ORGANIC LETTERS

1999
Vol. 1, No. 7
1111−1113

Synthesis and Fluoride-Promoted Wittig Rearrangements of α-Alkoxysilanes

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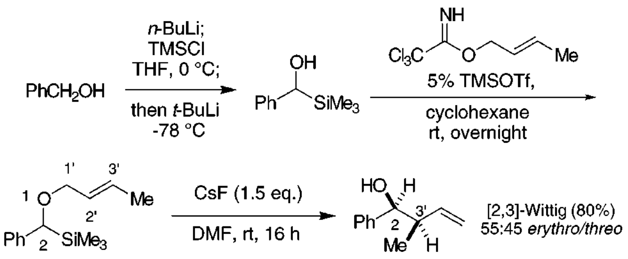
Received August 5, 1999

ABSTRACT

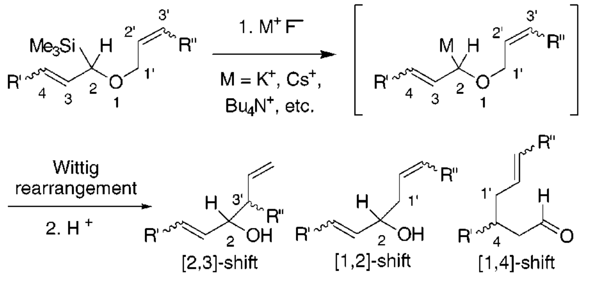


Lewis acid-catalyzed reaction of allyl and benzyl trichloroacetimidates with α-silyl alcohols was found to be a general method for the synthesis of α-alkoxysilanes. Upon exposure to CsF, these α-alkoxysilanes could be made to undergo [2,3]-Wittig rearrangement with an efficiency similar to that realized by the analogous but inherently more toxic α-alkoxystannanes.

For over 20 years Wittig rearrangements have elicited the attention of synthetic and physical organic chemists alike.[1] Reactions of this class are typically initiated by the formation of an α-metalated ether which undergoes a subsequent rearrangement, usually in the form of a [2,3]-, [1,2]-, or [1,4]-shift. While direct deprotonation of an ether at the α-carbon, usually facilitated by the presence of anion-stabilizing groups such as carbonyls, nitriles, allyl, benzyl, or propargyl moieties,[1] can be used to initiate the sigmatropic event, this approach is limited to those compounds possessing sufficiently acidic α hydrogens. In 1978, Still and Mitra showed that this restriction could be overcome by generating the α-alkoxy carbanion via tin−lithium exchange.[2] In the years following their pioneering work, the Wittig−Still rearrangement has earned its place as a powerful synthetic tool. Despite its demonstrated potential, broad application of this protocol has been governed by its reliance on the relatively toxic[3] organostannanes as well as the need for strong air- and moisture-sensitive bases such as n-BuLi.

To circumvent these two limitations, we considered the general possibility of α-alkoxysilanes being made to undergo [2,3]-sigmatropic rearrangement by the action of fluoride (Scheme 1). Not surprisingly such an approach has been the subject of prior, although very limited, investigations (Scheme 2).[4−6] In fact prior to the original disclosure of Still,[2] Reetz

Scheme 1



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[1] (a) Nakai, T.; Tomooka, K. *Pure Appl. Chem.* **1997**, *69*, 595−600. (b) Nakai, T.; Mikami, K. *Org. React.* **1994**, *46*, 105−209. (c) Marshall, J. A. In *Comprehensive Organic Synthesis*; Pattenden, G., Ed.; Pergamon: London, 1991; Vol. 3, pp 975−1014. (d) Brückner, R. In *Comprehensive Organic Synthesis*; Pattenden, G., Ed.; Pergamon: London, 1991; Vol. 6, pp 873−908.

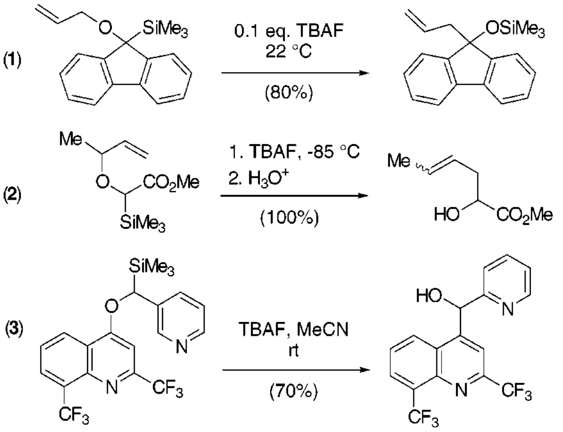
[2] Still, W. C.; Mitra A. *J. Am. Chem. Soc.* **1978**, *100*, 1927−1928.

[3] (a) *Chemistry of Tin*; Smith, P. J., Ed.; Blackie Academic & Professional: New York, 1998. (b) Davies, A. G. In *Organotin Chemistry*; VCH: New York, 1997. (c) Pereyre, M.; Quintard, J.-P.; Rahm, A. In *Tin in Organic Synthesis*; Butterworth: Toronto, 1987.

[4] Reetz, M. T.; Greif, N. *Chem. Ber.* **1977**, *110*, 2958−2959.

10.1021/ol9909132 CCC: $18.00

Scheme 2

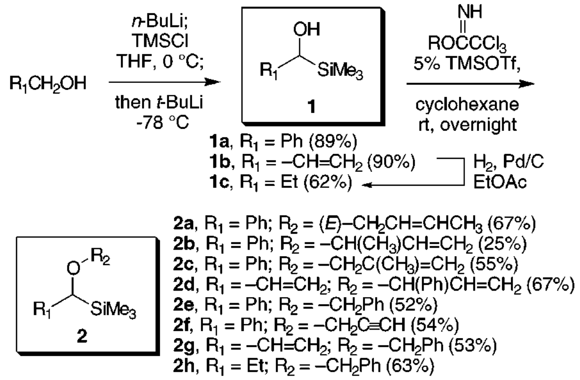


and Greif had shown[4] (Scheme 2; entry 1) that the thermal rearrangement of silylfluorene derivatives could be facilitated by catalytic quantities of tetrabutylammonium fluoride (TBAF). Several years later, Nakai reported[5] the fluoride ion-promoted [2,3]-Wittig rearrangement of two *C*-silylated α-allyloxy esters (Scheme 2; entry 2). To our knowledge the only other report of a fluoride triggered Wittig rearrangement was by Adam, who converted α-phenoxybenzylsilane into an alcohol which would appear to be the product of a [1,2]-Wittig (Scheme 2; entry 3).[6] However, the author makes the point that this reaction proceeds via an intramolecular ipso-substitution as opposed to the radical pair dissociation−recombination mechanism[7] of an actual [1,2]-Wittig rearrangement.

Given the mechanistic uncertainties and narrow substrate scope of these previous studies, coupled with little advancement of this field in over a decade, we decided to explore the generality of fluoride-promoted Wittig rearrangements of α-alkoxysilanes (Scheme 1). Key to our study would be an examination of substrates which would allow the direct comparison of α-alkoxysilanes with the more established α-alkoxystannanes. Furthermore, we sought to determine if such rearrangements could be carried out on relatively unactivated substrates.

Upon beginning our study, we were quick to realize that few general methods exist for the synthesis of α-alkoxysilanes with more complexity than that of the (TMS)methyl ethers.[8,9] (Perhaps one reason for the lack of progress in this area.) Although the substituted α-hydroxysilanes (**1**) (Scheme 3) are easily obtained via retro-Brook rearrangement,[10] the alkylation of these alcohols in situ[11] or under basic conditions proved difficult.[12] Furthermore, while we could efficiently tosylate α-hydroxybenzylsilane, nucleophilic displacement of the product also failed to provide any of the desired ethers.

Scheme 3



Several literature reports had demonstrated the compatibility of α-hydroxysilanes to acid-catalyzed methylation and acetalizations.[11,13] Following this lead, we found that TMSOTf-catalyzed etherification of aliphatic, allylic, or benzylic α-hydroxysilanes via the trichloroacetimidates of benzyl, propargyl, and various allylic alcohols[14] afforded the desired α-alkoxysilanes typically in 50−70% yields[15] after silica gel chromatography (Scheme 3).

With our general route to α-alkoxysilanes in place, we set out to explore the action of fluoride on these substrates. Surveying several fluoride sources, we found that contrary to previous reports, TBAF was not especially effective at promoting Wittig rearrangement. For example, reaction of **2b** with TBAF in the presence of 4 Å molecular sieves gave the [2,3]-rearrangement product **4** in only 20% yield. Similarly, neither tetrabutylammonium difluorotriphenylstannate[16] or KF provided any Wittig products. On the other hand, CsF in DMF proved to be relatively efficient at the promotion of [2,3]-Wittig rearrangements (Table 1). With CsF all of our substrates capable of undergoing a [2,3]-shift (**2a**−**d**) gave [2,3]-products in yields that were comparable to the analogous lithium anion-initiated rearrangements.[1]

While the scope of this preliminary investigation limits us in making any extensive stereochemical comparisons to

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[5] Takahashi, O.; Maeda, T.; Mikami, K.; Nakai, T. *Chem. Lett.* **1986**, 1355−1358.

[6] Adam, S. *Tetrahedron* **1989**, *45*, 1409−1414.

[7] (a) Tomooka, K.; Yamamoto, H.; Nakai, T. *Liebigs Ann. Chem.* **1997**, 1275−1281. (b) Maleczka, R. E., Jr.; Geng, F. *J. Am. Chem. Soc.* **1998**, *120*, 8551−8552 and references therein.

[8] (a) Suga, S.; Miyamoto, K.; Watanabe, M.; Yoshida, J. *Appl. Organomet. Chem.* **1999**, *13*, 469−474. (b) Mulzer, J.; List, B. *Tetrahedron Lett.* **1996**, *37*, 2403−2404 and references therein.

[9] For a retro [1,4]-Brook rearrangement approach to α-alkoxysilanes see: Hoffmann, R.; Brückner, R. *Chem. Ber.* **1992**, *125*, 1471−1484.

[10] (a) Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2392−2398. (b) Brook, A. G.; Pascoe, J. D. *J. Am. Chem. Soc.* **1971**, *93*, 6224−6627. (c) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77−84. (d) Brook, A. G.; Bassindale, A. R. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, pp 149−227.

[11] For successful examples of an in situ methylation and silylation, see: Murai, A.; Abiko, A.; Shimada, N.; Masamune, T. *Tetrahedron Lett.* **1984**, *25*, 4951−4954.

[12] For examples of some common side reactions under Williamson ether conditions, see (a) Kreeger, R. L.; Menard, P. R.; Sans, E. A.; Shechter, H. *Tetrahedron Lett.* **1985**, *26*, 1115−1118. (b) Sans, E. A.; Shechter, H. *Tetrahedron Lett.* **1985**, *26*, 1119−1122. (c) Chakraborty, T. K.; Reddy, G. V. *J. Chem. Soc., Chem. Commun.* **1989**, 251−253.

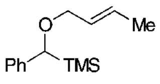
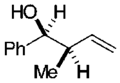
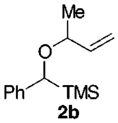
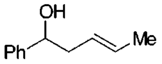
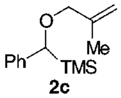
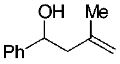
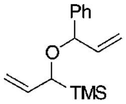
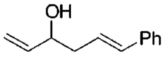
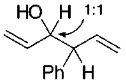
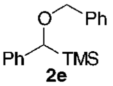
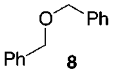
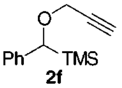
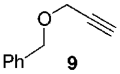
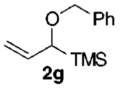
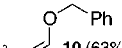
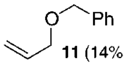
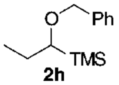
[13] Tsuge, O.; Kanemasa, S.; Nagahama, H.; Tanaka, J. *Chem. Lett.* **1984**, 1803−1806.

[14] Wessel, H. P.; Iversen, T.; Bundle, D. R. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2247−2250.

[15] Varied regioselectivity was observed with trichloroacetimidates derived from allylic alcohols. For example, etherification of **1a** with the trichloroacetimidate of crotyl alcohol gave a separable mixture of **2a** (67%)-and **2b** (25%), while reaction of **1b** with the trichloroacetimidate of cinnamyl alcohol gave **2d**, exclusively,

[16] Gingras, M. *Tetrahedron Lett.* **1991**, *32*, 7381−7384.

Table 1. Reaction of α-Alkoxysilanes with CsF[17]

entry	starting material	products (yield)	
1	 **2a**	 **3**	[2,3]-Wittig (80%) 55:45 *erythro/threo*
2	 **2b**	 **4**	[2,3]-Wittig (60%)
3	 **2c**	 **5**	[2,3]-Wittig (79%)
4	 **2d**	 **6** [2,3]-Wittig (54%)	 **7** [1,2]-Wittig (13%)
5	 **2e**	 **8**	(61%)
6	 **2f**	 **9**	(54%)
7	 **2g**	 **10** (63%) 88:12 *E/Z*	 **11** (14%)
8	 **2h**	No Reaction (80% recovery of **2h**)	

the rearrangement of analogous α-lithio compounds, the rearrangement of **2a** did exhibit the same (albeit poor) inherent stereochemical bias toward the erythro product, as its lithio counterpart.[1,18] Likewise, the exclusive *E*-olefin formation observed in entries 2 and 4 (Table 1) would suggest that the fluoride induced Wittigs proceed via the same *exo*-transition state preferred by traditional Wittig rearrangements.[1,19]

Our initial results do indicate that efficient fluoride promotion may be primarily limited to [2,3]-sigmatropic events. Only entry 4 (Table 1) showed any propensity for another Wittig manifold, providing the [1,2]-species as a minor product. Only loss of the silyl group was observed for other substrates (Table 1; entries 5−7) set up to undergo [1,2]-Wittig rearrangement. This observation that the fluoride-promoted rearrangements mimic their lithio counterparts during the concerted [2,3]-shift, but not during the radical pair dissociation−recombination driven [1,2]-Wittig rearrangement,[20] suggests the involvement of a metal-associated carbanionic intermediate. This would contrast with the traditional Wittig−Still, for which Brückner[21] has put forth experimental evidence of a metal free carbanion. What is less clear is whether these fluoride-promoted Wittigs involve a pentavalent silicon intermediate[8b,22] and/or the type of cation coordinated species suggested by ab initio calculations.[23]

Finally, it would appear that some activation of the starting material (benzylic or allylic) is required. Aliphatic α-alkoxysilanes (Table 1; entry 8), for example, failed to react under our conditions.

In summary, α-alkoxysilanes can be prepared via Lewis acid-catalyzed reaction of allyl and benzyl trichloroacetimidates with α-silyl alcohols and then made to undergo efficient Wittig rearrangement by reaction with CsF in DMF. Further synthetic and modeling studies aimed at expanding the scope and increasing our mechanistic knowledge of these rearrangements are currently underway and will be reported in due course.

Acknowledgment. Generous support was provided by the NIH (HL-58114) and the MSU Department of Chemistry (start-up funds for R.E.M. and a Harold Hart Graduate Fellowship for F.G.). We also thank Dr. P. G. Spoors (SmithKline Beecham) for valuable discussions.

Supporting Information Available: Spectroscopic data for all new compounds pictured as well as detailed experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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[17] All reactions were run with 3.0 equiv of CsF in DMF at room temperature over 16 h. See Supporting Information for more details.

[18] Schöllkopf, U.; Fellenberger, K.; Rizk, M. *Liebigs Ann. Chem.* **1970**, *734*, 106−115.

[19] Rautenstrauch, V. *J. Chem. Soc., Chem. Commun.* **1970**, 4−6.

[20] For data on the lithium base-promoted rearrangements of the substrates in Table 1, see the accompanying letter (Maleczka, R. E., Jr.; Geng, F. *Org. Lett.* **1999**, *1*, 1115−1118).

[21] Kruse, B.; Brückner, R. *Tetrahedron Lett.* **1990**, *31*, 4425−4428.

[22] Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371−1448.

[23] Wu, Y.-D.; Houk, K. N.; Marshall, J. A. *J. Org. Chem.* **1990**, *55*, 1421−1423.