

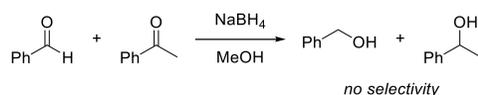


Selective Reduction of Aldehydes and Ketones Using Disilane as a Terminal Reductant

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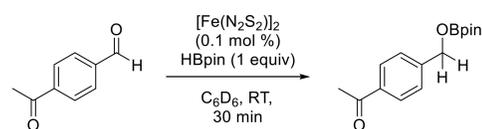
Introduction

Reduction reactions are currently hindered by a lack of functional group tolerance when using traditional reducing agents like boron and aluminum hydrides and catalytic hydrogenations. As a result, reactions such as the Luche reduction, and more recently hydrosilylations, have been developed.¹ However, these reactions do not allow for selective reduction of aldehydes and ketones when similar carbonyl functional groups are present, although there have been reports of aldehydes being selectively reduced by iron-imine catalyzed hydroboration and iron-complex catalyzed hydrogenation.²

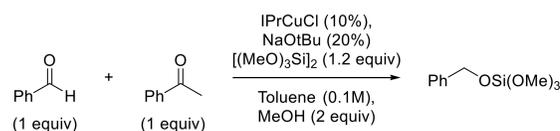


Herein, we report a reaction that does selectively reduce aldehydes or ketones in the presence of other readily reducible functional groups by using a copper catalyst and disilane as a terminal reductant. As a result, aldehydes and ketones were reduced to alcohols via a mechanism involving a 1,2-Brook Rearrangement.³ We found that this method can also selectively reduce aldehydes over ketones when both functional groups are present and allows for a broad substrate scope, enabling a greater range of reactions.

previous work:

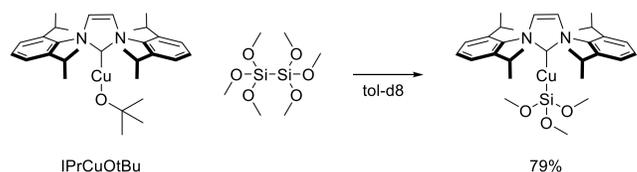


current work



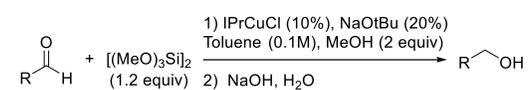
Previous Work

Previous work demonstrated copper alkoxides can activate a disilane.⁴ The copper-silyl complex showed mild reactivity which suggested it may undergo selective transformations when paired with an electrophile that has little steric bulk.

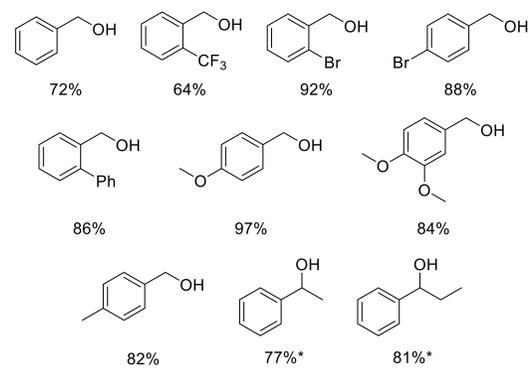


Substrate Scope

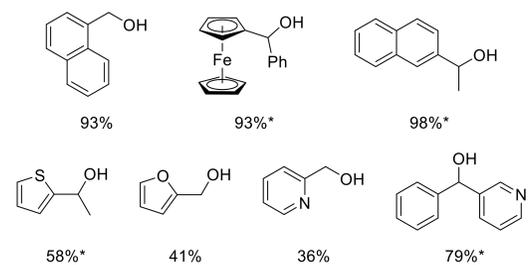
The copper silyl complex could be used as a catalyst to selectively reduce aldehydes and ketones, although ketones required excess silane and methanol.



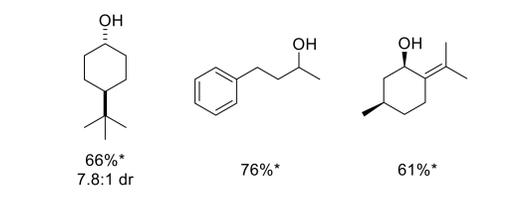
aromatic aldehydes and ketones:



hetero- and polyaromatics:



aliphatic ketones:

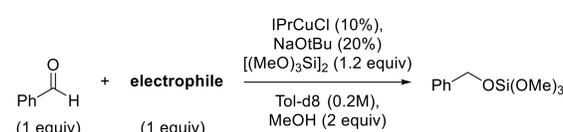


* 2.5 equiv of Si₂(OMe)₆ and 3.0 equiv of MeOH was used.

Overall, the reduction worked well with both electron-rich and electron-poor carbonyls. Additionally, poly- and heteroaromatics worked well, except smaller heteroaromatics tended to have poor yields because of increased water solubility. Aliphatic ketones also worked well with good stereoselectivity.

Functional Group Compatibility

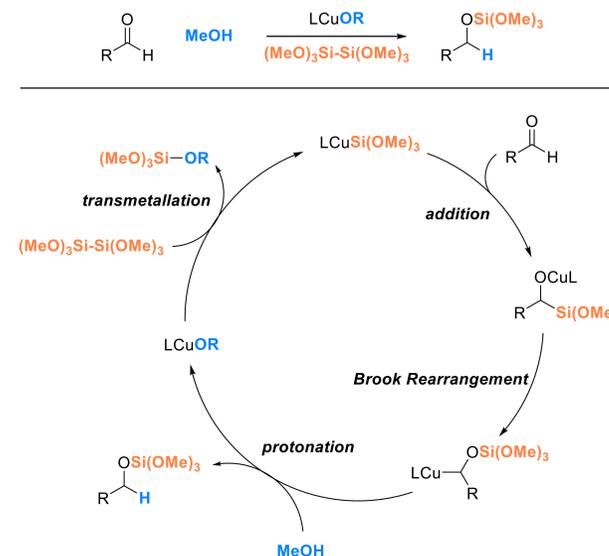
Selectivity was tested through a series of competition experiments. Despite the steric and electronic similarities between benzaldehyde and other electrophiles, the reaction still preferred to reduce benzaldehyde.



entry	electrophile	aldehyde reduction	selectivity
1		51%	5:1
2		78%	>20:1
3		87%	12:1
4		82%	>20:1
5		84%	>20:1
6		85%	>20:1
7		70%	>20:1
8		80%	8:1

Yields and ratios were determined by NMR using mesitylene as an internal standard.

Proposed Mechanism



The Brook Rearrangement of an α -silyl alcohol is an intramolecular migration of a silyl group from carbon to oxygen in the presence of a catalytic amount of base.⁵

Future Directions

1. Complete mechanistic studies to gain insight into the transformation.
2. Perform an asymmetric reduction using chiral ligands.
3. Form the α -silyl alcohol rather than the Brook Rearrangement product by using a different disilane.

Conclusions

We have shown that the silylation of benzaldehyde favors formation of a silyl ether through Brook Rearrangement. The silyl ether can be easily cleaved to reveal an alcohol. Overall, this reduction is highly selective for aldehydes over a number of other easily reducible functional groups. Future work will focus on understanding the mechanism further and expanding our understanding of the reaction to other transformations.

Acknowledgements

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