Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 48 (2007) 8356–8359
Tetrahedron Letters

3-Silyloxytetrahydrofurans via sulfoxonium ylide reactions with α-silyloxyepoxides

Paul S. Sabila, Yanke Liang and Amy R. Howell*

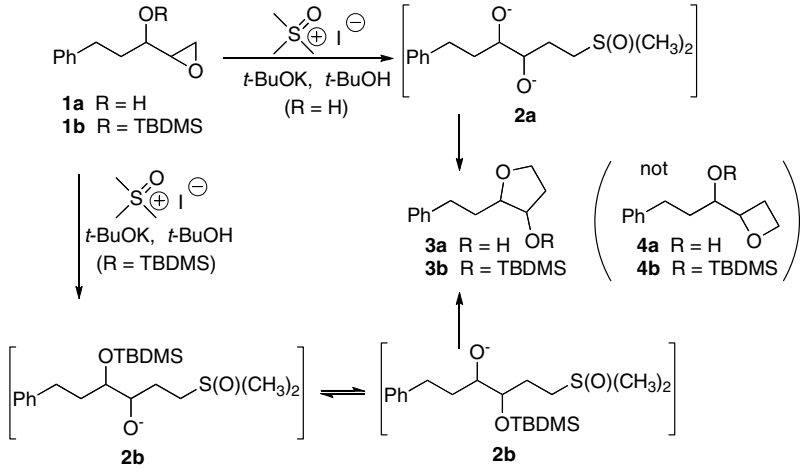
Department of Chemistry, University of Connecticut, Storrs, CT 06269-3060, United States

Received 4 July 2007; revised 7 September 2007; accepted 18 September 2007
Available online 21 September 2007

Abstract—α-Silyloxyepoxides were found to undergo sulfoxonium ylide induced ring-opening, followed by silyl-migration and intramolecular S_N2 reaction, resulting in 3-silyloxytetrahydrofurans. Studies on the scope and utility of this transformation are described.

In the accompanying paper we describe the conversion of α-mesyloxyoxetanes to 2-alkylidene oxetanes by a base promoted 1,2-elimination.[1] The alkylidene oxetane precursors were prepared by sulfoxonium ylide mediated ring expansion of protected α-hydroxyepoxides. During that investigation it became apparent that the success of this expansion for accessing α-hydroxyoxetanes was dependent on the presence and nature of the protecting group on the OH moiety. With benzyl protection, as described in the accompanying paper, hydroxyoxetane **4a** was obtained in good yield after cleavage of the benzyl group. In the absence of a protecting group or with a silyl group a different outcome was observed, as is described here.

Initially, ring expansion with unprotected α-hydroxyepoxide **1a** was attempted (Scheme 1). The major product was the corresponding tetrahydrofuran (THF) **3a**, rather than oxetane **4a**. In retrospect, the outcome was not surprising, as under the strongly basic conditions dialkoxide **2a** would be an intermediate, and cyclization to the 5-membered THF ring would be favored over oxetane formation. Consequently, the α-hydroxy moiety was protected with a TBDMS group to give **1b**. When



Scheme 1.

* Corresponding author. E-mail: amy.howell@uconn.edu

0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2007.09.113

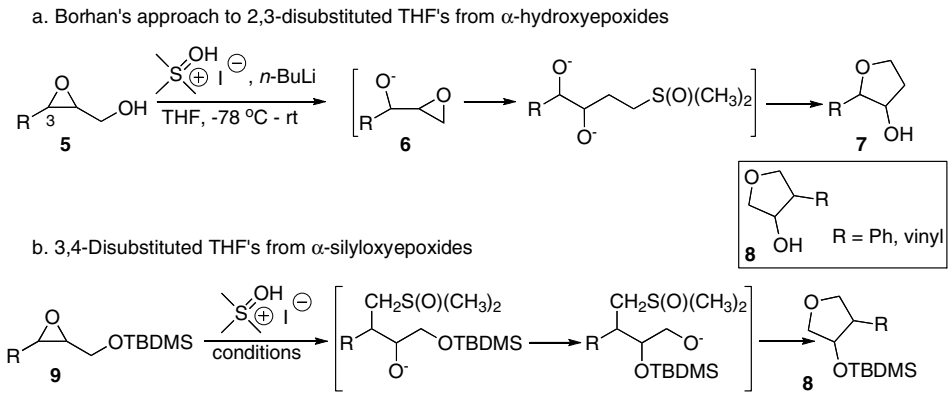
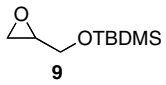
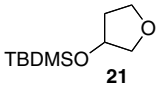
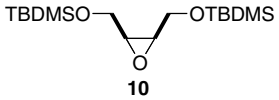
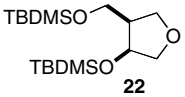
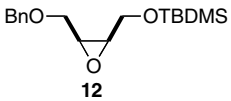
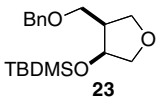
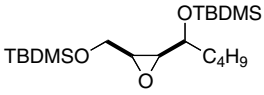
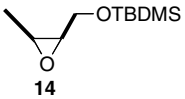
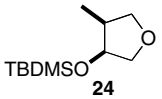
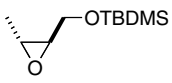
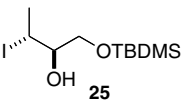
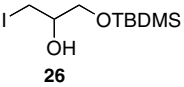


Figure 1. Disubstituted THF's from epoxides with vicinal oxygenation.

this was treated with dimethylsulfoxonium methylide, silyl-protected THF **3b** resulted (60% yield, 1:1 mixture of diastereomers), rather than the desired oxetane. Again, with hindsight the silyl migration was not sur-

Table 1. Reactions of α-silyloxyepoxides with dimethylsulfoxonium methylide

Epoxide	Condition	Product	Yield (%)
 **9**	1	 **21**	70
 **10**	2	 **22**	72
 **11**	1 or 2	NR	
 **12**	2	 **23**	44
 **13**	1 or 2	NR	
 **14**	2	 **24**	50
 **15**	1 or 2	NR	
15	3	 **25**	49
9	3	 **26**	78

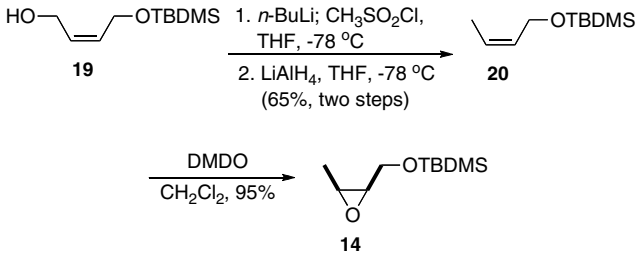
Conditions: (1) $(CH_3)_3SOI$, *t*-BuOK, *t*-BuOH; (2) $(CH_3)_3SOI$, *n*-BuLi (6–10 equiv), 24–32 h; (3) $(BF_3{\cdot}OEt_2)$ + epoxide followed by addition of preformed ylide.

prising[2,3] However, we decided to explore the scope and utility of this silyl-migratory entry to 3-silyloxy-THF's.

Subsequent to this initial observation of the conversion of α-silyloxyepoxide **1b** to 3-silyloxy-THF **3b**, Borhan and co-workers reported the conversion of epoxyalcohols **5** to 2,3-disubstituted THF's **7** in the presence of excess dimethylsulfoxonium methylide (Fig. 1a).[4] This process exploited the enhanced reactivity of epoxides **6**, formed by Payne rearrangement of **5**, and is attractive because of the ease of asymmetric synthesis of the chiral epoxides **5** and because of the stereoselectivity of the transformation. Yields were best when the 'R' group contained an α-oxygen; simple alkyl groups resulted in more complex product mixtures and low yields of **7** because of competing reaction by the ylide at C3 of epoxyalcohols **5**. In fact, 3,4-disubstituted-THF's **8** were isolated as the major product, albeit in modest yields (30–50%) when R was phenyl or vinyl. We recognized that the conversion of **5** to **7** was similar to our initial result, as the intermediates **6** correspond to our starting epoxides **1**, and the number of steps to access **3b** is identical using the chemistry in Scheme 1 or following the silylation of **7** (if R = PhC_2H_4). However, neither our initial studies nor Borhan's work provided an effective synthesis of 3,4-disubstituted THF's **8**. Here we describe our progress toward this goal (see Fig. 1b), which requires regioselective attack of dimethylsulfoxonium methylide on a 1,2-disubstituted epoxide.

A series of epoxides, shown in Table 1, was prepared to probe scope and utility of the silyl-migratory pathway to the functionalized THF's, especially 3,4-disubstituted-THF's. The epoxides were chosen to look at the effects of both stereochemistry and substituents on reaction outcome. Racemic epoxides **9**,[5] **10**,[6,7] **11**,[8] **12**,[9,10] and **15**[11] are known compounds. Epoxide **13** was prepared from known aldehyde **16**,[12] as shown in Scheme 2. Nucleophilic addition of *n*-butyllithium provided allyl alcohol **17**. Epoxidation gave an approximately 1:1 mixture of diastereomers **18**, which was protected to provide doubly silylated epoxide **13**. *cis*-Epoxide **14** was prepared by oxidation of TBDMS-protected alcohol **20**, available from the reduction[13] of known,[14] monoprotected diol **19** (Scheme 3).

The epoxides were reacted with dimethylsulfoxonium methylide, either generated in situ by reaction of trimethylsulfoxonium iodide with potassium *t*-butoxide in *t*-butanol (condition 1 in Table 1) or preformed by treatment of the sulfoxonium iodide with *n*-BuLi in

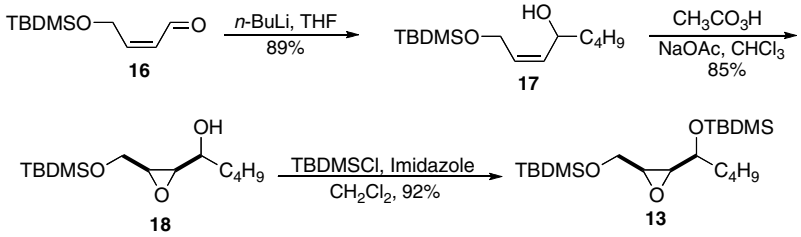


Scheme 3.

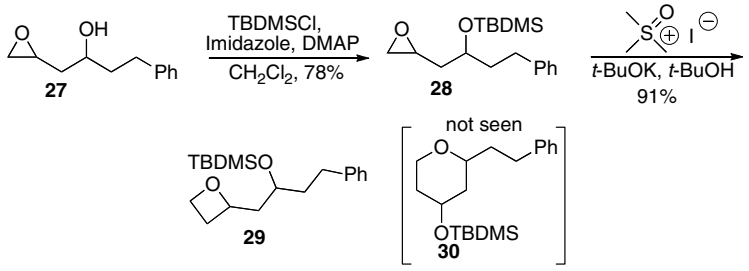
THF (condition 2 in Table 1). As anticipated, the simple model glycidol-derived epoxide **9** underwent smooth conversion to 3-silyloxy-THF **21**. The *cis*,bis-TBDMS protected epoxide **10** reacted stereospecifically with similar efficiency to provide 3,4-disubstituted THF **22**, while the corresponding trans-isomer **11** did not react. Differentially protected epoxide **12** gave THF **23**. Although the yield was lower than for the formation of **22**, compound **23** was the major product, and no other product was identifiable. The more sterically encumbered *cis*,bis-silyl epoxide **13** did not undergo reaction with the sulfoxonium ylide generated under either condition 1 or 2. With *cis*-epoxide **14**, having only single α-oxygenation, ring expansion gave **24** in moderate yield, with no readily identifiable by-products. As with *trans*-epoxide **11** versus cis-isomer **10**, the trans-diastereomer **15** of **14** did not react with the sulfoxonium ylide.

Attempts to effect the desired reaction by Lewis acid ($BF_3{\cdot}OEt_2$) activation of the epoxide (**15** or **9**) gave iodohydrins (**25** or **26**, respectively), rather than THF's. The outcome was the same whether the ($BF_3{\cdot}OEt_2$) was added to the epoxide prior to addition of the ylide or added to the reaction mixture subsequent to combining all the other reagents. Moreover, varying the number of equivalents of ($BF_3{\cdot}OEt_2$) did not substantially alter the results. Attempts to scavenge the iodide counterion subsequent to generating the ylide were unsuccessful. Use of trimethysulfoxonium chloride, containing the less nucleophilic chloride counterion, as the source of the sulfoxonium ylide, resulted in the corresponding chlorohydrin. These results suggest that the Lewis basicity of the ylide would complicate any efforts to use Lewis acids to activate the epoxides.

We also investigated the outcome with a silyloxy group beta to the epoxide. Known β-hydroxyoxirane **27**[15] was silylated (Scheme 4); the resultant β-silyloxyoxirane **28**



Scheme 2.



Scheme 4.

was then reacted with dimethylsulfoxonium methylide, generated by treatment of trimethylsulfoxonium iodide with potassium *t*-butoxide in *t*-butanol. Oxetane **29** was isolated in excellent yield, and no pyran formation (**30**) was seen, indicating that 1,5-silyl-migration did not compete with oxetane formation.

In conclusion, we have demonstrated that cis-1,2-disubstituted epoxides with an α-OTBDMS group undergo ring-opening with concomitant silyl-migration and cyclization to 3,4-disubstituted THF's upon treatment with dimethylsulfoxonium methylide. *trans*-Epoxides fail to react under the same conditions. With the ready availability of homochiral α-hydroxyepoxides, the approach described herein complements the preparation of 2,3-disubstituted THF's reported by Borhan and coworkers.

Acknowledgement

This manuscript is based upon work supported by the National Science Foundation (NSF) under Grant No. CHE-0111522.

Supplementary data

Full experimental procedures and characterization data are provided as supplementary data. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.09.113.

References and notes

1. Sabila, P. S.; Howell, A. R. *Tetrahedron Lett.* **2007**, *48*, doi:10.1016/j.tetlet.2007.09.109.
2. Teranishi, K.; Ueno, F. *Tetrahedron Lett.* **2003**, *44*, 4843–4848.
3. Molander, G. A.; Swallow, S. *J. Org. Chem.* **1994**, *59*, 7148–7151.
4. Schomaker, J. M.; Pulgam, V. R.; Borhan, B. *J. Am. Chem. Soc.* **2004**, *126*, 13600–13601.
5. Trost, B. M.; Kulawiec, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 2027–2036.
6. Righi, G.; Pescatore, G.; Bonadies, F.; Bonini, C. *Tetrahedron* **2001**, *57*, 5649–5656.
7. Ittah, Y.; Sasson, Y.; Shahak, I.; Tsaroom, S.; Blum, J. *J. Org. Chem.* **1978**, *43*, 4271–4273.
8. Bajwa, J. S.; Anderson, R. C. *Tetrahedron Lett.* **1991**, *32*, 3021–3024.
9. Azzena, F.; Calvani, F.; Crotti, P.; Gardelli, C.; Macchia, G.; Pineschi, M. *Tetrahedron* **1995**, *51*, 10601–10626.
10. Fujii, N.; Nakai, K.; Habashita, H.; Hotta, Y.; Tamamura, H.; Otaka, A.; Ibuka, T. *Chem. Pharm. Bull.* **1994**, *42*, 2241–2250.
11. Gao, Y.; Klunder, J. M.; Hanson, R. M.; Masamune, H.; Ko, S. Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.
12. Ramachandran, P. V.; Liu, H.; Reddy, M. V. R.; Brown, H. C. *Org. Lett.* **2003**, *5*, 3755–3757.
13. Vedejs, E.; Buchanan, R. A.; Conrad, P. C.; Meier, G. P.; Mullins, M. J.; Schaffhausen, J. G.; Schwartz, C. E. *J. Am. Chem. Soc.* **1989**, *111*, 8421–8430.
14. Ding, P.; Miller, M. J.; Chen, Y.; Helquist, P.; Oliver, A. J.; Wiest, O. *Org. Lett.* **2004**, *6*, 1805–1808.
15. Rychnovsky, S. D.; Griesgraber, G.; Zeller, S.; Skalitzky, D. J. *J. Org. Chem.* **1991**, *56*, 5161–5169.