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Red-Al® Reduction of 4-Silyloxy Propargylic Alcohols. A Surprising Round Trip for the Silyl Group

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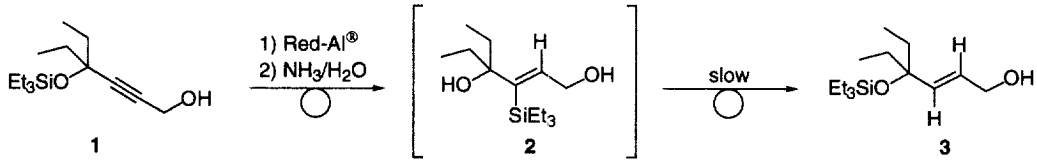
Abstract

The Red-Al® reduction of 4-silyloxy propargylic alcohols to 4-silyloxy allylic alcohols involves two consecutive regio- and stereospecific 1,3 silyl migrations — from oxygen to carbon and then back to the original oxygen.

Keywords: aluminium and compounds; rearrangements; silicon and compounds

A synthesis in our laboratories required the preparation of the monoprotected building block (E)-2-butene-1,4-diol **3**. We wish to report here the unexpected silatropic rearrangements involved in the Red-Al® reduction of its precursor **1.**



When propargylic alcohol **1**[1] was treated with Red-Al® in THF[2] and the reaction was quenched with 30% aqueous ammonia and then stirred for several hours at ambient temperature,[3] the expected (E) allylic alcohol **3** was obtained. However, when the reaction mixture was extracted with ether immediately after the aqueous quench, surprisingly the crystalline (Z) diol **2** (m.p. 76-77°C) was isolated along with **3**.[6] The double bond configuration in **2** was determined by double NOE difference experiments. The diol **2** evidently arises from the hydroalumination of **1**, followed by a new 1,3 silatropic rearrangement which proceeds with retention of the double bond configuration.

Thus, the reduction of **1** with Red-Al® followed by aqueous ammonia quench to give **3** should involve regio- and stereospecific double silyl migration via the (Z) diol intermediate **2**. Indeed, isolated vinylsilane **2** yielded **3** exclusively under the same reaction conditions. Moreover, the rearrangement is catalytic in aluminum reagent as 10 mol% of Red-Al®, when quenched with aqueous ammonia, catalyzed the rearrangement of **2**.[7] Other silyl groups (TMS and TBS) in **1** are transferred with equal ease. We expect this protocol to be useful when selective silyl mono-protection of an 1,4-enediol is desired.[8] Substituted diols of type **2** are alternatively available from aldehydes or ketones and 1-silylated alkynes.[9,10]

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While related 1,4-silyl shifts are known to occur in allylic alcohols,[11-13] the 1,3-silyl shift has been observed only in the C→O direction with potassium or sodium hydride in HMPA,[14,15] and selectivity has not been considered. In retrospect, these rearrangements are formally equilibrium processes, the O→C silyl shift being controlled under aprotic conditions by the high oxophilicity of aluminum. The driving force for the reverse catalytic rearrangement[16,17] of **2** to **3** under protic conditions is the stronger silicon-oxygen bond. While the exact nature of the catalyst for the latter rearrangement is not known, only the combination of an aluminum alkoxide with aqueous ammonia has been found to catalyze this silyl migration.[18]

From the mechanistic perspective it is interesting to note, that the 1,3-C→O silyl shift in **2** takes place exclusively. No products from the alternative 1,4-shift, which would have resulted from the silylation of the less hindered primary allylic alcohol, were detected. A similar preference has been previously noted for carbon to carbon silyl shifts in lithiated 1,2-diphenylethanes.[19] In that study, competition experiments suggested a preference for a 1,3- over a 1,4-C,C-shift, but the result is equivocal as it may reflect essentially the relative rates of lithiation, rather than silyl migration.

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References and Notes

1 Compound **1** was prepared from 3-ethyl-1-pentyn-3-ol by silylation (TESCl, DMAP, DMF), followed by hydroxymethylation (i. BuLi, THF; ii. paraformaldehyde). Selected analytical data: ^{1}H-NMR ($CDCl_3$, 400 MHz) 4.30 (d, J=4.3 Hz, 2H), 1.64 (q, J=7.7 Hz, 4H), 1.47 (br. s, 1H), 0.99-.92 (m, 15H), 0.67 (q, J=7.7 Hz, 6H); ^{13}C-NMR ($CDCl_3$, 100 MHz) 89.7, 82.5, 73.0, 51.3, 34.6, 8.6, 7.1, 6.2.

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3 Between 5-10% of allenic alcohol was also formed in the reduction of **1** by silyloxide elimination.[4,5] However, this byproduct was not formed in the rearrangement of **2** (see below).

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6 A 3M Red-Al® solution in toluene (3.7 mL, 11 mmol) was added dropwise to a solution of **1** (2.56 g, 10 mmol) in THF (10 mL) at -70°C. Temperature control below -70°C was required to minimize silyloxide elimination. After stirring for 2 h at 0°C the mixture was quenched by addition of 30% aqueous ammonia (4.5 mL). Then the mixture was immediately diluted with ether, the solids were removed by filtration and the filtrates were washed with 2N HCl, then with satd aq. $NaHCO_3$ and brine. After solvent evaporation, **2** (1.50 g, 58%) crystallized out from hexane. Selected analytical data for **2**: ^{1}H-NMR ($CDCl_3$, 400 MHz) 6.02 (t, J=6.0 Hz, 1H, NOE-1), 4.08 (d, J=6.0 Hz, 2H, NOE-2), 3.6 (br. s, 1H), 2.0 (br. s, 1H), 1.37 (q, J=6.8 Hz, 4H, NOE-1), 0.74 (t, 9H), 0.61 (t, 6H), 0.53 (q, J=7.7 Hz, 6H, NOE-2); ^{13}C-NMR (DMSO-d_6, 100 MHz) 142.7, 141.3, 78.1, 60.1, 32.8, 8.0, 7.8, 5.6.

7 In a typical experiment, pure (Z) diol **2** (2.58 g, 10 mmol) was dissolved in THF (10 mL) and the solution was cooled to 0°C. Red-Al® solution 3M in toluene (330 µL, 10 mol%) was added, followed by a 30% aq ammonia solution (400 µL), and the mixture was stirred vigorously for 5 h at 40°C. The solution was then decanted from the solids and the solvents were evaporated in vacuum to yield 2.56 g (99%) of pure (E) allylic alcohol **3**. ^{1}H-NMR ($CDCl_3$, 300 MHz) 5.76 (dt, J=15.6/5.4 Hz, 1H), 5.64 (d, J=15.6 Hz, 1H), 4.16 (d, J=4.8 Hz, 2H), 1.55 (dq, J=2.7/7.4 Hz, 4H), 1.38 (br. s, 1H), 0.95 (t, 9H),), 0.82 (t, 6H), 0.58 (q, J=7.8 Hz, 6H); ^{13}C-NMR ($CDCl_3$, 100 MHz) 137.3, 127.5, 77.8, 63.6, 32.5, 8.3, 7.1, 6.9.

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18 $Al(O^iPr)_3$ in 30% aq ammonia/THF (1:1) also promoted the rearrangement of **2** to **3**, while either of these reagents alone was ineffective.

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