



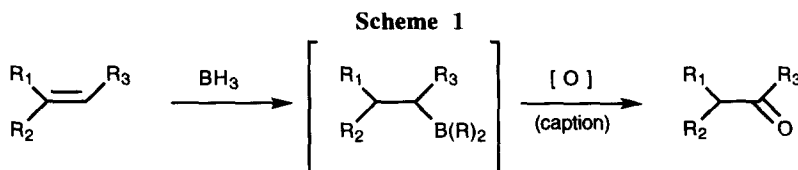
One-Pot Conversion of Olefins to Carbonyl Compounds by Hydroboration / NMO-TPAP Oxidation

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ABSTRACT: An efficient method to oxidize an olefin to the less substituted carbonyl compound is described. This new methodology utilizes borane dimethyl sulfide followed by tetrapropylammonium perruthenate *N*-methylmorpholine *N*-oxide to oxidize the resulting alkylborane. © 1997 Elsevier Science Ltd.

Alkylboranes have played a central role in organic synthesis during the past 40 years.¹ These organometallics, commonly prepared by hydroboration of an olefin, are frequently subjected to oxidative treatment in order to create "anti-Markovnikov" alcohols. Often, this "hydroboration-oxidation" of an olefin must be carried out as a prelude to further oxidation of the intermediate alcohol to a carbonyl unit. Therefore, a method for the direct conversion of olefins to carbonyl compounds could represent a generally useful synthetic technique, since it avoids the intermediate isolation of an alcohol. The first method to achieve this transformation (Scheme 1) was described in 1961 by H. C. Brown, and it entailed attack of the intermediate alkylboranes with chromic acid.² This protocol was suitable for the creation of ketones, but not aldehydes (overoxidation). In 1979, Brown extended the use of the reaction to include aldehydes by using PCC as the oxidant.³ The desire to avoid the use of toxic Cr(VI) reagents in many oxidations induced us to explore the use of the tetrapropylammonium perruthenate - *N*-methylmorpholine-*N*-oxide (TPAP-NMO)⁴ system for the oxidation of boranes to carbonyl compounds. In this Letter, we describe the successful realization of this general idea, thereby providing a new technique for the conversion of an olefin to a carbonyl derivative⁵ under mild conditions and in an environmentally benign manner.

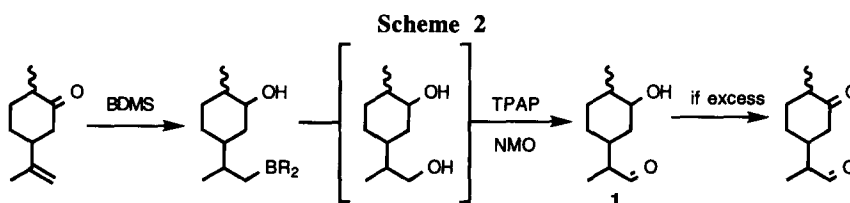


[O] = H₂CrO₄ (R₃ ≠ H; ref. 2); PCC (ref.3); cat. TPAP-NMO (this work).

A typical procedure involves the addition of 0.33 equiv. of borane-dimethyl sulfide complex (BDMS) to a stirred solution of the olefin in anhydrous ether. Upon completion of the hydroboration step, the ether solution is diluted with CH₂Cl₂ and treated with excess NMO, followed by a catalytic amount of TPAP, added approximately 1 h after the NMO (*vide infra*). The reaction is normally complete in about 5 minutes, and it is worked up in a

standard fashion.⁴ A detailed experimental procedure is provided below, while a summary of representative experiments appears in Table 1.

Borane and alkylboranes are known to reduce carbonyl groups.¹ This could pose a problem in the use of this methodology on molecules where a carbonyl group exists. For instance, reaction of dihydrocarvone with 0.33 equiv. of $\text{BH}_3\cdot\text{SMe}_2$ produced a mixture of boranes wherein the ketone had been reduced to an alcohol. Oxidation of this borane mixture under standard Ley conditions (1.5-2.5 equiv. of NMO, cat. TPAP) produced a mixture of products in which hydroxyaldehyde **1** was dominant (Scheme 2). This is consistent with Ley's report that TPAP will selectively oxidize primary alcohols over secondary ones.⁴ The desired ketoaldehyde was a minor component, and seemingly unreacted dihydrocarvone was also detected.⁶ However, the dicarbonyl compound is cleanly obtained by increasing the amount of borane and NMO to 0.7 and 5 equivalents, respectively. Excess BDMS clearly ensures complete reduction of the ketone *and* hydroboration of the olefin.



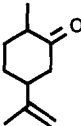
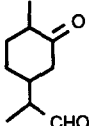





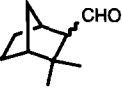







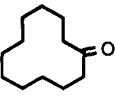


It is not fully clear whether the NMO-TPAP system acts at the level of the intermediate alkylboranes, or whether conversion of these to alcohols by NMO is necessary prior to further oxidation. In any event, the overall process takes place in a convenient one-pot fashion. It should be noted that oxidation of alkylborane mixtures that had been subjected to aqueous workup (removal of unreacted BH_3 and Me_2S) occurred quite rapidly (ca. 5 minutes). Thus, direct oxidation of the alkylboranes may not be excluded. However, *in situ* oxidation of such borane mixtures was most efficient when about 1 h contact time with NMO was allowed prior to TPAP addition.⁷ Under these conditions, significant conversion of the alkylboranes to alcohols was apparent (TLC).

Typical experimental conditions are as follows:

Method A (one-pot oxidation). A solution of borane dimethyl sulfide (BDMS) in hexanes (2M; 0.33 mmol, 150 μL) was added (syringe) at room temperature to a stirred solution of an olefin (1 mmol) in anhydrous ether (5 mL) under argon. The reaction was allowed to stir at room temperature for 3 hours, then it was diluted with freshly distilled CH_2Cl_2 (3 mL) and maintained under argon (balloon). Crushed 4 \AA molecular sieves were added to the stirred mixture, followed by 3 mmol of NMO. The mixture was stirred for 1 h prior to addition of 5 mol % TPAP. A color change from dark green to jet black signals completion of the reaction. Slow oxidations may be forced to complete by the addition of a small additional amount of TPAP. The solution was filtered through a plug of silica gel with ethyl acetate directly into a flask containing activated charcoal. The mixture was stirred briefly, then it was filtered again (celite) and carefully evaporated (some products are volatile), leaving a residue of essentially pure carbonyl compound.

Method B (one-pot oxidation of olefin in the presence of a carbonyl). A solution of BDMS in hexanes (2M; 0.66 mmol, 300 μL) was added (syringe) at room temperature to a stirred solution of an olefin (1 mmol) in anhydrous ether (5 mL) under argon. The reaction was allowed to stir at room temperature for 3 hours, then it

Table 1: Conversion of representative olefins to carbonyl compounds by hydroboration/TPAP oxidation

Substrate	Product	Entry	Conditions ^a	Yield % ^b
		1	A	50
		2	B	80
		3	A	70
		4	A	70
		5	A	78
		6	A	50
		7	A	61
C_8H_{17} 	C_8H_{17} 	8	A	72
		9	C	85
		10	A	98
		11	A	84

^aSee text; ^bYields of pure compounds (NMR, TLC). The identity and purity of the products was ascertained by comparison of their NMR spectra with those of authentic materials.

was diluted with freshly distilled CH_2Cl_2 (3 mL) and maintained under argon (balloon). Crushed 4Å molecular sieves were added to the stirred mixture, followed by 6 mmol of NMO. The mixture was stirred for 1 h prior to addition of 7 mol % TPAP. Slow oxidations may be forced to complete by the addition of a small additional amount of TPAP. The reaction was then processed as described above.

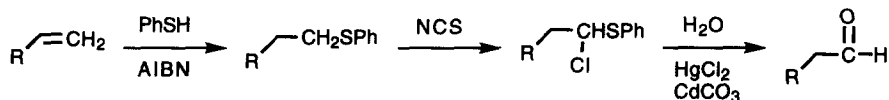
Method C (oxidation after aqueous workup of the boranes). A solution of BDMS in hexanes (2M; 0.33 mmol, 150 μL) was added (syringe) at room temperature to a stirred solution of an olefin (1 mmol) in anhydrous ether (5 mL) under argon. The reaction was allowed to stir at room temperature for 3 hours, then it was quenched with DI water and washed with brine. The organic layer was dried (Na_2SO_4) and evaporated. The residual paste of alkylboranes was immediately dissolved in freshly distilled CH_2Cl_2 and maintained under argon (balloon). Crushed 4Å molecular sieves were added to the stirred mixture, followed by 3 mmol NMO and 5 mol % mol TPAP. The reaction was then processed as described above.

In summary, a useful, mild technique for the oxidative conversion of an olefin into a carbonyl compound is now possible through the formal oxidation of alkylboranes with the Ley TPAP-NMO system.

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References and Footnotes

1. For excellent reviews of organoboron chemistry see: (a) Brown, H.C. *Organic Synthesis via Boranes*; Wiley-Interscience: New York, NY, 1975; (b) Pelter, A.; Smith, K.; Brown, H.C. *Borane Reagents*, Academic Press: New York, NY, 1988.
2. Brown, H. C.; Garg, C. *J. Am. Chem. Soc.* **1961**, *83*, 2952.
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4. Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625. For an excellent review see: Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis*, **1994**, 639.
5. For an alternative method to convert an olefin into a carbonyl compound through radical chemistry (diagram below) see: Paquette, L. A.; Klobucar, W. D.; Snow, R. A. *Syn. Commun.*, **1976**, *6*, 575.



6. This might have been unreacted starting material or it might have formed during the TPAP/NMO oxidation from the alcohol arising from carvone by carbonyl reduction, but not hydroboration of the olefin.
7. When NMO and TPAP were added simultaneously to the crude mixture of boranes the yields were very poor and continuous addition of extra TPAP was necessary to drive the reaction to completion. The TPAP is likely reacting with the residual borane, which is probably quenched when allowed to stir with NMO or with aqueous workup.

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