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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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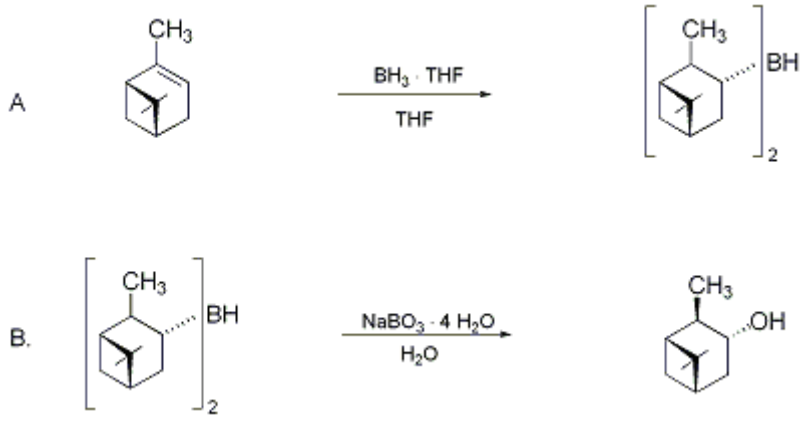
A SIMPLE AND CONVENIENT METHOD FOR THE OXIDATION OF ORGANOBORANES USING SODIUM PERBORATE: (+)-ISOPINOCAMPHEOL

[Bicyclo[3.1.1]heptan-3-ol, 2,6,6-trimethyl-, [1S-(1α,2β,3α,5α)]-]



Submitted by George W. Kabalka, John T. Maddox, Timothy Shoup, and Karla R. Bowers[1].
Checked by C. Huart and Leon Ghosez.

1. Procedure

CAUTION! This procedure should be conducted in an efficient fume hood to assure the adequate removal of hydrogen, a flammable gas which forms explosive mixtures with air.

A. *(+)-Diisopinocampheylborane*. A dry, 250-mL, three-necked, round-bottomed flask, equipped for magnetic stirring, and with a nitrogen inlet vented through a mercury bubbler, a rubber septum, and a thermometer, is flushed with nitrogen and charged with 13.75 g (0.101 mol) of (−)-α-pinene and 25 mL of tetrahydrofuran (Note 1),(Note 2),(Note 3)). The mixture is cooled to 0°C in an ice-water bath, magnetic stirring is initiated, and 58.0 mL (0.055 mol) of 0.95 M borane-tetrahydrofuran solution (Note 4) is added via syringe at a rate such that the temperature of the reaction mixture remains below 5°C. After the addition is complete, the cooling bath is removed. The reaction mixture is allowed to warm to room temperature and stir for 2 hr to ensure complete reaction.[2]

B. *(+)-Isopinocampheol*. To the stirred solution of (+)-diisopinocampheylborane in tetrahydrofuran, prepared above, 50 mL of distilled water is *slowly* added dropwise via syringe [*CAUTION!*] (Note 5) followed by the slow addition of 16.41 g (0.107 mol) of solid sodium perborate tetrahydrate (Note 6) through an appropriate addition funnel at a rate such that the temperature of the reaction mixture does not exceed 35°C (Note 7). Stirring is continued at room temperature (22°C) for 2 hr to ensure completion of the oxidation reaction. The contents of the flask are then poured into 70 mL of ice-cold water in a separatory funnel. After thorough mixing, the organic layer is removed and the aqueous layer is extracted twice with 25 mL of ether. The combined ether extracts are washed twice with 20-mL portions of water and then with 50 mL of saturated aqueous sodium chloride solution. The ether layer is dried over anhydrous magnesium sulfate, filtered, and concentrated on a rotary evaporator. The crude product is purified by short-path vacuum distillation to give 14.1–14.3 g (91–92%) of isopinocampheol, bp 68°C (0.7 mm), as white needles (mp 53–55°C) that crystallize in the receiving flask (Note 8). Recrystallization from pentane gives pure isopinocampheol as needles, mp 54–55°C (uncorrec.), $[\alpha]_D^{25}$ 34.4° (benzene, *c* 10) indicating 96.4% enantiomeric purity based on the highest reported literature value of 35.7° (Note 9).[3]

2. Notes

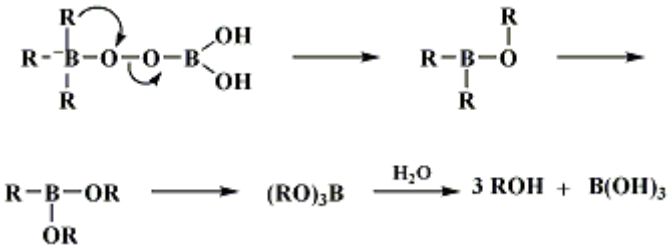
1. All glassware was predried at 140°C for at least 4 hr, assembled hot, flame dried, and cooled under a stream of nitrogen.
2. (1S)-(−)-α-Pinene [99%, 98% optical purity, $[\alpha]_D^{25}$ −50.6° neat] was purchased from Aldrich Chemical Company, Inc., and distilled under reduced pressure from lithium aluminum hydride before use.[2]
3. Tetrahydrofuran was distilled under nitrogen from sodium benzophenone ketyl.
4. Borane-tetrahydrofuran complex (1.0 M) was obtained from Aldrich Chemical Company, Inc., and the concentration of the solution determined using the literature procedure.[4]
5. *Since the hydroboration only proceeds to the dialkylborane stage, a large amount of hydrogen is evolved on hydrolysis. Very slow dropwise addition of water and adequate ventilation are recommended.*
6. Sodium perborate tetrahydrate was purchased from Aldrich Chemical Company, Inc. and used as received.
7. During the addition of sodium perborate the reaction flask is kept in a water bath (25°C).
8. An air condenser is employed for the distillation. The receiving flask is immersed in an ice bath.
9. The product exhibits the following spectral properties: IR (melt) cm^{-1}: 3300 (OH), 2930, 1472, 1450, 1384, 1367, 1050, 1015; ^1H NMR (250 MHz, $CDCl_3$) δ: 0.92 (s, 3 H), 1.04 (d, 1 H, J = 9), 1.13 (d, 3 H, J = 7), 1.22 (s, 3 H), 1.67–2.11 (m, 5 H), 2.30–2.58 (m, 2 H), 4.06 (dt, 1H); ^{13}C NMR (62.87 MHz, $CDCl_3$) δ: 20.7, 23.7, 27.7, 34.4, 38.1, 39.1, 41.8, 47.8, 47.9, 71.7.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

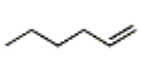
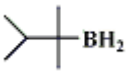
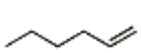
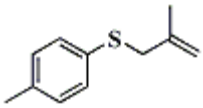
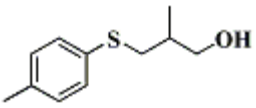
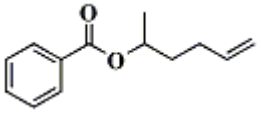
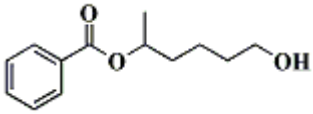
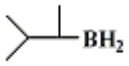
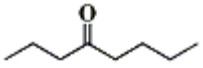
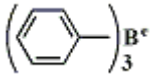
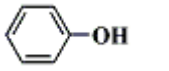
3. Discussion

This procedure illustrates the simplest and most convenient method for oxidizing organoboranes, in the present example a dialkylborane. It uses sodium perborate,[5] an inexpensive, safe, and easily handled reagent, as the oxidizing agent. The reaction proceeds under mild conditions and the yield of the product alcohol is generally as high or higher than that obtained in the sodium hydroxide/hydrogen peroxide oxidation procedure.[6] Thus, the sodium perborate method is an attractive alternative to the base/hydrogen peroxide oxidation procedure. In the case described above, the perborate procedure produces higher yields of (−)-isopinocampheol than the sodium hydroxide/hydrogen peroxide procedure with comparable stereoselectivity.[7] Although the mechanism of the oxidation has not been investigated in detail, sodium perborate does not appear to be acting as a simple mixture of hydrogen peroxide and sodium borate.[8,9,10,11] Presumably, borate is a more effective leaving group (Scheme 1) than hydroxide ion which is generated during oxidation by hydrogen peroxide .



Sodium perborate, owing to its stability, commercial availability, and ease of handling, should prove to be a popular reagent for oxidizing organoboranes. Some representative examples of the oxidation of organoboranes bearing a variety of alkyl and aryl groups are listed in Table I.[12,13]

TABLE I
SODIUM PERBORATE OXIDATION OF ORGANORANES[a]

Alkene	Reagent	Product	Yield(%) [b]
			93
			99
	BH_3		92
	BH_3		86
			84
			87

[a]The organoboranes were formed via the hydroboration of the alkene listed. [b]Isolated yield. [c]One equivalent of 2,3-dimethyl-2-butanol was isolated in addition to 2 equiv of 2-hexanol. [d]One equivalent of 1,4-cyclooctanediol was isolated in addition to the 1-hexanol. [e]Triphenylborane was purchased from Aldrich Chemical Company, Inc.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);

(Registry Number)

(−)-α-pinene

sodium benzophenone ketyl

(−)-ISOPINOCAMPHEOL

(1S)-(−)-α-Pinene

Benzene (71-43-2)

ether (60-29-7)

hydrogen (1333-74-0)

sodium chloride (7647-14-5)

nitrogen (7727-37-9)

hydrogen peroxide (7722-84-1)

Pentane (109-66-0)

magnesium sulfate (7487-88-9)

borane (7440-42-8)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

sodium borate

sodium perborate tetrahydrate (10486-00-7)

Isopinocampheol,
(+)-Isopinocampheol (27779-29-9)

(+)-Diisopinocampheylborane (21947-87-5)

SODIUM PERBORATE

Bicyclo[3.1.1]heptan-3-ol, 2,6,6-trimethyl-, [1S-(1α,2β,3α,5α)]- (24041-60-9)