

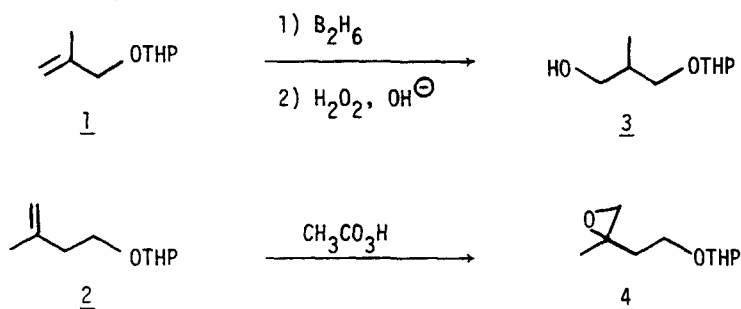
DETONATION ASSOCIATED WITH OXIDATIONS OF TETRAHYDROPYRANYL
ETHER DERIVATIVES. A SERIOUS NOTE OF CAUTION

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We wish to call attention to a potentially dangerous situation which arises out of a commonly employed synthetic procedure. Recent experience in these laboratories with violent explosions encountered in the hydroboration-oxidation of methallyl alcohol-THP (1) and the epoxidation of isoprenol-THP (2) leads us to suspect that the THP-protecting group forms sensitive organic peroxides when in contact with peroxy reagents. In both of these reactions, the precautions normally utilized in isolation of such products failed to destroy the sensitive components.

For example, the hydroboration product of 1 was routinely oxidized using alkaline hydrogen



peroxide and after workup, which included washing with 10% sodium sulfite, gave a negative starch-KI test. Nevertheless, upon attempted distillation (pot temp 120°; 0.05 mm) of the final product 3, a violent explosion ensued, without prior warning, resulting in serious injury. In another instance, the epoxidation of 2 using a 40% solution of peracetic acid gave the epoxide 4 which was similarly washed with 10% sodium sulfite and gave a negative starch-KI test. Distillation of 4, proceeded without event, but the small forerun obtained (bp 40-70°, 0.75 mm) detonated violently upon merely placing the collection flask in a glassware bin. Subsequent to the latter detonation, the remaining distillation fractions [bp 70-75° (0.75 mm); 75-80° (0.75 mm)] were examined for traces of peroxides. Both fractions gave negative starch-KI tests yet produced strong positive tests for organic peroxides using EM Reagent-ether peroxide test paper. Stirring a dilute methylene chloride solution of these fractions with 10% aqueous sodium sulfite did not destroy these

peroxides. Similar treatment with $\text{Na}_2\text{S}_2\text{O}_5$ which is purported to rapidly destroy ether peroxides¹ rendered the solution peroxide-free only after several hours.

In both ill-fated procedures this sensitive contaminant, possibly a secondary product derived from 2-hydroperoxytetrahydropyran,² was not detectable by routine tlc, nmr, or infrared methods employed. Due to the severity of the explosions, no additional experiments were performed to specifically identify the contaminant. In our judgment, the THF and other related acetals (1,3-dioxolanes, methoxymethyl ethers, etc.) should be presumed to be incompatible with peroxy reagents. When their use is essential to synthetic strategy, the utmost care should be taken to destroy organic peroxides¹ before product isolation, particularly distillation.

EXPERIMENTAL Hydroboration of 1 - A solution of 1 (17 g) in dry THF was treated with 34 ml 1M BH_3 -THF (Aldrich) at 0° and stirred (N_2) for 2 hr at 0° and 1 hr at 25°. Excess diborane was destroyed by addition of 3 ml of water and 20 ml 3N NaOH was added followed by 20 ml 30% H_2O_2 . The H_2O_2 was added at a rate to maintain a reaction temperature between 30-35°. After stirring at 25° for 30 min, the solution was poured into ice-water (300 ml) and the organic layer separated. The aqueous portion was extracted with ether (2 X 500 ml) and the combined organic solution was washed with saturated brine until the aqueous layer was neutral. The organic layer was then washed with 10% sodium sulfite (2 X 100 ml) and gave a negative starch-KI test. The organic layer was dried (MgSO_4) and concentrated to give 16.56 g of crude 3 as a colorless oil. The distillation procedure began at 0.05 mm. On reaching a pot temperature of 120°, a violent explosion occurred.

Epoxidation of 2 - To a chilled solution of 2 (34.0 g, 0.2 moles) and sodium acetate (4.2 g) in 200 ml methylene chloride was added 55.0 g of a 40% solution (0.29 moles) of peracetic acid (FMC). After the addition, the solution was stirred for 2 hr at 25°. Aqueous sodium sulfite (10%) solution was added until the mixture did not give a positive test with starch-KI paper. The organic layer was separated and washed with saturated sodium bicarbonate, brine, and dried (MgSO_4). After evaporation of the solvent, the crude product was distilled at 75-80° (0.75 mm), main fraction, 32.5 g, 87.5%. The forerun [less than 1 ml, distilling at 45-70° (0.75 mm)] detonated violently upon placing the flask in a glass-washing bin.

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