

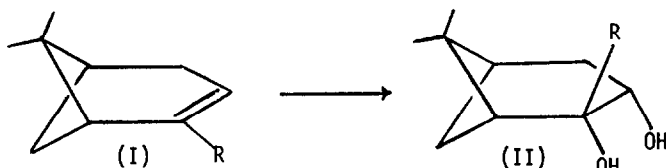
OSMIUM TETROXIDE CATALYZED HYDROXYLATION OF HINDERED OLEFINS

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Osmium tetroxide catalyzed hydroxylation of sterically hindered olefins proceeds efficiently with trimethylamine N-oxide as oxidizing agent in the presence of pyridine.

In a search for chiral sterically hindered diols which might form boronic esters useful for extending our recently developed synthetic methods¹, we attempted the dihydroxylation of some α -pinene derivatives (I) and found the known methods to be impractical.



(a) R = CH₂CH₂OCH₂OCH₂CH₂OCH₃

(b) R = CH₂CH₂OCH₃

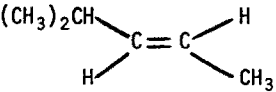
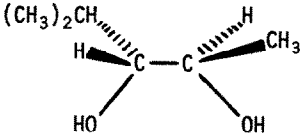
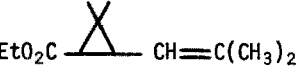
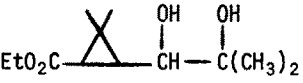
(c) R = CH₃ (opposite enantiomer)

Nopinol MEM ether (Ia), from (-)-nopinol and MEM chloride,^{2,3} on treatment with sodium chlorate and a catalytic amount of osmium tetroxide⁴ yielded only 10% of the diol (IIa) when it appeared that reaction had stopped as shown by thin layer chromatography. With *t*-butyl hydroperoxide, base, and OsO₄,⁵ the yield of (IIa) was 19-42%, but comparable amounts of ketol were also formed and required chromatography for separation. Alkaline potassium permanganate⁶ gave ~40% crude (IIa) containing lesser amounts of ketol and other byproducts. N-Methylmorpholine N-oxide and OsO₄ proved highly successful with less hindered olefins⁷. We used trimethylamine N-oxide instead because it was immediately available and with (Ia) obtained 27% of the diol (IIa) without byproducts after 30 hr reflux.

Noting that pyridine catalyzes formation⁴ and basic conditions favor hydrolysis⁵ of osmate esters, we added a little pyridine to the trimethylamine N-oxide-OsO₄, and the yield of (IIa) rose to 62%, with no ketol. Other olefins gave better yields, 78-93%, as shown in Table I. The 85% yield of 1,2-cyclo-octanediol compares favorably with the 79% reported for the best previous conditions⁷. The previous N-oxide method⁷ has failed with a tetrasubstituted olefin,^{5b} but our 83% yield of pinacol exceeds the 72% obtained with *t*-butyl hydroperoxide.^{5a}

Experimental. A solution of 20 mg of osmium tetroxide in 1 mL of *t*-butyl alcohol was added to a mixture of 25 mmol of the olefin, 3.75 g (34 mmol) of trimethylamine N-oxide dihydrate, 2 mL of pyridine, 15 mL of water, and 50 mL of *t*-butyl alcohol. The light purple solution was refluxed under an inert atmosphere 9-24 hr, cooled to 25°C, treated with 20 mL of 20% aqueous sodium bisulfite, concentrated under vacuum to remove *t*-butyl alcohol, saturated with sodium chloride, and extracted repeatedly with ether. The diol product was isolated analytically pure by vacuum bulb to bulb distillation. Tabulated b.p.'s are bath temperatures. Thin layer chromatography indicated no byproducts in all cases.

Table 1. Dihydroxylation of Olefins by OsO₄, (CH₃)₃NO, and Pyridine.

| Olefin | Time, hr | Diol | m.p. [b.p. of liq.] | %Yield |
|---|----------|---|------------------------------------|-----------------|
| (Ia) | 24 | (IIa) | [130-140°C/0.2 Torr] ³ | 62 ^a |
| (Ib) | 17 | (IIb) | [100-105°C/0.2 Torr] ³ | 78 |
| (Ic) (+)-enantiomer | 17 | (IIc) | 55-55.5°C (lit. ⁸ 56°C) | 93 |
|  | 10 |  | 56-57.5°C (lit. ⁹ 59°C) | 78 |
| Cyclooctene | 9 | cis-Cyclooctane-1,2-diol | 77-78°C (lit. ¹⁰ 79°C) | 85 |
|  (cis and trans mixture) | 24 |  | [100-105°C/0.2 Torr] ³ | 91 |
| (CH ₃) ₂ C=C(CH ₃) ₂ | 23 | Pinacol | 41-43°C | 83 ^b |

^aAfter 40 hr reflux, 55%. ^b91% contained (NMR analysis) in mixture with pyridine before redistillation, 108-110°/62 Torr.

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References and Notes

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