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Oxidation of Organoboranes with Trimethylamine N-Oxide Dihydrate

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Summary

Recently it has been reported that the commercially available, easily handled trimethylamine N-oxide dihydrate is an effective oxidizing agent for organoboranes. An examination of the efficiency and reactivity of this reagent under various reaction conditions was conducted. Alkenes were hydroborated to the corresponding alkylboranes, and the subsequent oxidations to alcohols were carried out using a slight excess of trimethylamine N-oxide dihydrate. The product yields at different time intervals were determined by glpc analysis.

The oxidation can be carried out in hydrocarbon as well as ethereal solvents. The rate of the oxidation is proportional to temperature. Furthermore, long reaction times at moderate temperatures are not detrimental to yields. The rates of reaction of alkyl groups in the organoborane were determined to be tertiary > cyclic secondary > acyclic secondary > n-primary > branched primary > vinyl.

Introduction

The oxidation of organoboranes has become an increasingly important reaction as the role of organoboranes in organic synthesis has expanded. The initial synthetic application of the organoboranes was oxidation with alkaline hydrogen peroxide to give the corresponding alcohols in quantitative yields.[1]

$$R_3B \xrightarrow[OH^-]{H_2O_2} 3\ ROH$$

The organoboranes are now utilized as intermediates in a wide range of conversions leading to such classes of compounds as carboxylic acids, aldehydes, ketones, nitriles, amines, and alkyl halides.[2] Although these reactions differ in the reagents used to effect the conversions, almost all of them require either oxidation or protonolysis in the final step to remove boron from the product.

The standard oxidation methods which have been developed for the oxidation of organoboranes[2] have associated features which make them undesirable as oxidative procedures in certain instances. For example, the aldehyde products from the hydroboration-oxidation of terminal alkynes are unstable to the strongly basic conditions of alkaline hydrogen peroxide oxidation,[3] oxidation with molecular oxygen is non-sterospecific,[4] and the anhydrous amine oxide is tedious to prepare.[5]

Recently, it has been reported that the commercially available, easily handled, solid trimethylamine N-oxide dihydrate is an efficient reagent for organoborane oxidation.[6] In addition, the reagent will tolerate a wide variety of functional substituents. Such advantageous properties in an oxidizing agent made it desirable to determine under what circumstances trimethylamine N-oxide dihydrate could be employed. A systematic study was undertaken to investigate the effects of solvent, temperature, and structure upon the oxidation of organoboranes to alcohols. The results are reported in the present paper.

RESULTS AND DISCUSSION

Solvent Effects. Oxidations of organoboranes with trimethylamine N-oxide dihydrate (TMAO) can be carried out in either hydrocarbon or ethereal solvents. The rate of oxidation appears to be largely insensitive to the solvents utilized, especially at the higher temperature. The results for the oxidation of tricyclohexylborane are summarized in

Figure 1. Results obtained utilizing other organoboranes are similar; the only significant difference being variations in overall yield.

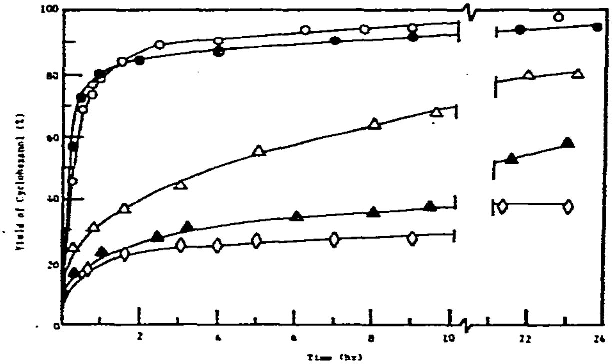


Figure 1. Solvent effects on the oxidation of tricyclohexylborane with TMAO.
○, Toluene, 66°; ●, THF, 66°; △, $CHCl_3$, 25°, ▲, THF, 25°; ◇, Toluene, 25°.

TMAO exists as a suspension in tetrahydrofuran (THF), toluene, and chloroform. Because of TMAO's low solubility, the reaction rates are often dependent on the stirring rate; in all oxidations with TMAO, vigorous stirring should be maintained. Only at the lower temperature and over longer reaction times is there any noticeable solvent effect on product yield. The tendency for TMAO to aggregate in solution appears to decrease in the order $CHCl_3$ > toluene > THF. Polar aprotic solvents such as nitrobenzene or dimethyl sulfoxide do not solvate the amine oxide. TMAO is soluble in protic polar solvents such as ethanol. However, organoboranes are only sparingly soluble in alcoholic solvents and little efficiency is gained by dissolving the TMAO in ethanol prior to the oxidations. The absence of solvent effects at the higher temperature can be attributed to the increased solubility of TMAO as its melting point of 91°C is approached.

Hydroborations which are commonly performed in ethereal solvents can now be followed by oxidation in either ethereal or hydrocarbon solvents using

TMAO. Furthermore, since the addition of a large quantity of water (as would be the case in aqueous peroxide oxidations) is no longer a necessity using TMAO, product isolation is often more simple.

Temperature Effects. The rate of the oxidation reaction is temperature dependent. The yield of alcohol increases with increasing temperature. The results are shown in Figures 2 and 3.

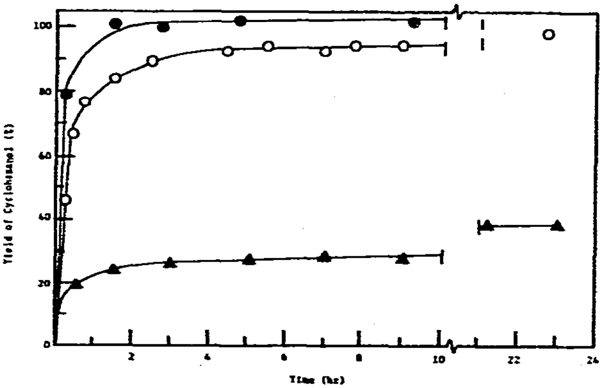
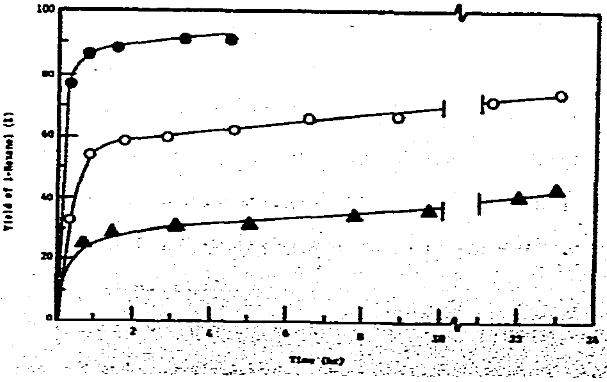


Figure 2. Temperature effects on the oxidation of tricyclohexylborane with TMAO. ●, 110°; ○, 66°; ▲, 25°. The solvent was toluene. The percent yield of alcohol is normalized for a 94% theoretical yield of 1-hexanol.



Previous work had indicated that the second and third alkyl groups on the organoborane are removed more slowly than the first,[5] requiring either higher temperatures or longer reaction times. That the reaction can be made to be selective by proper choice of temperature is illustrated in the oxidation of tri-n-hexylborane, Figure 3. At 25°, one alkyl group is removed at 66°, two alkyl groups are removed and at 138°, the reaction is complete. An identical result is observed with tri-n-octylborane.

The oxidation can be initiated at one temperature and then concluded at a higher temperature. Whether the reaction is manipulated in this manner or conducted entirely at the higher temperature, the yield of alcohol is identical. If only moderate reaction temperatures can be tolerated by reactants or products, lengthening the reaction time will be adversely affect the yield of alcohol.

Structural Effects. Symmetrical trialkylboranes. The rate of oxidation is very sensitive to the structure of the alkyl groups in the organoborane. The rate of oxidation decreases in the order s-cycloalkyl > s-alkyl > n-alkyl > β-branched p-alkyl. The results are summarized in Figure 4. In the

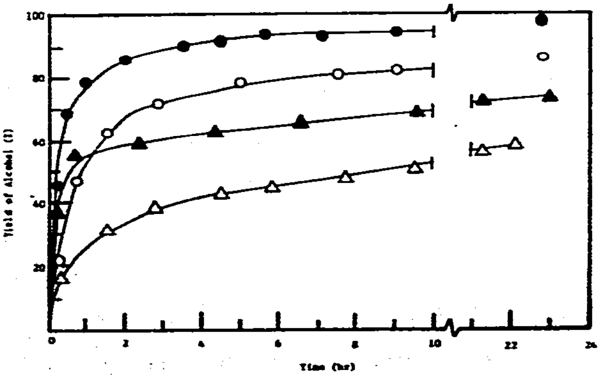


Figure 4. Structural effects on the oxidation of trialkylboranes with TMAO. ●, Tricyclohexylborane; ○, Tris-(2- and 3-octylborane). ▲, Tri-n-hexylborane; △, Tris-2-methylpentylborane. The oxidations were performed in toluene at 66°. The percent yield of alcohol is normalized for a 94% theoretical yield of 1-hexanol, and a 79% theoretical yield of 2-methyl-1-pentanol. The yield of octanol represents the combined yields of 2- and 3-octanol.

hydroboration of 1-hexene, 6-7% of the secondary alkylborane is formed,[7] and consequently, the product contains approximately 7% of the secondary alcohol. Although the reaction is not quantitative for all the trialkyl-boranes at 66°, the oxidation can be completed by increasing the temperature.

Mixed trialkylboranes. When mixed trialkylboranes are oxidized with TMAO, the rate order 3° > 2° > 1° is observed.

When the mixed borane, dicyclohexyl-n-octylborane, is oxidized with two equivalents of TMAO in THF at 66°, the secondary cyclohexyl group is preferentially removed with 14% ± 3% of the theoretical amount of 1-octanol found.

In the oxidation of those mixed boranes containing the tertiary thexyl (2,3-dimethyl-2-butyl) radical, the product analysis always indicated more thexyl alcohol than any other alcohol component. (Although the yield of thexyl alcohol could not be quantitatively determined, its presence was discernible by glpc). For example, the oxidation of thexyl-di-n-octylborane with one equivalent of TMAO in THF at 26° produced only 21.6 ± 3% of the "theoretical amount" of 1-octanol after 10 hrs. Likewise, when thexylcyclohexyl-n-octylborane was oxidized with one equivalent of TMAO in THF at 26°, 39.9 ± 3% of the theroetical amounts of cyclohexanol and 14.4 ± 3% of the theoretical amount of 1-octanol were found after 12 hrs.

Vinyldialkylboranes. The oxidation of the vinyl group with TMAO is very slow.[8] When dicyclohexyl-1-hexenylborane was oxidized with the stoichiometric amount of TMAO in diglyme at 130° for 1.5 hr., only 38.7% of the vinyl groups had been oxidized to hexanal. During this time, both of the cyclohexyl groups would have been oxidized. Thus, the vinyl moiety is the slowest in the rate ordering of structural groups. The rates of alkyl group migration are in agreement with those from studies using other oxidizing agents.[9]

Conclusions

The use of trimethylamine N-oxide dihydrate as an oxidizing agent for organoboranes should be considered as a viable alternative to the standard alkaline hydrogen peroxide oxidation procedure.

Experimental Section

Proton NMR spectra were recorded on a Varian Associates T-60 spectrometer. The yield of oxidation products was determined using glpc, (except for 1-hexanal which was determined by nmr), using a 10 ft column of 5% SE-30 on Chromosorb W. The instrument was a Varian Associates Model 90-P. The alcohol products were analyzed as the silyl ether derivatives.

Materials. Tetrahydrofuran was dried with excess lithium aluminum hydride and distilled under nitrogen. Diglyme was dried with calcium hydride and lithium aluminum hydride and distilled under reduced pressure. Borane solution in THF was prepared from sodium borohydride and boron trifluoride etherate. Trimethylamine N-oxide dihydrate and all of the organic compounds used are commercially available, and were used as received.

Preparation of Organoboranes. The monoalkyl-, dialkyl-, and trialkylboranes were prepared according to published procedures.[2,10,11]

Oxidation of organoboranes with trimethylamine N-oxide dihydrate. The appropriate solvent (20 ml) was added to a solution of organoborane (5.0 mmole) in tetrahydrofuran. The tetrahydrofuran was then removed under reduced pressure, and a glpc or nmr internal reference was introduced. While the apparatus was flushed with nitrogen, the solid trimethylamine N-oxide dihydrate (16.5 mmole, 1.83 g) was added through the neck of the flask. Vigorous stirring was initiated and the flask was immediately submerged in a constant temperature bath (I^2R Therm-O-Watch Electronic Controller).

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