The [1,5]-Brook Rearrangement: An Initial Application in Anion Relay Chemistry

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The Brook rearrangement comprises the anionic migration of a silyl group from a carbon atom to an oxygen atom, thereby converting an oxyanion (typically a lithium alkoxide) to a carbanion (an organolithium).[1] The simplest [1,2]-form is illustrated in Figure 1. The mechanism, studied extensively by Brook and co-workers, has been shown to proceed intramolecularly, via a hypervalent pentacoordinate silicon species with retention of configuration at
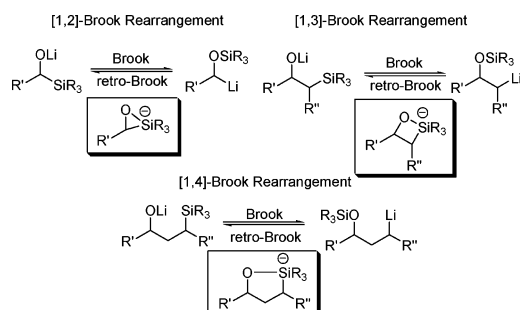
Figure 1. The family of Brook rearrangements.

silicon and inversion of configuration at carbon.[1] Typically Brook rearrangements are reversible processes. The strength of the Si—O bond (ca. 119—124 kcal/mol) compared with the Si—C bond (ca. 75—83 kcal/mol) often favors carbanion formation over alkoxide formation in polar solvents;[1] however, in some cases the greater stability of the oxyanion vs the carbanion outweighs the bond energy differences.[2] Although the original Brook rearrangement encompassed [1,2]-rearrangements, numerous examples of [1,3]- and [1,4]-migrations are now known.[3,4] The [1,3]-Brook rearrangement and the Peterson olefination are believed to share a similar pentacoordinate 1,2-oxasilatanide intermediate.[5] The retro-Brook (or West) rearrangement[2] has also been reported; both rearrangements are now well-established transformations in organic synthesis. There are also several examples which may involve [1,5]- or [1,6]-Brook or retro-Brook rearrangements;[6] however, no evidence was provided that the silyl migrations occur via an intramolecular process.[6]

Recently significant interest has developed in the utility of Brook and retro-Brook rearrangements in tandem reactions, or those combining these rearrangements with bond forming steps.[5] Examples include our multicomponent linchpin coupling[7] and our recently introduced anion relay chemistry (ARC);[8] both transformations are based on the [1,4]-Brook rearrangement. To expand the scope of these synthetic tactics, we became interested in the possibility of longer-range {i.e., [1, *n*]- (*n* ≥ 5)} Brook rearrangements. Herein, we report the first documented examples of [1,5]-Brook rearrangements involving intramolecular silyl migration in conjunction with an initial application in anion relay chemistry.

To explore the feasibility of long-range Brook rearrangements we selected silyl dithianes. This choice was based on the fact that anion stabilizing groups (cf. dithiane) on carbon accelerate the rate

Scheme 1
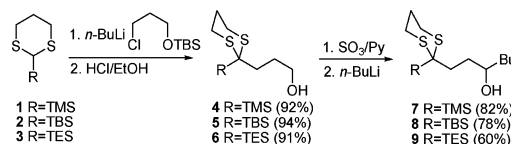
of silyl migration.[5] Toward this end, hydroxyl dithianes **7**−**9** were prepared from the corresponding 2-silyl-1,3-dithianes in four steps (Scheme 1).

Hydroxyl dithiane **7** was then subjected to a variety of conditions (Table 1). For example, treatment with lithium bases (*t*-BuLi, *n*-BuLi, or LHMDS, 1.1 equiv) at room-temperature results in slow (18 h) silyl migration to furnish the [1,5]-migration product in 30−40% yield (entries 1 and 2). When we employed sodium or potassium bases such as NaHMDS and KHMDS at 0 °C, the rate of silyl migration increased dramatically to furnish the [1,5]-Brook rearrangement product **10** in high yield. A similar rate enhancement was observed with the Schlosser base (*t*-BuOK/*n*-BuLi). These results were not completely unexpected, since weaker ion pairing (cf. sodium or potassium) is known to increase the reactivity of the alkoxide and thereby shift the equilibrium in favor of silyl ether formation.[5,9]
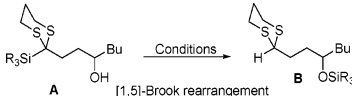
Table 1. Base and Temperature Effects on the Brook Rearrangement of **7**

| entry	base	temp	time	yield of 10
1	*t*-BuLi or *n*-BuLi	rt	overnight	<30%
2	LHMDS	rt	overnight	40%
3	NaHMDS	0 °C	30 min	88%
4	KHMDS	0 °C	30 min	92%
5	*t*-BuOK/*n*-BuLi	0 °C	60 min	89%

We next examined a series of solvents and temperature regimes with substrates **7**−**9** (Table 2). In THF, TMS migration proceeds readily even at −78 °C in the presence of potassium bases (KHMDS or Schlosser's base), whereas in Et$_2$O TMS migration was completely suppressed at −78 °C, although warming to 0 °C did lead to rearrangement. Not surprisingly TBS migration proved less facile than that of TMS because of steric hindrance. For example, in THF at −78 °C, only a trace amount of the TBS migration product was observed after 1 h, whereas warming to 0 °C led to complete migration. Again in Et$_2$O, TBS migration was significantly suppressed even at 0 °C. In anticipation of the ARC tactic, we were pleased to find that addition of HMPA triggers silyl transfer in Et$_2$O at low temperature. Similar effects were observed for the TES congener.

To establish the mode of silyl migration (i.e., intra- or intermolecular), a crossover experiment was carried out, wherein an equimolar mixture of **5** and **7** was treated with KHMDS in THF (Scheme 2). No crossover products were observed. Thus, silyl
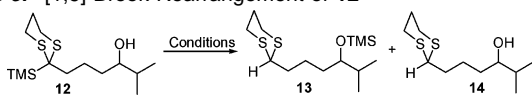
Table 2. [1,5]-Brook Rearrangements of **7**−**9**

| entry	−SiR₃	base 1.1 equiv	solvent	temp °C	time min	result
1	TMS	KHMDS	THF	−78	60	**B** (93%)
2	TMS	*t*-BuOK/*n*-BuLi	THF	−78	60	**B** (93%)
3	TMS	KHMDS	Et₂O	0	60	**B** (92%)
4	TMS	KHMDS	Et₂O	−78	60	**A** (>95%), **B** (<5%)
5	TBS	KHMDS	THF	0	30	**B** (95%)
6	TBS	*t*-BuOK/*n*-BuLi	THF	0	60	**B** (85%)
7	TBS	KHMDS	THF	−78	60	**A** (>95%), **B** (<5%)
8	TBS	KHMDS	Et₂O	0	60	**A** (82%), **B** (11%)
9	TBS	KHMDS	Et₂O/HMPA	−30	60	**B** (90%)
10	TES	KHMDS	THF	0	60	**B** (95%)

Scheme 2
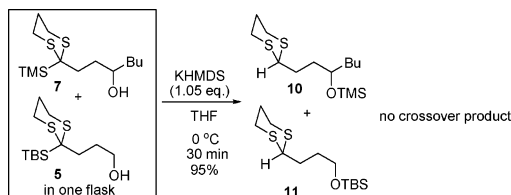
migration occurs intramolecularly, presumably via a 1,6-cyclic, hypervalent pentacoordinate intermediate.

Encouraged by the viability of the [1,5]-Brook rearrangement, we turned to the possibility of a [1,6]-Brook rearrangement, employing **12** as the model system (Table 3). Treatment of **12** with KHMDS in THF at 0 °C furnished silyl ether **13**, albeit with concomitant formation of the desilylated product **14** (entry 1). No reaction occurred in THF when NaHMDS was employed as the base (entry

Table 3. [1,6]-Brook Rearrangement of **12**

entry	base (1.1 equiv)	solvent	temp °C	time	result (**13/14**)
1	KHMDS	THF	0	1 h	47%: 31%
2	NaHMDS	THF	0	1 h	no reaction
3	NaHMDS	DMF	0	5 min	59%: 28%
4	KHMDS	DMF	0	5 min	13%: 76%

2). However use of DMF as solvent did result in complete conversion within 5 min (entries 3 and 4), although a significant amount of desilylated product **14** was also observed. That silyl transfer was occurring, at least in part via an intermolecular pathway, was demonstrated by a crossover experiment involving a mixture of **12** and **15** (1:1); crossover product **16** was produced in 24% yield (Scheme 3). Thus the conditions that effect facile intramolecular [1,5]-migration do not readily lead to intramolecular [1,6]-silyl transfer, presumably because of an unfavorable seven-membered transition state.

Scheme 3
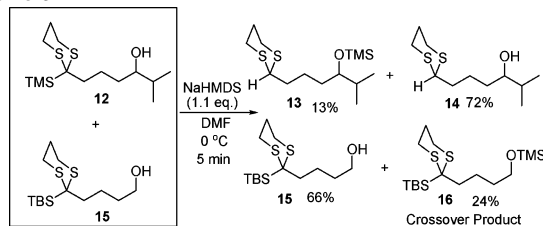
To explore the feasibility of the [1,5]-Brook rearrangement in the ARC tactic, we first carried out a deuterium oxide quench experiment (Scheme 4). Sequential treatment of the lithium alkoxide

Scheme 4
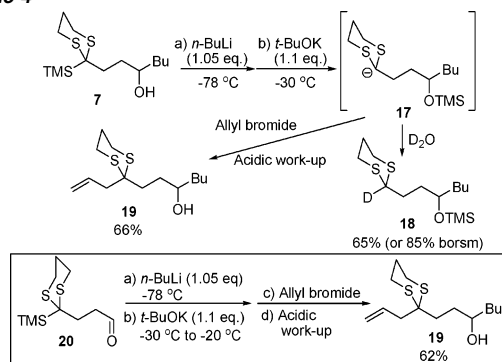
generated from alcohol **7** with *n*-BuLi, followed in turn by addition of *t*-BuOK and then D₂O, furnished the deuterated product **18** in good yield. This result suggests *t*-BuOK transmetalates the lithium alkoxide to trigger the Brook rearrangement and as a consequence generates a reactive dithiane anion. Indeed, when allyl bromide was employed in place of D₂O, adduct **19** was produced in 66% yield. The possibility that these reactions occur via rapid equilibration of the oxy and carbon anion and/or via a pentavalent silyl ate nuclephile cannot be ruled out at this time.

Encouraged by these results, a tricomponent ARC sequence was explored by adding *n*-BuLi to aldehyde **20**, followed in turn by the addition of *t*-BuOK to trigger the silyl migration and allyl bromide to capture the derived anion; tricomponent ARC adduct **19** was produced in 62% yield.

In summary, [1,5]-Brook rearrangements proceed efficiently with sodium and potassium bases to furnish silyl ethers in excellent yield; less effective are lithium bases even at room temperature with HMPA. That the mode of silyl migration is intramolecular was demonstrated by a crossover experiment. Finally, the tricomponent ARC coupling tactic was demonstrated employing a [1,5]-Brook rearrangement. Further exploration of Brook rearrangements in conjunction with the ARC tactic continue in our laboratory.

Supporting Information Available: Spectroscopic and analytical data and selected experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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