Graphical Abstract

Tandem Epoxysilane Rearrangement/Wittig-Type Reactions Using γ-Phosphinoyl- and γ-Phosphonio-αβ-epoxysilane
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Tandem Epoxysilane Rearrangement/Wittig-Type Reactions Using γ-Phosphinoyl- and γ-Phosphonio-α,β-epoxysilane

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Abstract—Reaction of γ-phosphinoyl- and γ-phosphonio-α,β-epoxysilane with a base followed by addition of a ketone or an aldehyde afforded dienol silyl ether derivatives via a tandem process that involves base-induced ring opening of the epoxide, Brook rearrangement, and Wittig-type reaction. © 2007 Elsevier Science. All rights reserved

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Recently we have developed the epoxysilane rearrangement that converts γ-metalated α,β-epoxysilanes into β-siloxyallylic carbanion derivatives, which are often difficult to generate in other ways. During the exploration of the possibility of cascade reactions initiated by the rearrangement, we became interested in its use in Wittig-type reactions (Scheme 1) by introduction of a heteroatom substituent such as a phosphonyl group as an α-carbanion-stabilizing group, allowing a direct access to dienol silyl ethers. Dienol silyl ethers have been used as versatile building blocks in a variety of synthetic transformations, including Diels-Alder reaction, γ-selective reaction with electrophiles in dienolates, and modular synthesis of a polyenic backbone. Although this has led to considerable efforts toward developing methods for synthesizing such conjugated systems, most of which use α,β-unsaturated aldehydes as a starting material, only a few methods of synthesis have so far been reported.

First we prepared γ-phosphoryl dienol silyl ether 6 from the known epoxy silane 5 and examined the tandem epoxysilane rearrangement/Horner-Wadsworth-Emmons reaction. Treatment of 6 with LDA followed by addition of hexanal afforded the adduct 8 (single diastereomer) and the protonated product 9 in 19% and 38% yields, respectively, no desired product 7 being obtained.

The result can be understood by considering that cycloelimination from betaine intermediates does not readily occur when electron-withdrawing groups in the phosphonate reagents are absent. Next we focused on a phosphine oxide-based approach, which can afford condensation products directly in the presence of potassium ion without isolation of the adducts. When phosphine oxide 11, prepared from 10 via the reaction with lithium diphenyolphosphate followed by H₂O₂ oxidation and then epoxidation, was treated with KHMDMS followed by cyclohexanone, dienol silyl ether 13 and protonated products 14 were obtained in low yield together with decomposition products (Scheme 3). In contrast, the use of n-BuLi produced adducts of ketone 12 in 64% yield, which were converted into 13 by exposure to KHMDMS. These results prompted us to change a counter cation from lithium to potassium or sodium in situ after the formation of lithium salt of 12.

Lithium salt 12', generated from 11 with n-BuLi and cyclohexanone, was treated with KHMDMS or NaHMDS in situ (Table 1). The best result was obtained by 3 equiv of NaHMDS to afford 13 (Table 1) in 77% yield. Reactions with aldehydes resulted in low yields.

We next turned our attention to Wittig reaction using γ-phosphonio derivative 4c, the synthesis of which using the corresponding halides we had attempted at the initial stage of the project but had given up on because of unavailability of isolable and purifiable material. Encouraged by the above result with the phosphine oxide, we decided to reexamine the preparation of 4c. After extensive experimentation, we found triflate derivative 16, readily prepared by the sequence shown in Scheme 4, to be suitable for our purposes. When 16 was treated with n-BuLi at -80 °C over a period of 15 min followed by addition of cyclohexanone and then warmed to room temperature,
The reactions with aldehydes gave somewhat better results in terms of yield and Z/E selectivity of the enol silyl ether moiety. Thus, when 16 was reacted with n-BuLi and then benzaldehyde at -80 °C, 17 was obtained in 47% yield in a ratio of 3.4 (Z/E) (Table 1, entry 1). The yield was improved to 75% yield when the reaction was conducted at 15 °C (entry 2). The reactivity and selectivity of the reaction were affected by a change in the solvent from THF to CH2Cl2. Although the reaction in CH2Cl2 under the same reaction conditions led to recovery of the starting material (entry 3), lowering the reaction temperature to -40 °C gave 17 in the Z selectivity (entry 4).

In conclusion, we have demonstrated further possibilities of the epoxysilane rearrangement as an initiator in cascade reactions. A unique feature of this method is that, in addition to the tandem nature of the process, the starting phosphonium salt is a stable crystalline solid that is readily derived from propargyl alcohol and can be stored for several months without significant decomposition.

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8. We found that 16 is a stable crystalline compound (mp 126 °C) when stored at room temperature.