JOC*Note*

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

Zhenfeng Xi,*,† Xiaozhong Liu,† Jianming Lu,† Fengyu Bao,†,‡ Hongtao Fan,† Zhiping Li,†,‡ and Tamotsu Takahashi*,‡

Peking University-Hokkaido University Joint Lab, College of Chemistry, Peking University, Beijing 100871, China, and Catalysis Research Center and Graduate School of Pharmaceutical Sciences, Hokkaido University, and SORST, Japan Science and Technology Corporation (JST), Sapporo 001-0021, Japan

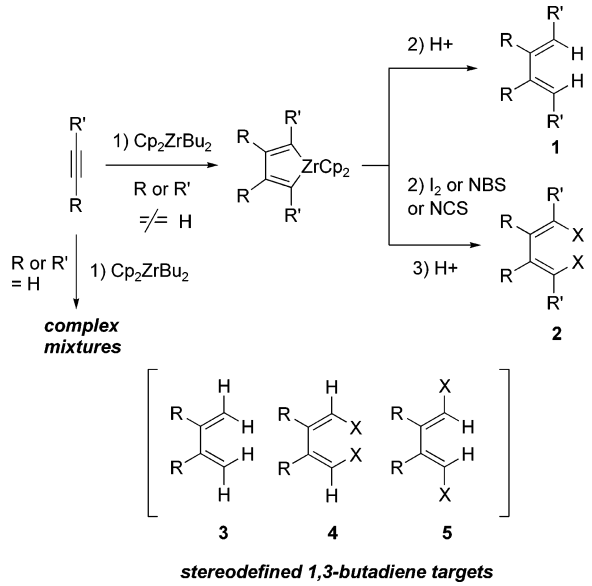
tamotsu@cat.hokudai.ac.jp

Received June 22, 2004

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 Br_2 in CH_2Cl_2, (*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 reaction 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 alkyes with Cp_2ZrBu_2 (Negishi reagent) generally affords complex mixtures.

SCHEME 1



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′ = $SiMe_3$).[5] On the other hand, hydrolysis−desilylation of vinylsilanes using CF_3CO_2H 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 CF_3CO_2H 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 CF_3CO_2H gave **3a** and **3b** in similar yields.

* To whom correspondence should be addressed. Phone: +81-11-706-9149. Fax: +81-11-706-9150.
† Peking University.
‡ Hokkaido University.

(1) (a) Fringuelli, F.; Taticchi, A. *Dienes in the Diels−Alder Reaction*; Wiley: New York, 1990. (b) Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, U.K., 1991; Vol. 5, p 315. (c) Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167. (d) Kumar, A. *Chem. Rev.* **2001**, *101*, 1.

(2) For reviews, see: (a) Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (c) Suzuki, A. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998; p 49. (d) Miyaura, N. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: London, U.K., 1998; Vol. 6, p 187.

(3) (a) Baird, M. S.; Jefferies, I. *Tetrahedron Lett.* **1986**, *27*, 2493. (b) Gundersen, G.; Nielsen, C. J.; Thomassen, H. G.; Becher, G. *J. Mol. Struct.* **1988**, *176*, 33. (c) Dedek, V.; Chvatal, Z. *J. Fluorine Chem.* **1986**, *31*, 363. (d) Engman, L.; Bystrom, S. E. *J. Org. Chem.* **1985**, *50*, 3170. (e) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001.

(4) (a) Chen, J.; Song, Q.; Wang, C.; Xi, Z. *J. Am. Chem. Soc.* **2002**, *124*, 6238. (b) Chen, J.; Song, Q.; Li, P.; Guan, H.; Jin, X.; Xi, Z. *Org. Lett.* **2002**, *4*, 2269. (c) Song, Q.; Chen, J.; Jin, X.; Xi, Z. *J. Am. Chem. Soc.* **2001**, *123*, 10419. (d) Xi, Z.; Song, Q.; Chen, J.; Guan, H.; Li, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1913. (e) Xi, Z.; Song, Q. *J. Org. Chem.* **2000**, *65*, 9157.

(5) (a) Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829. (b) Takahashi, T.; Kageyama, M.; Denisov, V.; Hara, R.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 687. (c) Xi, Z.; Hara, R.; Takahashi, T. *J. Org. Chem.* **1995**, *60*, 4444. (d) Hara, R.; Xi, Z.; Kotora, M.; Xi, C.; Takahashi, T. *Chem. Lett.* **1996**, 1003. (e) Takahashi, T.; Xi, C.; Xi, Z.; Kageyama, M.; Fischer, R.; Nakajima, K.; Negishi, E. *J. Org. Chem.* **1998**, *63*, 6802.

(6) (a) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1989**, *111*, 2870. (b) Takahashi, T.; Kotora, M.; Kasai, K.; Suzuki, N. *Organometallics* **1994**, *13*, 4183. (c) Xi, C.; Huo, S.; Afifi, T. H.; Hara, R.; Takahashi, T. *Tetrahedron Lett.* **1997**, *38*, 4099. (d) Yamaguchi, S.; Jin, R.; Tamao, K.; Sato, F. *J. Org. Chem.* **1998**, *63*, 10060. (e) Liu, Y.; Xi, C.; Hara, R.; Nakajima, K.; Takahashi, T. *J. Org. Chem.* **2000**, *65*, 6951. See also (f) Fukuhara, K.; Takayama, Y.; Sato F. *J. Am. Chem. Soc.* **2003**, *125*, 6884. (g) Deals, C.; Urabe, H.; Sato F. *Chem. Commun.* **2002**, 820.

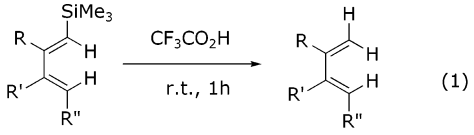
(7) Takahashi, T.; Xi, Z.; Fischer, R.; Huo, S.; Xi, C.; Nakajima, K. *J. Am. Chem. Soc.* **1997**, *119*, 4561.

(8) (a) Fleming, I.; Dunogues, J. Smithers, R. *Org. React.* **1989**, *37*, 57−575. (b) Asaoka, M.; Shima, K.; Takei, H. *J. Chem. Soc., Chem. Commun.* **1988**, 430. (c) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371. (d) Hudrlik, P. F.; Kassim A. M.; Agwaramgbo, E. L. O.; Doonquah, K. A.; Roberts, R. R.; Hudrlik A. M. *Organometallics* **1993**, *12*, 2367. (e) Ahmar, M.; Duyck, C.; Fleming, I. *Pure Appl. Chem.* **1994**, *66*, 2049.

(9) (a) Araki, S.; Ohmura, M.; Butsugan, Y. *Synthesis* **1985**, 963. (b) Luo, F.-T.; Fwu, S.-L.; Juang, W.-S. *Tetrahedron Lett.* **1992**, *33*, 6839.

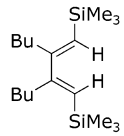
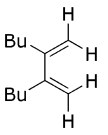
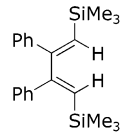
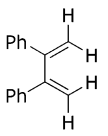
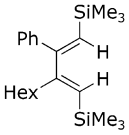
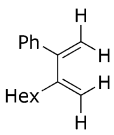
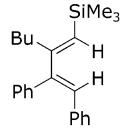
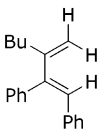
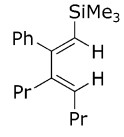
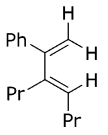
10.1021/jo048940f CCC: $27.50
Published on Web 11/04/2004

TABLE 1. Formation of 2,3-Disubstituted or 1,2,3-Trisubstituted 1,3-Butadienes via Protonation−Desilylation of Silylated 1,3-Butadienes[a]



(1)

1 **3**

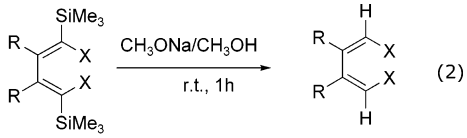
run	silylated butadiene **1**		product **3**		yield of **3**/%[b]
1		**1a**		**3a**	98 (75)
2		**1b**		**3b**	91 (82)
3		**1c**		**3c**	95 (85)
4		**1d**		**3d**	94 (82)
5		**1e**		**3e**	92 (77)

[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 CF_3CO_2H, 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).

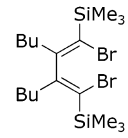
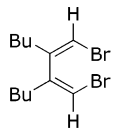
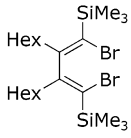
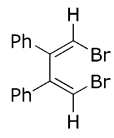
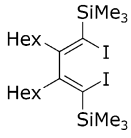
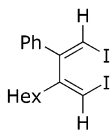
An interesting and potentially very useful product, (*E*)-2,3-dialkyl-1,1,4,4-tetrabromo-2-butenes **6**, was obtained when we attempted to prepare the (*E*,*E*)-2,3-dialkyl-1,4-bis(trimethylsilyl)-1,4-dibromo-1,3-butadiene **5** by halogenation−desilylation of silylated 1,3-butadienes **1**. As demonstrated 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]



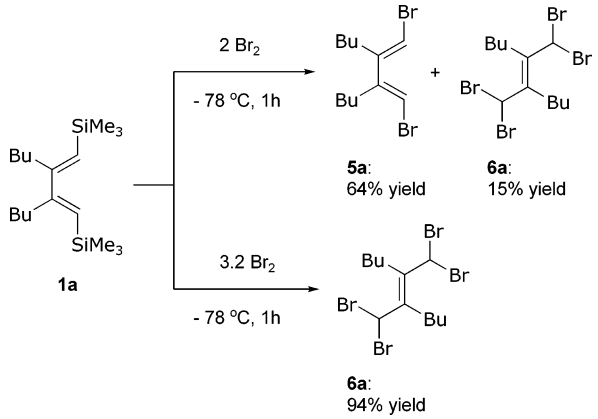
(2)

2 **4**

run	silylated butadiene **2**		product **4**		yield of **4**/%[b]
1		**2a**		**4a**	88
2		**2b**		**4b**	74
3		**2c**		**4c**	84

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

SCHEME 2



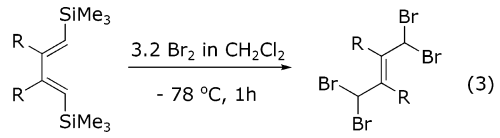
reactive toward bromine. 1,4-Addition of bromine to **5a** proceeded.[10] The structure of **6a** has been determined by single-crystal X-ray analysis.

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-

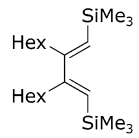
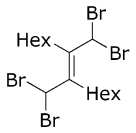
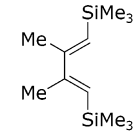
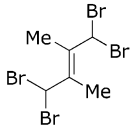
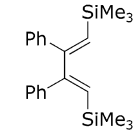
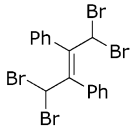
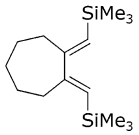
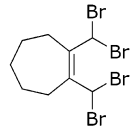
(10) Horasan, N.; Kara, Y.; Azizoglu, A.; Balci, M. *Tetrahedron* **2003**, *59*, 3691.

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



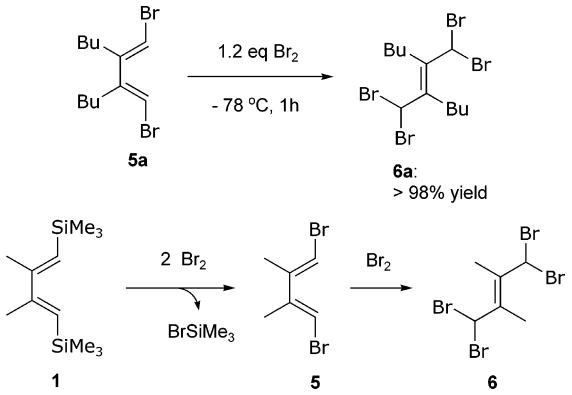
(3)

1 **6**

run	silylated butadiene **1**	product **6**	yield of **6**/%[b]
1			
	1f	**6b**	98
2			
	1g	**6c**	84
3			
	1b	**6d**	98
4			
	1h	**6e**	83

[a] Reaction conditionswere as shown in eq 3. [b] Isolated yields.

SCHEME 3



rabromo-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 CH_2Cl_2 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 $NaHCO_3$. Products were extracted with ether, washed with H_2O and brine, dried with $MgSO_4$, and evaporated. Separation by column chromatography afforded butadienes.

2,3-Dibutyl-buta-1,3-dienes (3a).[9a] Colorless liquid. GC yield 98%, isolated yield 75%; ^{1}H NMR ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) δ 14.0 (2C), 22.6 (2C), 30.9 (2C), 34.0 (2C), 111.2 (2C), 148.0 (2C); HRMS calcd for $C_{12}H_{22}$ 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 CH_2Cl_2) and freshly prepared CH_3ONa in CH_3OH (5.0 mL, 2.0 M) was stirred for 1 h at room temperature. The reaction mixture was added to 10.0 mL saturated $NaHCO_3$ and extracted with ether (3 × 10.0 mL). The extract was washed with water, NH_4Cl, and saturated NaCl and dried over $MgSO_4$. 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); ^{1}H NMR ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.4, 29.2, 35.3, 102.8, 144.6; HRMS calcd for $C_{12}H_{20}Br_2$ 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 CH_2Cl_2 was added 6.4 mL of a 0.5 M solution of Br_2 in CH_2Cl_2 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 $Na_2S_2O_3$ 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 colum chromatography. When the amount of added solution of Br_2 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); ^{1}H NMR ($CDCl_3$) 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); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.4, 29.4, 30.6, 105.2, 145.8; HRMS calcd for $C_{12}H_{20}Br_2$ 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 Br_2; ^{1}H NMR ($CDCl_3$) 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); ^{13}C NMR (CDC l$_3$) δ 13.8, 23.3, 29.6, 32.6, 42.4, 135.3; mp 97−98 °C. Anal. Calcd for $C_{12}H_{20}$ Br_4: C, 30.01; H, 4.20; Br, 65.79. Found: C, 29.88; H, 4.17; Br, 65.77.

Acknowledgment. This work was partially supported by National Science Fund for Distinguished Young Scholars (29825105), the Major State Basic Research Development Program (G2000077502-D), and the National Natural Science Foundation of China (29702001, 20172003 and 20232010). Cheung Kong Scholars Program and Qiu Shi Science & Technologies Foundation are gratefully acknowledged.

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.

JO048940F