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HIGHLY DIASTEREOSELECTIVE OXIDATIONS OF A THIOETHER APPENDED WITH A NEIGHBORING HYDROXYL GROUP

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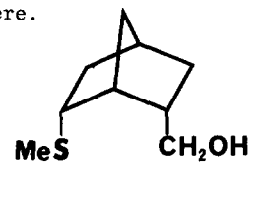
Abstract. Highly diastereoselective oxidations of endo-alcohol 1 to the corresponding sulfoxides, the relative stereochemistries of these sulfoxides and that of an intermediary alkoxysulfonium salt determined by X-ray crystallographic analysis is reported.

Anodic oxidation of endo-alcohol 1 occurs at an unusually low potential.[1] If oxidation of the thioether moiety is facilitated by neighboring group participation[2] by the hydroxyl group, the two electron oxidation product is expected to be alkoxysulfonium salt 2. Chemical oxidation of endo-alcohol 1 has been studied to afford an authentic sample of this salt to be compared with the product obtained by anodic oxidation. Chemical oxidation of endo-alcohol 1 to give alkoxysulfonium salt 2 and sulfoxide alcohol 3 is highly stereoselective. Because of the interest in the stereochemistry of such oxidations[3], and our unusual results, our studies are reported here.



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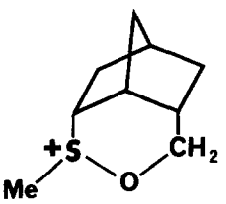

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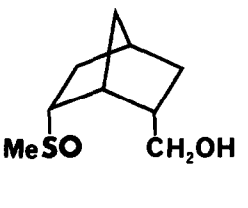

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Treatment of endo-alcohol 1[4] with an excess of tert-butyl hypochlorite followed by one equivalent of mercury(II)chloride[5] gives alkoxysulfonium salt 2 which is indefinitely stable at room temperature. Only one diastereomer of 2 is obtained as shown by ^{1}H NMR analysis. Base-promoted hydrolysis of this salt produces exclusively one diastereomeric sulfoxide alcohol, 3a. Oxidation of endo-alcohol 1 with m-chloroperoxybenzoic acid yields predominantly the other diastereomeric sulfoxide alcohol 3b with a diastereomer ratio of 16:1 as determined by ^{1}H NMR spectroscopic analysis. Thus, depending on the method of oxidation of endo-alcohol 1, either diastereomeric sulfoxide can be secured with excellent stereochemical control.

The relative configuration of the alkoxysulfonium salt obtained by sequential treatment of endo-alcohol 1 with tert-butyl hypochlorite and mercury(II)chloride has been unequivocally established by a single crystal X-ray diffraction study. This salt crystallizes in the monoclinic space group $P2_1/c$ with a = 10.152(3)Å, b = 11.857(4)Å, c = 12.087(3)Å, β = 97.98(2)°, and Z = 4. The structure was solved by the heavy atom method. The position of the mercury atom was located from a three-dimensional Patterson map. The remaining atoms were located by subsequent structure factor calculations and difference electron density maps. Full-matrix least-squares refinement led to a conventional R factor of 0.062 after several cycles of anisotropic refinement. The relative configuration is as shown in the Scheme below for 2a, and a stereoview of the molecule is shown in Fig. 1.

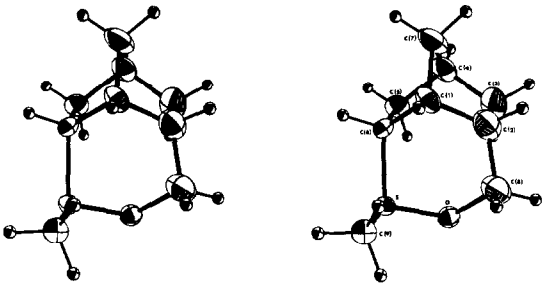


Fig. 1. ORTEP[6] stereoview of alkoxysulfonium salt 2 without the anion. The hydrogen atoms have been assigned arbitrary thermal parameters. Thermal ellipsoids are drawn to enclose 30% of the probability distribution.[19]

The relative configuration of sulfoxide alcohol 3b obtained by m-chloroperoxybenzoic acid oxidation of endo-alcohol 1 has been unambiguously determined by X-ray crystallographic analysis. Sulfoxide alcohol 3b crystallizes in the monoclinic space group C2/c with a = 6.289(2)Å, b = 16.005(5)Å, c = 18.951(8)Å , β = 93.40(3)°, and Z = 8. The nonhydrogen atoms were located by direct methods.[7] Full-matrix least-squares refinement led to a conventional R value of 0.036 after several cycles of anisotropic refinement. The relative configuration is as shown below for 3b, and an ORTEP stereoview of the molecule is shown in Fig. 2. Since sulfoxide alcohol 3a, obtained by hydrolysis of alkoxysulfonium salt 2a, is the diastereomer of 3b its relative con-

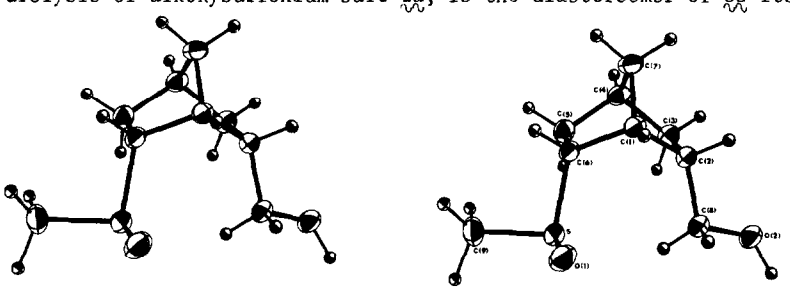
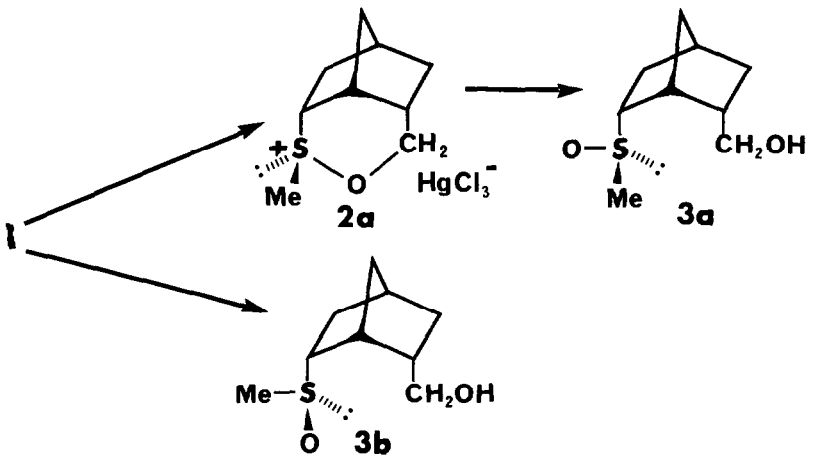


Fig. 2. ORTEP[6] stereoview of sulfoxide alcohol 3b. The hydrogen atoms have been assigned arbitrary thermal parameters. Thermal ellipsoids are drawn to enclose 30% of the probability distribution.

figuration must be as shown in the Scheme on the next page. Comparison of the stereochemistry of alkoxysulfonium salt 2a with its hydrolysis product 3a reveals that the hydrolysis occurs with inversion of the configuration at the sulfur atom as expected. Hydrolysis of alkoxysulfonium salts in base has been reported to occur with inversion of configuration at the sulfur atom.[8]

Consideration of the stereochemical results summarized in the Scheme reveals an unusual feature. The relative stereochemistry of alkoxysulfonium 2a and the predominant sulfoxide alcohol obtained by m-chloroperoxybenzoic acid oxidation are the same. This is the opposite of the usual result.[9] For example, oxidation of 4-substituted thianes with m-chloroperoxybenzoic acid give predominantly the equatorial sulfoxides, whereas oxidation with tert-butyl hypochlorite

SCHEME



affords the axial sulfoxides.[9] m-Chloroperoxybenzoic attacks from the sterically less hindered equatorial direction to introduce an equatorial oxygen atom.[10] Attack by tert-butyl hypochlorite on the thianes also occurs from the sterically less encumbered equatorial direction generating a chlorosulfonium salt with the chlorine atom occupying the equatorial position.[5,11,12] Displacement by alcohol on this chlorosulfonium salt occurs with inversion at the sulfur atom to form the axially substituted alkoxysulfonium salt. The alkoxysulfonium salt then undergoes solvolysis under the reaction conditions[5,11-13] with C-O bond cleavage resulting in retention of configuration at the sulfur atom to afford the axial sulfoxide.[14] Oxidation of endo-alcohol 1 on the one hand with tert-butyl hypochlorite followed by base hydrolysis of the isolated alkoxysulfonium salt and, on the other hand, with m-chloroperoxybenzoic acid results in forming sulfoxides of opposite stereochemistry only because of inversion of configuration at the sulfur atom on hydrolysis of alkoxysulfonium salt 3a. In effect, the direction of approach of m-chloroperoxybenzoic acid to deliver an oxygen atom and tert-butyl hypochlorite to deliver a chlorine atom (assuming inversion of configuration on subsequent intramolecular hydroxyl group displacement) to endo-alcohol 1 is opposite. Although the basis for these results is not known, an appealing rationalization follows. The direction of attack by tert-butyl hypochlorite on endo-alcohol 1 is in accord with expectations based solely on steric effects in the diastereomeric transition states leading to the intermediary chlorosulfonium salts.[14,15] The stereochemistry of the sulfoxide alcohol obtained by m-chloroperoxybenzoic acid oxidation is that expected on consideration of steric effects in the diastereomeric transition states in which the peracid is hydrogen bonded to the alcohol moiety. Similar transition states are well established for reaction of allylic alcohols with peracids.[16] Directing effects by hydroxyl groups[13,14,17] and carboxylic acid groups[18] in oxidation of sulfides with peracids have also been previously reported. The basis for such direction has not been established although hydrogen bonding effects have been listed among other possibilities.

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