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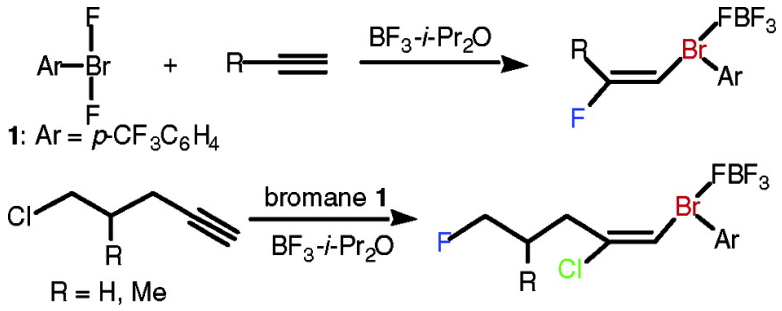

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Synthesis and Characterization of β-Haloalkenyl-λ³-bromanes: Stereoselective Markovnikov Addition of Difluoro(aryl)-λ³-bromane to Terminal Acetylenes

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Hypervalent 1-alkenyl(phenyl)-λ³-iodanes enjoy their rich chemistry in modern organic synthesis.[1] Because of the very high leaving group ability of phenyl-λ³-iodanyl groups,[2] they undergo unusual vinylic S_N2 displacement by the reaction with a wide range of nucleophiles.[3] They also serve as excellent progenitors for generation of alkylidene carbenes.[4]

In a marked contrast, little is known concerning the chemistry of the closely related group 17 1-alkenyl-λ³-bromanes because a method for their syntheses is not available and no well-established 1-alkenyl-λ³-bromanes are known. In 1985, Olah and co-workers reported the preparation of vinyl(methyl)(hexafluoroantimonato)-λ³-bromane in chlorosulfonyl fluoride solution;[5] alkylation of vinyl bromide with a large excess of methyl fluoride−antimony pentafluoride complex at −78 °C in SO_2ClF afforded a light-yellow colored solution of the vinyl(methyl)-λ³-bromane, whose ^{13}C NMR spectrum at −90 °C showed three absorptions at δ 132.9(C_β), 120.9 (C_α), and 44.1(Me) ppm. The vinyl(methyl)-λ³-bromane was found to be stable at −78 °C for only several hours (ca. 4 h), after which polymerization sets in. We report herein, for the first time, the synthesis, isolation, and characterization of β-fluoro- and β-chloroalkenyl(aryl)-λ³-bromanes.

Recently, we reported the synthesis of 1-alkynyl(aryl)(tetrafluoroborato)-λ³-bromanes through ligand exchange of difluoro-λ³-bromane **1** with 1-alkynylstannanes;[6] thus, reaction of 1-(trimethylstannyl)-1-alkynes with *p*-trifluoromethylphenyl(difluoro)-λ³-bromane (**1**) in the presence of BF_3−Et_2O at −78 °C in dichloromethane afforded 1-alkynyl(aryl)-λ³-bromanes in high yields. Use of unsubstituted terminal alkynes instead of 1-alkynylstannanes, however, dramatically changed the reaction course and resulted in fluoro-λ³-bromanation of the triple bonds in a Markovnikov fashion, yielding β-fluoroalkenyl-λ³-bromanes **2** (Scheme 1).

Exposure of 1-decyne to difluoro-λ³-bromane **1** (1.5 equiv) and BF_3−Et_2O (1.5 equiv) at −78 °C in dichloromethane under argon afforded a 62% yield of β-fluoro-1-decenyl-λ³-bromane **2a** (R = n-C_8H_{17}) stereoselectively in an *E:Z* ratio of 96:4 after repeated decantation with hexane (Table 1, entry 2). In this reaction, (*E*)-β-ethoxy-**3a** (7%) and (*E*)-β-chloro-1-decenyl-λ³-bromane **3b** (4%) were obtained as byproducts. Without using BF_3, no formation of these vinyl-λ³-bromanes was observed. Hypervalent F−Br−F bonding in **1** is efficiently polarized by the coordination of BF_3, and the positive charge on the bromine(III) is increased. In contrast to ethoxy-λ³-bromane **3a**, which gradually decomposes even during purification by hexane decantation, fluoro-λ³-bromane **2a** is stable and no decomposition was detected when it was left standing in a refrigerator over 1 month. The β-ethoxy group of **3a** originates from the ligand Et_2O of Lewis acid BF_3,[7] and the formation of β-alkoxybromanes can be controlled by using sterically more demanding BF_3-*i*-Pr_2O (Table 1, entry 6). The solvent dichloromethane transfers the chlorine atom to the electron-deficient reactive species, such as carbocations and carbenes, via the intermediacy of chloronium ions and ylides, respectively,[8] and in our reactions, it gives rise to the other byproduct, β-chlorodecenyl-λ³-bromane **3b**. In fact, use of a less nucleophilic solvent,[8a] such as chloroform or carbon tetrachloride, showed no evidences for formation of **3b**, whereas more nucleophilic 1,2-dichloroethane resulted in an increased yield (19%) of **3b** at the expense of the formation of **2a** (Table 1, entries 7−9). $AgBF_4$ also activates difluorobromane **1** in the reaction but affords a moderate yield of **2a** with a low stereoselectivity (Table 1, entry 10).[9]

Scheme 1

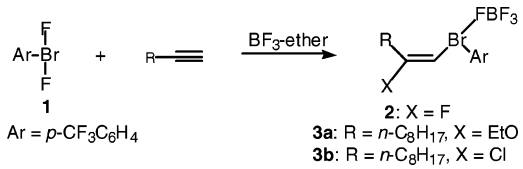

Table 1. Addition of Difluoro-λ³-bromane **1** to 1-Decyne, Yielding β-Fluorodecenyl-λ³-bromane **2a**[a]

entry	BF_3–ROR′ (equiv)	solvent	temp (°C)	time (h)	yield (%)[b]	ratio *E:Z*
1[c]	Et_2O (1.1)	CH_2Cl_2	−78	3	50[d,e]	95:5
2	Et_2O (1.5)	CH_2Cl_2	−78	3	62[d,e]	96:4
3	Et_2O (3)	CH_2Cl_2	−78	3	61[d,e]	98:2
4	THF (1.5)	CH_2Cl_2	−78	5	56	96:4
5	*t*-BuOMe (1.5)	CH_2Cl_2	−78 to 25	5	33[e]	87:13
6	*i*-Pr_2O (1.5)	CH_2Cl_2	−78 to 25	5	72[e]	96:4
7[f]	*i*-Pr_2O (1.5)	$CHCl_3$	−60 to 25	3.5	74	94:6
8	*i*-Pr_2O (1.5)	CCl_4	−20 to 25	3.5	60	95:5
9	*i*-Pr_2O (1.5)	$Cl(CH_2)_2Cl$	−30 to 25	3.5	47[g]	92:8
10	$AgBF_4$ (1.5)	$CHCl_3$	−60 to 25	3.5	44	75:25

[a] Conditions: difluorobromane **1** (1.5 equiv), Ar. [b] Yields after purification by repeated decantation with hexane. [c] Difluorobromane **1** (1.1 equiv). [d] (*E*)-β-Ethoxybromane **3a** (7−15%) was obtained. [e] (*E*)-β-Chlorobromane **3b** (3−13%) was obtained. [f] Difluorobromane **1** (2 equiv). [g] **3b** (19%) was obtained.

Table 2 summarizes the results of regio- and stereoselective fluoro-λ³-bromanation of terminal alkynes in chloroform in the presence of BF_3-*i*-Pr_2O. Acetoxy, chloro, methoxycarbonyl, and methoxy groups are compatible with our β-fluorovinyl-λ³-bromane synthesis (Table 2, entries 6−9). Interesting methine fluorination of the *iso*-butyl group afforded difluorinated vinyl-λ³-bromane **2k** (R = Me_2CFCH_2) as a minor product (Table 2, entry 3). In the reaction of sterically demanding 3,3-dimethyl-1-butyne, competition between β-fluorination and β-methylation via 1,2-methyl shift takes place and gave a mixture of β-fluorovinyl-λ³-bromane **2f** (40%) and (*Z*)-3-fluoro-2,3-dimethyl-1-butenyl-λ³-bromane (13%) (Table 2, entry 5).

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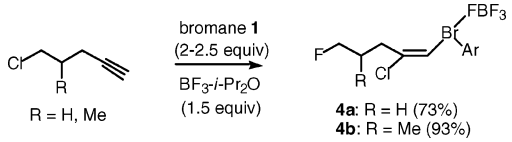
Table 2. Synthesis of β-Fluorovinyl-λ^3-bromanes **2**[a]

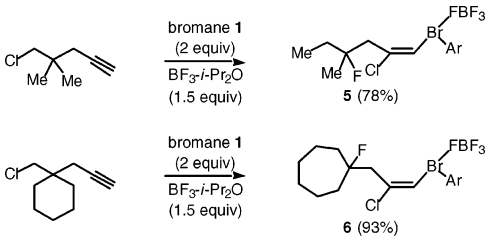
entry	R	difluoro-λ^3-bromane **1** (equiv)	**2**	yield (%)[b]	ratio *E*:*Z*
1	*n*-Bu	2.5	**2b**	88[c]	93:7
2	*n*-C_6H_{13}	2	**2c**	75	95:5
3	*i*-Bu	2.5[d]	**2d**	81[e]	91:9
4	$Me_2CH(CH_2)_2$	2	**2e**	82[c]	93:7
5	*t*-Bu	2.5	**2f**	40[f]	86:14
6	$AcO(CH_2)_9$	2	**2g**	60	94:6
7	$Cl(CH_2)_9$	2	**2h**	72	97:3
8	$MeO_2C(CH_2)_8$	2.5	**2i**	62	95:5
9	$MeO(CH_2)_9$	2	**2j**	65	97:3

[a] Conditions: $CHCl_3$, BF_3-*i*-Pr_2O (1.5 equiv), −60 to 25 °C (3.5 h), Ar. [b] Yields after purification by repeated decantation with hexane. [c] Contaminated with a small amount of impurities. [d] BF_3-*i*-Pr_2O (2.5 equiv). [e] Vinyl-λ^3-bromane **2k** (16%) was obtained. [f] (*Z*)-3-Fluoro-2,3-dimethylbutenyl-λ^3-bromane (13%) was obtained.

Scheme 2



Scheme 3



To develop an efficient method for the synthesis of β-chlorovinyl-λ^3-bromanes, use of an external chloride anion, Bu_4NCl, as an additive was examined but found to be fruitless;[10] however, we found that the internal delivery of a soft chlorine atom will make possible the formation of β-chlorovinyl-λ^3-bromanes. Thus, 5-chloro-1-pentyne and 5-chloro-4-methyl-1-pentyne by the reaction with difluorobromane **1** produced (*E*)-β-chloro-ω-fluorovinyl-λ^3-bromanes **4a** and **4b**, respectively, in high yields (Scheme 2). These reactions are exclusively stereoselective to the limits of ^{1}H NMR (400 MHz) detection, and no formation of *Z*-isomers was observed. The reaction probably involves a 1,4-chlorine shift from sp^3 to sp^2 carbon atoms as a key step[11] and is termed a domino λ^3-bromanation−chlorine shift−fluorination reaction. The λ^3-bromane **4** contains three kinds of halogen atoms, F, Cl, and Br, in the molecule.

Very interestingly, in the case of 4,4-dialkyl-1-pentynes, the domino reaction was accompanied by an additional 1,2-alkyl rearrangement. For instance, 5-chloro-4,4-dimethyl-1-pentyne afforded (*E*)-β-chloro-δ-fluorohexenyl-λ^3-bromane **5** in 78% yield (Scheme 3). The domino λ^3-bromanation−chlorine shift−alkyl shift−fluorination reaction of 1-chloromethyl-1-propynylcyclohexane resulted in the ring-enlargement of cyclohexane, yielding fluorocycloheptane **6** in 93% yield.

X-ray crystallographic analysis of fluorocycloheptane **6**, shown in Figure 1, illustrates a T-shaped structure with one fluorine atom of the BF_4 ligand at the apical site of the bromine(III) center with a near-linear C1−Br1···F7 triad (172.6(2)°). The root mean square deviation of the four atoms (Br1, C1, C11, and F7) from their least-squares planes is 0.071(2) Å.

Reaction mechanism involving the formation of tetracoordinated λ^3-bromane **7** (Scheme 4) is compatible with the formation of unrearranged and rearranged β-haloalkenyl(aryl)-λ^3-bromanes.

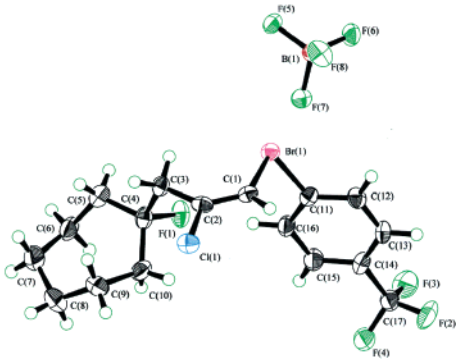
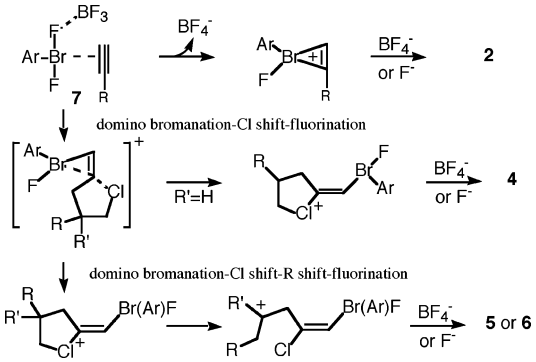


Figure 1. ORTEP drawing of **6**. Selected bond lengths (Å) and angles (deg): Br(1)−C(1) 1.886(5), Br(1)−C(11) 1.908(5), C(1)−C(2) 1.312(8), Br(1)···F(7) 2.766(3), C(1)−Br(1)−C(11) 96.8(2), C(1)−C(2)−C(3) 130.1-(4).

Scheme 4



Supporting Information Available: Experimental procedures, compound characterization data, and X-ray crystallographic data in CIF format for **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) When the reaction of entry 2 in Table 1 was carried out in the presence of Bu_4NCl (1.5 equiv), a decreased yield (23%) of **2a** and (*E*)-1,2-dichloro-1-decene (19%) was obtained. These results probably reflect partial oxidation of the chloride anion to Cl_2 by difluorobromane **1** during the reaction.

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