

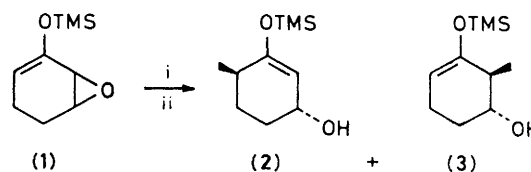
The Selective Opening of α,β -Epoxyketone Trimethylsilyl Enol Ethers by Cuprate Reagents: Selectivity Reversal in Tetrahydrofuran[†]

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Lithium dialkylcuprates in tetrahydrofuran give direct opening of α,β -epoxyketone trimethylsilyl enol ethers, in contrast to the allylic opening with cuprate reagents in diethyl ether.

The addition of organometallic compounds to allylic epoxides gives the products of either direct or allylic attack, depending on the reagent.¹ In the course of our study of analogous additions to trimethylsilyl (TMS) enol ethers of α,β -epoxyketones, independent results in this area were published.² While our data support the latter findings, the present report concerns a peculiar solvent effect, which leads to a reversal of the selectivity, as shown in Scheme 1.[§]



Scheme 1. i, Cuprate, 45 min; ii, NH_4Cl (aqueous).[§]

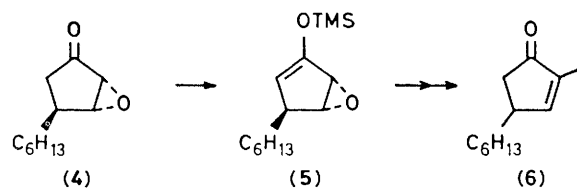
[†] This work is taken from part of the PhD Thesis of M. F. Schlecht, Columbia University, 1980.

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[§] TMS enol ethers were prepared in the usual manner (ref. 2). The yields given are for isolated products. For (2): ^1H n.m.r. (CDCl_3) δ 0.19 (s, 9H), 0.91 (d, 3H, J 7.5 Hz), 4.27 (q, 1H, J 4 Hz), and 4.89 (d, 1H, J 4 Hz); i.r. ν (thin film) 3600–3100, 3030, and 1655 cm^{-1} . For (3): ^1H n.m.r. (CDCl_3) δ 0.19 (s, 9H), 0.95 (d, 3H, J 7.5 Hz), 3.58 (m, 1H), 4.79 (br. s, 1H); i.r. ν (thin film) 3600–3100, 3030, and 1655 cm^{-1} . Ratios given are based on n.m.r. integrals of the oxomethine protons. Ratios in parentheses reflect quantitative g.l.p.c. analysis of the mixtures of cyclohexenones resulting from hydrolysis and dehydration of the products from separate runs. The selectivity for LiCuMe_2 in diethyl ether found in these laboratories was not as high as that reported by Wender *et al.*, in ref. 2.

Conditions	(2):(3)	Overall yield, %
1.5 equiv. LiCuMe_2 , THF, -20°C	0:100 (6:94)	62
4 equiv. LiCuMe_2 , diethyl ether, -40°C	59:41 (65:35)	81
4 equiv. $\text{LiCu}(\text{CN})\text{Me}$, diethyl ether, -40°C	100:0 (96:4)	77

Lithium dimethylcuprate in tetrahydrofuran (THF)³ gives direct opening of the epoxide TMS enol ether (1) to yield (3). Similar results are obtained when (1) is treated with lithium di-*n*-butylcuprate in THF. No significant quantity of the corresponding hydroxy ketone is isolated, indicating that the reaction is not occurring *via* the enolate, and is probably not



due to free methyl-lithium. No reaction takes place at -40°C in THF. The mechanistic implication of this solvent effect remains an open question.

In a second example, treatment of the TMS enol ether (5) of epoxyketone (4) with lithium dimethylcuprate in THF, followed by hydrolysis and acid-catalysed dehydration, yields the known cyclopentenone (6)¹ in 40% overall yield from (4).

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- 3 A ¹H n.m.r. study of cuprates in ethereal solvents suggests temperature dependent equilibria: E. C. Ashby and J. J. Watkins, *J. Chem. Soc., Chem. Commun.*, 1976, 784.
- 4 T. A. Rudol'fi and A. A. Skorubskii, *Zh. Prikl. Spektrosk.*, 1975, **22**, 1062; *Chem. Abstr.*, **83**, 113199d. For (6): ¹H n.m.r. (C₆D₆) δ 1.71 (s, 3H), 6.60 (s, 1H); i.r. (CHCl₃) 1690 cm⁻¹.