Allylic Alcohols by Methylene Transfer from *N*-Lithiomethyl-*N*,*N*′,*N*″,*N*″-tetramethyldiethylenetriamine to Epoxides

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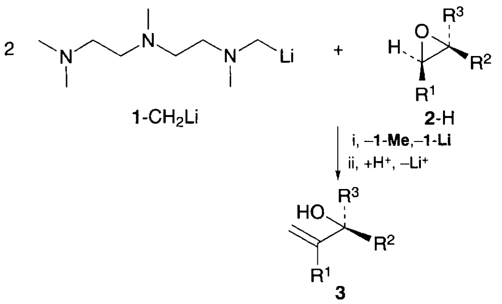
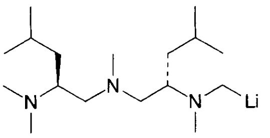
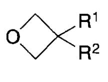
Allylic (homoallylic) alcohols are obtained from epoxides (and certain oxetanes) and *N*-lithiomethyl-*N*,*N*′,*N*″,*N*″-tetramethyldiethylenetriamine.

Treatment of 2 equiv. of *N*-lithiomethyl-*N*,*N*′,*N*″,*N*″-tetramethyldiethylenetriamine **1-CH$_2$Li**, recently described by us,[1] with 1 equiv. of an epoxide having at least one oxiranyl hydrogen **2-H** constitutes a new path to those versatile building blocks of modern organic synthesis, allylic alcohols **3**.

Yields are moderate (Table 1); however, the procedure is very simple,† clean and, as indicated by preliminary experiments, seems rather adaptable. Reaction between cyclohexene oxide and **5-CH$_2$Li**, a chiral derivative of **1-CH$_2$Li** obtained from L-leucine, gave **3d** in 75% e.e.‡ Use of oxetanes **6a,b** in the reaction with **1-CH$_2$Li** (room temp., 24 h) led to homoallylic alcohols **7a** (10%) and **7b** (80%).§ Entry 3 of Table 1 hints at a method for systematic construction of carbohydrate-type compounds from allylic alcohols by repetitive application of the sequence Sharpless oxidation/OH-protection/methylenation.




5-CH$_2$Li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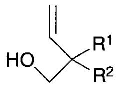
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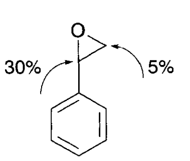
a R^1 = R^2 = Et
b R^1 = Me, R^2 = CH$_2$OMe



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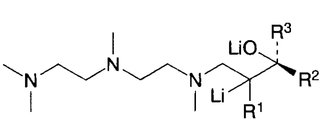
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The formation, from cyclooctene oxide, of *endo*-2-bicyclo-[3.3.0]octanol, the characteristic product of α-lithiocyclooctene oxide[4] {35%, besides 7% of the allylic alcohol **3** [R^1 = R^2 = –(CH$_2$)$_6$–, R^3 = H]}, and the preferred mode of attack on styrene oxide by **1-CH$_2$Li** (*cf.* **8**, evidenced by the mixture of isomeric alcohols obtained) suggest that the initial products from **2-H** and **1-CH$_2$Li** and its analogues are α-lithioepoxides **2-Li**.¶ As in 'reductive alkylation' of epoxides with 'normal' organolithiums,[6] **2-Li** adds a second equiv. of **1-CH$_2$Li** to give **9** which, instead of the 'normal' elimination of lithium oxide to form allylic amine, undergoes elimination of **1-Li** to give the lithium alkoxide of **3**.[7]

The marked protophilicity of **1-CH$_2$Li** could be due to its monomeric nature. The diamine corresponding to **1-CH$_2$Li**, Me$_2$NCH$_2$CH$_2$N(Me)CH$_2$Li,[8] whose organic part does not contain sufficient nitrogen atoms to support a monomeric structure, reacts with **2-Ha** to form **3a** together with the product of nucleophilic ring opening in the ratio 2 : 1.‖

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Table 1 Transformation of epoxides **2-H** into allylic alcohols **3**

Entry	Epoxide 2-H	R^1	R^2	R^3	Allylic alcohol 3	Yield (%)[a]
1	**a**	H	H	(CH$_2$)$_5$Me	**a**	61
2	**b**	H	H	(CH$_2$)$_4$CH=CH$_2$	**b**	54
3	**c**	H	H	CH$_2$OBu^t	**c**	72
4	**d**	H	–(CH$_2$)$_5$–		**d**	60
5	**e**	–(CH$_2$)$_4$–		H	**e**	42
6	**f**	H	Me	Ph	**f**	44

[a] Isolated yields.

Footnotes

† *Standard procedure*: To a 0.2 mol dm^{-3} solution of **1-CH$_2$Li** in pentane (2 equiv.) under argon, the epoxide **2-H** (1 equiv.) was added dropwise with a syringe at 0 °C. The reaction mixture was stirred at room temp. for 1–3 h, quenched with water, acidified and extracted with diethyl ether.

‡ Determined by ^{1}H NMR with Eu(TFC)$_3$. According to its optical rotation, our major enantiomer, ultimately derived from cyclohexene, is the same as that obtained before in 60% e.e. *via* a route starting from cyclohexanone.[2]

§ 3-(Methoxymethyl)oxetanes exhibit enhanced reactivity towards alkyllithiums.[3] In the case of **6a**, low reactivity combines with limited stability of **1-CH$_2$Li** under the conditions of reaction.

¶ This contrasts with the behaviour of related (dipole-stabilised) *N*-alkylmethyl anion equivalents R–N(XC=Y)CH$_2$Li (X, Y = H, NR; OLi, O; R, O; SLi, S) which, with epoxides $\mathrm{HR^1\overbrace{C{-}C}^{O}R^2R^3}$, give the products of nucleophilic substitution (nucleophilic aminoalkylation), R–N(XC=Y)-CH$_2$(HR^1)CC(R^{2}R^3)COLi, *cf.* ref. 5.

|| A single case in the literature, known to us, of an epoxide methylenation resembling ours, is a two-step procedure: addition of dimsyl sodium is followed by thermolysis of the hydroxysulfoxide obtained.[9]

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