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Selective Deoxygenation of Allylic Alcohols and Acetates by Lithium Perchlorate Promoted Triethylsilane Reduction

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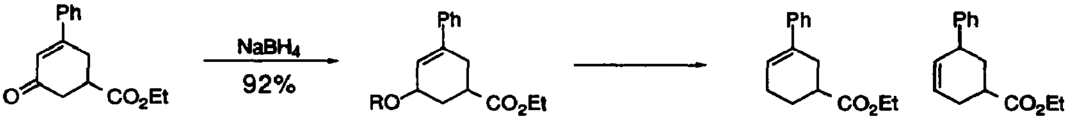
Abstract: A series of cyclic secondary allylic alcohols and acetates was deoxygenated using triethylsilane in the presence of ethereal lithium perchlorate. Under these conditions the allylic oxygen functionality was selectively removed in the presence of esters, isolated olefins, ketals and tertiary alcohols. Primary allylic alcohols were not deoxygenated under these conditions.

We recently required a method for the deoxygenation of ketone **1**.[1] The Clemenson and the Wolf-Kishner reductions failed to produce the desired arylcyclohexene **3**. This prompted us to investigate the reductive deoxygenation of the allylic alcohol **2a** which could be readily obtained from enone **1** via sodium borohydirde reduction.

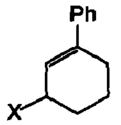


1 **2a** R = H **2b** R = Ac **3** **4**

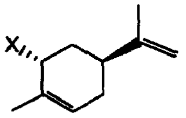
While allylic acetate **2b** was easily reduced by sodium cyanoborohydride in the presence of a catalytic amount of palladium tetrakistriphenylphosphine,[2] we desired a method which would directly deoxygenate allylic alcohol **2a** without reducing its ester functionality. Direct reduction of allylic (or benzylic alcohols) usually requires more forcing conditions. For example, reduction of alkyl and benzylic hydroxyl groups can be effected by aluminum hydride complexes.[3] Unsaturated ketones have also been deoxygenated under these conditions.[4] Recently triethylsilane in the presence of trifluoroacetic acid[5] and ammonium fluoride[6] has also been shown to reductively deoxygenate benzylic alcohols. However, a variety of functional groups will not tolerate such harsh conditions. Selective deoxygenation of allylic alcohols requires that the reaction be carried out under milder conditions.

Grieco and Pearson have both recently reported on the use of ethereal solutions of lithium perchlorate to promote the displacement of allylic oxygen functionalities by a variety of nucleophiles.[7,8b] Ethereal lithium perchlorate has also been shown to cause the rearrangement of allylic ethers.[8] In accord with Winstein's earlier findings,[9] the lithium perchlorate-ether medium is thought to promote the ionization of the allylic oxygen bond activating it toward nucleophilic substitution. If a hydride could act as a nucleophile in such a reaction, a relatively mild method of allylic alcohol reduction could be effected.

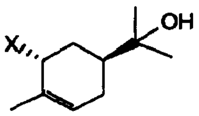
This reasoning led us to attempt the reduction of alcohol **2a** with triethylsilane in a 3M ethereal lithium perchlorate solution. These conditions converted alcohol **2a** to the desired cyclohexene **3** in 89% yield along with 5% of the undesired isomer **4**. To investigate the scope of this reaction a series of cyclohexenyl alcohol and acetate substrates shown below was subjected to these conditions and the results are listed in the Table.



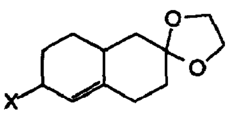
5a X = OH
5b X = OAc
6 X = H



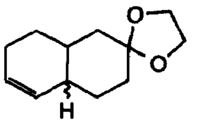
7 X = OH
8 X = H



9 X = OH
10 X = H



11 X = OAc
12 X = H



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Table[10]

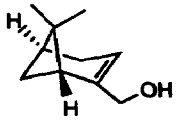
Substrate	Product (Yield)
2a	**3** (89), **4**(5)
2b	**3** (89), **4**(5)
5a	**6** (92)
5b	**6** (92)
7	**8** (68)
9	**10** (52)
11	**12** (48), **13** (12)

As can be seen from the Table, the reaction works equally well with both allylic alcohols and allylic acetates. Both allylic acetates **2b** and **5b** underwent reduction to their respective products **3** (along with a small amount of **4**) and **6**. There seems to be no significant difference either in the rate of reduction or yields for allylic acetates and allylic alcohols. Alcohols **7** and **9** were also successfully reduced using these conditions, despite the fact they contain no exocyclic substitution on the olefin.[8b] Perhaps this explains their somewhat diminished yields as compared to **2a** and

5a. The isolated olefin found in **7** as well as the tertiary hydroxyl functionality found in **9** were unaffected by these conditions. Deoxygenation of alcohol **11** gave a mixture of **12** as well as products arising from double bond isomerization.

Consistent with other silane reductions[5] we found triethylsilane to be a superior reducing reagent to the more hindered *tert*-butyldimethylsilane and triisopropylsilane. These silanes were considerably slower in reducing the allylic alcohol in the presence of etheral lithium perchlorate. However we are continuing to evaluate alternative hydride sources in these laboratories.

While the reaction seems general for cyclic secondary allylic alcohols and acetates, primary allylic alcohols and acetates were not reduced under these conditions. No reaction was observed with the primary allylic alcohol **14**. Similarly neither cinnamyl alcohol **15a** nor the corresponding acetate **15b** reacted under these conditions. This contrasts with the earlier work of Pearson[6] in which a silylketene acetal was added to cinnamyl acetate **15b** under similar conditions as shown below to give ester **16**. Presumably the greater neucleophillic strength of the ketene silyl acetal allows this reaction to proceed.



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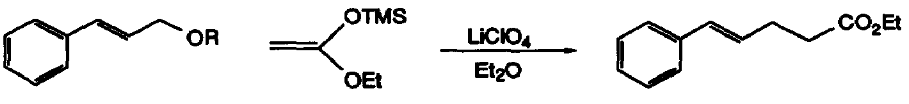

15a R = H
15b R = Ac

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Thus allylic deoxygenation for cyclohexenyl alcohols can be conveniently carried out using triethylsilane in the presence of ethereal lithium perchlorate. Unlike other methods of allylic dexygenation it does not require conversion to the acetate or expensive transition metal catalysts. A variety of functional groups are tolerated including esters, hydroxyls and ketals .

General Procedure

Lithium perchlorate solutions were freshly prepared from reagent grade lithium perchlorate which had been dried for 8 hours at 170°C under vacuum. The substrate, at a concentration 0.25M in 3.0M lithium perchlorate-diethyl ether solution, was treated with 3 equivalents of triethylsilane at room temperature, and the reaction was stirred under nitrogen for 16 hours. The mixture is partitioned between water and diethyl ether. The organic layer was dried with $MgSO_4$ and concentrated. The crude products were purified by column chromatography.

Acknowledgment Prof. William Pearson (Univ. of Michigan) is acknowledged for helpful discussions during the preparation of this manuscript and for alerting us to an example similar to our work in the recently published doctoral thesis of Jeff Schkeryantz (University of Michigan, 1993).

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10. All products had satisfactory NMR, and mass spectral analysis. Where possible compounds were compared with authentic samples by TLC.

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