Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 47 (2006) 6565–6568

Studies on the deprotonation and subsequent [1,4]-Wittig rearrangement of α-benzyloxyallylsilanes

Edith N. Onyeozili and Robert E. Maleczka, Jr.*

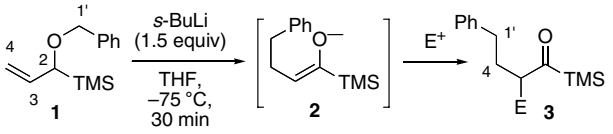
Department of Chemistry, Michigan State University, East Lansing, MI 48824, USA

Received 22 June 2006; revised 6 July 2006; accepted 6 July 2006
Available online 31 July 2006

Abstract—Upon exposure to *s*-BuLi, benzyloxyallylsilane undergoes an unusually rapid and efficient [1,4]-Wittig rearrangement. Herein we describe efforts aimed at trapping the intermediate α-carbanion with an electrophile prior to rearrangement. The results of these experiments indicate that α-deprotonation and bond reorganization are separate events. Findings herein further indicate that the future success of benzyloxyallylsilanes in [1,4]-Wittig rearrangements will likely hinge on the acidity of the benzylic protons.

In an earlier letter,[1] we described the [1,4]-Wittig rearrangement[2] of benzyloxyallylsilane (**1**) (Scheme 1). Upon treatment with *s*-BuLi, compound **1** rapidly undergoes the [1,4]-Wittig shift to afford enolate **2** in high yield after only 30 min at −75 °C. To the best of our knowledge, this represents the most rapid, selective, and efficient [1,4]-Wittig rearrangement of α-alkoxysilanes in particular, and allyl benzyl ethers in general, ever reported. Furthermore, enolate **2** could be effectively quenched with various electrophiles to generate a range of corresponding acylsilanes (**3**).

The mechanism by which the [1,4]-Wittig rearrangement occurs appears to be substrate dependent, with radical/radical anion dissociation/recombination or concerted pathways possible.[3] For **1**, the observed ratio of [1,4]- to [1,2]-products was reliant on the reaction temperature, with the [1,2]-Wittig rearrangement intruding at higher temperatures. We interpreted these results as evidence of a concerted rearrangement of deprotonated



Scheme 1. [1,4]-Wittig rearrangement of 1.

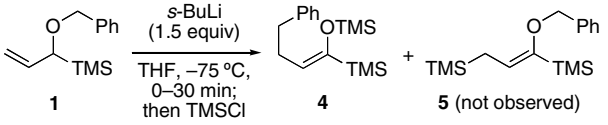
Keywords: [1,4]-Wittig rearrangement; Deprotonation; Organosilanes; Carbanion.
* Corresponding author. Tel.: +1 517 355 9715; fax: +1 517 353 1793; e-mail: maleczka@chemistry.msu.edu

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.07.018

1. In search of additional support for that conclusion and as a prelude to future experiments aimed at elucidating the stereochemical course of the rearrangement, we sought to trap the anion of **1** prior to bond reorganization.

In their own studies on the mechanism and synthetic utility of the Wittig rearrangement, Schlosser and Strunk[3d] had developed conditions that allowed virtually quantitative metalation and subsequent silylation of allyl ethers with little competition from [1,2]- and/or [1,4]-rearrangements. Following their lead, we treated cold (−75 °C) THF-solutions of **1** with *sec*-BuLi followed after some period of time by chlorotrimethylsilane (TMSCl) (Scheme 2). Given the short reaction times (<30 min) we expected to obtain mixtures of silylenol ether **4** and bissilane **5**. However, **5** was never observed. Even when the reaction was quenched early, only **4**[1] and unreacted starting material (**1**) could be identified in the crude reaction mixtures.

Given these results, the unusually high reaction rate, and the complete absence of [1,2]-Wittig products, we had to consider the option that the deprotonation step and the rearrangement of **1** were happening



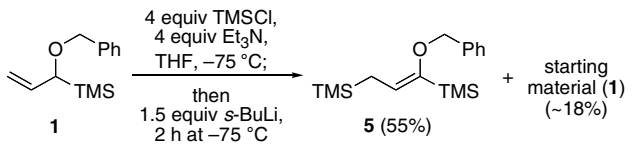
Scheme 2.

simultaneously. Although such a concerted course of action would be unusual in carbanion chemistry, analogous mechanisms include the widely accepted enzyme catalyzed depronation/electrophilic capture sequence.[4]

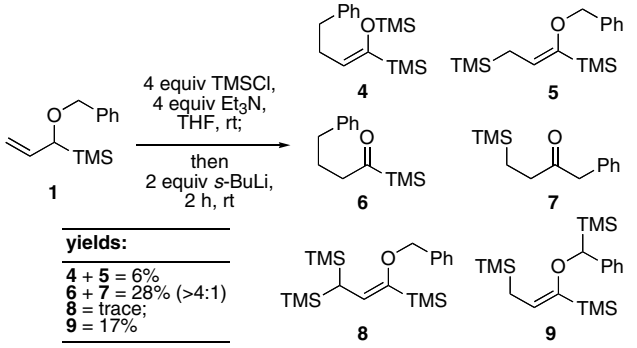
Of course it was just as likely, if not more, that deprotonation and Wittig rearrangement were separate steps, the former leading to a carbanion intermediate that simply rearranged prior to the addition of the electrophile. To test for this possibility, we sought to take advantage of the relatively slow reaction between TMSCl and alkyllithiums[5] and deprotonate **1** in the presence of TMSCl. In practice, slowly adding *s*-BuLi (1.5 equiv as a 1.3 M solution in cyclohexane added at 1.0 mL/70 min) to a −78 °C mixture of **1**, TMSCl (4.0 equiv), and triethylamine (4.0 equiv) in THF, followed by stirring for 1 h at that temperature and then an aqueous workup, resulted in the isolation of compound **5**[6] (55%) and unreacted starting material (18%) (Scheme 3). The geometry of **5** was ascertained by transient NOE experiments and is consistent with an intramolecular coordination between lithium and the substrate oxygen.[3d,e] Similarly, the silylation occurred exclusively at the γ-position, which was consistent with previously documented reports.[3d,7]

These results certainly implied that **1** underwent deprotonation followed by a separate rearrangement step. However, as a final test of this conclusion, we ran a control experiment where **1** was reacted with 4 equiv TMSCl and 4 equiv triethylamine in THF at −78 °C, without *s*-BuLi. Under these conditions, no reaction occurred, ruling out the possibility that Et_3N was deprotonating **1**. This negative result, combined with the in situ trapping experiments described above, and the absence of any observable Wittig products during those same experiments are firm indications that the α-deprotonation and [1,4]-Wittig rearrangement of **1** are not concerted events.

As electrophile capture superceded rearrangement at low temperatures, we next asked what would happen at elevated temperatures. Thus, the in situ trapping experiment was repeated at room temperature (Scheme 4). The outcome of this reaction was generation of at least six compounds. [1,4]- and [1,2]-Derived Wittig products **6**[8] and **7**[8] (4:1) along with silylated enol ether **4**[1] contributed to over 30% of the reaction's yield. A trissilylated byproduct (**9**[6]) was also isolated in approximately 17%, as were small amounts of **5** and a second trissilylated byproduct (**8**[6]). As these data clearly showed rearrangement to be competitive with in situ TMS trapping at room temperature, the above query was answered. However, the formation of trissilylated products (**8** and **9**) raised new questions. In attempts to drive



Scheme 3.



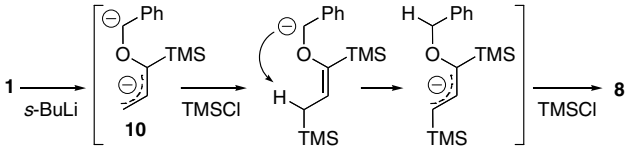
Scheme 4.

the low temperature reactions to completion (Scheme 3), compound **1** was reacted with 2.5 equiv of *s*-BuLi (vs. 1.5 equiv). While excess base did allow for the complete consumption of starting material, it also gave rise to trissilylated byproducts **8** and **9** (see Scheme 4 for structures). When the *s*-BuLi was added at approximately 1.0 mL/30 min **5**, **8**, and **9** were produced in a ratio of 5.9:1.0:2.8 with a combined 66% yield. Even more rapid addition of the base (>1.0 mL/15 min) increased the formation of **8** and **9** to where they became the major products (**5**:**8**:**9** 1.0:1.1:4.4) (85% combined yield).

Compounds **8** and **9** could originate from the deprotonation of **5**. To gauge the likelihood of this option, we added *s*-BuLi at ~1.0 mL/40 min to a mixture of TMSCl, Et_3N, and **5**. Surprisingly, during each of two runs **5** reacted very slowly. Analysis of the reactions after the typical 2 h at −78 °C revealed only trace amounts of **8** and **9**. Quenching the reaction after 24 h, gave 85% of **5** along with a 1.0:1.7 mixture of **8** and **9**.[9] These data argue against **8** and **9** coming exclusively from **5**. Barring aggregate effects or increases in the heats of mixing, it is also difficult to relate changes in site selectivity during the deprotonation of **5** with differences in the *s*-BuLi addition rate.

If **5** is not chiefly responsible for the formation of **8** and **9**, then perhaps the dianion of **1** (**10**), resulting from the sudden presence of excess *s*-BuLi is operative. Such a dianion could afford **9** directly. Though purely conjecture, **8** could arise from a process where silylation of dianion **10** at the γ-position was followed by an intramolecular proton shift[9] to afford the silyl stabilized allyl anion (Scheme 5).

While the mechanism by which **8** and **9** originate remains speculative, any potential dianion formation under the Wittig conditions would have consequences for future applications of the reaction. The [1,4]-Wittig



Scheme 5.

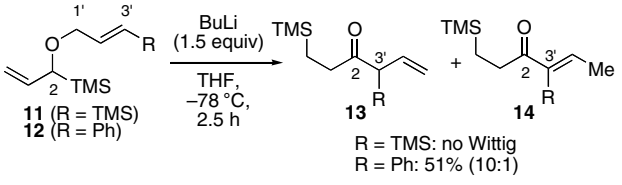
rearrangement of **1** typically requires 1.5 equiv of base to go to completion. Thus, excess base is available for a second deprotonation. Furthermore if dianion formation of **1** is relatively facile with excess base, then increasing the acidity of protons at the migrating center could make some dianion formation unavoidable even with only 1.0 equiv of base. Such dianions would be very sluggish toward rearrangement, thereby limiting substrate scope.

To probe this issue further we examined the reaction of compound **11**.[10] While the relative acidities of protons at C-2 and C-1′ should be similar,[11] mono deprotonation at either position would generate anionic intermediates capable of [2,3]-, [1,2]-, or [1,4]-Wittig rearrangement. Despite multiple Wittig pathways, exposure of **11** to our normal [1,4]-Wittig conditions showed little evidence of a reaction (Scheme 6, R = TMS). Even at room temperature, the consumption of starting material was slow and the product mixture complex.

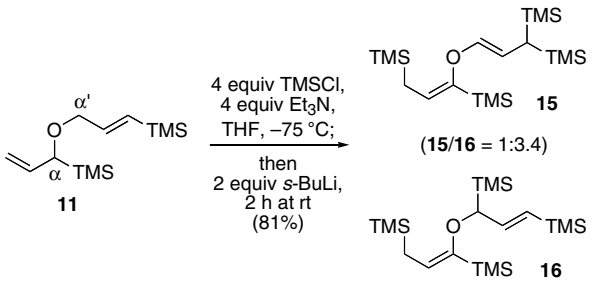
This stood in contrast to the reaction of compound **12**,[10] which with either *s*-BuLi or *n*-BuLi underwent facile [2,3]-Wittig rearrangement followed by TMS group migration[8] to afford **13**[6] and a minor amount (10%) of its conjugated isomer (**14**[6]) (Scheme 6, R = Ph). No [1,2]- or [1,4]-Wittig products were observed during the reaction of **12**. Furthermore, while the isolated yield of **13** and **14** was only 51%; the crude material appeared to be fairly clean, indicating a very efficient transformation.

We suspected that the key difference between the TMS (**11**) and Ph (**12**) analogues is that **11** has a higher kinetic acidity[11,12] at C-1′ and thus is able to form a rearrangement inhibiting dianion. With this in mind, we again looked to in situ trap the carbanion intermediate(s) generated during the reaction of **11**. Treatment of a −78 °C THF solution of **11**, 4 equiv TMSCl, and 4 equiv Et_3N with 2 equiv *s*-BuLi afforded tetrasilylated compounds **15**[6] and **16**[6] (1.0:3.4) in 86% yield after column chromatography on $AgNO_3$-impregnated silica gel[13] (Scheme 7). While we cannot rule out stepwise installment of the TMS groups, these products are consistent with dianion formation. Irrespective of the mechanistic details, the different reactivities of **11** and **12** indicate that the future success of α-alkoxyallylsilanes in [1,4]-Wittig rearrangements will likely hinge on the relative acidity of the α and α′ ethereal protons.

In conclusion, through the in situ trapping of the carbanion intermediate, we have shown that deprotonation and [1,4]-Wittig rearrangement of α-alkoxysilanes are not concerted but rather separate events. As an outgrowth



Scheme 6.



Scheme 7.

of these experiments, we determined that the presence of anion stabilizing groups on the migrating substituent could be detrimental to the success of the reaction. Studies aimed at determining the role of these substituent effects (i.e., dianion formation) as well as a broader survey of the substrate scope are on-going and will be reported in due course.

Acknowledgements

We thank the NIH (HL-58114), NSF (CHE-9984644), and the Astellas USA Foundation for their generous support.

Supplementary data

Experimental details and compound characterization data are available on-line at http://www.sciencedirect.com/. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.07.018.

References and notes

1. Onyeozili, E. N.; Maleczka, R. E., Jr. *Chem. Commun.* **2006**, 2466–2468.
2. For Wittig rearrangement reviews see: (a) Nakai, T.; Mikami, K. *Org. React.* **1994**, *46*, 105–209; (b) Tomooka, K.. In *Chemistry of Organolithium Compounds*; Rappoport, Z., Ilan, M., Eds.; Wiley: London, 2004; Vol. 2, pp 749–828.
3. (a) Felkin, H.; Frajerman, C. *Tetrahedron Lett.* **1977**, *18*, 3485–3488, and references cited therein; (b) Sayo, N.; Kimura, Y.; Nakai, T. *Tetrahedron Lett.* **1982**, *23*, 3931–3934; (c) Hayakawa, K.; Hayashida, A.; Kanematsu, K. *J. Chem. Soc., Chem. Commun.* **1988**, 1108–1110; (d) Schlösser, M.; Strunk, S. *Tetrahedron* **1989**, *45*, 2649–2664; (e) Nakazaki, A.; Nakai, T.; Tomooka, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2235–2238.
4. Gerlt, J. A.; Gassman, P. G. *J. Am. Chem. Soc.* **1992**, *114*, 5928–5934.
5. Bey, A. E.; Weyenberg, D. R. *J. Org. Chem.* **1966**, *31*, 2036–2037.
6. The structure assigned to each new compound is in accord with its IR, ^1H NMR and ^{13}C NMR spectra, as well as appropriate parent ion identification by HRMS. See Supplementary data for additional details.
7. Murai, A.; Abiko, A.; Shimada, N.; Masamune, T. *Tetrahedron Lett.* **1984**, *25*, 4951–4954.

8. Maleczka, R. E., Jr.; Geng, F. *Org. Lett.* **1999**, *1*, 1115–1118.
9. We are tempted to speculate that the minimization of $A_{1,2}$-strain within **5** accounts for the seemingly slow intermolecular deprotonation of the allylic protons.
10. Compounds **11** (46% (Lewis acid = $BF_3{\cdot}Et_2O$)) and **12** (17% (Lewis acid = TMSOTf)) were generated from the corresponding trichloroacetimidate as generally described in Maleczka, R. E., Jr.; Geng, F. *Org. Lett.* **1999**, *1*, 1111–1113 and the Supplementary data.
11. For the deprotonation and rearrangement of vinylogous α-alkoxysilanes see: (a) Mikami, K.; Kishi, N.; Nakai, T. *Chem. Lett.* **1989**, 1683–1686; (b) Greeves, N.; Lee, W.-M. *Tetrahedron Lett.* **1997**, *38*, 6445–6448.
12. It is difficult to estimate the p*K* differences between **11** and **12**, but intrinsic silyl stabilization is said to be worth about 2–3 p*K* units for delocalized carbon acids. See Streitwieser, A.; Xie, L.; Wang, P.; Bachrach, S. M. *J. Org. Chem.* **1993**, *58*, 1778–1784.
13. Lawrence, B. M. *J. Chromatogr. A* **1968**, *38*, 535–537.