Full Length Articles

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

Yuki Kitamura,[a] Mio Matsumura,[a] Yuki Murata,[a] Mizuki Yamada,[a] Naoki Kakusawa,[b] Motohiro Tanaka,[a] Hiroyuki Okabe,[c] Hiroshi Naka,[c,**] Tohru Obata,[a,***] Shuji Yasuike[a,*]

[a]*School of Pharmaceutical Sciences, Aichi Gakuin University, 1-100 Kusumoto-cho, Chikusa-ku, Nagoya 464-8650, Japan*

[b]*Faculty of Pharmaceutical Sciences, Hokuriku University, Ho-3 Kanagawa-machi, Kanazawa 920-1181, Japan*

[c]*Research Center for Materials Science and Graduate School of Science, Nagoya University, Chikusa, Nagoya 464-8602, Japan*

*Corresponding author.

**Corresponding author.

***Corresponding author.

E-mail address: s-yasuik@dpc.agu.ac.jp (S. Yasuike)

h_naka@nagoya-u.jp (H. Naka)

tobata@dpc.aichi-gakuin.ac.jp (T. Obata)

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

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.

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], IF_5 [16], F_2 [17], Et_2NSF_3 [7], methyl 3-azidotetrafluoropropionate ($N_3CF_2CF_2CO_2Me$) [18], and triphenylbismuth difluoride (Ph_3BiF_2) [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., $HBF_4{\cdot}OEt_2$, $NOBF_4$, and Bu_4NBF_4) and boron trifluoride (e.g., $BF_3{\cdot}OEt_2$) 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 NB_4, 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 ($NOBF_4$) 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 CH_2Cl_2 at room temperature under aerobic conditions (entries 1–11). Among these reagents, $NOBF_4$, NO_2BF_4, and IPy_2BF_4 afforded the expected triphenylantimony difluoride (**2a**) in good to high yields (entries 3–5). $NOBF_4$ 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 $NOBF_4$ (entries 3, 12–14). The best result was observed in the reaction of **1a** with $NOBF_4$ in the ratio 1:2 (entry 3). It seems that one of the four fluorine atoms on the B atom in $NOBF_4$ was involved in the antimony–fluorine bond formation. Moreover, an excess amount of $NOBF_4$ seems to injure the product (entry 14). Screening of solvent showed that the reaction proceeded effectively in CH_2Cl_2 (84%), toluene (71%), and CH_3CN (59%). Other solvents such as tetrahydrofuran and MeOH could not be used because of the poor solubility and low stability of $NOBF_4$. Consequently, the best result was obtained when **1a** was treated with $NOBF_4$ (2 eq) in CH_2Cl_2 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 Ar_3Sb (**1b–m**) and $NOBF_4$ were investigated under the optimized conditions. The results are shown in Table 2. The yields of Ar_3SbF_2 were sensitive to the electronic nature of the substituents on the phenyl rings. The Ar_3Sb 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 $NOBF_4$ at room temperature gave the expected **2b** in 25% yield and 4-nitrosoanisole as a side product in 24% yield (entry 1). It was assumed that 4-nitrosoanisole was formed by the nitroso-induced *ipso*-deantimonation of **1b** with $NOBF_4$. Therefore, the reaction of **1b** and $NOBF_4$ 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 $NOBF_4$ 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 $NOBF_4$ [31, 32]. Fig. 1 shows a possible mechanism for the synthesis of triarylantimony difluorides from Ar_3Sb and $NOBF_4$. 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 $H_2N_2O_2$ (**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 (IC_{50} = 5.13–15.2 μM). 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*-Tol_3SbF_2 (**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. ^{1}H NMR (TMS: δ: 0.00 ppm or CH_2Cl_2: 5.30 ppm as an internal standard) and ^{13}C NMR ($CDCl_3$: δ: 77.00 ppm as an internal standard) spectra were recorded on JEOL JNM-AL400 (400 MHz and 100 MHz respectively) spectrometers in $CDCl_3$. ^{19}F NMR (α,α,α-trifluorotoluene: δ: –64.0 ppm as an internal standard) spectra were recorded on JEOL ECA-600 spectrometers in $CDCl_3$. Mass spectra were obtained on a JEOL JMP-DX300 instrument (70 eV, 300 μA). 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 F_{254}). 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 CH_2Cl_2 (3.0 mL) was added $NOBF_4$ (1.0

mmol) at –20 or 0 ºC. The reaction mixture was stirred at –20 ºC or room temperature for the indicated time (2–5 h) until complete consumption of the starting material, as monitored by TLC. After dilution with CH_2Cl_2 (20 mL) and water (20 mL), the organic layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (20 mL × 2). The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (**2a**, **c**–**e**, **h**, and **2j** : *n*-hexane:Et_2O = 5:1, **2b**: CH_2Cl_2), 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 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ : 7.52–7.53 (m, 9H, Ar-H), 8.14–8.19 (m, 6H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 129.5, 132.1, 134.1 (t, $^2J_{C,F}$ = 15.3 Hz), 135.3 (t, $^3J_{C,F}$ = 5.0 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ : –153.5 (s, 2F). LRMS (EI): *m/z* 390 (M^+, 20%), 313 (95%), 154 (100%). HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{15}F_2Sb$: 390.0180. Found: 390.0183.

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

Brown oil (108 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ : 3.83 (s, 9H, Me), 7.04 (d, 6H, *J* = 8.8 Hz, Ar-H), 8.04–8.07 (m, 6H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{19}F NMR (565 MHz, $CDCl_3$) δ : –151.1 (s, 2F); LRMS (EI): *m/z* 480 (M^+, 45%), 373 (100%), 214 (90%); HRMS: *m/z* $[M]^+$ calcd for $C_{21}H_{21}F_2O_3Sb$: 480.0494. Found: 480.0497.

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

Colorless prism (153 mg, 71%), mp 113–115 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ : 21.4, 130.2, 130.9 (t, $^2J_{C,F}$ = 15.2 Hz), 135.1 (t, $^3J_{C,F}$ = 5.0 Hz), 142.5;

^{19}F NMR (565 MHz, $CDCl_3$) δ: –152.8 (s, 2F). LRMS (EI): *m/z* 432 (M^+, 10%), 341 (100%), 182 (80%). HRMS: *m/z* $[M]^+$ calcd for $C_{21}H_{21}F_2Sb$: 432.0650. Found: 432.0652.

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

Colorless plates (176 mg, 79%), mp 65–67 ºC (from *n*-hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.22–7.27 (m, 6H, Ar-H), 8.13–8.27 (m, 6H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 117.0 (d, $^2J_{C,F}$ = 16.6 Hz), 128.6 (td, $^2J_{C,F}$ = 16.5, 3.3 Hz), 137.5 (dt, $^3J_{C,F}$ = 9.0, 5.0 Hz), 165.6 (d, $^1J_{C,F}$ = 253.2 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) 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 $C_{18}H_{12}F_2Sb$: 443.9897. Found: 443.9894.

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

Pale yellow plates (210 mg, 85%), mp 114–116 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52–7.54 (m, 6H, Ar-H), 8.06–8.08 (m, 6H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 130.0, 131.5 (t, $^2J_{C,F}$ = 16.1 Hz), 136.5 (t, $^3J_{C,F}$ = 5.4 Hz), 139.4; ^{19}F NMR (565 MHz, $CDCl_3$) δ: –152.7 (s, 2F); LRMS (EI): *m/z* 494 (M^+, 15%), 383 (100%), 222 (80%); HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{12}Cl_3F_2Sb$: 493.8981. Found: 493.8977.

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

Pale yellow plates (270 mg, 86%), mp 111–113 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, 6H, *J* = 7.8 Hz, Ar-H), 7.99 (d, 6H, *J* = 8.8 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 128.0, 132.0 (t, $^2J_{C,F}$ = 15.7 Hz), 132.8, 136.6 (t, $^3J_{C,F}$ = 4.1 Hz); ^{19}F NMR (565 MHz, $CDCl_3$) δ: –153.1 (s, 2F). LRMS (FAB): *m/z* 625 (M^+, 10%), 609 (100%), 297 (10%). HRMS: *m/z* $[M]^+$ calcd for $C_{18}H_{12}Br_3F_2Sb$: 625.7475. Found: 625.7478.

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

Colorless needles (258 mg, 85%), mp 121–123 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.40 (t, 9H, *J* = 7.3 Hz, Me), 4.41 (q, 6H, *J* = 7.3 Hz, CH_2), 8.20 (d, 6H, *J* = 8.3 Hz, Ar-H), 8.26 (d, 6H, *J* = 8.3 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) 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; ^{19}F NMR (565 MHz, $CDCl_3$) δ: –152.4 (s, 2F). LRMS (FAB): *m/z* 606 (M^+, 25%), 587 (100%), 253 (15%). HRMS: *m/z* $[M]^+$ calcd for $C_{27}H_{27}F_2O_6Sb$: 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 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, 6H, *J* = 7.8 Hz, Ar-H), 8.32 (d, 6H, *J* = 7.8 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) 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); ^{19}F NMR (565 MHz, $CDCl_3$) 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 $C_{21}H_{12}F_{11}Sb$: 593.9802. Found: 593.9806.

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

Colorless prism (182 mg, 78%), mp 147–150 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.85 (d, 6H, *J* = 7.8 Hz, Ar-H), 8.29 (d, 6H, *J* = 7.8 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$) 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); ^{19}F NMR (565 MHz, $CDCl_3$) δ: –154.5 (s, 2F); LRMS (EI): *m/z* 465 (M^+, 5%), 363 (100%), 242 (35%). HRMS: *m/z* $[M]^+$ calcd for $C_{21}H_{12}F_2N_3Sb$: 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 ºC (from *n*-hexane–CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) 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, $^{4}J_{C,F}$ = 2.5 Hz), 126.5, 131.6 (t, $^{3}J_{C,F}$ = 9.9 Hz), 135.0, 136.8 (t, $^{2}J_{C,F}$ = 15.7 Hz), 142.9; ^{19}F NMR (565 MHz, $CDCl_3$) δ: –112.0 (s, 2F); LRMS (EI): *m/z* 414 ($[M\text{-}F]^+$, 70%), 412 (95%), 341 (100%). HRMS: *m/z* $[M\text{-}F]^+$ calcd for $C_{21}H_{21}FSb$: 414.0744. Found: 414.0740.

4.3. Antitumor activity

Mouse melanoma cells B16-F10, human promyelocytic leukemia cells HL-60, human fiblosarcoma 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: IR (%) = (1 – T/C) × 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.

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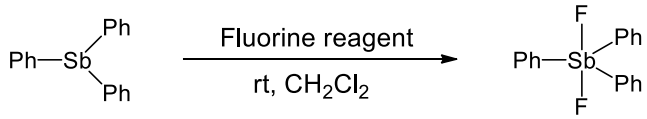
Table 1

Reaction of triphenylstibane **1a** with fluorine reagents.[a]



1a **2a**

Entry	Reagent (eq)	Time (h)	Yield (%)[b]	
			2a	Recovery
1	$HBF_4{\cdot}Et_2O$ (2)	24	4	92
2	$Bu_4N{\cdot}BF_4$ (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

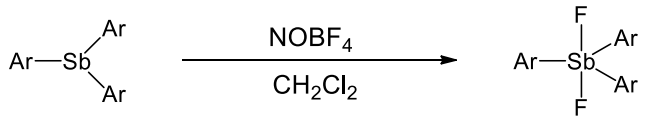
[a] Conditions: **1a** (0.5 mmol), CH_2Cl_2 (3 mL), rt, under air.

[b] Isolated yield.

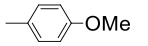
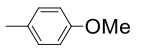
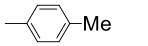
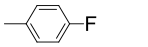
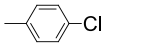
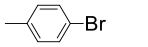
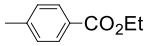
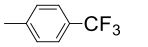
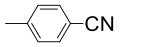
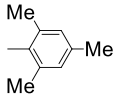
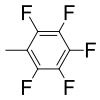
[c] **1a** (10 mmol), CH_2Cl_2 (60 mL).

Table 2

Synthesis of triarylantimony difluorides.[a]



1b-m **2b-m**

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), $NOBF_4$ (1.0 mmol), CH_2Cl_2 (3 mL), rt, under air.
[b] Isolated yield.
[c] Yield of 4-nitrosoanisole in parentheses .
[d] –20°C.

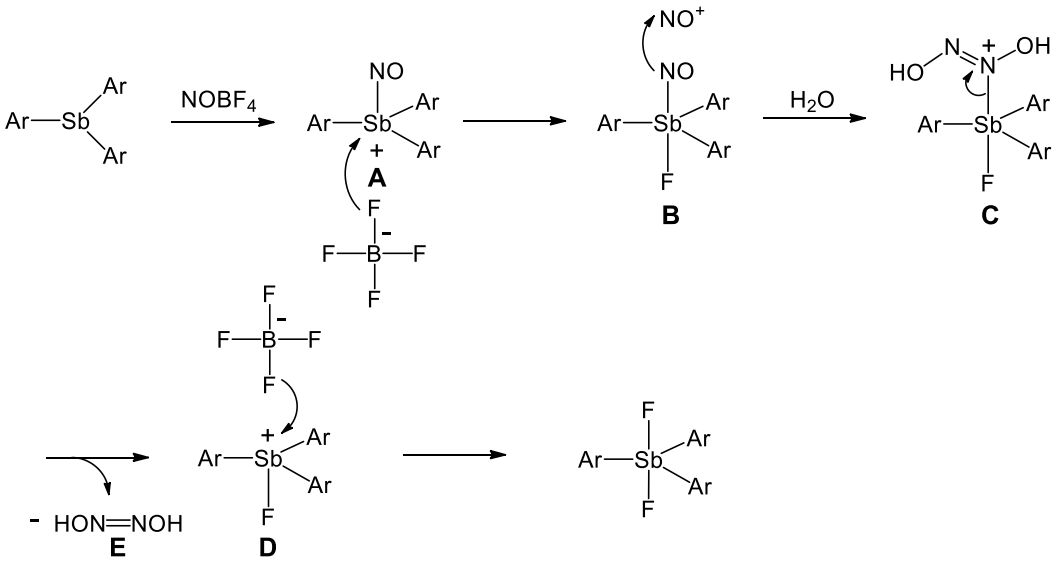


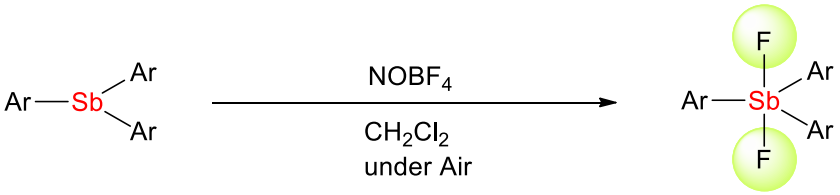
Fig. 1. Possible Mechanism

Table 3

IC_{50}[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] IC_{50} values (μM) were showed the mean ± SD.



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

Supporting information

X-ray structure of compound **2i**.

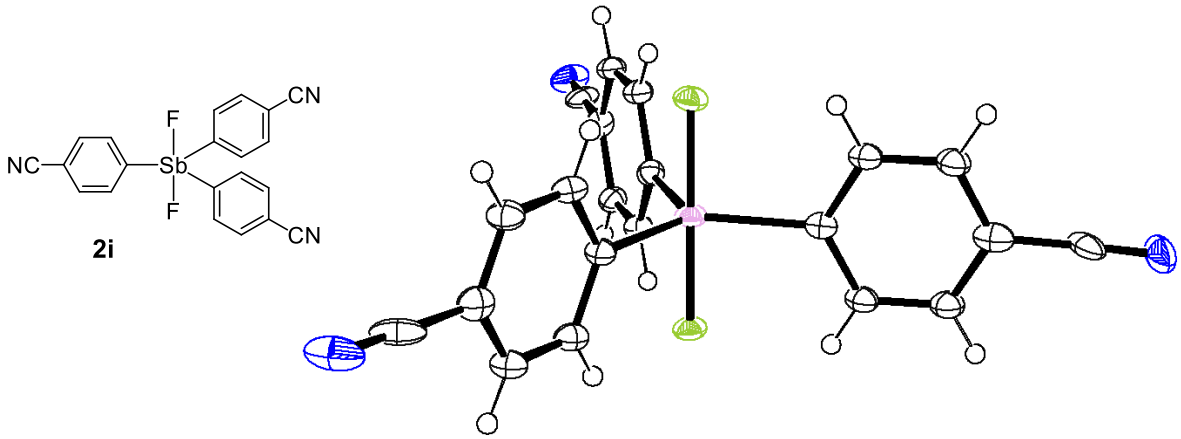


Fig. 1. ORTEP drawing of compound **2i** with 50% probability.

The crystal data of **2i** remains a matter of solution due to the low quality of the crystal measured, but the structure of pentavalent antimony was sure.

The structure has the problems such as follow.

- This structure contains poorly resolved solvate molecules.
- Failure to treat them by modeling as disorder resulted in high occupancy of other groups.