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Facile O-Deallylation of Allyl Ethers via S_N2' Reaction with *tert*-Butyllithium

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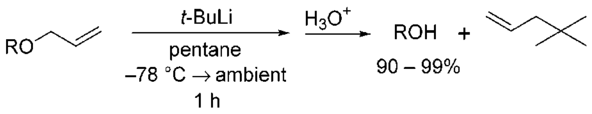
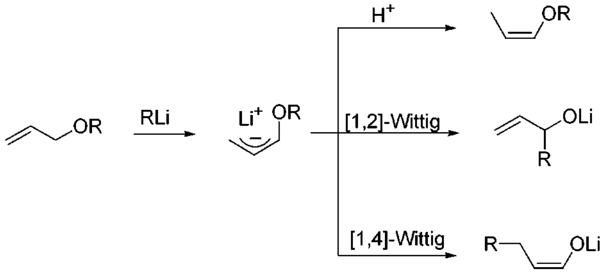
ABSTRACT



Allylic ethers are converted to the corresponding alcohol or phenol in virtually quantitative yield at temperatures below ambient simply by stirring a hydrocarbon solution of the ether with 1 molar equiv of *tert*-butyllithium. The reaction, which produces 4,4-dimethyl-1-pentene as a coproduct, most likely involves an S_N2' attack of the organolithium on the allyl ether.

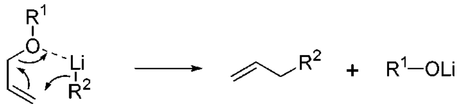
The selective metalation resulting from treatment of simple allyl ethers with an organolithium reagent has been known for over 25 years.[1] As illustrated in Scheme 1, the *Z*-configured allyloxy organometallic species produced by deprotonation at the allylic position[2] may be trapped by electrophiles at low temperature,[1] while at higher temperatures [1,2]- and [1,4]-Wittig rearrangements are observed.[3] It is significant that in virtually all of these studies a strongly lithiophilic solvent such as THF was used for the deprotonation.[1,2]

Scheme 1



In light of the facility with which allyl ethers are deprotonated in the presence of an organolithium, we were intrigued by a 1965 paper by Broaddus reporting the cleavage of several alkyl allyl ethers upon treatment with *n*-butyllithium in a hydrocarbon solution at 70 °C to give the lithium alkoxide and 1-heptene.[4] The reaction was formulated (Scheme 2) as an S_N2' process in which coordination of the organolithium with the ether oxygen provides a cyclic transition state for the cleavage.[4]

Scheme 2



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(1) (a) Evans, D. A.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560. (b) Still, W. C.; Macdonald, T. L. *J. Am. Chem. Soc.* **1974**, *96*, 5563. (c) Hartmann, J.; Muthukrishnan, R.; Schlosser, M. *Helv. Chim. Acta* **1974**, 57, 2261. (d) Still, W. C.; Macdonald, T. L. *J. Org. Chem.* **1976**, *41*, 3620. (e) Hoppe, D. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 932 and references therein.

(2) Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1979**, 1.

(3) (a) For a review of the literature dealing with Wittig rearrangements, see: Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 763. (b) For a discussion of the synthetic utility of the [1,4]-Wittig rearrangement, see: Schlosser, M.; Strunk, S. *Tetrahedron* **1989**, *45*, 2649.

(4) Broaddus, C. D. *J. Org. Chem.* **1965**, *30*, 4131.

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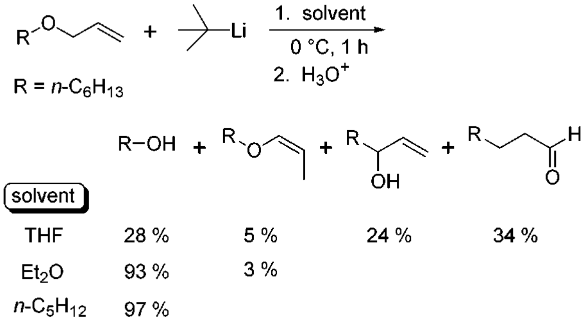
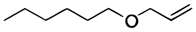
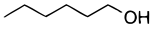
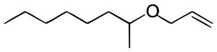
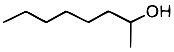
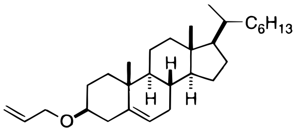
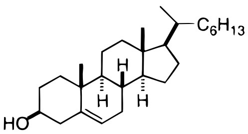
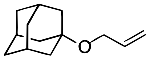
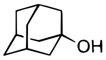
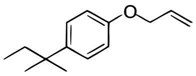
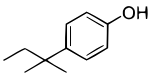
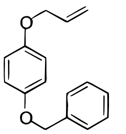
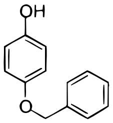
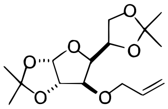
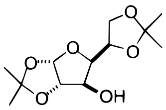
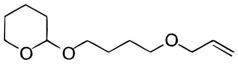
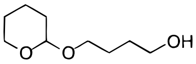
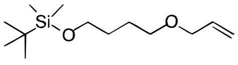
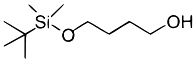
It would appear that solvent has a profound effect on the outcome of the reaction of an organolithium with an allyl ether, and this suggests that the state of aggregation of the organolithium may be the factor responsible for the course of the reaction. It occurred to us that it might be possible to test this hypothesis by observing the outcome of the reaction of an allyl ether with *tert*-butyllithium (*t*-BuLi) in various solvents since it is known that *t*-BuLi is predominantly tetrameric in hydrocarbon solution,[5] dimeric in diethyl ether,[6] and monomeric in THF.[7] As demonstrated by the results presented below, the degree of association of *t*-BuLi has a dramatic effect on the course of the reaction of this reagent with an allyl ether. Herein we report that a variety of allyl ethers may be deallylated in virtually quantitative yield at temperatures below ambient simply by stirring a hydrocarbon solution of the ether with 1 equiv of *t*-BuLi.

Scheme 3



Treatment of allyl hexyl ether in THF, Et_2O, or *n*-pentane solution with 1 equiv of *t*-BuLi in pentane for 1 h at 0 °C leads to complete consumption of the ether as adjudged by GC analysis of the crude reaction mixtures. However, as illustrated in Scheme 3, the course of the reactions is quite solvent dependent: in THF the principal products arise from [1,2]- and [1,4]-Wittig rearrangement of the lithiated ether[3] and in Et_2O the major course of the reaction is cleavage of the allyl ether, while in a pentane solution the exclusive

Table 1. *t*-BuLi-Induced Deallylation (Scheme 4)[a]

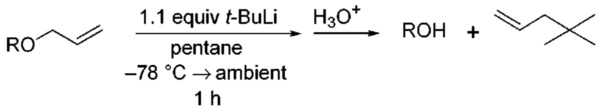
entry	allyl ether	alcohol	yield,[b] %
1			92
2			97
3			99
4			94
5			94
6			89
7			98
8			89
9			91

[a] A solution of the allyl ether in dry *n*-pentane (typically 1 mL per mmol of ether) was cooled to −78 °C, 1.1 equiv of *t*-BuLi in pentane was added, and the resulting solution was allowed to warm and stand at room temperature for 1 h before being quenched with 10% aqueous HCl. [b] Isolated yield of chromatographically pure product.

product is 1-hexanol (it should be noted that an equivalent amount of 4,4-dimethyl-1-pentene is also produced); there was no evidence of any products arising from deprotonation of the allyl hexyl ether in the pentane solution. Clearly, *t*-BuLi in pentane is an effective reagent for O-deallylation of allyl hexyl ether and, as demonstrated by the results summarized in Table 1, this reaction appears to be quite general.

The allyl unit is widely used as a robust protecting group for alcohols and phenols, and a variety of methods have been developed for its removal.[8] Most deprotection methods rely on a two-step process involving isomerization of the allyl ether to an enol ether and subsequent hydrolysis or oxidation[8] although one-pot procedures have been recently developed.[9] The facile cleavage of allyl ethers upon treatment with *t*-BuLi in hydrocarbon solution (Scheme 4) provides an alternative and very convenient method for the selective removal of an allyl protecting group.

Scheme 4



The O-deallylation of an allyl ether is easily accomplished by adding slightly more than 1 molar equiv of *t*-BuLi in either pentane or heptane to a cold[10] solution of the allyl ether in dry pentane (ca. 1 mL/mmol of ether), removing the cooling bath, and allowing the resulting solution to stand at room temperature for 1 h.[11] Addition of aqueous acid followed by simple extractive workup affords an essentially pure alcohol in high yield after removal of volatile components (including 4,4-dimethyl-1-pentene) by rotary evaporation. Examples representative of the scope of this O-deallylation protocol are presented in Table 1.[12]

Allyl ethers derived from primary, secondary, or tertiary alcohols (Table 1, entries 1−4) as well as those derived from a phenol (Table 1, entries 5 and 6) are cleaved cleanly and in excellent yield. It is significant that the allyl group may be selectively removed in the presence of a benzyloxy group (Table 1, entry 6). As might be expected, selective O-deallylation may be accomplished in the presence of an acetal (Table 1, entries 7 and 8) or a *tert*-butyldimethylsilyl protecting group (Table 1, entry 9).

The O-deallylation reaction outlined above (Scheme 4) provides a practical, convenient, and highly efficient method for the removal of an allyl protecting group, providing that the molecule is otherwise able to tolerate the use of *t*-BuLi. The mechanism of the cleavage reaction most likely involves a formal S_N2' process (Scheme 2) as first suggested by Broaddus in his pioneering study of the cleavage of alkyl allyl ethers by *n*-BuLi in hydrocarbon solution at elevated temperature.[4]

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Supporting Information Available: Experimental procedures describing the preparation of previously unreported compounds and general procedure for deallylation of allyl ethers. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) The reaction of *t*-BuLi with an allyl ether in pentane solution is typically quite exothermic, and for this reason it is prudent to initiate the reaction at a low temperature. The reactions summarized in Table 1 were initiated most conveniently by addition of *t*-BuLi to a −78 °C solution of the allyl ether in pentane and removal of the cooling bath. It might be noted that the reactions may be initiated at higher temperatures (i.e., 0 °C or higher) if care is taken to control the exotherm.

(11) As suggested by the results summarized in Scheme 3, the deallylation may also be run at low temperature using diethyl ether as solvent with only a slight diminution in yield. However, we favor the use of pentane (or similar hydrocarbon) as solvent due to the fairly rapid reaction of *t*-BuLi with diethyl ether at temperatures near ambient.

(12) All but two of the allyl ethers used in this study are known compounds whose physical and spectroscopic properties are fully in accord with those reported in the literature. The preparations of 1-allyloxy-4-(tetrahydropyran-2-yloxy)butane (Table 1, entry 8) and 1-allyloxy-4-(*tert*-butyldimethylsilyloxy)butane (Table 1, entry 9) are detailed in the Supporting Information accompanying this Letter.