Notes

A Remarkable Inversion in the Selective Oxidation of Organoboranes and Thioethers

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In recent years, borane–methyl sulfide (BMS) has emerged as a valuable reagent for the hydroboration of alkenes.[2] Its stability at room temperature, its availability in concentrated form, and its applicability in a wide variety of solvents all have combined to cause it to become a favorite reagent for such application. Following the hydroboration of alkenes with BMS, the organoborane is obtained in solution mixed with the methyl sulfide. In some cases, the presence of methyl sulfide does not interfere with the subsequent utilization of these boranes in further transformations. However, in other cases, e.g., in the alkylation reaction of α,β-unsaturated ketones with trialkylborane (which proceeds via a free-radical chain mechanism), methyl sulfide acts as an efficient free-radical scavenger and inhibits the reaction.[3] Hence, its complete removal from such reaction mixtures is important.

Recently, we synthesized for the first time borane–1,4-oxathiane (BOT) as a neat stable liquid, 8.0 M in borane, and have shown that it is an extremely useful reagent for the conversion of alkenes to organoboranes in a wide variety of solvents, minimizing the problems of odor encountered with BMS. Oxidation with alkaline hydrogen peroxide yielded the corresponding alcohols in excellent yields.[4] It was observed that during the oxidation of organoboranes from a solution containing thioethers, e.g., methyl sulfide or 1,4-oxathiane, use of the calculated amount of hydrogen peroxide is often associated with simultaneous oxidation of a considerable amount of the thioether.[5] Hence, an excess of hydrogen peroxide had to be used. In view of the discovery of the increasing number of borane reagents (as borane–thioether complexes) as useful hydroborating reagents, we thought it desirable to develop procedures which would allow one to oxidize, from a solution of organoborane and thioether, one component selectively, without affecting the other, or vice versa.

It is known that sodium hypochlorite oxidizes thioethers all the way to the sulfones.[6] We have, however, discovered that treatment of methyl sulfide and 1,4-oxathiane with a controlled quantity of sodium hypochlorite in the form of commercial Clorox (a 5.25% solution of NaOCl in water) or with calcium hypochlorite in 1:1 and 1:0.5 molar ratios, respectively, in tetrahydrofuran (THF) or diethyl ether at

25 °C results in the fast oxidation of such thioethers to the corresponding sulfoxides. The sulfoxides are then extracted into the aqueous layer. It is also known that sodium hypochlorite oxidizes organoboranes sluggishly at 25 °C.[7] It therefore appeared to us that the hypochlorites might be able to oxidize thioethers selectively from a solution of the organoborane without oxidizing the latter. Indeed, treatment of a 1.0 M solution of tri-n-octylborane and either methyl sulfide or 1,4-oxathiane in THF with an equimolar quantity of sodium hypochlorite at 25 °C results in the complete oxidation of the thioether, as is evident by analysis for the thioether by GC using an internal standard. The reaction is fast, complete at 25 °C within minutes of the addition of the oxidizing agent. The organic layer containing the organoborane was recovered and dried. Examination of the ^{11}B NMR spectrum showed the absence of any product derived from oxidation of the tri-n-octylborane. Removal of the THF yielded tri-n-octylborane in a yield of 96%. This was then oxidized by the standard procedure with alkaline hydrogen peroxide. 1-Octanol was isolated in a yield of 84%. The above reaction with calcium hypochlorite was not as clean as that with sodium hypochlorite, and was accompanied by the oxidation of some of the tri-n-octylborane.

The sulfoxides produced in these oxidations are highly soluble in water. Consequently, they are readily washed away from the reaction mixture to leave the organoborane behind in a form suitable for further transformations.

We next turned our attention to finding a reagent which would oxidize the organoborane cleanly to alcohol, without oxidizing the thioether, when both are present in solution. Thioethers are oxidized by 30% hydrogen peroxide to sulfoxide at 25 °C, and the reaction is known to be acid catalyzed.[8] Thus, the oxidation in water or alcohol (which play the role of acid) is very fast, and the rate is ~12 times faster than that in Et$_2$O.[8] The oxidation of thioether from a 1.0 M THF solution is comparatively slow, but is complete within 2 h at 25 °C. The oxidation is still slower when the reaction mixture in THF contains ~20% aqueous sodium hydroxide (2 h at 25 °C and 0.5 h at 55 °C). This observation, coupled with the fact that alkaline hydrogen peroxide oxidizes organoborane rapidly to alcohol at 25 °C,[9] led us to believe that strongly alkaline hydrogen peroxide would be the reagent of choice for the selective oxidation of organoborane in the presence of thioether. Thus, treatment of a solution of 1 mol of tri-n-octylborane and 1 mol of methyl sulfide or 1,4-oxathiane in 0.5 M THF with 1 mol of sodium hydroxide (as a 3 M solution) and 3 mol of hydrogen peroxide (standard oxidation procedure for organoborane) results in the oxidation of 80% of the tri-n-octylborane and 20% of the thioether. Thus, the reaction was only partially selective. We then reasoned that an increase in the amount of base in the above oxidation above the standard amount should suppress the oxidation of the thioether, thereby allowing the organo-

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borane to be oxidized quantitatively. Indeed, when 3 mol of sodium hydroxide (3 M solution) was used in the above reaction, oxidation of thioether was totally suppressed and the tri-n-octylborane was quantitatively oxidized to the corresponding alcohol (98% yield by GC).

We have therefore demonstrated that from a solution of organoborane and thioether, by a careful choice of reagent, it is possible to oxidize the organoborane in the presence of the thioether or to oxidize the thioether in the presence of the organoborane.

Experimental Section

All operations were carried out under nitrogen. THF, Et$_2$O and 1-octene were distilled from lithium aluminum hydride and stored under nitrogen. Methyl sulfide and 1,4-oxathiane were distilled from 9-borabicyclo[3.3.1]nonane (9-BBN) and stored under nitrogen. Commercial Clorox (5.25% sodium hypochlorite in water) was used as the source of sodium hypochlorite.

Tri-n-octylborane. To a well-stirred solution of borane–methyl sulfide (5.4 mL, 50 mmol) at 20 °C there was added under nitrogen 1-octene (23.6 mL, 150 mmol) dropwise over a period of 15 min. The reaction mixture was stirred at this temperature for an additional 15–20 min. Methyl sulfide was removed under vacuum (15 mm, 1 h) to leave essentially pure tri-n-octylborane (100%) in the flask.

Oxidation of Thioether from a Solution of Tri-n-octylborane in 1.0 M THF with Sodium Hypochlorite. Oxidation of methyl sulfide in the presence of tri-n-octylborane is described as representative. With the usual experimental setup,[10] the reaction flask was charged with tri-n-octylborane (2.21 mL, 5 mmol), methyl sulfide (0.38 mL, 5 mmol), n-decane (0.38 mL, 2 mmol), and THF (2.03 mL) to make the reaction mixture 1.0 M in borane. The flask was surrounded by a water bath (20 °C) and sodium hypochlorite (7.2 mL, corresponding to 5 mmol of NaOCl) was added dropwise over a period of 10–12 min while the contents of the flasks were stirred. After 15 min, the aqueous layer was saturated with anhydrous potassium carbonate and the organic layer was analyzed by GC using 10% SE-30 on Chromosorb (60/80), 6 ft × 0.25 in. column. GC analysis revealed the absence of methyl sulfide, indicating thereby its 100% conversion to the sulfoxide. The ^{11}B NMR spectrum of the organic layer indicated the presence of only trialkylborane at δ +85.7 (relative to BF$_3$·OEt$_2$) and no oxidation product arising from the trialkylborane.

For the isolation of tri-n-octylborane or its oxidation product, 1-octanol, after the selective removal of methyl sulfide, the following experiments were done. Tri-n-octylborane (6.63 mL, 15 mmol) and methyl sulfide (1.14 mL, 15 mmol) in THF (7.23 mL) were placed in a flask surrounded by a water bath (20 °C). Sodium hypochlorite (21.6 mL, 15 mmol of NaOCl) was added dropwise over 25–30 min. After 10 min at this temperature, the aqueous layer was saturated with anhydrous potassium carbonate. The THF layer was separated under nitrogen. The aqueous layer was washed with 2 × 5 mL of THF and the washings were transferred to the main solution. The organic layer was dried over anhydrous magnesium sulfate under nitrogen and filtered, and removal of the solvents yielded 5.05 g (96%) of the tri-n-octylborane. Alternatively, the above tri-n-octylborane (4.42 mL, 10 mmol) was dissolved in THF (5.58 mL) and the reaction mixture was oxidized by adding 3 M sodium hydroxide (3.7 mL, 11 mmol) followed by 30% hydrogen peroxide (4.0 mL, 32 mmol). After 1 h at 50 °C, the aqueous layer was saturated with anhydrous potassium carbonate and the organic layer was separated. The aqueous layer was extracted with two 15-mL portions of ether and the combined extract was washed with saturated brine solution (15 mL). The organic layer was dried over anhydrous magnesium sulfate. Removal of solvent and distillation afforded 3.28 g of 1-octanol (84%) (containing 5–6% of 2-octanol), bp 85–87 °C (15 mm).

Oxidation of Tri-n-octylborane from a Solution of Thioether in 0.5 M THF with Alkaline Hydrogen Peroxide. The oxidation of tri-n-octylborane from a solution of 1,4-oxathiane is described as representative. The reaction flask containing

tri-n-octylborane (2.21 mL, 5 mmol), 1,4-oxathiane (0.47 mL, 5 mmol), n-tetradecane (0.52 mL, 2 mmol), and THF (6.8 mL) was surrounded by a water bath (20 °C). Sodium hydroxide (3 M, 5.0 mL, 15 mmol) was added followed by 30% hydrogen peroxide (1.88 mL, 15 mmol) dropwise over a period of 10 min. After an additional 2 h at 25 °C, the aqueous layer was saturated with anhydrous potassium carbonate. Analysis of the organic layer by GC revealed 14.67 mmol of 1-octanol and 2-octanol (93:7), a yield of 98%.

Registry No. Borane–methyl sulfide, 13292-87-0; 1-octene, 111-66-0; tri-n-octylborane, 3248-78-0; methyl sulfide, 75-18-3; methyl sulfoxide, 67-68-5; 1-octanol, 111-87-5; 2-octanol, 123-96-6; borane-1,4-oxathiane, 72525-30-5.

Anhydrous Copper(II) Sulfate: An Efficient Catalyst for the Liquid-Phase Dehydration of Alcohols

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A fundamental organic transformation for which a great number of methods have been reported is the conversion of alcohols to olefins. These methods include both direct dehydration of the alcohol with numerous reagents and elimination in alcohol derivatives, usually esters.[1] New procedures and reagents appear regularly, each of which offers certain advantages over other methods.[2] We wish to report that anhydrous copper(II) sulfate, prepared by heating copper(II) sulfate pentahydrate at 200–300 °C for 2 days, serves as an effective catalyst for the dehydration of secondary, tertiary, benzylic, and allylic alcohols to the corresponding olefins. This reagent was first employed with tertiary alcohols in 1933[3] and has been nearly ignored since. We find that it is a valuable alternative to other dehydration reagents and works for a variety of alcohol types.

Of greatest note is the extreme simplicity of the method. The neat alcohol and the solid catalyst are heated at an appropriate temperature (vide infra), and the olefin distills from the reaction mixture. Dehydration occurs in the liquid phase so that gas-phase flow systems are unnecessary, the conditions are fairly mild (100–160 °C), and the time required is relatively short (0.5–15 h). Furthermore, the olefin product is uncontaminated with byproducts other than the evolved water; filtration through a cotton pad gives pure product.

Experimental Guidelines. Anhydrous copper(II) sulfate can be prepared in large batches and stored indefinitely in a desiccator. It was found that an alcohol-catalyst ratio of 1:0.75 gave the best results. The temperature required for smooth dehydration varies with the alcohol structure—the order of reactivity being tertiary ≈

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