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Tandem epoxysilane rearrangement/Wittig-type reactions using γ-phosphinoyl- and γ-phosphonio-α,β-epoxysilane

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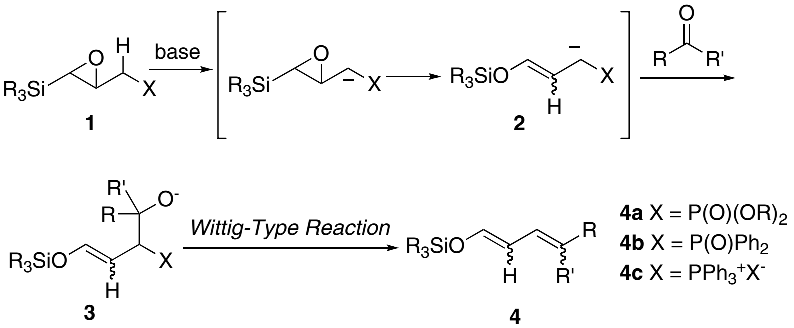
Abstract—Reaction of γ-phosphinoyl- and γ-phosphonio-α,β-epoxysilane with a base followed by addition of a ketone or an aldehyde afforded dienol silyl ether derivatives via a tandem process that involves base-induced ring opening of the epoxide, Brook rearrangement, and Wittig-type reaction.

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.[1] During the exploration of the possibility of cascade reactions initiated by the rearrangement, we became interested in its use in Wittig-type reactions[2] (Scheme 1) by the introduction of a heteroatom substituent such as a phosphonoyl 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,[3] γ-selective reaction with electrophiles in dienolates,[4] and modular synthesis of a polyenic backbone.[5] Although this has led to considerable efforts toward developing methods for synthesizing such conjugated systems,[6] 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 derivative **6** from the known epoxy silane **5** and examined the tandem epoxysilane rearrangement/Horner–Wadsworth–Emmons reaction. Treatment of **6** with LDA followed by the addition of hexanal afforded adduct **8** (single diastereomer) and the protonated product **9** in 19% and 38% yields, respectively, no desired product **7** being obtained (Scheme 2).

The result can be understood by considering that cycloelimination from betaine intermediates does not readily occur when electron-withdrawing groups in the



Scheme 1. Epoxysilane **1** as a precursor of dienol silyl ethers.

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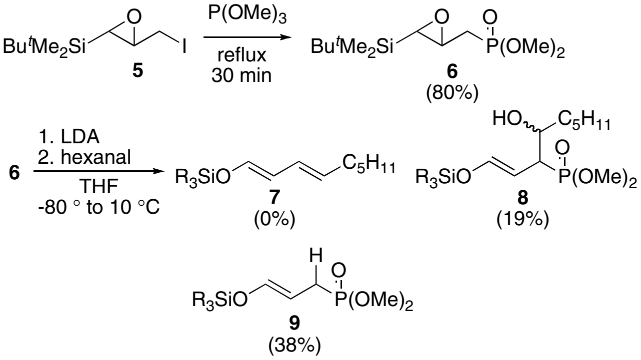
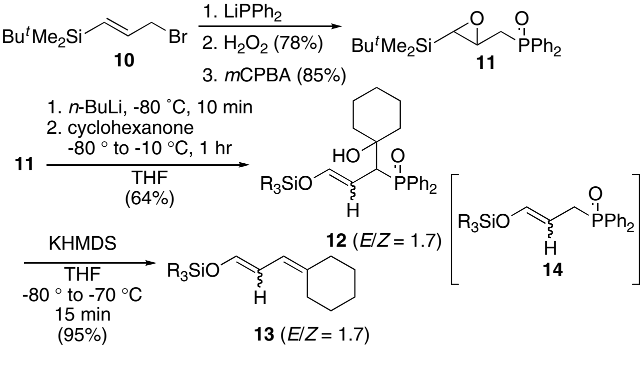


Scheme 2. Preparation of **6** and its reaction with hexanal.

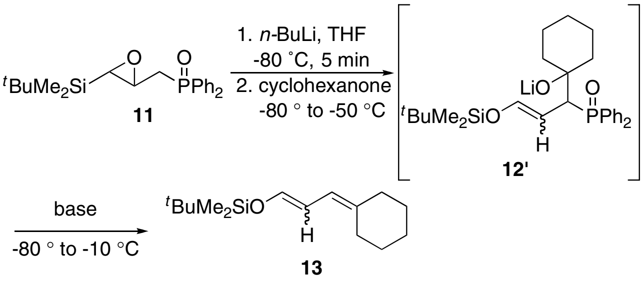
phosphonate reagents are absent.[2b] Next we focused on a phosphine oxide-based approach, which can afford condensation products directly in the presence of potassium ion without isolation of the adducts. When phosphine oxide **11**, prepared from **10** via the reaction with lithium diphenylphosphide followed by H_2O_2 oxidation and then epoxidation, was treated with KHMDS followed by cyclohexanone, dienol silyl ether **13** and protonated products **14** were obtained in a low yield together with decomposition products (Scheme 3). In contrast, the use of *n*-BuLi produced adducts of ketone **12** in a 64% yield, which were converted into **13** by exposure to KHMDS. These results prompted us to change a counter cation from lithium to potassium or sodium in situ after the formation of the lithium salt of **12**.[7]

Lithium salt **12′**, generated from **11** with *n*-BuLi and cyclohexanone, was treated with KHMDS or NaHMDS in situ (Scheme 4). The best result was obtained by 3 equiv of NaHMDS to afford **13** (Scheme 4) in a 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 an extensive experimentation, we found triflate derivative **16**,[8] readily prepared by the sequence shown in Scheme 5, to be suitable for our purposes. When **16** was treated with *n*-BuLi at −80 °C over a period of 15 min followed by the addition of cyclohexanone and then warmed to room temperature, dienol silyl ethers **13** were obtained in a 40% yield in a ratio of 1.6 (*Z*/*E*) (Scheme 5).



Scheme 3. Preparation of **11** and its reaction with cyclohexanone.



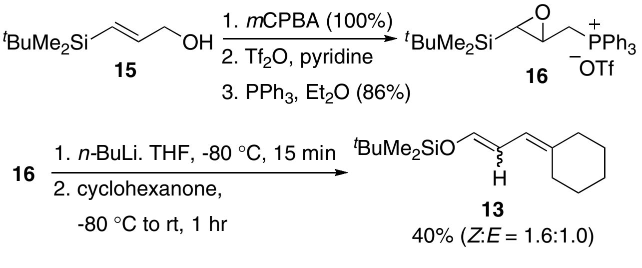
entry	base (equiv)	yield (%) **12** (*E*/*Z*)	yield (%) **13** (*E*/*Z*)
1	KHMDS (2.0)	17 (1.3)	38 (1.0)
2	NaHMDS (2.0)	19 (1.0)	58 (1.3)
3	NaHMDS (3.0)	-	77 (1.0)

Scheme 4. One-pot synthesis of **13**.

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 a 47% yield in a ratio of 3.4 (*Z*/*E*) (Table 1, entry 1). The yield was improved to a 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 CH_2Cl_2. Although the reaction in CH_2Cl_2 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).

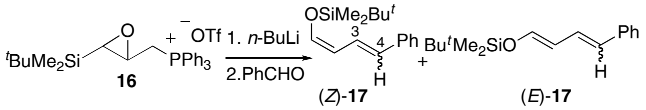
A similar trend was observed with the reactions with other aldehydes (Table 2).

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.



Scheme 5. Preparation of **16** and its reaction with cyclohexanone.

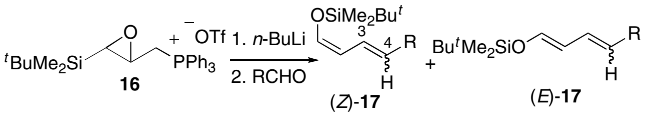
Table 1. Reaction of **16** with benzaldehyde



Entry	Conditions	Solvent	Yield (%)	Z/E[a]
1	1. −80 °C, 15 min 2. −80 °C, 30 min	THF	47	3.4
2	1. 15–20 °C, 3 min 2. 15–20 °C, 5 min	THF	75	3.4
3	1. 15–20 °C, 3 min 2. 15–20 °C, 10 min	CH_2Cl_2	0	—
4	1. −40 °C to −35 °C, 3 min 2. −40 °C to −30 °C, 25 min	CH_2Cl_2	65	9.4

[a] The ratios of 3E/3Z were almost 1.0.

Table 2. Reaction of **16** with aldehydes



Entry	R	Conditions[a]	Yield (%)	Z/E[b]
1	n-C_5H_{11}	A	77	4.4
2	n-C_5H_{11}	B	60	8.0
3	$(CH_3)_2CH$	A	68	10.6
4	$(CH_3)_2CH$	B	58	8.0
5	c-C_6H_{11}	A	69	6.6
6	c-C_6H_{11}	B	48	9.1
7	$(CH_3)_3C$	A	50	Z only[c]
8	$(CH_3)_3C$	B	42	Z only[c]

[a] Condition A: 1. 15–20 °C, 3 min, 2. 15–20 °C, 5 min in THF; condition B: 1. −40 °C to −35 °C, 3 min, 2. −40 °C to −30 °C, 25 min in CH_2Cl_2.

[b] The ratios of 3E/3Z were almost 1.0.

[c] 3Z isomer was formed exclusively.

Acknowledgments

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