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Twofold Brook rearrangement-mediated tandem reactions of δ-silyl-γ,δ-epoxy-α,β-unsaturated acylsilanes with a cyanide ion

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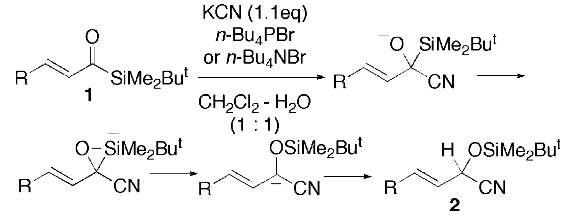
Abstract—Reaction of δ-silyl-γ,δ-epoxy-α,β-unsaturated acylsilanes with KCN in the presence of chloro or cyanoformates gives highly functionalized dienol silyl ether derivatives via a twofold Brook rearrangement-induced tandem sequence.

Several years ago, we reported that reactions of acylsilanes **1** with KCN under liquid–liquid phase-transfer catalytic conditions proceed smoothly via a Brook rearrangement to produce *O*-silyl cyanohydrin derivatives **2** in excellent yields without trapping of the α-silylalkoxide by water (Scheme 1).[1–3] These results suggest that acylsilanes can be equivalent to *O*-silyl cyanohydrin α-carbanions in combination with cyanide ion.

We also established that *O*-silyl cyanohydrins of β-silyl-α,β-epoxyaldehydes **3** readily undergo base-induced ring opening/Brook rearrangement/allylic alkylation to produce enol silyl ether derivatives **4** (Scheme 2).[4]

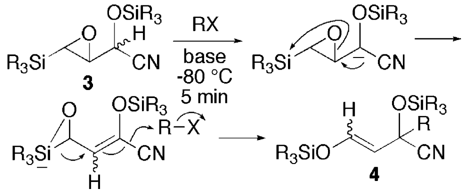
The above studies led us to attempt the reaction of β-silyl-α,β-epoxyacylsilanes **5** with cyanide ion in the presence of an electrophile, which would afford **8** according to a tandem sequence expressed in Scheme 3. Thus, nucleophilic attack of a cyanide ion on acylsilane **5** would generate silicate intermediate **6** that should undergo Brook rearrangement-induced ring opening of the epoxide followed by the second Brook rearrangement in **7** and subsequent reaction with an electrophile at the allylic position to give **8**.



Scheme 1. Reaction of acylsilanes with KCN under phase-transfer catalytic conditions.

Unfortunately, we could not prepare **5** in a reasonable yield because of the tendency in the stage of epoxidation of the corresponding α-silylalcohol to undergo a silyl-migration reaction.[5] We decided to use a vinylogous derivative **11**, which was prepared by the Horner–Wadsworth–Emmons reaction of aldehyde **9**[4b] with phosphonate **10** (Scheme 4).[6]

When acryloylsilane **11** was treated with KCN in the presence of *n*-Bu$_4$NBr or *n*-Bu$_4$PBr in CH$_2$Cl$_2$–H$_2$O, *O*-silyl cyanohydrin derivative **16** was obtained together with α-silyl alcohol **15**, a product that was protonated before the formation of the second silicate intermediate **14** (Scheme 5).[7] The trend that a better result was obtained with *n*-Bu$_4$PBr than with *n*-Bu$_4$NBr is the same as that in the case of **1**. The ratio of **16** to **15** increased



Scheme 2. Tandem base-promoted ring opening/Brook rearrangement/allylic alkylation of γ-silyl-β,γ-epoxybutanenitriles.

Keywords: Tandem reaction; Brook rearrangement; Acylsilanes; Epoxysilanes.

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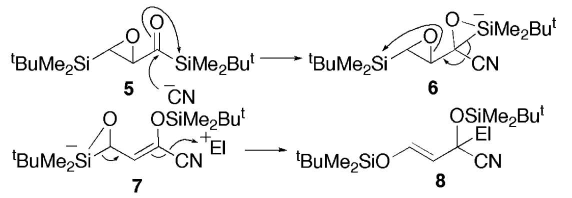
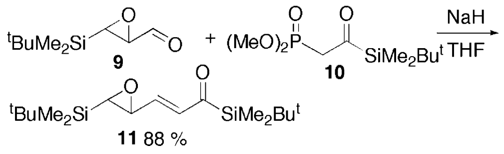
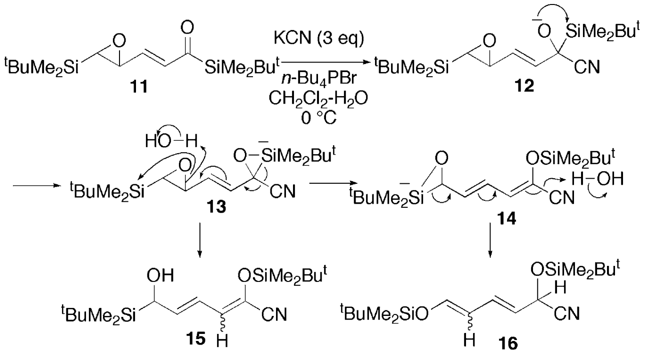


Scheme 3. Twofold Brook rearrangement-mediated tandem reaction of **5** with a cyanide ion.



Scheme 4. Synthesis of **11**.



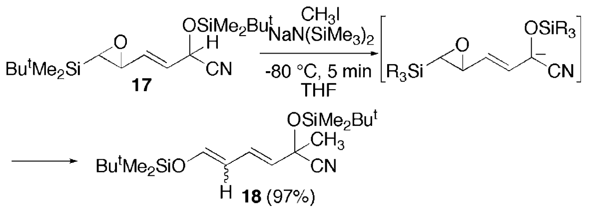
catalyst	mol%	time (h)	**15**	**16** (*E*/*Z*)
^{n}Bu$_4$NBr	0.5	10	32	24 (11)
^{n}Bu$_4$NBr	5	7.5	35	31 (5.2)
^{n}Bu$_4$NBr	50	1.5	9	49 (1)
^{n}Bu$_4$PBr	0.5	7.5	42	34 (only *E*)
^{n}Bu$_4$PBr	5	1.5	32	31 (6.75)
^{n}Bu$_4$PBr	50	5 (min)	5	50 (0.72)

Scheme 5. Reaction of **11** with KCN under liquid–liquid phase-transfer catalytic conditions.

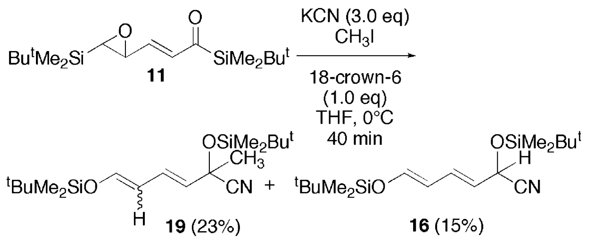
with increasing amounts of the catalyst, presumably because of rate acceleration to **16** by the increase in the ionic character in the silicate intermediate **14** due to the change in the counter cation from potassium to ammonium or phosphonium ions. The fact that **11** can undergo a twofold Brook rearrangement in the presence of water to give **16** as a major product without interception of intermediates such as **12** by water prompted us to examine the reaction of **11** with electrophiles in non-hydroxylic solvents.

We first examined the reaction of **11** with MeI as an electrophile, because we recently reported that related cyanohydrin derivatives **17** undergo a base-induced alkylation reaction involving a tandem process similar to that in the case of **3** at −80 °C to give **18** in an excellent yield (Scheme 6).[4b]

When a solution of **11** and MeI in THF was treated with KCN in the presence of 18-crown-6 at 0 °C, only a 23% yield of **19** together with **16** (15%) was obtained (Scheme 7). We could not improve the yield of **19** after extensive examination of the reaction conditions including solvents and additives. A possible reason for the failure can be that an immediate precursor for **19** is unstable under the conditions (e.g., 0 °C) required for its formation. The fact that warming the reaction of **17** with $NaN(SiMe_3)_2$ to 0 °C in the absence of MeI led to complex product mixtures is supportive of our analysis.



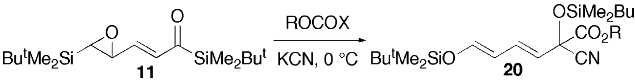
Scheme 6. Base-induced isomerization of **17** followed by methylation.



Scheme 7. Reaction of **11** with KCN in the presence of MeI.

We next turned our attention to chloroformates as more reactive electrophiles. When **11** was reacted with *n*-butyl chloroformate in the presence of KCN and 18-crown-6, ester derivative **20** was obtained in varying yields depending on the reaction conditions. Thus, addition of KCN and 18-crown-6 to a CH_2Cl_2 solution of **11** and *n*-butyl chloroformate (method A) afforded **20** in 31% yield (Table 1, entry 1). Changes in the solvent from CH_2Cl_2 to THF and Et_2O resulted in decomposition (entries 2 and 3). We reasoned that the low yield of **20** resulted from the competing nucleophilic attack of the cyanide ion at the carbonyl groups of the acylsilane and the chloroformate. Considering the possibility that cyanoformate, generated in situ in the reaction, is an actual electrophile, we next examined a method that involves reacting preformed cyanoformate[8] in situ with **11** (method B). When **11** was added to a solution of cyanoformate that was generated by treating chloroformate with KCN and 18-crown-6, the yield was improved. The best result was obtained with 0.1 equiv of 18-crown-6 and use of Et_2O (0.05 M) as a solvent, which afforded **20** in 90% yield (entry 7). Similar results were obtained with ethyl and benzyl chloroformates (entries 8 and 9). Johnson has recently reported that the reaction of acylsilanes with cyanoformates affords acylated products through a cyanation/Brook rearrangement/C-acylation reaction.[9] Treatment of **11** with cyanoformates under Johnson's conditions produced **20** in excellent yields (entries 10–12).

Table 1. Reaction of **11** with chloro and cyanoformates



Entry	R	X	Method	18-Crown-6 (equiv)	Solvent	Concn (M)	Time (h)	Yield (%)
1	*n*-Bu	Cl	A	1.0	CH_2Cl_2	0.5	5 (min)	31
2	*n*-Bu	Cl	A	1.0	THF	0.5	1	—[a]
3	*n*-Bu	Cl	A	1.0	Et_2O	0.5	12	—[a]
4	*n*-Bu	Cl	B	0.4	CH_2Cl_2	0.05	3	49
5	*n*-Bu	Cl	B	0.4	Et_2O	0.05	20	56
6	*n*-Bu	Cl	B	0.1	CH_2Cl_2	0.05	48	24
7	*n*-Bu	Cl	B	0.1	Et_2O	0.05	2	90
8	Et	Cl	B	0.1	Et_2O	0.05	5	80
9	$PhCH_2$	Cl	B	0.1	Et_2O	0.05	9	80
10	*n*-Bu	CN	B	0.1	Et_2O	0.05	1.5	89
11	Et	CN	B	0.1	Et_2O	0.05	1	93
12	$PhCH_2$	CN	B	0.1	Et_2O	0.05	15 (min)	81

[a] A complex mixture was obtained.

In conclusion, we have demonstrated that reactions of δ-silyl-γ,δ-epoxy-α,β-unsaturated acylsilanes with KCN and chloro and cyanoformates produce highly functionalized dienol silyl ethers via a tandem sequence featuring a twofold Brook rearrangement. Investigation of chirality transfer from the epoxide to the quaternary center using optically active **11** is currently underway.

Acknowledgements

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Supplementary data

Information available: Full experimental details and spectral data. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.08.157.

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