Pergamon

Tetrahedron Letters 41 (2000) 6589–6592

TETRAHEDRON LETTERS

Reverse Brook rearrangement of 2-alkynyl trialkylsilyl ether. Synthesis of optically active (1-hydroxy-2-alkynyl)trialkylsilane

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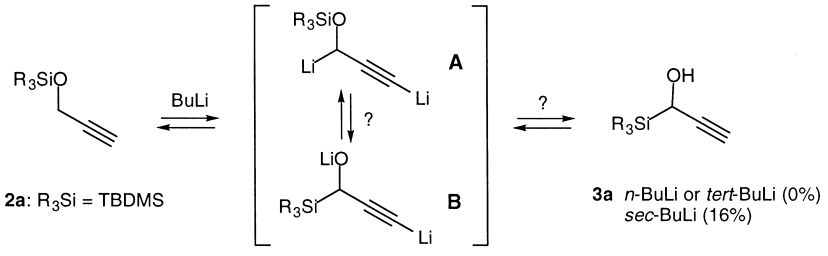
Received 5 June 2000; revised 22 June 2000; accepted 23 June 2000

Abstract

A new method for the synthesis of optically active α-hydroxyalkynylsilane **3** is described. The key step of the conversion to **3** was the use of the reverse Brook rearrangement of the 2-alkynyl silyl ether **2**.

Keywords: reverse Brook rearrangement; α-hydroxyalkynylsilane; 2-alkynyl silyl ether.

The (1-hydroxy-2-alkynyl)trialkylsilane (α-hydroxyalkynylsilane) derivative, possessing a chiral α-hydroxysilane group convertible to an aldehyde or a carboxylic acid, has received considerable attention owing to its potential utility as a building block in organic synthesis.[1] However, methodology for its preparation has been limited to the use of a nucleophilic addition reaction, i.e. addition of an alkynyl anion to trialkylsilylformaldehyde.[2] In this report, we wish to describe an efficient entry to the synthesis of (1-hydroxy-2-alkynyl)trialkylsilane **3** by means of reverse Brook rearrangement of 2-alkynyl trialkylsilyl ether **2**.



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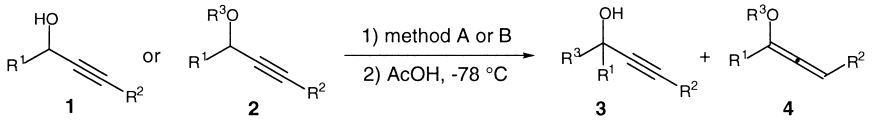
0040-4039/00/$ - see front matter
PII: S0040-4039(00)01086-8

Treatment of a 2-alkenyl silyl ether with a strong base is well known to undergo the reverse Brook rearrangement to give (1-hydroxy-2-alkenyl)trialkylsilane,[3] while no successful example regarding the reverse Brook rearrangement employing 2-alkynyl silyl ether has been reported to date, due probably to the instability of the 2-alkynylalkoxylithium intermediate **B** (Eq. (1)). In fact, treatment of the propargyl silyl ether **2a** with *n*- or *tert*-BuLi resulted in a complete recovery of the starting material. On the other hand, the use of 3 equiv. of *sec*-BuLi was found to effect the desired rearrangement to give **3a** in 16% yield,[4] apparently indicating the presence of an equilibrium between **A** and **B**.[5]

Encouraged by this finding, we attempted to improve its yield. Finally, the yield was optimized to 70% when unprotected propargyl alcohol (**1a**) was treated with the following sequence of reactions in one pot (method A): (1) TBDMSCl and *n*-BuLi in THF; (2) 3 equiv. of *sec*-BuLi at –45°C for 22 h; and (3) acetic acid in THF at –78°C (Table 1, entry 1).[5,6] This method was applied to other 2-alkyn-1-ols (**1b–d**). The reaction of 2-butyn-1-ol (**1b**) using 1.2 equiv. of *n*-BuLi for the rearrangement step provided **3b** in 86% yield (entry 2), while the use of the isolated TBDMS ether **2b** (method B) afforded the same product in 45% yield (entry 7), where the yield was improved to 78% by using 3 equiv. of *n*-BuLi (entry 8). 2-Octyn-1-ol (**1c**) using TMSCl and *tert*-BuLi[7] afforded the α-hydroxytrimethyl-silane **3c** in 45% yield (entry 4). In this case, method A was slightly superior to method B (35%, entry 9) in terms of yield. Next, we examined these

Table 1
The reverse Brook rearrangement of 2-alkylnyl trialkylsilyl ether



1 2 3 4

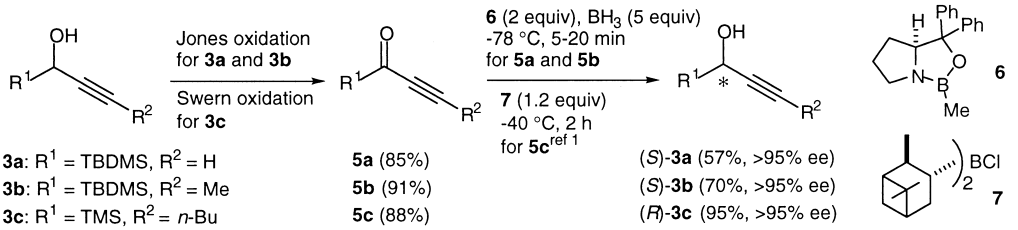
	substrate	R^1	R^2	R^3	method,[a] base (equiv)	time (h)	product yield (%)				addition of LiCl (equiv) product yield (%)				
1	**1a**	H	H	TBDMS	A, *sec*-BuLi (3)	22	**3a**	70	**4a**	4					
2	**1b**	H	Me	TBDMS	A, *n*-BuLi (1.2)	2	**3b**	86	**4b**	0					
3	**1b**	H	Me	TBDMS	A, *n*-BuLi (1.2)[b]	2	**3b**	32	**4b**	0					
4	**1c**	H	*n*-Bu	TMS	A, *tert*-BuLi (1.2)	2	**3c**	45	**4c**	0					
5	**1d**	Me	*n*-Bu	TMS	A, *tert*-BuLi (3)[c]	3	**3d**	34[d]	**4d**	0					
6	**2a**	H	H	TBDMS	B, *sec*-BuLi (3)	22	**3a**	16[e]	**4a**	8	(3)	**3a**	28[f]	**4a**	0
7	**2b**	H	Me	TBDMS	B, *n*-BuLi (1.2)	1.5	**3b**	45[g]	**4b**	<2[h]	(1)	**3b**	58	**4b**	0
8	**2b**	H	Me	TBDMS	B, *n*-BuLi (3)	1.5	**3b**	78	**4b**	<2[h]	(3)	**3b**	85	**4b**	0
9	**2c**	H	*n*-Bu	TMS	B, *tert*-BuLi (3)	1.5	**3c**	35	**4c**	<2[h]	(3)	**3c**	44	**4c**	0
10	**2d**	Me	*n*-Bu	TMS	B, *tert*-BuLi (3)[c]	3	**3d**	67	**4d**	31	(3)	**3d**	52[i]	**4d**	0

[a]Method A (one-pot preparation, see ref 6): (1) 2-alkyn-1-ol (**1**), *n*-BuLi (1.05 equiv), chlorotrialkylsilane (1.05 equiv), THF, 25 °C, (2) alkyllithium, -45 °C; method B: isolated silyl ether **2**, alkyllithium, THF, -45 °C.
[b]TBDMSOTf was used instead of chlorotrialkylsilane.
[c]Reaction was carried out at -20 °C.
[d]28% of **1d** was recovered.
[e]22% of **2a** was recovered.
[f]12% of **2a** was recovered.
[g]35% of **2b** was recovered.
[h]Determined by ^{1}H NMR.
[i]38% of **2d** was recovered.

methods for the conversion of the secondary propargyl alcohol **1d** or its silyl ether **2d** into the corresponding α-substituted-α-hydroxysilane **3d**, which has a sterically crowded tertiary hydroxy group. Method A using TMSCl and *tert*-BuLi was quite effective for this conversion to give **3d** in 67% yield (entry 10), together with the allenol ether **4d**[8] (31%, vide infra).[9] Thus, the reverse Brook rearrangement was found to be an efficient method for the preparation of various types of the (1-hydroxy-2-alkynyl)trialkylsilanes **3a**–**d**.

One question arose from the above results, namely, why did direct treatment of the silyl ether **2** with the base (method B) result in a significant decrease in the yields of the α-hydroxysilane **3** in comparison with its one-pot preparation (method A) where LiCl, produced at the silylation step, existed in the reaction? To understand the role of LiCl, the following experiments were performed: (1) the use of TBDMSOTf instead of TBDMSCl for method A; and (2) the addition of LiCl to method B. The reaction of **1b** using TBDMSOTf gave **3b** in 32% yield which was much lower than that obtained using TBDMSCl (entry 3). Addition of LiCl (1–3 equiv.) to the reaction of the silyl ethers **2a**–**c** resulted in a slight increase in the yields, respectively (entries 6–9), which were, however, still lower than those obtained by method A. It is noted that none of the allenol ethers **4a**–**c** were by-produced by the addition of LiCl. These results indicate that LiCl plays an important role to obtain better yields in both methods, and prevents the formation of the allenol ethers in method B, which would be produced through an intermediate such as **A** in Eq. (1). However, the real role of LiCl in the present reaction is not clearly understood at this stage, although it has been reported that lithium halides affect the equilibrium of the Brook rearrangement.[8c]

The conversion of the resulting **3a**–**c** into their optically active forms was accomplished as shown in Scheme 1. Jones oxidation of **3a** gave the silyl ketone **5a** in good yield. Enantioselective reduction of **5a** with 5 equiv. of BH_3 in the presence of 2 equiv. of (*S*)-oxazaborolidine **6**[10] afforded the optically active (1-hydroxy-2-alkynyl)trialkylsilane (*S*)-**3a**[11] (57% yield, >95% ee).[12,13] The α-hydroxysilane (*S*)-**3b**[11] (>95% ee)[12] was synthesized in the same manner. On the other hand, the α-hydroxysilane **3c** was converted to the silyl ketone **5c** by Swern oxidation because of its instability under the acidic conditions. Successful conversion of **5c** into the optically active α-hydroxysilane (*R*)-**3c**[11] (>95% ee)[12] using (–)-*B*-chloro diisopinocamphenylborane (**7**, (–)-DIP-Cl)[14] has been reported.[1,15]



Scheme 1.

In summary, we have found that the reverse Brook rearrangement is a useful method for the conversion of the 2-alkynyl trialkylsilyl ether **2** into the (1-hydroxy-2-alkynyl)trialkylsilane **3**, whose optically active form was prepared by oxidation and subsequent enantioselective reduction.

References

1. Sakaguchi, K.; Mano, H.; Ohfune, Y. *Tetrahedron Lett*. **1998**, *39*, 4311–4312.
2. Linderman, R. J.; Suhr, Y. J. *J. Org. Chem*. **1988**, *53*, 1569–1572.
3. (a) Brook, A. G. *Acc. Chem. Res*. **1974**, 77–84. (b) Danheiser, R. L.; Fink, D. M.; Okano, K.; Tsai, Y.-M.; Szczepanski, S. W. *J. Org. Chem*. **1985**, *50*, 5393–5396. (c) Danheiser, R. L.; Fink, D. M.; Okano, K.; Tsai, Y.-M.; Szczepanski, S. W. In *Org. Synth. Coll. Vol. VIII;* John Wiley & Sons: New York, 1993; pp. 501–505.
4. When a nearly stoichiometric amount of the base was used for method B, the yields of **3a**–**d** decreased and a significant amount of **2a**–**d** was recovered, respectively.
5. The yields of **3a** decreased when the reaction (entry 1) was quenched at elevated temperature (–45°C, 13% of **3a** and 13% of **4a**; 0°C, 9% of **3a** and 17% of **4a**). The corresponding silyl ether **2a** was not recovered at all.
6. Representative experimental procedure for the reverse Brook rearrangement by method A: To a solution of **1b** (10.0 g, 142.7 mmol) in THF (180 mL), was added *n*-BuLi in *n*-hexane (149.8 mmol) at –78°C, and the mixture was stirred at 0°C for 30 min. To the solution was added a solution of TBDMSCl (22.6 g, 149.8 mmol) in THF (30 mL) at –78°C. After stirring at room temperature for 4 h, *n*-BuLi (171.2 mmol) in *n*-hexane at –78°C was added to the solution dropwise, and the mixture was stirred at –45°C for 2 h. The reaction was quenched by 10% AcOH in THF at –78°C. The mixture was extracted with Et_2O, and the organic phase was washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (*n*-hexane/Et_2O, 30/1) to give **3b** (22.5 g, 86%) as a colorless oil.
7. The use of *n*-BuLi for the reaction of the TMS ether **2c** or **2d** resulted in cleavage of the TMS group.
8. Preparation of silyl allenol ether from (1-substituted-1-hydroxy-2-alkynyl)trimethylsilane, see: (a) Kuwajima, I.; Kato, M. *Tetrahedron Lett*. **1980**, *21*, 623–626. (b) Reich, H. J.; Olson, R. E.; Clark, M. C. *J. Am. Chem. Soc*. **1980**, *102*, 1423–1424. (c) Reich, H. J.; Eisenhart, E. K.; Olson, R. E.; Kelly, M. J. *J. Am. Chem. Soc*. **1986**, *108*, 7791–7800.
9. Treatment of the TBDMS-substituted analogue of **2d** with *n*-, *sec*-, or *tert*-BuLi resulted in a complete recovery of the starting material.
10. (a) Corey, E. J.; Bakshi, R. K.; Shibata, K. P. *J. Am. Chem. Soc*. **1987**, *109*, 5551–5553. For reviews, see: (b) Singh, V. K. *Synthesis* **1992**, 605. (c) Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1992**, *3*, 1475–1504. (c) Deloux, L.; Srebnik, M. *Chem. Rev*. **1993**, 93, 763–784.
11. (*S*)-**3a**: Colorless oil, $[\alpha]_D^{25}$ –75.6° (*c* 0.62, $CHCl_3$, >95% ee); (*S*)-**3b**: Colorless oil, $[\alpha]_D^{25}$ –80.0° (*c* 1.20, $CHCl_3$, >95% ee); (*R*)-**3c**: Colorless oil, $[\alpha]_D^{25}$ +78.5° (*c* 2.00, $CHCl_3$, >95% ee).
12. The optical purity and absolute configuration of **3a**–**c** were determined by the modified Mosher method using ^1H NMR. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc*. **1991**, *113*, 4092–4093.
13. The TIPS-substituted analogue of (*S*)-**3a** ($[\alpha]_D^{25}$ –66.0° (*c* 0.89, $CHCl_3$, >95% ee)[12] was also prepared (64%) using oxazaborolidine **6** from its racemic form which was prepared from **1a** using TIPSCl by the reverse Brook rearrangement (70%, method A).
14. (a) Sonderquist, E. J.; Anderson, C. L.; Miranda, E. I.; Rivera, I. *Tetrahedron Lett*. **1990**, *31*, 4677–4680. (b) Dahr, R. K. *Aldrichimica Acta* **1994**, *27*, 43–51.
15. (–)-DIPCl (**7**) was also effective for the enantioselective reduction of **5b** to give (*R*)-**3b** (82% yield, >95%) ee.[12]