Carbon–Carbon Bond Formation via Opening of Epoxysilanes with Organometals Containing Lithium and Copper

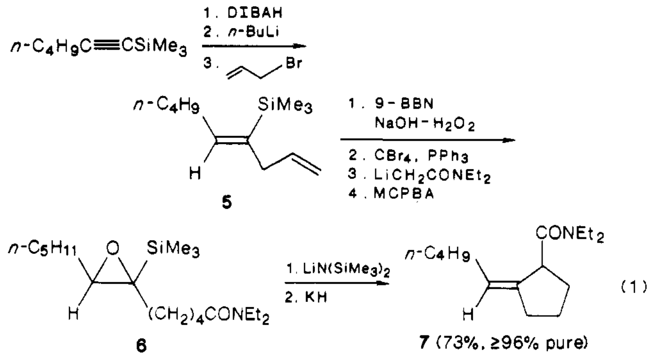
Summary: Various types of organometals containing lithium and copper react with *E* and *Z* epoxysilanes to produce adducts which, either under the reaction conditions or upon treatment with a base, e.g., KH, can be stereospecifically converted to the corresponding *E* and *Z* alkenes, respectively.

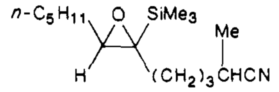
Sir: We recently reported a stereospecific procedure for preparing oxygenated heterocycles containing an exocyclic alkene group[1] using Hudrlik's epoxysilane opening reactions with heteroatom nucleophiles.[2] Our attempts to develop a similar method for preparing carbocycles containing exocyclic alkenes, however, were hampered by the paucity of satisfactory procedures for the required carbon–carbon bond formation via epoxysilane opening.[3-5] The only satisfactory examples known at the outset of our study were those involving $LiCu(Pr\text{-}n)_2$ and $LiCu(Bu\text{-}n)_2$.[3a] The corresponding reaction of Grignard reagents mainly proceeds via isomerization to aldehydes or ketones and halohydrin formation.[3b]

We therefore undertook a study of the reaction of epoxysilanes with various types of organometals containing three metals that have been most successfully used in the carbon–carbon bond formation via epoxide opening, i.e., Li,[6] Al,[6] and Cu,[7] and we have found that organolithiums and organocoppers containing aryl, alkenyl, alkynyl, amido, cyano, and dithiane groups can indeed react with *E* and *Z* epoxysilanes (**1** and **2**) to produce adducts which, either under the reaction conditions or upon treatment with a base, e.g., KH, can be stereospecifically converted to the corresponding *E* and *Z* alkenes, respectively (Scheme I). One key finding is that Li is a satisfactory countercation used in conjunction with relatively weak carbanion bases, such as alkynyl, amidoalkyl, cyanoalkyl, and dithiane carbanion, while the use of Cu is either preferable or necessary in cases where more basic carbanions, such as alkenyl and aryl, are employed. The use of organolithiums in the latter cases tends to lead to competitive side reactions, most notably direct attack at Si by carbanions. Organoalkanes either did not readily react with epoxysilanes or induced the formation of halohydrins.

The experimental results are summarized in Table I. The required (*E*)-epoxysilanes were prepared via lithiation of (*E*)-1-iodo-1-alkenes with 2 equiv of *t*-BuLi, silylation with Me_3SiCl, and epoxidation with *m*-chloroperbenzoic acid (MCPBA). (*E*)-1-Iodo-1-alkenes were in turn prepared via hydroalumination of 1-alkynes and iodination with I_2.[8] (*Z*)-Epoxysilanes were prepared via hydroalumination–hydrolysis–epoxidation of 1-(trimethylsilyl)-1-alkynes.[8] All of the epoxysilanes used in this study were stereoisomerically >98% pure. The disubstituted alkene products (**3** and **4**) were also stereoisomerically >95% pure.

The favorable results obtained in developing procedures for intermolecular carbon–carbon bond formation via epoxysilane opening prompted us to explore the feasibility of applying the method developed above to the stereoselective synthesis of exocyclic alkenes containing carbocycles. 1-(Trimethylsilyl)-1-hexyne was converted into **5** via hydroalumination with DIBAH, ate complexation with *n*-BuLi, and allylation with allyl bromide.[1] Conversion of **5** into **6** was then achieved in 71% overall yield via hydroboration–oxidation with 9-borabicyclo[3.3.1]nonane (9-BBN) and $NaOH\text{–}H_2O_2$ (86%), bromination with CBr_4 and PPh_3 (93%), alkylation with $LiCH_2CONEt_2$ (97%), and epoxidation with MCPBA (92%). The reaction of **6** with $LiN(SiMe_3)_2$ produced an adduct, which was then treated with KH to afford a 73% yield of **7** as an isomerically >96% pure compound (eq 1). The preparation of **8** and its conversion into **9** were similarly performed. Although the isolated yield of **9**, which was isomerically ≥96% pure, was 60% based on **8**, GLC analysis of the reaction mixture revealed that **8** was still remaining unreacted to the extent of 30–35%. The corresponding reaction of **10** only produced **11** in 87% yield. Finally, all attempts to induce cyclization of **12** to give **13** were unsuccessful. Presumably, the two carbon centers that must interact each other are sterically too crowded to form a carbon–carbon bond.





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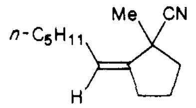

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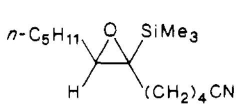

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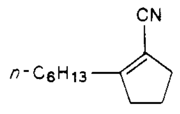

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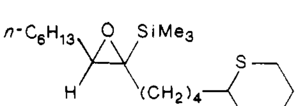

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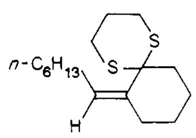

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[1] Luo, F. T.; Negishi, E. *J. Org. Chem.* **1983**, *48*, 5144.

[2] Hudrlik, P. F.; Hudrlik, A. M.; Rona, R. J.; Misra, R. N.; Withers, G. P. *J. Am. Chem. Soc.* **1977**, *99*, 1973 and pertinent references therein.

[3] (a) Hudrlik, P. F.; Peterson, D.; Rona, R. J. *J. Org. Chem.* **1975**, *40*, 2263. (b) Hudrlik, P. F.; Hudrlik, A. M.; Misra, R. N.; Peterson, D.; Withers, G. P.; Kulkarni, A. K. *J. Org. Chem.* **1980**, *45*, 4444 and pertinent references therein.

[4] During the course of our investigation, a paper reporting the reaction of epoxysilanes with organocoppers to produce 1,2-diols was published [Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4413].

[5] After this study had been completed, two additional papers on the reaction of epoxysilanes with organocopper reagents have been presented. (a) Alexakis, A.; Normant, J. F.; Jachiet, D. 196th ACS National Meeting, Los Angeles, September 25–30, 1988; ORGN-300. (b) Soderquist, J. A.; Santiago, B. 196th ACS National Meeting, Los Angeles, September 25–30, 1988; ORGN-368.

[6] For a review with pertinent references, see: Negishi, E. *Organometallics in Organic Synthesis*; John Wiley and Sons: New York, 1980.

[7] For a review, see: Posner, G. H. *An Introduction to Synthesis Using Organocopper Reagents*; John Wiley and Sons: New York, 1980.

[8] Zweifel, G.; Miller, J. A. *Org. React.* **1984**, *32*, 375.

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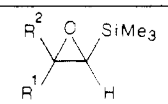
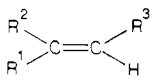
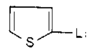
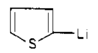
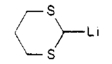
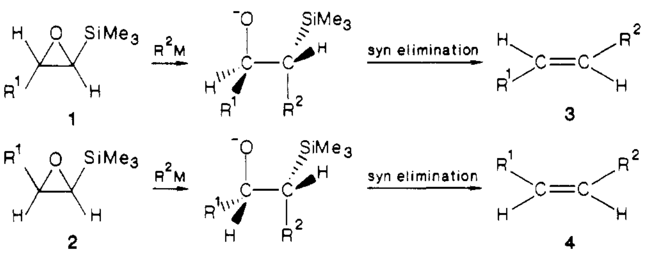
Table I. Reaction of Epoxysilanes with Organometals[a]

			yield,[b] % of		
R^1	R^2	R^3M		stereoselectivity, %	others
n-C_5H_{11}	H	Li_2CuPh_2CN	94 (>95)	>95	
H	n-C_5H_{11}	Li_2CuPh_2CN	77 (82)	>95	
H	n-C_4H_9	PhLi	- (50)	>95	$PhSiMe_3$ (50%)
n-C_4H_9	H		82	>95	
H	n-C_4H_9		80	>95	
n-C_4H_{11}	H	$Li_2Cu(CH{=}CH_2)CN$	80	>95	
n-C_4H_9	H	n-$C_4H_9C{\equiv}CLi$	95	>95	
H	n-C_5H_{11}	n-$C_4H_9C{\equiv}CLi$	92	≥98	
H	n-C_4H_9	$LiAlClEt_2(C{\equiv}C_4H_9$-$n)$	0		n-$C_4H_9CH(OH)CHClSiMe_3$ (96%)
H	n-C_5H_{11}	$LiCH_2CONEt_2$	95[c]		
H	n-C_6H_{13}		83	≥98	

[a] Organolithium reactions were run at -78 to 25 °C by gradually warming the reaction mixture, while organocopper reactions were run at -50 to -20 °C followed by warming to 25 °C. [b] Isolated yield. The number in parentheses is a GLC yield. [c] Yield of N,N-diethyl-4-hydroxy-3-(trimethylsilyl)nonanamide.

Scheme I[a]



[a] R^1 and R^2 = carbon groups. M = Li and Cu.

The following two procedures are representative. **2-[(*Z*)-1-Octenyl]-1,3-dithiane.** To a solution of 1,3-dithiane (0.255 g, 2.12 mmol) in 6 mL of THF at -25 °C was added n-BuLi (2.7 M in hexane, 0.82 mL, 2.22 mmol). The reaction mixture was stirred at 25 °C for 1-2 h, followed by addition of (*Z*)-1-(trimethylsilyl)-1-octene oxide (0.425 g, 2.12 mmol) in 2 mL of THF. The resulting mixture was stirred overnight at 25 °C, quenched with 3 N HCl, extracted with ether, washed with $NaHCO_3$, dried over $MgSO_4$, and distilled to give 0.41 g (83%) of the title compound as an isomerically >98% pure material: bp 105-108 °C (0.05 mmHg); IR (neat) 785 (m) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.88 (t, J = 7 Hz, 3 H), 1.0-1.7 (m, 8 H), 1.7-2.4 (m, 4 H), 2.6-3.0 (m, 4 H), 4.90 (d, J = 9 Hz, 1 H), 5.2-5.7 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.30, 22.79, 25.22, 28.00, 29.10, 29.58, 30.55, 31.88, 43.46, 126.01, 134.75. Anal. Calcd for $C_{12}H_{22}S_2$: C, 62.55; H, 9.62. Found: C, 62.36; H, 9.71. **(*E*)-1,3-Nonadiene.** To a suspension of CuCN (0.43 g, 4.8 mmol) in 4 mL of THF at -78 °C was added vinyllithium (1.85 M in ether, 5.2 mL, 9.6 mmol).[9] The reaction mixture was warmed to 0 °C, and the resulting clear solution was cooled to -20 °C. To this was added (*Z*)-1-trimethyl-1-heptene oxide (0.74 g, 4 mmol) in 4 mL of THF. The mixture was gradually warmed to 25 °C and stirred for 2-3 h. Quenching with aqueous NH_4Cl, extractive workup, and distillation gave 0.40 g (80%) of the title compound[10] as an isomerically >96% pure substance: IR (neat) 1650 (w), 1010 (m), 910 (s), 750 (s) cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, J = 6 Hz, 3 H), 1.0-1.7 (m, 6 H), 2.0-2.4 (m, 2 H), 4.7-5.2 (m, 2 H), 5.5-6.6 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 14.15, 22.69, 29.07, 31.60, 32.67, 114.62, 131.11, 135.72, 137.60.

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Supplementary Material Available: Experimental data for synthesized compounds (5 pages). Ordering information is given on any current masthead page.

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Synthesis of Oxidized Spiroketals via 2-Furyl Ketone Oxidation-Rearrangement

Summary: A new method for the synthesis of highly oxidized spiroketals has been developed via the oxidation-rearrangement of 2-furyl ketones, readily available by the reaction of furyllithium reagents with lactones. Spiroketals hydroxylated in the 2-position are produced as slowly equilibrating mixtures of diastereomers in good yield. The method has been applied to the synthesis of trioxadispiroketals modeling those present in the polyether antibiotics salinomycin, narasin, and their analogues.

Sir: Spiroketals are important subunits of a growing variety of naturally occurring compounds of considerable current importance and interest. Although simple derivatives of both the 1,7-dioxaspiro[5.5]undecane (1) and

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