Synthetic Methods

1-Alkynyl(aryl)(tetrafluoroborato)-λ³-bromanes as Highly Efficient Michael Acceptors: Uncatalyzed Conjugate Addition of 1-Alkynyl(trialkyl)stannanes To Yield Symmetrical and Unsymmetrical 1,3-Butadiynes**

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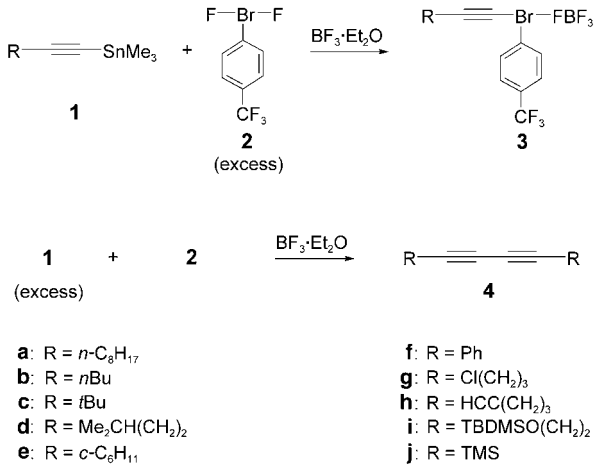
In contrast to alkynylboron, -aluminium, and -nickel reagents, alkynylcopper species do not efficiently transfer the alkynyl group to electron-deficient olefins and alkynes in a conjugate fashion owing to the strength of the alkynyl–copper(I) bond.[1,2] Michael addition of alkynylstannanes appears to be a very difficult process, probably owing to the low polarity of a C–Sn bond, and there are no well-established precedents for the direct reaction. Specially designed alkynylstannanes with enhanced reactivity such as ynaminostannanes ($R_2NCCSnMe_3$) undergo conjugated addition toward acetylenedicarboxylates in MeCN under heating at reflux.[3] Palladium(0)-catalyzed Michael-type addition of alkynylstannanes to conjugated ynones and alkynoates by using an iminophosphine ligand was recently reported.[4] Herein we report bromine(III)-mediated homocoupling of alkynylstannanes to yield symmetrical 1,3-butadiynes that involves uncatalyzed Michael addition reactions of alkynylstannanes to highly electron-deficient alkynyl-λ³-bromanes.

Despite extensive studies on the chemistry of 1-alkynyl(phenyl)-λ³-iodanes,[5] little is known about the closely related group 17 1-alkynyl(aryl)-λ³-bromanes **3**, mostly because of the considerable difficulty of their synthesis. Recently, we reported the synthesis and characterization of 1-alkynyl(aryl)(tetrafluoroborato)-λ³-bromanes **3** through ligand exchange of a difluoro-λ³-bromane with alkynylstannanes.[6] Thus, exposure of 1-(trimethylstannyl)-1-alkyne **1** to an excess of *para*-trifluoromethylphenyl(difluoro)-λ³-bromane (**2**; 1.5 equiv; prepared from *para*-trifluoromethylphenyl(trimethyl)silane by ligand exchange with bromine trifluoride at −78 to −25 °C in dichloromethane) in the presence of $BF_3{\cdot}Et_2O$ at −78 °C in dichloromethane afforded 1-alkynyl(aryl)-λ³-bromane **3** in high yields (Scheme 1). Use of excess amounts of the 1-alkynylstannanes **1** (>2 equiv) relative to difluoro(aryl)-λ³-bromane **2** dramatically changed the reaction course and afforded the homocoupling products 1,3-butadiynes **4** in good yields.



Scheme 1. TBDMS = *tert*-butyldimethylsilyl, TMS = trimethylsilyl.

Rigid and sterically undemanding diacetylene moieties are frequently embodied in many natural products and find increasing application as key structural elements in synthetic receptors for molecular recognition.[7] Reaction of difluoro-λ³-bromane **2** with 2.2 equivalents of 1-decynylstannane **1a** in the presence of $BF_3{\cdot}Et_2O$ (1.2 equiv) from −78 °C to room

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temperature in dichloromethane under argon resulted in oxidative homocoupling with the formation of icosa-9,11-diyne (**4a**) in 69% yield (Table 1, Entry 3). The use of 2 equivalents of $BF_3{\cdot}Et_2O$ led to a slight improvement in the yield (72%), whereas in the absence of $BF_3{\cdot}Et_2O$ no formation of the diyne **4a** was observed. 1-Decynyl(tributyl)-stannane also afforded the diyne **4a** in 78% yield. However, the attempted dimerization of 1-decynyl(trimethyl)silane and -germane gave poor results and large amounts of the reactants were recovered (Table 1, Entries 6 and 7).

Table 1: Reaction of substituted 1-alkynes with difluoro-λ^3-bromane **2**.[a]

Entry	1-Alkynes	$BF_3{\cdot}Et_2O$ [equiv]	4	Yield [%][b]
1	**1a**	0	**4a**	0
2	**1a**	1[c]	**4a**	49
3	**1a**	1.2	**4a**	69
4	**1a**	2	**4a**	72
5	n-C_8H_{17}—≡—$SnBu_3$	1.2	**4a**	78
6	n-C_8H_{17}—≡—$GeMe_3$	1.2	**4a**	17
7	n-C_8H_{17}—≡—$SiMe_3$	1.2	**4a**	0

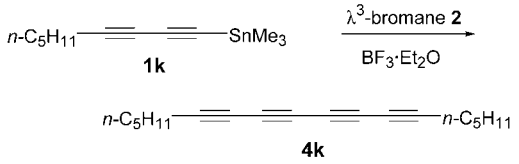
[a] Unless otherwise noted, reactions were carried out by using 2.2 equivalents of an alkyne in dichloromethane in the presence of $BF_3{\cdot}Et_2O$ from −78 °C to room temperature during 5 h under argon. [b] Isolated yields. [c] Reaction conditions: −78 °C, 2.5 h.

Our initial examination of the substrate generality for oxidative homocoupling of 1-alkynylstannanes **1** is shown in Table 2. Dimerization of simple primary, secondary, and tertiary alkylethynyl(trimethyl)stannanes afforded the 1,3-butadiynes **4b–e** in good yields (74–83%). 1,10-Dichlorodecadiyne **4g** was obtained in 69% yield from 5-chloropentynylstannane **1g**. However, phenylethynyl(trimethyl)stannane (**1f**) gave 1,4-diphenyl-1,3-butadiyne (**4f**) in only 33% yield. Ethynyl- and siloxy-substituted alkynyl(trimethyl)stannanes **1h** and **1i** gave 1,3-diynes in moderate yields. Selective coupling of trimethyl(trimethylsilylethynyl)stannane (**1j**) resulted in the formation of bis(trimethylsilyl)-1,3-diyne **4j**, although in a low yield (27%). The use of trimethylstannyl-1,3-diyne **1k** provided directly the conjugated octatetrayne **4k** (40%; Scheme 2). Both tetrabutylstannane and phenyltrimethylstannane do not undergo oxidative homocoupling.

Table 2: Oxidative homocoupling of alkynylstannanes **1** by reaction with difluoro-λ^3-bromane **2**.[a]

Entry	1	4	Yield [%][b]
1	**1b**	**4b**	74
2	**1c**	**4c**	83
3	**1d**	**4d**	76 (87)
4	**1e**	**4e**	80
5	**1f**	**4f**	33
6	**1g**	**4g**	69 (84)
7	**1h**	**4h**	45
8	**1i**	**4i**	47
9	**1j**	**4j**	27

[a] Reactions were carried out by using 2.2 equivalents of an alkyne **1** in dichloromethane in the presence of $BF_3{\cdot}Et_2O$ (1.2 equiv) from −78 °C to room temperature during 5 h under argon. [b] Isolated yields. Yields obtained after GC are quoted in parentheses.



Scheme 2.

On the basis of our previous report[6] as well as the observation that the oxidative homocoupling of 1-alkynylstannane **1a** to yield the diyne **4a** does not take place in the absence of $BF_3{\cdot}Et_2O$ (Table 1, Entry 1),[8] it seems reasonable to assume that the bromine(III)-mediated homocoupling of 1-alkynylstannane **1** probably involves the initial formation of 1-alkynyl(aryl)(tetrafluoroborato)-λ^3-bromane **3** through ligand exchange and its further reaction with excess 1-alkynylstannane **1**. In fact, treatment of 1-decynyl-λ^3-bromane **3a** with 1-alkynylstannane **1a** at room temperature under argon afforded the 1,3-diyne **4a** in 59% yield. The reaction does not require activation with Lewis acids. Interestingly, in this reaction a 4% yield of the cyclopentene **5** was also produced.[9] The reaction with 1-decynyl(trimethyl)germane provided a comparable result with formation of a small amount of **5** (Table 3, Entry 2).

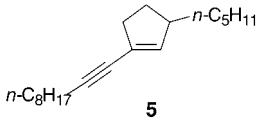
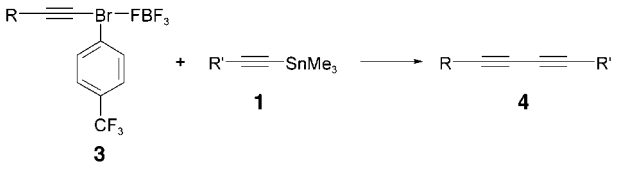


Table 3: Uncatalyzed cross-coupling of alkynyl-λ^3-bromanes **3** with alkynylstannanes **1** and -germanes.[a]

Entry	3	Alkyne	4	Yield [%][b]
1	**3a**	**1a**	**4a**	59
2	**3a**	n-C_8H_{17}—≡—$GeMe_3$	**4a**	64
3	**3a**	**1c**	**4l**	76
4	**3a**	**1e**	**4m**	71
5	**3a**	**1f**	**4n**	66
6	**3c**	**1a**	**4l**	76
7	**3c**	**1e**	**4o**	74
8	**3e**	**1a**	**4m**	71

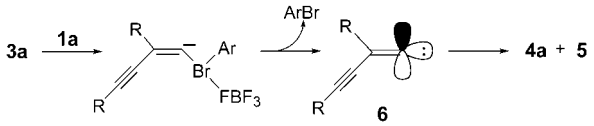
[a] Reactions were carried out by using 2.2 equivalents of an alkyne in dichloromethane at room temperature for 5 h under argon. [b] Isolated yields.

The cross-coupling reaction makes it possible to synthesize unsymmetrically substituted 1,3-butadiynes **4l–o** (Scheme 3, Table 3). For instance, reaction of **3a** with alkynylstannanes **1c** and **1e** afforded the unsymmetrical butadiynes **4l** (76%) and **4m** (71%; Table 3, Entries 3 and 4), which were also produced by the reaction of the inverse combinations (reaction of **1a** with **3c** and **3e**, respectively).



Scheme 3.

Isolation of the byproduct cyclopentene **5** clearly indicates that the reaction of **3a** with **1a** involves the intermediacy of alkylidene carbene **6**, which is produced by Michael addition of 1-alkynylstannane **1a** and the subsequent reductive elimination of the aryl-λ^3-bromanyl group (Scheme 4). A



Scheme 4. R = *n*-C_8H_{17}, Ar = *p*-$CF_3C_6H_4$.

1,2-shift of the alkynyl group in **6** produces **4a**, while competing intramolecular 1,5 carbon–hydrogen insertion affords **5**.[5,10] High migratory aptitude of alkynyl groups in alkylidene carbenes and carbenoids are well established.[11]

The most important step in this mechanism should be an uncatalyzed Michael addition of 1-alkynyl(trimethyl)stannane **1** with rather low nucleophilicity to 1-alkynyl-λ^3-bromane **3**. Entry 2 in Table 3 shows that the less nucleophilic 1-decynyl(trimethyl)germane also serves as an efficient Michael donor toward **3**. The question arises why simple alkynylstannanes and -germanes undergo uncatalyzed conjugate addition toward **3**. We believe that the highly electron-deficient nature of 1-alkynyl-λ^3-bromanes **3**, evoked by a large electron-withdrawing inductive effect of an aryl(tetrafluoroborato)-λ^3-bromanyl group with a substituent constant σ_I of 1.63 (for PhBr(BF_4)),[12] will be responsible for this unusual addition reaction. Actually, 1-alkynyl(aryl)-λ^3-iodanes associated with a reduced inductive effect ($\sigma_I = 1.35$ for PhI(BF_4)) do not function as Michael acceptors, and no formation of 1,3-butadiyne **4a** was observed in the attempted reaction of 1-decynyl(*para*-trifluoromethylphenyl)(tetrafluoroborato)-λ^3-iodane with 1-alkynylstannane **1a** under the conditions described.

To better understand these differences in reactivity in λ^3-bromanes and λ^3-iodanes, density functional theory (DFT) calculations on the simplified 1-propynyl derivatives **7** were carried out (Figure 1). The acetylenic π^* orbital (LUMO+4) of 1-propynyl(phenyl)(fluoro)-λ^3-bromane **7a** is lower in energy than that for the λ^3-iodane **7b** (LUMO+4; 0.04672 eV for **7a**, 0.04778 eV for **7b**). Mulliken atomic charges show that the Cβ carbon atom in **7a** is apparently more positive than that in **7b**.

In summary, we have presented the first example of uncatalyzed Michael addition reactions of simple 1-alkynyl-(trimethyl)stannanes, a reaction which is involved in difluoro-λ^3-bromane-mediated coupling of 1-alkynylstannanes to yield

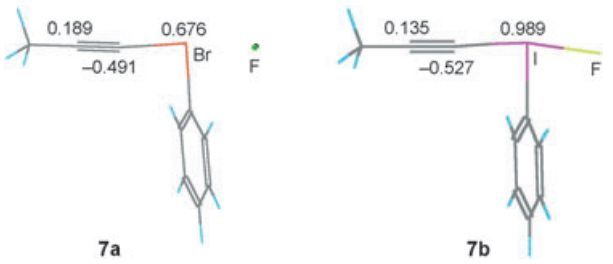


Figure 1. Mulliken atomic charges at Cα, Cβ, Br, and I calculated with the B3LYP/LanL2DZ method (Gaussian 03W).

symmetrical 1,3-butadiynes. Tandem Michael addition–carbene rearrangements of 1-alkynyl(aryl)-λ^3-bromanes with 1-alkynylstannanes provides a new route for the synthesis of unsymmetrical 1,3-butadiynes.[7]

Experimental Section

4a (Table 1, Entry 3): A solution of difluoro[4-(trifluoromethyl)-phenyl]-λ^3-bromane (**2**; 34 mg, 0.13 mmol) in dichloromethane (0.2 mL) followed by $BF_3{\cdot}Et_2O$ (22 mg, 0.16 mmol) were added dropwise to a stirred solution of 1-decynyl(trimethyl)stannane (**1a;** 86 mg, 0.29 mmol) in dichloromethane (0.8 mL) at −78 °C under argon. The mixture was gradually warmed to room temperature over 5 h. The reaction mixture was quenched with water and extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate and concentrated under aspirator vacuum to give an oil, which was purified by preparative TLC (SiO_2, hexane/dichloromethane 4:1) to give a mixture (25.9 mg) of **4a** and **5** (95:5; 69% and 4%, respectively). **4a**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.25$ (t, $J =$ 7.4 Hz, 4H), 1.52 (quint, $J = 7.4$ Hz 4H), 1.41–1.33 (m, 4H), 1.33–1.21 (m, 16H), 0.88 ppm (t, $J = 6.3$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 77.5$, 65.3, 31.9, 29.2, 29.1, 28.9, 28.4, 22.7, 19.2, 14.1 ppm; IR (neat): $\tilde{\nu} = 2925$, 2855, 2233, 1465, 1377, 722 cm^{-1}; MS (70 eV): *m*/*z* (%): 274 (2) [M^+], 245 (3), 231 (3), 217 (9), 203 (8), 189 (4), 175 (10), 161 (19), 147 (22), 133 (31), 119 (43), 105 (56), 91 (100), 79 (65); HRMS: calcd for $C_{20}H_{34}$ [M^+]: 274.2661; found: 274.2663. A pure sample of **5** was obtained by preparative GC (20% silicon GE SF-96, 3 m). **5**: ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.89$ (br s, 1H), 2.69 (m, 1H), 2.46–2.34 (m, 2H), 2.31 (t, $J = 7.4$ Hz 2H), 2.12–2.02 (m, 1H), 1.53 (quint, $J = 7.4$ Hz 2H), 1.45–1.21 (m, 19H), 0.95–0.84 ppm (6H); IR ($CHCl_3$): $\tilde{\nu} = 2928$, 2856, 1465, 1265 cm^{-1}; MS (70 eV): *m*/*z* (%): 274 (22) [M^+], 203 (100) [M^+-C_5H_{11}]; HRMS: calcd for $C_{20}H_{34}$ [M^+]: 274.2661; found: 274.2651. **4l** (Table 3, Entry 7)**: 1a** (59 mg, 0.2 mmol) was added to a stirred solution of 3,3-dimethyl-1-butynyl-λ^3-bromane **3c** (35 mg, 0.09 mmol) in dichloromethane (2 mL) at room temperature under argon. The reaction mixture was stirred for 5 h, quenched with water, and extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate and concentrated under aspirator vacuum to give an oil, which was purified by preparative TLC (SiO_2, hexane) to give **4l** as a colorless oil (15 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.25$ (t, $J = 7.2$ Hz, 2H), 1.51 (quint, $J = 7.2$ Hz, 2H), 1.42–1.33 (m, 2H), 1.32–1.25 (m, 8H), 1.24 (s, 9H), 0.88 ppm (t, $J = 6.7$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) $\delta = 85.0$, 78.8, 65.0, 63.9, 31.9, 30.6, 29.2, 29.1, 28.9, 28.4, 27.9, 22.7, 19.3, 14.1 ppm; IR ($CHCl_3$): $\tilde{\nu} = 2929$, 2858, 2147, 1457 cm^{-1}; MS (70 eV): *m*/*z* (%): 218 (9) [M^+], 203 (24), 189 (50), 175 (22), 161 (61), 147 (58), 133 (61), 119 (96), 105 (100), 91 (60); HRMS: calcd for $C_{16}H_{26}$ [M^+]: 218.2035; found: 218.2041.

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[8] Ligand exchange of difluoro-λ^3-bromane **2** with alkynylstannanes **1** to yield 1-alkynyl-λ^3-bromanes **3** requires activation with $BF_3{\cdot}Et_2O$ with which hypervalent F-Br-F bonding in **2** is efficiently polarized by the coordination of BF_3 and the positive charge on the bromine(III) is increased.

[9] Cyclopentene **5** was also obtained as a byproduct (3–5%) in the bromine(III)-mediated homocoupling of **1a** (Table 1, Entries 2–4).

[10] An alternative ligand-coupling pathway on bromine(III) of (n-$C_8H_{17}CC)_2Br(p$-$CF_3C_6H_4$), produced by ligand exchange through the nucleophilic attack of alkynylstannane **1a** at the polarized bromine of **3a**, could account for the formation of 1,3-butadiyne **4a**. The observation that the diphenyls Ph-Ph and p-$CF_3C_6H_4Ph$ are not formed on the attempted dimerization of phenyl(trimethyl)stannane by the reaction with difluoro-λ^3-bromane **2** strongly suggests a tandem Michael addition–carbene rearrangement pathway. However, involvement of the ligand-coupling reaction as a competing minor process can not be rigorously ruled out. For ligand coupling in hypervalent compounds, see: a) S. Oae, Y. Uchida, *Acc. Chem. Res.* **1991**, *24*, 202; b) M. A. Carroll, S. Martin-Santamaria, V. W. Pike, H. S. Rzepa, D. A. Widdowson, *J. Chem. Soc. Perkin Trans. 2* **1999**, 2707; c) K. Akiba, T. Okinaka, M. Nakatani, Y. Yamamoto, *Tetrahedron Lett.* **1987**, *28*, 3367; d) J. P. Finet, *Ligand Coupling Reactions with Heteroatomic Compounds*, Pergamon, Oxford, **1998**.

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