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Novel Conversion of Epoxides to One Carbon Homologated Allylic Alcohols by Dimethylsulfonium Methylide

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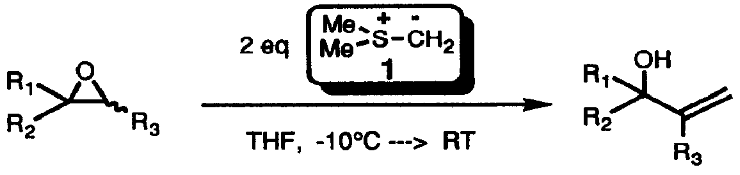
Abstract: The reaction of excess of dimethylsulfonium methylide with terminal, allylic, or benzylic epoxides affords good to excellent yields of one carbon homologated allylic alcohols.

The ready accessibility of a wide variety of epoxides in racemic or chiral form has made them popular intermediates in organic synthesis[1]. For example, numerous methods are available for their conversion to the corresponding allylic alcohols[2]. Epoxides can also be alkylated by phosphorus and oxosulfonium ylides leading, generally, to phosphoranes[3] and oxetanes[4], respectively. Herein, we report that with excess dimethylsulfonium methylide **1** (Scheme 1), terminal, allylic and benzylic epoxides are smoothly converted directly to one carbon homologated allylic alcohols in good to excellent yields. This methodology complements the reaction of **1** with halides and mesylates described in the following communication.

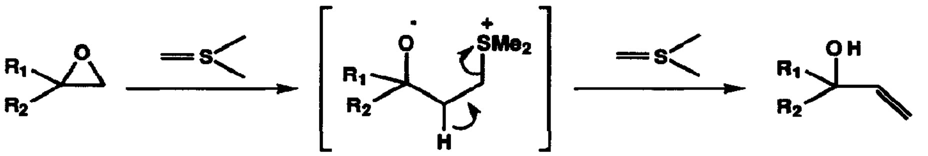


$R_1 = R_2$ = alkyl or R_1 = H, R_2 = alkyl, benzyl; R_3 = H
$R_1 = R_2$ = H or R_1 = H, R_2 = alkyl, benzyl; R_3 = benzyl

Scheme 1

The interaction of excess **1** with some representative epoxides is summarized in table 1. Monosubstituted epoxides (entries 1 and 2) gave allylic alcohols resulting from exclusive addition at the less hindered carbon. In contrast to trimethylsulfoxonium ylide, no evidence of oxetane formation or β-elimination was observed. Likewise, good yields of homologated alcohols were obtained from acyclic (entry 3) and cyclic (entry 4) 1,1-disubstituted epoxides. The conformationally rigid 4-*tert*-butylcyclohexylmethylene oxides (entries 5 and 6) furnish the corresponding axial and equatorial allylic alcohols in comparable yields. It is worth noticing that the addition of vinyl Grignard to 4-*tert*-butylcyclohexanone[5] leads to a 3:2 mixture of both isomers whereas the axial and equatorial epoxides can be obtained stereoselectively by using either the dimethylsulfoxonium or dimethylsulfonium methylides respectively[6,7]. Allylic epoxides (entries 7 and 8) lead to allylic alcohols resulting from the nucleophilic attack at the less hindered epoxide carbon. In the case of styrene oxide (entry 9), competing reactivity at the terminal and benzylic positions led to a *ca.* 8:1 mixture of α- and β- regioisomers, respectively, in 94% combined yield. Noteably, 1,2-dialkylsubstituted and 1,1,2-trisubstituted epoxides as well as oxetanes were refractory and starting material was recovered unchanged. Benzylic 1,2-disubstituted epoxides (entry 10), on the other hand, proved to be more reactive and gave exclusive addition at the benzylic position. Despite its steric hindrance, *trans*-stilbene oxide (entry 11) also furnished allylic alcohol in modest yield as the only reaction product along with recovered starting material (50%). Significantly, the normally base sensitive indene oxide (entry 12) underwent homologation to the corresponding *exo*-cyclic allylic alcohol in excellent yield.

The above result suggests that our earlier report of the conversion of ketones to one-carbon homologated allylic alcohols[8] using excess **1** proceeds *via* an epoxide intermediate. While the mechanistic details of the current reaction are not known, the proposed mechanism shown in scheme 2 is consistent with the stoichiometry of the reaction, *i.e.*, two or more equivalents of ylide are required for olefin formation whereas addition of one equivalent of epoxide to one equivalent of ylide **1** leads to a 1:1 mixture of starting product and desired allylic alcohol in high combinated yield.

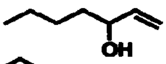
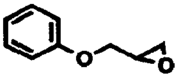
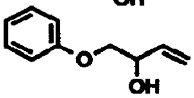
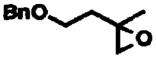
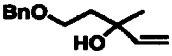
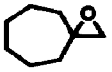
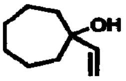
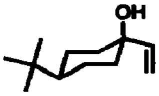
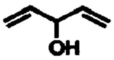
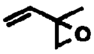
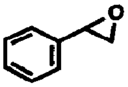
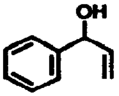
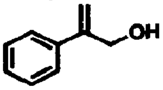
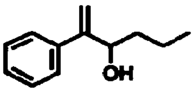
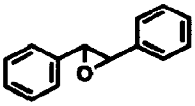
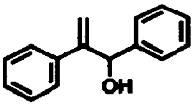
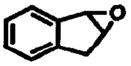
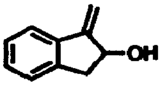


Scheme 2

Representative procedure :

To a -10°C suspension of trimethylsulfonium iodide (857 mg, 4.2 mmol, 3 equiv) in dry THF (13 ml) was added *n*-BuLi (1.6 M in hexane, 2.56 ml, 4.1 mmol, 2.9 equiv). After 30 min, 1-hexene oxide (140 mg, 1.40 mmol, 1 equiv) in THF (2 ml) was introduced, producing a milky suspension. The reaction was allowed to warm to 0 °C over about 30 minutes and then to room temperature and stirred for 2 hours. The reaction was quenched with water at 0 °C, extracted with ether and the combined organic layers dried over magnesium sulfate. SiO_2 chromatography of the crude afforded 1-heptene 3-ol (127 mg, 1.12 mmol, 80%) as a colorless oil identical in all respects with an authentic sample[9].

Table 1 . Conversion of epoxides into allylic alcohols

Entry	Substrate	Product	Yield (%)*
1			80
2			96
3			89
4			89
5			90
6			88
7			83
			11
8			93
9			81
			13
10			79
11			45**
12			92

* isolated yields

** recovered starting material 50%

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7. Other cases of such a stereoselective epoxide formation from cyclic ketones have been reported. In these cases, our reaction appears as an interesting stereochemical alternative to the less selective addition of vinyl Grignard to a carbonyl. For examples see: Bly, R. K.; Bly, R. S. *J. Org. Chem.* **1963**, *28*, 3165-3172. Carlson, R. G.; Behn, N. S. *J. Org. Chem.* **1967**, *32*, 1363-1367. Bly, R. S.; DuBose, C. M.; Konizer, G. B. *J. Org. Chem.* **1968**, *33*, 2188-2193. Cook, C. E.; Corley, R. C.; Wall, M. E. *J .Org. Chem.* **1968**, *33*, 2789-2793. Ballantine, J. D. ; Sykes, P. J. *J. Chem. Soc.(C)* **1970**, 731-735. Carruthers, W. ; Qureshi, M. I. *J. Chem. Soc.(C)* **1970**, 2238-2244.
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9. All compounds were fully characterized by NMR (^1H,^{13}C), mass spectroscopy and combustion analysis.

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