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LETTERS

A safe, scaleable method for the oxidation of carbon–boron bonds with Oxone®

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Abstract

A new procedure for the oxidation of carbon–boron bonds to the corresponding alcohol with Oxone® is described. © 2000 Elsevier Science Ltd. All rights reserved.

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The oxidation of carbon–boron bonds to the corresponding alcohol can be achieved with a wide range of oxidants.[1] The most common method used is hydrogen peroxide in a basic medium, although trimethylamine *N*-oxide (TMANO),[2] peracids,[3] chromium reagents,[4] sodium perborate,[5] sodium percarbonate,[6] and many others can be used. Most of these methods are of limited utility on a large-scale due to safety, reproducibility, or reagent waste concerns. Herein, we report a general, safe, and reproducible method for the oxidation of carbon–boron bonds with Oxone® ($2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$).

While investigating the hydroboration of **7**, we encountered difficulty in the oxidative workup of the reaction. In order to fully convert the alkyl–borane to the secondary alcohol, the reaction had to be heated to reflux with 30% hydrogen peroxide and NaOH for 2 full hours. From this procedure, an 88% yield of material could be isolated after column chromatography. This substrate is particularly slow to oxidize, possibly because of intramolecular coordination of the tertiary amine to the alkyl–borane intermediate. This procedure is not optimal for large-scale work for a number of reasons, including the inherent instability of the hydrogen peroxide solution.[7] Accelerating Rate Calorimetry (ARC™) revealed a primary exotherm that was sufficient to raise the reaction temperature to the onset of a secondary exothermic decomposition occurring near 110°C, which could contribute to potential runaway conditions on scale.

We found that working this reaction up with Oxone® (3 equivalents, 5 volumes water) provided the corresponding alcohol in 92% yield and higher purity than any of the other procedures

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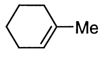
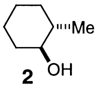
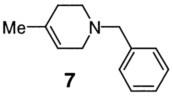
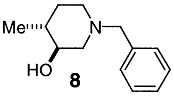
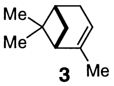
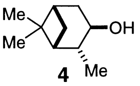
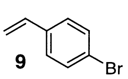
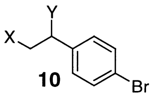
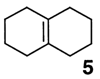
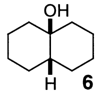
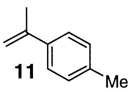
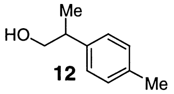
investigated.[8] Oxone®, in direct comparison, has a higher onset of decomposition than 30% hydrogen peroxide and liberates less energy. This reaction is performed at lower temperature, which provides a larger margin of safety, and is dose-rate controlled by addition of Oxone® solution, providing a better overall safety profile for the oxidation.[9] Additionally, Oxone® is a solid, allowing for the addition of precisely weighed amounts of reagent to be used in the reaction. A minimum of 3 equivalents of Oxone® are necessary to drive the oxidation to completion.

This reaction is general and works on a range of organoboranes to provide the alcohol products in good yield (Table 1).[10] [11]

Table 1[a]

Starting Material	Product	Isolated Yield	Starting Material	Product	Isolated Yield
 **1**	 **2**	50	 **7**	 **8**	92
 **3**	 **4**	95	 **9**	 **10** 4.6 X=OH, Y=H : 1 X=H, Y=OH	75
 **5**	 **6**	90	 **11**	 **12**	85

a) All reactions were run on 10 mmol scale, with the exception of **7**-**8** which was run on 100 mmol (18.7 g) scale. See footnote 10 for experimental details.

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7. DSC for 30% aqueous H_2O_2: Exothermic decomposition from 31 to 100°C liberating 747 J/g of energy. Reaction calorimetry was performed in an Accelerating Rate Calorimeter (ARC^{TM}).
8. No chromatography was necessary. A variety of methods were investigated including TMANO, MCPBA, and sodium perborate. These methods all suffered from either safety concerns (TMANO), incomplete reaction (perborate), or side reactions (MCPBA).
9. DSC for 30% aqueous Oxone®: Exothermic decomposition from 56 to 127°C liberating 86 J/g of energy. Reaction calorimetry was performed in a CRC90e^{TM} reaction calorimeter.
10. A typical procedure is as follows: To a solution of alkene **7** (18.7 g, 100 mmol) in THF (150 mL) was added $NaBH_4$ (6.5 g, 170 mmol) at room temperature under N_2. The slurry was cooled to 0°C, and $BF_3{\cdot}OEt_2$ (15 mL, 16.8 g, 118.3 mmol) in THF (25 mL) was slowly added through an addition funnel. The addition was kept slow enough to keep the temperature of the reaction mixture below 0°C. After the addition the reaction mixture was stirred at 0°C for 1 h and at room temperature for 1.5 h. The reaction was re-cooled to 0°C and water (50 mL) was

added slowly to destroy the excess borane. The reaction was stirred at rt for 2 h, followed by the addition of Oxone® (110 g, 342.8 mmol) in water (500 mL) at 0°C. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched by adding $NaHSO_3$ (solid) until all excess oxidant was destroyed (KI/starch test paper). The pH of the reaction mixture was 1–2. The reaction mixture was extracted with ethyl acetate (3×50 mL), and the aqueous layer was adjusted to pH 12 with 6 N NaOH and extracted with ethyl acetate (4×100 mL). The organic layer was washed with brine, dried over $NaSO_4$, and concentrated in vacuo. The residue obtained is pure alcohol (19.0 g, 92%).

11. Compounds **2**, **4** and **10** were compared to authentic samples purchased from Aldrich. Compounds **6**, **8** and **12** were compared to data reported in the literature. Compound (**6**): *J. Am. Chem. Soc.* **1989**, *111*, 6749; compound (**8**): *Tetrahedron* **1970**, *26*, 5519; compound (**12**): *J. Org. Chem.* **1982**, *47*, 4692.