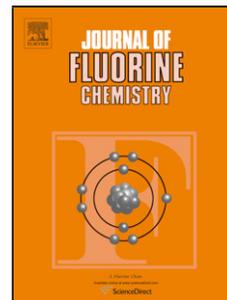


Accepted Manuscript

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PII: S0022-1139(17)30047-7
DOI: <http://dx.doi.org/doi:10.1016/j.jfluchem.2017.04.004>
Reference: FLUOR 8969

To appear in: *FLUOR*

Received date: 18-2-2017
Revised date: 8-4-2017
Accepted date: 8-4-2017

Please cite this article as: Yuki Kitamura, Mio Matsumura, Yuki Murata, Mizuki Yamada, Naoki Kakusawa, Motohiro Tanaka, Hiroyuki Okabe, Hiroshi Naka, Tohru Obata, Shuji Yasuike, A versatile synthesis of triarylantimony difluorides by fluorination of triarylstibanes with nitrosyl tetrafluoroborate and their antitumor activity, Journal of Fluorine Chemistry <http://dx.doi.org/10.1016/j.jfluchem.2017.04.004>

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Full Length Articles

A versatile synthesis of triarylantimony difluorides by fluorination of triarylstibanes with nitrosyl tetrafluoroborate and their antitumor activity

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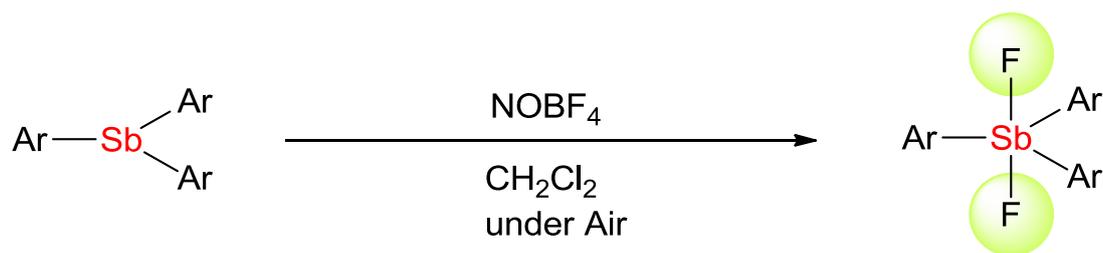
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Graphical abstract



IC_{50} for antitumor activity = 2.43 - 43.8 μM against 5 cell lines

Highlights:

Triarylantimony difluorides were synthesized by oxidative fluorination of triarylstibanes with NOBF_4 .

The antitumor activity of triarylantimony difluorides exhibited good anti-proliferation activity against tumor cell lines.

p- Tol_3SbF_2 exhibited the best antitumor activity among the compounds in this series.

ABSTRACT

Triarylantimony difluorides were synthesized in moderate to excellent yields by oxidative fluorination of triarylstibanes with nitrosyl tetrafluoroborate (NOBF_4) under aerobic conditions. This reaction is the first example of fluorination of trivalent organoantimony compounds using NOBF_4 as a fluorinating agent. The triarylantimony difluorides exhibited good anti-proliferation activity against tumor cell lines. In particular, the IC_{50} of *p*- Tol_3SbF_2 (**2c**) was the lowest in each cell lines.

Keywords:

Triarylantimony difluoride

Nitrosyl tetrafluoroborate

Fluorination

Antimony

Antitumor

1. Introduction

Organoantimony compounds have attracted much interest because of their use as important reagents in organic synthesis and their potential biological activities [1–4]. Among these, triarylantimony difluorides are used as precursors of pentavalent organoantimony compounds in main-group element chemistry [5–7]. These triarylantimony difluorides have been typically synthesized by fluorination of organoantimony compounds [5, 7–19]. Oxidative fluorination of triarylstibanes is a straightforward strategy and has been widely conducted using fluorinating reagents such as HF/*t*BuOOH [15], IF₅ [16], F₂ [17], Et₂NSF₃ [7], methyl 3-azidotetrafluoropropionate (N₃CF₂CF₂CO₂Me) [18], and triphenylbismuth difluoride (Ph₃BiF₂) [19]. However, most of these fluorinating reagents are difficult to handle and can cause glass corrosion. In 2012 Fuchigami et al. reported a single example of electrochemical fluorination of triphenylstibane (0.1 mmol scale) using KF as an inexpensive and less glass-corrosive reagent in the presence of poly(ethylene glycol) [14]. However, substrate scope and scalability of this reaction remains unclear. On the other hand, tetrafluoroborates (e.g., HBF₄·OEt₂, NOBF₄, and Bu₄NBF₄) and boron trifluoride (e.g., BF₃·OEt₂) act as nucleophilic fluorinating reagents that are easy to handle and do not cause glass corrosion [20]. For example, they are used in the fluorination of aliphatic cyanoazides [21, 22], and α -diazo- β -keto esters [23, 24] and in the ring-opening fluorination of epoxides [25]. To the best of our knowledge, the synthesis of triarylantimony difluorides by the reaction of triarylstibanes with tetrafluoroborate has not hitherto been reported.

We have recently reported the synthesis and biological activity of organoantimony compounds [26–30]. Among these, 1-[(2-di-*p*-tolylstibanophenyl)diazenyl]pyrrolidine [28] and 2-(di-*p*-tolylstibano)-*N*-*p*-tolylbenzamide [29] showed potent anti-proliferative activity against

human tumor cell lines such as NB₄, HeLa, L1210, Mm1, and DLD-1. Moreover, tris(pentafluorophenyl)stibane induced gene expression of metallothionein (MT)-1A and -2A, which are the subisoforms of MT in bovine aortic endothelial cells [30]. This knowledge shows that organoantimony compounds with fluorine atoms possibly show potent biological activity. As a continuation of our previous studies, we now report a versatile synthesis of triarylantimony difluorides by the fluorination of triarylstibanes with nitrosyl tetrafluoroborate (NOBF₄) and their antitumor activity.

2. Results and discussion

2.1. Synthesis of triarylantimony difluorides

We initially determined the optimum conditions for the fluorination of triphenylstibane (**1a**) with fluorine reagents such as tetrafluoroborate and boron trifluoride. The results of the search for active agents and the optimum amount of fluorine reagents for the reaction are summarized in Table 1. The progress of the reaction was monitored by thin-layer chromatography (TLC), and the reaction time was determined when **1a** disappeared on TLC. First, we performed the reaction of **1a** with a variety of fluorine agents (2 eq) to compare their reactivity in CH₂Cl₂ at room temperature under aerobic conditions (entries 1–11). Among these reagents, NOBF₄, NO₂BF₄, and IPy₂BF₄ afforded the expected triphenylantimony difluoride (**2a**) in good to high yields (entries 3–5). NOBF₄ appeared to be the best reagent for this reaction in terms of the yield (84%) of the fluorinated product (**2a**) and reaction time (3 h) (entry 3). Next, the optimum amount of fluorine reagent was determined by the reaction of **1a** with NOBF₄ (entries 3, 12–14). The best result was observed in the reaction of **1a** with NOBF₄ in the ratio 1:2 (entry 3). It seems that one of the four fluorine atoms on the B atom in NOBF₄ was involved in the antimony–fluorine bond formation. Moreover, an excess amount of NOBF₄ seems to injure the product (entry 14). Screening of solvent showed that the reaction proceeded effectively in CH₂Cl₂ (84%), toluene (71%), and CH₃CN (59%). Other solvents such as tetrahydrofuran and MeOH could not be used because of the poor solubility and low stability of NOBF₄. Consequently, the best result was obtained when **1a** was treated with NOBF₄ (2 eq) in

CH₂Cl₂ at room temperature. This reaction could also be scaled up to 10 mmol and the desired product **2a** was obtained in excellent yields of up to 88%, i. e., 3.44 g of the product could be generated (entry 15).

Table 1

To demonstrate the efficiency and generality of the abovementioned protocol, the reactions of various Ar₃Sb (**1b–m**) and NOBF₄ were investigated under the optimized conditions. The results are shown in Table 2. The yields of Ar₃SbF₂ were sensitive to the electronic nature of the substituents on the phenyl rings. The Ar₃Sb with electron-withdrawing groups (**1d–i**) were fluorinated smoothly in good to excellent yields, whereas those without an electron-attracting group (**1b** and **1c**) gave **2b** and **2c** in moderate yields (entries 2–9). The reaction of **1b**, which has a methoxy group on the phenyl ring, with NOBF₄ at room temperature gave the expected **2b** in 25% yield and 4-nitroanisole as a side product in 24% yield (entry 1). It was assumed that 4-nitroanisole was formed by the nitroso-induced *ipso*-deantimonation of **1b** with NOBF₄. Therefore, the reaction of **1b** and NOBF₄ was performed at low temperature (–20 °C), and **2b** was obtained in 45% yield without any side product (entry 2). Comparison of methyl-substituted antimony substrates (**1c**, **1j**, and **1k**) showed remarkable influence of the steric hindrance (entries 3, 10, and 11). The most bulky mesityl derivative **1k** was totally unreactive (entry 11). Fluorination of **1l** and **1m** with NOBF₄ gave a complex mixture (entries 12 and 13).

Table 2

At present, the mechanism of the fluorination of organoantimony compounds is unclear. We consider a similar reaction mechanism proposed by Olah and Prakash et al. for the desulfurative fluorination of sulfides and fluorination of arylacetylenes using NOBF₄ [31, 32]. Fig. 1 shows a possible mechanism for the synthesis of triarylantimony difluorides from Ar₃Sb and NOBF₄. The first step of

the reaction involves the generation of stibonium ion **A** from Ar_3Sb (**1a–j**) with NO^+ . Intermediate **B** is obtained through nucleophilic attack by F^- from BF_4^- . The reaction of **B** with NO^+ affords stibonium ion **D** and $\text{H}_2\text{N}_2\text{O}_2$ (**E**) *via* intermediate **C**. **E** decomposes to N_2O and H_2O [33]. Intermediate **D** is converted to triarylantimony difluorides (**2a–j**) by the nucleophilic attack of F^- . This mechanism is in line with the fact that the present fluorination protocol requires 2 equivalents of NOBF_4 (Table 1, entries 3, 12, and 13).

Fig. 1

2.2. Antitumor activity

The biological activity of the synthesized triarylantimony difluorides (**2a–j**) was evaluated in terms of the antitumor effect in mouse and human cultured tumor cell lines. The tested compounds presented good anti-proliferation activity against all the cell lines (Table 3). This series of compounds exhibited antitumor activity against not only the mouse and human leukemia cell lines but also human solid tumor cell lines such as colon and breast tumors. In particular, the IC_{50} of *p*- Tol_3SbF_2 (**2c**) with the *p*-tolyl functional group was the lowest values (2.43–3.97 μM) in each cell lines, indicating that this compound exhibited the best antitumor activity among those studied. In our previous paper [29], we reported the anti-proliferative activity of cisplatin (CDDP, 1.0–6.2 μM against 6 tumor cell lines), a famous platinum-based antitumor drug. Interestingly, the antitumor activity of *o*- Tol_3SbF_2 (**2j**), a regioisomer of **2c**, was significantly lower ($\text{IC}_{50} = 5.13\text{--}15.2 \mu\text{M}$). It seems that the difference in the position of the methyl functional group caused a conformational change and a consequent lack of interaction between the molecule and the unidentified biological target. Furthermore, the electron-donating and electron-withdrawing substituents on the aromatic ring were not affected significantly in this assay system. However, **2i** having benzonitrile as an aromatic side chain showed remarkably reduced sensitivity in all the tumor cell lines. Although the mechanism of this organoantimony series for anti-proliferation in tumor cells is still unclear, these compounds may become key molecules in the development of potent antitumor agents.

Table 3

3. Conclusion

In conclusion, we have developed a novel fluorination of triarylstibanes by using nitrosyl tetrafluoroborate as the fluorine source under aerobic conditions. Various triarylstibanes with electron-donating and electron-withdrawing functional groups afforded the corresponding triarylantimony difluorides in moderate to excellent yields. These compounds exhibited potent antitumor activity against several cultured tumor cell lines. Particularly, the sensitivity of *p*-Tol₃SbF₂ (**2c**) was higher than that of the other triarylantimony difluorides in all the tested cell lines. These findings indicate that the potential application of organoantimony compounds with fluorine atoms may be extended to the development of a superior antitumor drug.

4. Experimental

4.1. General

Melting points were measured on a Yanagimoto micro melting point hot-stage apparatus (MP-S3) and reported as uncorrected values. ¹H NMR (TMS: δ : 0.00 ppm or CH₂Cl₂: 5.30 ppm as an internal standard) and ¹³C NMR (CDCl₃: δ : 77.00 ppm as an internal standard) spectra were recorded on JEOL JNM-AL400 (400 MHz and 100 MHz respectively) spectrometers in CDCl₃. ¹⁹F NMR (α,α,α -trifluorotoluene: δ : -64.0 ppm as an internal standard) spectra were recorded on JEOL ECA-600 spectrometers in CDCl₃. Mass spectra were obtained on a JEOL JMP-DX300 instrument (70 eV, 300 μ A). IR spectra were recorded on a Shimadzu FTIR-8400S spectrophotometer and reported in terms of frequency of absorption (cm⁻¹). Only selected IR bands are absorbencies reported. Chromatographic separations were carried out using Silica Gel 60N (Kanto Chemical Co., Inc.) under the solvent system stated. Thin-layer chromatography (TLC) was performed using Merck Pre-coated TLC plates (silica gel 60 F₂₅₄). Triphenylstibane (**1a**) was purchased from Sigma-Aldrich,

and other triarylstibanes of **1b**, **c**, **j** [15], **1d**, **e**, **g**, **h** [34], **1f** [35], and **1i** [36] were prepared according to the reported procedures.

4.2. General procedure for triarylantimony difluorides

To a solution of triarylstibane (**1a–j**: 0.5 mmol) in dry CH₂Cl₂ (3.0 mL) was added NOBF₄ (1.0 mmol) at –20 or 0 °C. The reaction mixture was stirred at –20 °C or room temperature for the indicated time (2–5 h) until complete consumption of the starting material, as monitored by TLC. After dilution with CH₂Cl₂ (20 mL) and water (20 mL), the organic layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (20 mL × 2). The combined organic layers were washed with water and brine, dried over anhydrous MgSO₄, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (**2a**, **c–e**, **h**, and **2j**: *n*-hexane:Et₂O = 5:1, **2b**: CH₂Cl₂), affording triarylantimony difluorides (**2a–e**, **h**, and **2j**). In the case of **2f**, **g**, and **2i**, the crude product was purified by recrystallization.

4.2.1. Triphenylantimony difluoride (**2a**) [15]

Pale yellow plates (164 mg, 84%). mp 106–109 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 7.52–7.53 (m, 9H, Ar-H), 8.14–8.19 (m, 6H, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 129.5, 132.1, 134.1 (t, ²J_{C,F} = 15.3 Hz), 135.3 (t, ³J_{C,F} = 5.0 Hz); ¹⁹F NMR (565 MHz, CDCl₃) δ: –153.5 (s, 2F). LRMS (EI): *m/z* 390 (M⁺, 20%), 313 (95%), 154 (100%). HRMS: *m/z* [M]⁺ calcd for C₁₈H₁₅F₂Sb: 390.0180. Found: 390.0183.

4.2.2. Tris(4-methoxyphenyl)antimony difluoride (**2b**)

Brown oil (108 mg, 45%). ¹H NMR (400 MHz, CDCl₃) δ: 3.83 (s, 9H, Me), 7.04 (d, 6H, *J* = 8.8 Hz, Ar-H), 8.04–8.07 (m, 6H, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 55.3, 115.1, 124.7 (t, ²J_{C,F} = 15.7 Hz), 136.6 (t, ³J_{C,F} = 5.0 Hz), 162.7; ¹⁹F NMR (565 MHz, CDCl₃) δ: –151.1 (s, 2F); LRMS (EI): *m/z* 480 (M⁺, 45%), 373 (100%), 214 (90%); HRMS: *m/z* [M]⁺ calcd for C₂₁H₂₁F₂O₃Sb: 480.0494. Found: 480.0497.

4.2.3. *Tris(4-tolyl)antimony difluoride (2c)* [37]

Colorless prism (153 mg, 71%), mp 113–115 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 2.38 (s, 9H, Me), 7.33 (d, 6H, *J* = 7.8 Hz, Ar-H), 8.01 (d, 6H, *J* = 8.3 Hz, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 21.4, 130.2, 130.9 (t, ²*J*_{C,F} = 15.2 Hz), 135.1 (t, ³*J*_{C,F} = 5.0 Hz), 142.5; ¹⁹F NMR (565 MHz, CDCl₃) δ: –152.8 (s, 2F). LRMS (EI): *m/z* 432 (M⁺, 10%), 341 (100%), 182 (80%). HRMS: *m/z* [M]⁺ calcd for C₂₁H₂₁F₂Sb: 432.0650. Found: 432.0652.

4.2.4. *Tris(4-fluorophenyl)antimony difluoride (2d)* [38]

Colorless plates (176 mg, 79%), mp 65–67 °C (from *n*-hexane). ¹H NMR (400 MHz, CDCl₃) δ: 7.22–7.27 (m, 6H, Ar-H), 8.13–8.27 (m, 6H, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 117.0 (d, ²*J*_{C,F} = 16.6 Hz), 128.6 (td, ²*J*_{C,F} = 16.5, 3.3 Hz), 137.5 (dt, ³*J*_{C,F} = 9.0, 5.0 Hz), 165.6 (d, ¹*J*_{C,F} = 253.2 Hz); ¹⁹F NMR (565 MHz, CDCl₃) δ: –151.1 (s, 2F), –107.6 (s, 3F); LRMS (EI): *m/z* 444 (M⁺, 10%), 349 (100%), 190 (80%); HRMS: *m/z* [M]⁺ calcd for C₁₈H₁₂F₂Sb: 443.9897. Found: 443.9894.

4.2.5. *Tris(4-chlorophenyl)antimony difluoride (2e)*

Pale yellow plates (210 mg, 85%), mp 114–116 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 7.52–7.54 (m, 6H, Ar-H), 8.06–8.08 (m, 6H, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 130.0, 131.5 (t, ²*J*_{C,F} = 16.1 Hz), 136.5 (t, ³*J*_{C,F} = 5.4 Hz), 139.4; ¹⁹F NMR (565 MHz, CDCl₃) δ: –152.7 (s, 2F); LRMS (EI): *m/z* 494 (M⁺, 15%), 383 (100%), 222 (80%); HRMS: *m/z* [M]⁺ calcd for C₁₈H₁₂Cl₃F₂Sb: 493.8981. Found: 493.8977.

4.2.6 *Tris(4-bromophenyl)antimony difluoride (2f)*

Pale yellow plates (270 mg, 86%), mp 111–113 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 7.68 (d, 6H, *J* = 7.8 Hz, Ar-H), 7.99 (d, 6H, *J* = 8.8 Hz, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 128.0, 132.0 (t, ²*J*_{C,F} = 15.7 Hz), 132.8, 136.6 (t, ³*J*_{C,F} = 4.1 Hz); ¹⁹F NMR (565 MHz, CDCl₃) δ: –153.1 (s, 2F). LRMS (FAB): *m/z* 625 (M⁺, 10%), 609 (100%), 297 (10%). HRMS: *m/z* [M]⁺ calcd for C₁₈H₁₂Br₃F₂Sb: 625.7475. Found: 625.7478.

4.2.7. Tris(4-ethoxycarbonylphenyl)antimony difluoride (**2g**)

Colorless needles (258 mg, 85%), mp 121–123 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 1.40 (t, 9H, *J* = 7.3 Hz, Me), 4.41 (q, 6H, *J* = 7.3 Hz, CH₂), 8.20 (d, 6H, *J* = 8.3 Hz, Ar-H), 8.26 (d, 6H, *J* = 8.3 Hz, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 14.2, 61.5, 130.3, 134.2, 135.3 (t, ³*J*_{C,F} = 5.0 Hz), 138.4 (t, ²*J*_{C,F} = 15.3 Hz), 165.6; ¹⁹F NMR (565 MHz, CDCl₃) δ: –152.4 (s, 2F). LRMS (FAB): *m/z* 606 (M⁺, 25%), 587 (100%), 253 (15%). HRMS: *m/z* [M]⁺ calcd for C₂₇H₂₇F₂O₆Sb: 606.0814. Found: 606.0811; IR (KBr): 1724 cm⁻¹.

4.2.8. Tris[4-(trifluoromethyl)phenyl]antimony difluoride (**2h**) [7]

Pale yellow plates (238 mg, 80%), mp 94–96 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 7.82 (d, 6H, *J* = 7.8 Hz, Ar-H), 8.32 (d, 6H, *J* = 7.8 Hz, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 123.4 (q, ¹*J*_{C,F} = 273.1 Hz), 126.4 (q, ³*J*_{C,F} = 1.7 Hz), 134.7 (q, ²*J*_{C,F} = 33.1 Hz), 135.9 (t, ³*J*_{C,F} = 5.4 Hz), 137.3 (t, ²*J*_{C,F} = 15.7 Hz); ¹⁹F NMR (565 MHz, CDCl₃) δ: –153.4 (s, 2F), –64.6 (s, 9F); LRMS (FAB): *m/z* 594 (M⁺, 15%), 575 (100%), 271 (60%). HRMS: *m/z* [M]⁺ calcd for C₂₁H₁₂F₁₁Sb: 593.9802. Found: 593.9806.

4.2.9. Tris(4-cyanophenyl)antimony difluoride (**2i**)

Colorless prism (182 mg, 78%), mp 147–150 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 7.85 (d, 6H, *J* = 7.8 Hz, Ar-H), 8.29 (d, 6H, *J* = 7.8 Hz, Ar-H); ¹³C NMR (100 MHz, CDCl₃) δ: 116.9, 117.4, 132.9, 136.1 (t, ³*J*_{C,F} = 5.3 Hz), 138.0 (t, ²*J*_{C,F} = 15.7 Hz); ¹⁹F NMR (565 MHz, CDCl₃) δ: –154.5 (s, 2F); LRMS (EI): *m/z* 465 (M⁺, 5%), 363 (100%), 242 (35%). HRMS: *m/z* [M]⁺ calcd for C₂₁H₁₂F₂N₃Sb: 465.0037. Found: 465.0034. IR (KBr): 2230 cm⁻¹.

4.2.10. Tris(2-tolyl)antimony difluoride (**2j**) [8]

Pale yellow plates (130 mg, 60%). mp 197–199 °C (from *n*-hexane–CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃) δ: 2.55 (s, 9H, Me), 7.31–7.37 (m, 6H, Ar-H), 7.45 (td, 3H, *J* = 7.6, 1.0 Hz, Ar-H), 7.73 (d,

3H, $J = 7.3$ Hz, Ar-H); ^{13}C NMR (100 MHz, CDCl_3) δ : 23.2 (t, $^4J_{\text{C,F}} = 2.5$ Hz), 126.5, 131.6 (t, $^3J_{\text{C,F}} = 9.9$ Hz), 135.0, 136.8 (t, $^2J_{\text{C,F}} = 15.7$ Hz), 142.9; ^{19}F NMR (565 MHz, CDCl_3) δ : -112.0 (s, 2F); LRMS (EI): m/z 414 ($[\text{M-F}]^+$, 70%), 412 (95%), 341 (100%). HRMS: m/z $[\text{M-F}]^+$ calcd for $\text{C}_{21}\text{H}_{21}\text{FSb}$: 414.0744. Found: 414.0740.

4.3. Antitumor activity

Mouse melanoma cells B16-F10, human promyelocytic leukemia cells HL-60, human fibrosarcoma cells HT-1080, human breast adenocarcinoma cell line MCF-7 and human colorectal adenocarcinoma cells DLD-1 were purchased from the American Type Culture Collection. The tested all cell lines were maintained at 37 °C and 5% CO_2 in RPMI-1640 medium supplemented with 10% heat-inactivated fetal bovine serum (FBS) and 1% penicillin-streptomycin. The growth-inhibitory effects of the compounds on tumor cells were examined using a colorimetric assay involving 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). Briefly, 198- μL aliquots of an exponentially growing cell suspension (10,000 cells/mL) were incubated with 2 μL of varying concentrations of compounds dissolved by dimethyl sulfoxide (DMSO). After exposure to the compounds for 72 h, 25 μL of MTT solution (3 mg/mL in PBS) was added to each well and the cell cultures were incubated at 37 °C for 4 h. After removal of the medium, the formed formazan was dissolved in 200 μL of DMSO. The absorbance of each well was measured at 570 nm with MTP-800AFC immunoreader (CORONA Electric), and the inhibition ratio (IR) was calculated using the following formula: $\text{IR} (\%) = (1 - \text{T}/\text{C}) \times 100$, where C is the mean of optical densities of the control group and T of the treatment group. The IC_{50} value was defined as the concentration of the compound needed to effect a 50% reduction in growth relative to the control. The IC_{50} value was determined by a graphical correlation of the dose-response curve with at least three compound concentration points.

Acknowledgments

Partial financial support for this work was provided by a research grant from Institute of Pharmaceutical Life Sciences, Aichi Gakuin University and Hokuriku University. We thank Takahiro Isogawa (Nagoya U) for his technical assistance.

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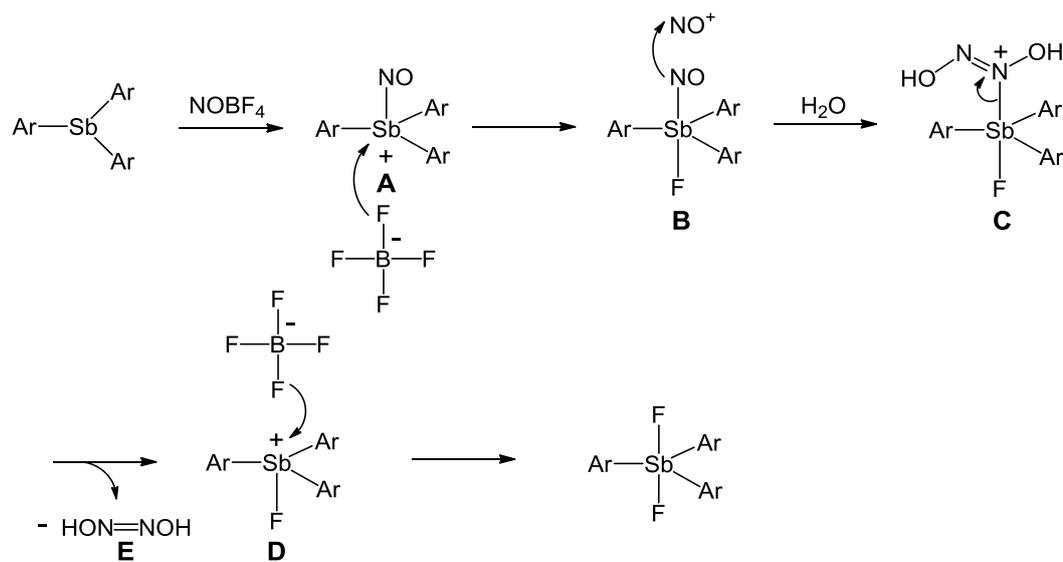
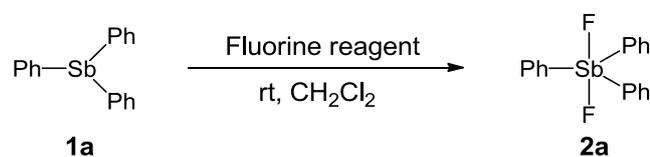


Fig. 1. Possible Mechanism

Table 1

Reaction of triphenylstibane **1a** with fluorine reagents.^a

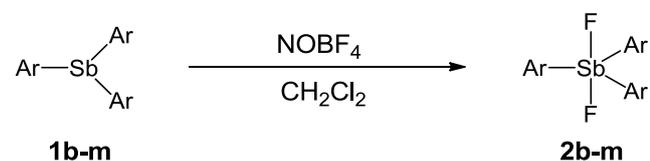


Entry	Reagent (eq)	Time (h)	Yield (%) ^b	
			2a	Recovery
1	$\text{HBF}_4 \cdot \text{Et}_2\text{O}$ (2)	24	4	92
2	$\text{Bu}_4\text{N} \cdot \text{BF}_4$ (2)	24	0	96
3	NOBF_4 (2)	3	84	0
4	NO_2BF_4 (2)	4	67	0
5	IPy_2BF_4 (2)	24	60	0
6	Cp_2FeBF_4 (2)	24	2	91
7	NaBF_4 (2)	24	0	98
8	NH_4BF_4 (2)	24	0	97
9	Et_3OBF_4 (2)	24	0	97
10	Et_2OBF_3 (2)	24	2	95
11	TBAF (2)	24	0	98
12	NOBF_4 (0.5)	24	22	69
13	NOBF_4 (1.0)	24	49	39
14	NOBF_4 (3)	3	50	0
15 ^c	NOBF_4 (2)	4	88	0

^a Conditions: **1a** (0.5 mmol), CH_2Cl_2 (3 mL), rt, under air.

^b Isolated yield.

^c **1a** (10 mmol), CH_2Cl_2 (60 mL).

Table 2Synthesis of triarylsantimony difluorides.^a

Entry	Substrate	Ar	Time (h)	Yield (%) ^b
1	1b		3	2b : 25 (24) ^c
2 ^d	1b		5	2b : 45
3	1c		3	2c : 71
4	1d		2	2d : 79
5	1e		3	2e : 85
6	1f		3	2f : 86
7	1g		2	2g : 85
8	1h		2	2h : 80
9	1i		3	2i : 78
10	1j		4	2j : 60
11	1k		24	2k : 0
12	1l		24	2l : 0
13	1m		24	2m : 0

^a Conditions: **1** (0.5 mmol), NOBF₄ (1.0 mmol), CH₂Cl₂ (3 mL), rt, under air.^b Isolated yield.^c Yield of 4-nitrosoanisole in parentheses .^d -20°C.**Table 3**IC₅₀^a for compounds **2a–j** in several tumor cell lines.

	B16-F10	HL-60	HT-1080	DLD-1	MCF-7
2a	7.17 ± 4.02	8.20 ± 2.72	13.2 ± 6.7	8.09 ± 3.05	14.2 ± 7.2
2b	5.60 ± 4.21	6.85 ± 1.01	9.77 ± 5.00	6.17 ± 1.26	10.2 ± 0.9
2c	2.43 ± 1.23	3.63 ± 0.73	3.97 ± 1.84	3.26 ± 1.45	3.78 ± 1.80
2d	6.78 ± 3.71	8.36 ± 2.76	7.82 ± 3.67	8.13 ± 4.24	13.4 ± 1.0
2e	3.85 ± 1.80	7.20 ± 3.64	8.76 ± 3.81	8.30 ± 3.66	7.16 ± 3.69
2f	3.91 ± 2.11	5.42 ± 1.13	5.48 ± 1.40	6.66 ± 3.09	7.22 ± 2.48

2g	3.20 ± 1.31	5.54 ± 1.84	7.39 ± 5.01	5.04 ± 1.30	5.69 ± 2.53
2h	4.43 ± 0.88	3.68 ± 0.86	5.38 ± 1.28	4.37 ± 1.34	5.23 ± 2.34
2i	34.2 ± 12.3	31.8 ± 7.1	40.1 ± 14.2	43.8 ± 19.5	30.3 ± 11.4
2j	5.13 ± 1.49	15.2 ± 11.1	10.4 ± 1.2	6.63 ± 2.12	12.2 ± 0.3

^a IC₅₀ values (μM) were showed the mean ± SD.