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AN EFFICIENT REDUCTION OF ACETALS AND KETALS TO METHYL ETHERS.

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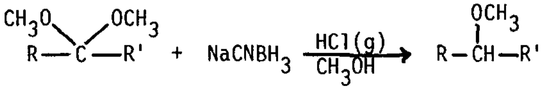
A number of reagents are known which can effect reductive cleavage of acetals and ketals to ethers. These include lithium aluminum hydride - Lewis acid mixtures,[1,2] diisobutylaluminum hydride,[3] hydrogen with rhodium on alumina catalyst,[4] and diborane in tetrahydrofuran.[5]

We have found that sodium cyanoborohydride in methanol with hydrogen chloride gas is also an efficient reagent for reduction of acetals and ketals to methyl ethers at ice-bath temperatures. This reagent mixture has the advantage that the reagents are readily available, easily stored, and the reaction is quick and efficient.



$$R{-}C(OCH_3)_2{-}R' + NaCNBH_3 \xrightarrow[CH_3OH]{HCl(g)} R{-}CH(OCH_3){-}R'$$

In each of the experiments listed in the table, hydrogen chloride gas was bubbled through a solution of a 1.5 molar ratio of sodium cyanoborohydride and one gram of the acetal or ketal in 10 ml of methanol at 0° until the reaction mixture remained acidic as determined by wet "Hydrion" paper. On the scales run the reaction times were about 10 minutes. The methyl ethers were isolated by pouring the reaction mixture over ice and extracting with pentane. The pentane extracts were washed with saturated sodium bicarbonate and dried over potassium carbonate. Pentane was removed and the product distilled.[6] GC analysis of the pentane extracts showed only the methyl ethers present.

The utility of the reaction can be seen from the data. Aliphatic acetals and ketals are efficiently reduced to methyl ethers. The dimethyl acetal of benzaldehyde is cleanly reduced to the methyl ether with no over-reduction to toluene observed by GC. Potentially acid sensitive 1,1-dimethoxy-2,4-pentadiene is also cleanly reduced to the corresponding allylic methyl ether without rearrangement or incorporation of hydrogen chloride.

When 2-phenyl-2-methyl-1,3-dioxolane is reduced under the above conditions the only product observed is 1-phenyl-1-methoxyethane. Presumably solvent intercepts the intermediate cation faster than hydride from the borohydride.

ACKNOWLEDGEMENT

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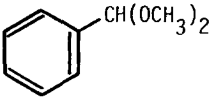
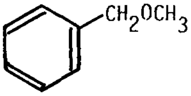
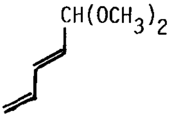
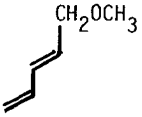
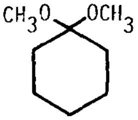
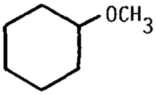
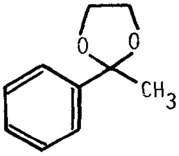
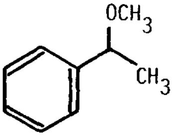
Table

Acetal or ketal	Product	% Yield[a]
$CH_3(CH_2)_8CH(OCH_3)_2$	$CH_3(CH_2)_8CH_2OCH_3$	83
		88[b]
		46 (94)
		78
		76

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a.) All yields are isolated yields except those in brackets which are GC yields (dodecane internal standard)

b.) No toluene observed by GC analysis.

REFERENCES AND NOTES

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6. All products gave spectra consistent with the assigned structures.