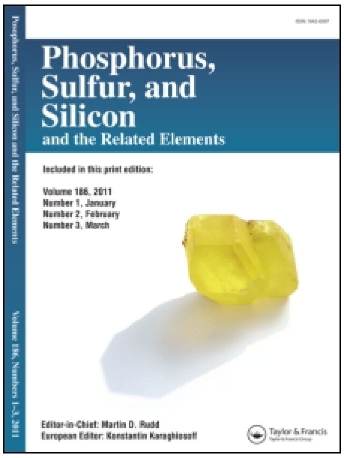

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LITHIATIONS OF 1-ALKYL-1H-1,2,4-TRIAZOL-5-YL SILANES: NOVEL ANION-MEDIATED CARBON-TO-CARBON SILICON MIGRATIONS

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Communication

LITHIATIONS OF 1-ALKYL-1H-1,2,4-TRIAZOL-5-YL SILANES: NOVEL ANION-MEDIATED CARBON-TO-CARBON SILICON MIGRATIONS

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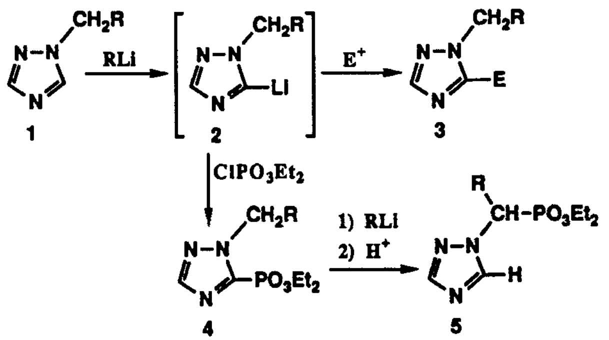
The lithiation chemistry of several 1-alkyl-1H-1,2,4-triazol-5-yl silanes has been investigated. Lithiation occurs exclusively on the 1-alkyl group, α to nitrogen, and on warming, an unusual anion-mediated carbon-to-carbon silicon migration occurs giving rise to novel 1H-1,2,4-triazol-1-yl alkyl silanes.

Key words: Lithiation, 1,2,4-triazol-5-yl silanes, 1-alkyl-1,2,4-triazole silanes, silicon migrations, anion mediated.

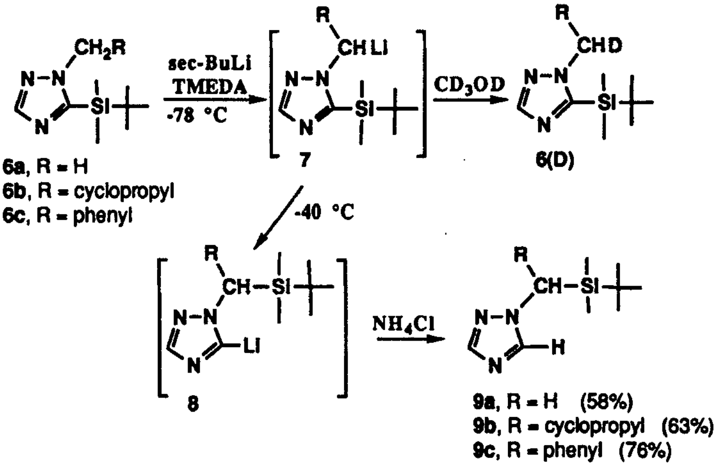
Electrophilic substitution of 1-alkyl-1H-1,2,4-triazoles **1** is known to be a general route to 5-substituted-1H-1,2,4-triazoles **3**.[1–4] We previously reported the first synthesis of 5-phosphono-1H-1,2,4-triazoles[4] **4** *via* this methodology. More recently, we reported[5] that attempts to lithiate the 3-position of **4** resulted instead in lithiation of the α-methylene unit of the 1-alkyl group and subsequent migration of the phosphonate group. This provided a convenient route to α-substituted 1-phosphonomethyltriazoles **5**, which are not easily prepared by the conventional "Mannich-type" approach (Scheme I).

We now report that certain 5-silyl-1H-1,2,4-triazoles **6** react similarly when treated with alkyl lithium reagents. Lithiation occurs exclusively on the α-methylene unit of the 1-alkyl substituent with no evidence of any lithiation at C-3 of the triazole ring. The lithiated intermediates **7** were reasonably stable at −78°C based on results of deuterium trapping experiments. When the reaction mixtures were quenched with CD_3OD at −78°C the deuteriated products **6(D)** were isolated. Deuterium incorporation was >90% based on integration of the α-methylene unit in the proton NMR spectra of **6(D)**. On the other hand, warming above −50°C led to substantial quantities of silyl migration products **9**. When the reactions were allowed to warm to −40°C before quenching, **9** became the major product with **6** as the only other component present by proton NMR (Scheme II).

Chromatographic separation of isomeric **9** from **6** was problematic. Fortunately, **9** is much more stable than **6** to protodesilylation with aqueous acid. Thus, treatment of the product mixture with aqueous HCl in acetone rapidly converted all remaining **6** to the more water soluble **1**, which could be easily removed by aqueous extraction. Chromatographic purification easily removed the silanol/siloxane side-products producing pure **9** in isolated yields of 58–76%.



SCHEME I



SCHEME II

This simple one step metalation procedure provides a convenient entry for the preparation of novel α-substituted 1-silylmethyl triazoles, **9**, which may exhibit unusual fungicidal activity but are not readily available by conventional synthetic methods.[6] While other examples of anion-mediated carbon to carbon silicon migrations have been reported,[7] to the best of our knowledge the conversion of **6** to **9** represents the first example of an anion-mediated 1,3 carbon-to-carbon silyl migration. Efforts are underway to determine the synthetic scope and general utility of this interesting transformation.

Representative Procedure—Preparation/Characterization of **9c**: A solution of **6c**[4] (3.0 g, 11 mmol) in anhydrous THF/TMEDA (200 mL/1.7 mL) was cooled to −78°C under N_2 and treated dropwise with a solution of *sec*-butyllithium (8.8 mL of a 1.5 M soln. in cyclohexane, 13 mmol) over 15 minutes. The resulting red-orange solution was stirred at −78°C for 1 hr, then warmed to −50°C and stirred for 3 hrs at −50 to −40°C. The reaction was quenched with NH_4Cl (several grams of solid), and warmed to 25°C. The mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissloved in ether (100 mL), washed with water (2 × 100 mL), brine (50 mL), and dried over $MgSO_4$. Filtration and concentration *in vacuo* gave 3.0 g of a yellow oil, which was a 4:1 mixture of **9c** and **6c**, respectively. This mixture was dissolved in 100 mL of acetone and treated with 1 mL of 10% HCl. After 10 minutes, the reaction was quenched with excess Na_2CO_3. Filtration and concentration of the filtrate *in vacuo* gave 2.9 g of a 4:1 mixture of **9c** and 1-benzyl-1H-1,2,4-triazole. This mixture was dissolved in cyclohexane (50 mL), washed with water (6 × 50 mL), brine (50 mL), and dried over $MgSO_4$. Filtration and concentration *in vacuo* gave 2.7 g of **9c** along with some silanol/siloxane. Chromatotron purification (EtOAc) gave 2.3 g (76%) of pure **9c** as a light yellow oil, which partially solidifies with time (m.p. 30–35°C). ^{1}H-NMR ($CDCl_3$, 360 MHz): δ 8.1 (1H, s), 7.95 (1H, s), 7.15–7.35 (5H, m), 5.1 (1H, s), 0.8 (9H, s), 0.2 (3H, s), 0.05 (3H, s); ^{13}C-NMR ($CDCl_3$, decoupled): δ 150.8, 143.1, 138.6, 128.1, 127.1, 126.6, 55.5, 26.7, 17.0, −6.0, −6.9; Anal. calcd. for $C_{15}H_{23}N_3Si_1$: C, 65.88; H, 8.48; N, 15.37; found: C, 65.60; H, 8.52; N, 15.21.

Characterization of **9a**: Compound **9a** was isolated in 58% yield as a colorless oil. ^{1}H-NMR ($CDCl_3$, 60 MHz): δ 7.9 (1H, s), 7.8 (1H, s), 3.7 (2H, s), 0.9 (9H, s), 0.1 (6H, s); Anal. calcd. for $C_9H_{19}N_3Si_1$: C, 54.77; H, 9.70; N, 21.29; found: C, 54.86; H, 9.75; N, 21.23.

Characterization of **9b**: Compound **9b** was isolated in 63% yield as a pale yellow oil. ^{1}H-NMR ($CDCl_3$, 60 MHz): δ 7.9 (1H, s), 7.8 (1H, s), 3.1 (1H, d, J = 10 Hz), 0.9 (9H, s), 0.3–1.7 (5H, unresolved m), 0.25 (3H, s), 0.1 (3H, s); ^{13}C-NMR ($CDCl_3$, decoupled): δ 151.0, 142.0, 56.1 26.8, 16.7, 13.3, 7.7, 4.8, −6.5, −7.4; Anal. calcd. for $C_{12}H_{23}N_3Si_1$: C, 60.71; H, 9.76; N, 17.70; found: C, 60.64; H, 9.80; N, 17.64.

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7. For example see: P. W. Rabideau, R. K. Dhar, D. K. Clawson and Z. Zhan, *Tetrahedron Lett.*, **32**, 3969–3972 (1991) and references cited therein.