

Synthesis of 1,1,4,4-Tetrabromo-2-butenes and Related Compounds via Desilylation–Bromination of Silylated 1,3-Butadiene Derivatives

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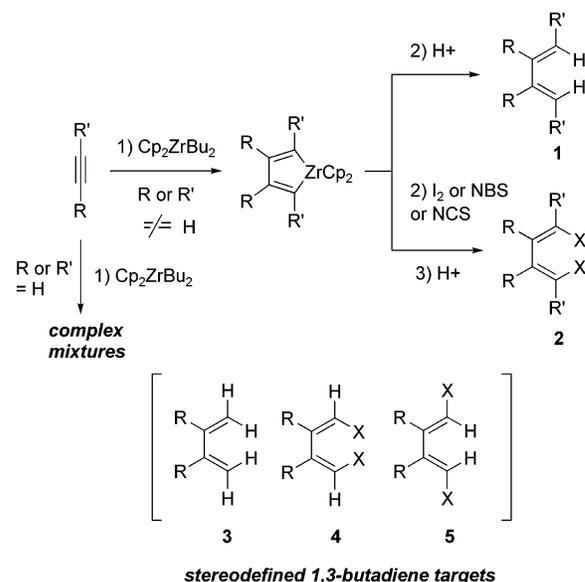
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Abstract: The combination of zirconocene-mediated coupling of silylated alkynes with a protonation–desilylation or bromination–desilylation process afforded otherwise unavailable butadiene derivatives. When (*E,E*)-2,3-dialkyl-1,4-bis(trimethylsilyl)-1,3-butadienes were treated with 3 equiv of Br₂ in CH₂Cl₂, (*E*)-2,3-dialkyl-1,1,4,4-tetrabromo-2-butenes were obtained in excellent yields with perfect stereoselectivity.

Stereodefined substituted 1,3-butadienes and 1,4-dihalo-1,3-butadienes are synthetically important intermediates.^{1–4} (**1–5** in Scheme 1). The zirconocene-mediated coupling of alkynes provides a convenient method for the preparation of the all-*trans* 1,2,3,4-tetrasubstituted 1,3-butadienes (**1**) and 1,4-dihalo-1,3-dienes (**2**, X = I, Br, or Cl).^{5–7} However, this zirconocene-mediated coupling reac-

SCHEME 1



tion cannot be applied for the preparation of important 1,3-butadiene derivatives **3**, **4**, or **5** (Scheme 1), because treatment of halogenated alkynes or terminal alkynes with Cp₂ZrBu₂ (Negishi reagent) generally affords complex mixtures.

It is known that terminally silylated alkynes undergo regio- and stereoselective coupling on low valent zirconocene species to afford silylated 1,3-butadienes (**1**, R' = SiMe₃).⁵ On the other hand, hydrolysis–desilylation of vinylsilanes using CF₃CO₂H or NaOMe and halogenation–desilylation of vinylsilanes using halogenation reagents are well-documented methods for alkenes and vinyl halides, respectively.⁸ Therefore, we combined these two synthetically useful protocols, trying to prepare hitherto unknown 1,3-butadiene derivatives **3**, **4**, or **5**.

As listed in Table 1, protonation–desilylation of mono- or disilylated 1,3-butadienes using CF₃CO₂H afforded their corresponding products in excellent yields. Both tri- or disubstituted 1,3-butadienes could be readily prepared.⁹ For the synthesis of **3a** and **3b**,^{3d,7} direct quench of the reaction mixtures of zirconacyclopentadienes using CF₃CO₂H gave **3a** and **3b** in similar yields.

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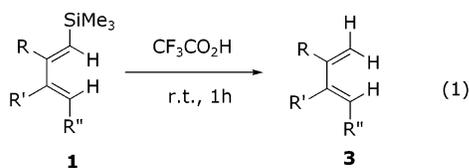
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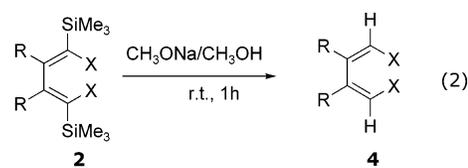
TABLE 1. Formation of 2,3-Disubstituted or 1,2,3-Trisubstituted 1,3-Butadienes via Protonation–Desilylation of Silylated 1,3-Butadienes^a

run	silylated butadiene 1	product 3	yield of 3 / ^b %
1			98 (75)
2			91 (82)
3			95 (85)
4			94 (82)
5			92 (77)

^a Reaction conditions were as shown in eq 1. ^b GC yields. Isolated yields are given in parentheses.

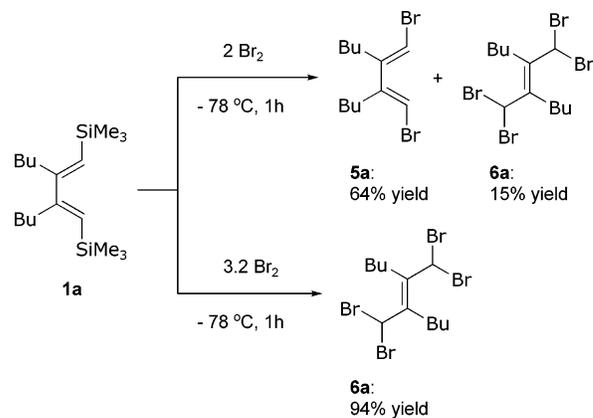
When 1,4-bis(trimethylsilyl)-1,4-dihalo-1,3-dienes **2** were treated with $\text{CF}_3\text{CO}_2\text{H}$, the desired products, (*Z, Z*)-1,4-dihalo-1,3-dienes **4**, were formed in very low yields, along with several unknown compounds. Fortunately, we found the desired products **4** could be obtained in high isolated yields when compounds **2** were treated with NaOMe (Table 2).

An interesting and potentially very useful product, (*E*)-2,3-dialkyl-1,1,4,4-tetrabromo-2-butenes **6**, was obtained when we attempted to prepare the (*E, E*)-2,3-dialkyl-1,4-bis(trimethylsilyl)-1,4-dibromo-1,3-butadiene **5** by halogenation–desilylation of silylated 1,3-butadienes **1**. As demonstrated in Scheme 2, when **1a** was treated with 2 equiv of Br_2 in CH_2Cl_2 , a mixture of two products was obtained. One was (*E, E*)-1,4-dibromo-1,3-butadiene **5**, which was formed as an isomer of **4a** in 64% isolated yield. The other was an unexpected product, (*E*)-2,3-dibutyl-1,1,4,4-tetrabromo-2-butene **6a**, which was obtained in 15% isolated yield. Fortunately, (*E*)-2,3-dibutyl-1,1,4,4-tetrabromo-2-butene **6a** could be prepared in almost quantitative yield when **1a** was treated with 3 equiv of Br_2 in CH_2Cl_2 at -78°C for 1 h. The formation of **5a** was not observed under the reaction conditions. This indicates that **5a** was formed first and that **5a** was

TABLE 2. Formation of 1,4-Dihalo-1,3-butadiene Derivatives via Desilylation of 1,4-Dihalo-1,4-disilyl-1,3-butadienes^a

run	silylated butadiene 2	product 4	yield of 4 / ^b %
1			88
2			74
3			84

^a Reaction conditions were as shown in eq 2. ^b Isolated yields.

SCHEME 2

reactive toward bromine. 1,4-Addition of bromine to **5a** proceeded.¹⁰ The structure of **6a** has been determined by single-crystal X-ray analysis.

Such 1,1,4,4-tetrabromo-2-butenes are allylic halides, which are versatile building blocks in synthetic chemistry. Furthermore, these 1,1,4,4-tetrabromo-2-butenes have multiple reactive sites. Therefore, rich and interesting reaction chemistry can be anticipated from these 1,1,4,4-tetrabromo-2-butene derivatives. Representative results are given in Table 3.

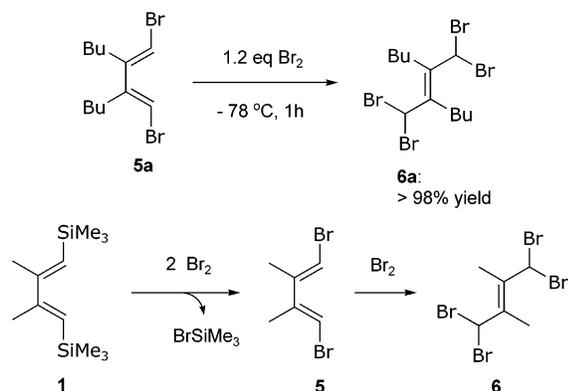
To obtain evidence for understanding reaction mechanisms, we treated the isolated pure **5a** with 1 equiv of Br_2 in solution CH_2Cl_2 . The starting compound **5a** was quantitatively transformed to (*E*)-2,3-dibutyl-1,1,4,4-tet-

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TABLE 3. Formation of 1,1,4,4-Tetrabromo-2-butene Derivatives via Bromination–Desilylation of Silylated 1,3-Butadienes

run	silylated butadiene 1	product 6	yield of 6 / ^a ^b
1			98
2			84
3			98
4			83

^a Reaction conditions were as shown in eq 3. ^b Isolated yields.

SCHEME 3

1,1,4,4-tetrabromo-2-butene **6a** (Scheme 3). This result, in conjunction with the results shown in Scheme 2, indicates that the (*E,E*)-1,4-dibromo-1,3-butadiene **5** is the key intermediate in the bromination-desilylation reaction process from **1** to **6**.

Experimental Section

Typical Procedure for Preparation of 3. To a solution of 2 mmol of 1,4-disilyl-1,3-butadienes **1** in 12 mL of CH₂Cl₂ was added 4 mmol of TFA dropwise at room temperature (or 2 mmol

TFA was added if only one TMS group was in the molecule). The reaction mixture was stirred for 1 h at the same temperature. The resulting mixture was quenched with saturated NaHCO₃. Products were extracted with ether, washed with H₂O and brine, dried with MgSO₄, and evaporated. Separation by column chromatography afforded butadienes.

2,3-Dibutyl-but-1,3-dienes (3a).^{9a} Colorless liquid. GC yield 98%, isolated yield 75%; ¹H NMR (CDCl₃) δ 0.89 (t, *J* = 7.2 Hz, 6H), 1.25–1.46 (m, 8H), 2.22 (t, *J* = 6.6 Hz, 4H), 4.90 (bs, 2H), 5.04 (bs, 2H); ¹³C NMR (CDCl₃) δ 14.0 (2C), 22.6 (2C), 30.9 (2C), 34.0 (2C), 111.2 (2C), 148.0 (2C); HRMS calcd for C₁₂H₂₂ 166.1722, found 166.1720.

Typical Procedure for Preparation of (*Z,Z*)-1,4-Dihalo-1,3-butadiene Derivatives 4. A solution of **2** (1.0 mmol in 4.0 mL of CH₂Cl₂) and freshly prepared CH₃ONa in CH₃OH (5.0 mL, 2.0 M) was stirred for 1 h at room temperature. The reaction mixture was added to 10.0 mL saturated NaHCO₃ and extracted with ether (3 × 10.0 mL). The extract was washed with water, NH₄Cl, and saturated NaCl and dried over MgSO₄. The solvent was evaporated in vacuo to give crude products. Chromatography using petroleum ether as the eluent provided the corresponding pure product **4**.

2,3-Dibutyl-1,4-dibromo-1,3-(*Z,Z*)-butadiene (4a). Colorless liquid, isolated yield 84% (270 mg); ¹H NMR (CDCl₃) δ 0.91 (t, *J* = 7.2 Hz, 6H), 1.29–1.47 (m, 8H), 2.19 (t, *J* = 6.8 Hz, 4H), 6.08 (s, 2H); ¹³C NMR (CDCl₃) δ 13.8, 22.4, 29.2, 35.3, 102.8, 144.6; HRMS calcd for C₁₂H₂₀Br₂ 321.9932, found 321.9932.

Typical Procedure for the Formation of 1,1,4,4-Tetrabromo-2-butenes via Bromination–Desilylation. To a solution of 1,4-bis(trimethylsilyl)-2-butene **1** (1.0 mmol) in 4.0 mL of CH₂Cl₂ was added 6.4 mL of a 0.5 M solution of Br₂ in CH₂Cl₂ at –78 °C. The mixture was stirred for 1 h and then stirred in an ice–salt bath for 1 h. Next, 10 mL of saturated Na₂S₂O₃ was added, and this reaction mixture was extracted with ether (3 × 10 mL), followed by drying. Evaporation in vacuo afforded crude product, which was purified by recrystallization or by column chromatography. When the amount of added solution of Br₂ was 4.2 mL (0.5 M, 2.1 mmol), 64% isolated yield of (*E,E*)-1,4-dihalo-1,3-butene **5a** and 15% isolated yield of 1,1,4,4-tetrabromo-2-butenes **6a** were obtained.

2,3-Dibutyl-1,4-dibromo-1,3-(*E,E*)-butadiene (5a). Colorless liquid, 64% isolated yield (206 mg); ¹H NMR (CDCl₃) δ 0.91 (t, *J* = 6.9 Hz, 6H), 1.30–1.39 (m, 8H), 2.33 (t, *J* = 7.5 Hz, 4H), 6.18 (s, 2H); ¹³C NMR (CDCl₃) δ 13.9, 22.4, 29.4, 30.6, 105.2, 145.8; HRMS calcd for C₁₂H₂₀Br₂ 321.9932, found 321.9933.

2,3-Dibutyl-1,1,4,4-tetrabromo-2(*E*)-butene (6a). Colorless crystal, isolated yield 94% for 3.2 equiv of Br₂; ¹H NMR (CDCl₃) δ 0.85 (t, *J* = 7.2 Hz, 6H), 1.27–1.57 (m, 8H), 2.26 (t, *J* = 8.1 Hz, 4H), 6.43 (s, 2H); ¹³C NMR (CDCl₃) δ 13.8, 23.3, 29.6, 32.6, 42.4, 135.3; mp 97–98 °C. Anal. Calcd for C₁₂H₂₀Br₄: C, 30.01; H, 4.20; Br, 65.79. Found: C, 29.88; H, 4.17; Br, 65.77.

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Supporting Information Available: Experimental procedures, characterization data, and NMR spectra of all new compounds, including crystallographic data for **6a**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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