** (5 mmol) in tetrahydrofuran (0.75 molar in borane).
[b] By G.L.C. analysis after oxidation.
[c] By G.L.C. analysis using 10% SE-30 on Chrom W (60/80), 6′ × 0.25″ column and *n*-tetradecane as the internal standard.
[d] Reactions were over after the addition of the alkenes, but were oxidized after specified time.
[e] Isolated yield; b.p. 85–87 °C/15 torr; n_D^{20}: 1.4296 [Lit. [12] b.p. 196 °C/760 torr; n_D^{20}: 1.4297].
[f] After 60 min at room temperature, 15 min under reflux.
[g] <1% *cis* isomer.
[h] Isolated yield; b.p. 138–139 °C/754 torr; n_D^{20}: 1.4521 [Lit. [12] b.p. 139–140 °C/760 torr; n_D^{20}: 1.4521].

These results establish borane:1,4-oxathiane to be a new convenient hydroborating agent with valuable characteristics.

Borane:1,4-Oxathiane (2):
All operations are carried out under nitrogen. Diborane gas is generated in a mini-version of the standard diborane generator by reacting sodium borohydride (21.6 g, 550 mmol) in diglyme (145 ml) with boron trifluoride etherate (91.2 ml, 724 mmol)[3] and passing the gas evolved into 1,4-oxathiane (**1**; 56.2 ml, 540 mmol) at room temperature to saturation. (Excess diborane is passed into dry tetrahydrofuran.) An aliquot of the neat reagent thus formed is analyzed by hydrolysis. The hydrogen evolved corresponds to a concentration of 8.0 molar in borane. On cooling the product to 0 °C, it crystallizes and these crystals melt at 11–15 °C.

(−)-*cis*-Myrtanol:
Hydroboration is carried out by adding (−)-β-pinene[9] (11.9 ml, 75 mmol; $[\alpha]_D^{23}$: −21.4°; 95.5% optical purity) dropwise to a well-stirred mixture of **2** (3.13 ml, 25 mmol) and pentane (18.3 ml) at room temperature (under nitrogen). The solution is allowed to stand for 15 min to complete the hydroboration. Then ethanol (15 ml) is added, followed by 3 molar sodium hydroxide solution[10] (25.0 ml, 75 mmol). The reaction mixture is then immersed in a cooling bath and 30% aqueous hydrogen peroxide (9.4 ml, 75 mmol) is added dropwise over 15 min at such a rate that the temperature does not rise above 35 °C (gentle reflux). The reaction mixture is then heated under reflux for 1 h and then poured into ice/water (300 ml). The mixture is extracted with ether (70 ml). The ether layer is washed thoroughly with water (3 × 200 ml), followed by saturated brine solution (50 ml). G.L.C. analysis of the organic layer showed only traces of **1**. The organic layer is dried with anhydrous potassium carbonate, filtered, and concentrated. Distillation under vacuum provides pure (−)-*cis*-myrtanol; yield: 9.0 g (79%); b.p. 68–69 °C/0.2 torr; n_D^{20}: 1.4912; $[\alpha]_D^{23}$: −20.8° (*c* 11.2, $CHCl_3$); Lit. [11], b.p. 70–72 °C/1 torr; n_D^{20}: 1.4910; $[\alpha]_D^{25}$: −21.0°].

Tri-*n*-octylborane:
To a well-stirred solution of **2** (3.13 ml, 25 mmol) in tetrahydrofuran (10.0 ml), making the solution 1.0 molar in borane, is added (under nitrogen) 1-octene (11.8 ml, 75 mmol) at room temperature. After about 10–15 min, aqueous sodium hypochlorite solution (Clorox; 3.86 ml, 275 mmol) is then added dropwise over 45 min at room temperature. Following the addition, the reaction mixture is stirred for 15 min. The aqueous layer is treated with sufficient potassium carbonate to give a separate aqueous phase in which the sulfoxide dissolves. The organic layer is separated under nitrogen. The aqueous layer is washed with tetrahydrofuran (2 × 8 ml). The combined extract is dried with anhydrous magnesium sulfate. Filtration yields a solution of tri-*n*-octylborane in tetrahydrofuran. Removal of solvent gives tri-*n*-octylborane; yield: 8.42 g (96%).

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[8] See Chapter 9 of ref. 3 for a review of techniques.
[9] We are indebted to Dr. Bernard J. Kane, SCM Glidden Durkee Organic Chemicals, for a gift of (−)-β-pinene.
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