BrF_3-KHF_2: An air-stable fluorinating reagent

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Abstract

BrF_3-KHF_2, an air-stable solid prepared from BrF_3 and KHF_2, was used in the various fluorination reactions, including desulfurizing fluorination reactions of benzylic sulfides, ketone and aldehyde dithioacetals, (phenylthio)glycosides, and trimethyl trithioorthocarboxylates. As the results, one to three fluorine atoms were selectively introduced to the substrates.

1. Introduction

Organofluorine compounds are widely used, as medicines, pesticides, functional materials, and so on [1]. They are generally prepared artificially using fluorinating reagents because organofluorine compounds are rare in nature. Therefore, the role of the fluorinating reagent is important for synthesizing desired organofluorine compounds, and many fluorinating reagents have been produced and used [2]. However, most of them are sensitive to moisture, and special skills and equipments are required for their use. Therefore, stable fluorinating reagent is desirable [3]. Recently, we reported the

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preparation of a new stable fluorinating reagent, IF_5-pyridine-HF, and its use in various fluorination reactions [4]. BrF_3 has been also used as a fluorinating reagent, and is more reactive than IF_5 [5]. Therefore, we attempted to synthesize a new stable fluorinating reagent from BrF_3.

2. Results and discussion

BrF_3 is known to make a complex of MBF_4 where M is Cs, Rb, K [6], or Me_4N [7]. However, their ability as a fluorinating reagent has not yet been studied. We attempted to synthesize a stable complex from BrF_3. Addition of BrF_3 to KF in CH_2Cl_2 was performed at -78 °C, and the cooling bath was removed. When the temperature reached room temperature, a violent exothermal reaction took place. As BrF_3 violently reacts with CH_2Cl_2 at room temperature, this result shows that free BrF_3 remains in the mixture and causes the violent reaction. On the other hand, when BrF_3 was added to an excess amount of KHF_2 in CH_2Cl_2, the exothermal reaction did not occur even after reaching room temperature. A slightly reddish supernatant was removed by decantation and the remaining solid was washed with CH_2Cl_2 several times. The remaining solvent was removed by blowing a nitrogen gas to the solid. The resulting pale yellow solid is air-stable and can be stored in a Teflon™ bottle in the refrigerator [8]. We applied this BrF_3-KHF_2 complex in various fluorination reactions.

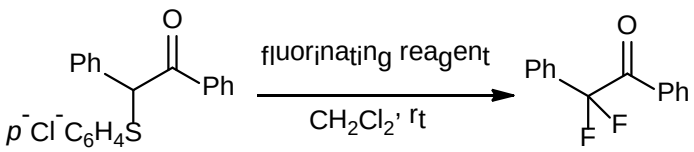
*2.1. Desulfurizing difluorination of benzylic sulfide **1** using BrF_3-KHF_2*

Initially, BrF_3-KHF_2 was used in a desulfurizing difluorination reaction of benzylic sulfide. When 2-[4-chlorophenyl)thio]-1,2-diphenyletanone (**1a**) was added to a

suspension of BrF_3-KHF_2 in CH_2Cl_2 at room temperature, the solution color became dark red, and 2,2-difluoro-1,2-diphenylethanone (**2a**) was formed in 88% yield. Although the yield of **2a** was comparable to that obtained by using IF_5-pyridine-HF [4a], the reaction was completed in a shorter time (15 min versus 5 h) (Table 1).

Table 1

Comparison of reactivity of BrF_3-KHF_2 and IF_5-pyridine-HF in desulfurizing difluorination of **1a** [a]



1a **2a**

Entry	Fluorinating reagent	Reaction time	Yield of **2a**(%)[b]
1	IF_5-pyridine-HF	5 h	88
2	BrF_3-KHF_2	15 min	89

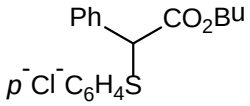
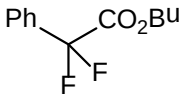
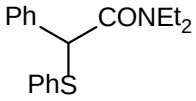
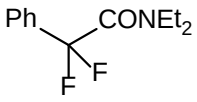
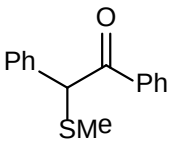
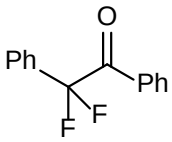
[a] 2eq of fluorinating reagent to **1a** was used.

[b]Isolated yield based on **1a** used.

In the reaction of BrF_3-KHF_2 with benzylic sulfides containg an electron-withdrawing group (**1b**-**d**), the corresponding desulfurizing difluorination products (**2a**-**c**) were obtained in high yields as shown in Table 2.

Table 2

Desulfurizing difluorination of **1** with BrF_3-KHF_2 [a]

Entry	Substrate **1**	Reacion time	Product **2**	Yield (%)[b]
1	 **1b**	3 h	 **2b**	(84)
2	 **1c**	15 min	 **2c**	76 (85)[c]
3	 **1d**	15 min	 **2a**	91 (99)[c]

[a]If otherwise not mentioned, the reaction was carried out in CH_2Cl_2 at room temperature using 2 eq of BrF_3-KHF_2 to **1**.

[b]Isloated yield based on **1** used. In parentheses, ^{19}F NMR yield.

[c]3eq of BrF_3-KHF_2 to **1** was used.

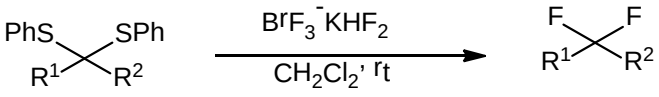
*2.2. Reaction of aldehyde and ketone dithioacetal **3** with BrF_3-KHF_2*

BrF_3-KHF_2 was also applied to the reaction with the ketone and aldehyde dithioacetals [3c, 5b, 9]. Reactions with diphenyl dithioacetals of aldehydes (**3a-c**) and ketones (**3d,e**) were completed in 1 h, and the corresponding *gem*-difluorides (**4a-e**) were obtained in

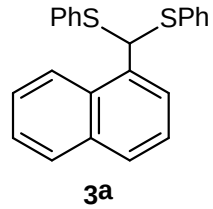
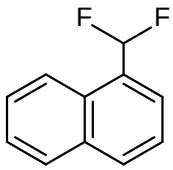
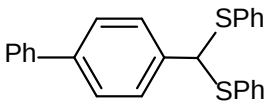
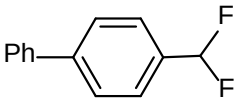
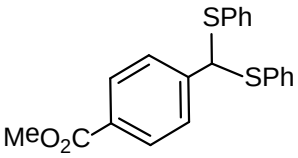
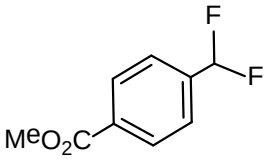
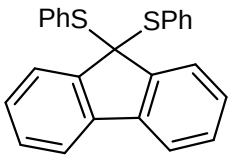
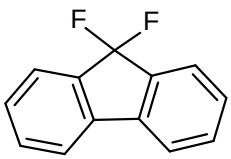
good yields, as shown in Table 3.

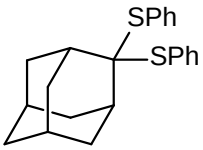
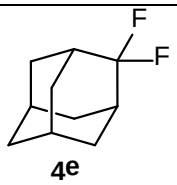
Table 3.

The reaction of aldehyde and ketone thioacetals with BrF_3-KHF_2 [a]



3 **4**

Entry	Substrate **3**	Reacion time (min)	Product **4**	Yield (%)[b]
1	 **3a**	45	 **4a**	(91)
2	 **3b**	45	 **4b**	81(90)
3	 **3c**	15	 **4c**	91(99)
4	 **3d**	45	 **4d**	(84)

5	 **3e**	60	 **4e**	(81)[c]

[a]If otherwise not mentioned, the reaction was carried out at room temperature using 2.2 eq of BrF_3-KHF_2 to **3**.

[b]Isolated yield based on **3**. In parentheses, ^{19}F NMR yield.

[c]The reaction was carried out at 0 °C.

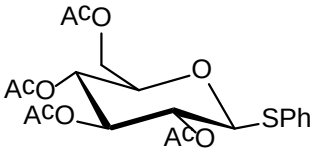
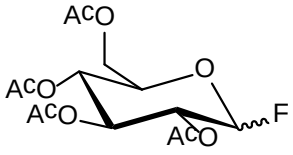
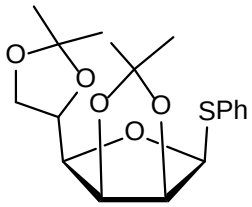
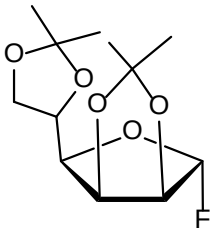
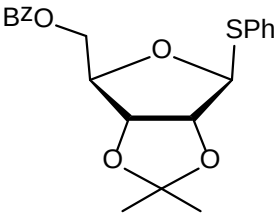
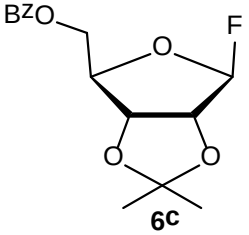
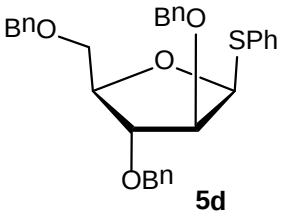
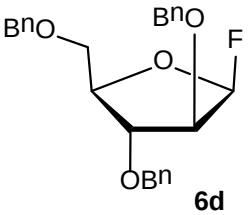
*2.3. Synthesis of glycosyl fluorides **6** by the reaction of (phenylthio)glycosides **5** with BrF_3-KHF_2*

Glycosyl fluorides have been widely used as glycosyl donors in glycosidation reactions [10]. They are generally prepared from the corresponding thioglycosides using a fluorination reagent with or without an oxidizing agent [11]. We applied BrF_3-KHF_2 for the synthesis of glycosyl fluorides (**6**) from the corresponding (phenylthio)glycosides (**5**). Both pyranosyl fluoride (**6a**) and furanosyl fluorides (**6b-d**) were prepared in good yield by the reaction of the corresponding (phenylthio)glycosides (**5a-d**) with BrF_3-KHF_2 in CH_2Cl_2 (Table 4). In the reaction with furanosyl derivatives, only one isomer was selectively formed (Entries 2-4).

Table 4.

The reaction of (phenylthio)glycosides with BrF_3-KHF_2 [a]

Entry	Substrate **5**	Reacion	Product **6**	Yield

		time		(%)[b]
1	 **5a**	4 h	 **6a**	83(86)[c] (α : β = 63:37)
2	 **5b**	15 min	 **6b**	89(94)[d] α only
3	 **5c**	15 min	 **6c**	87 β only
4	 **5d**	15 min	 **6d**	(66) β only

[a]If otherwise not mentioned, the reaction was carried out at room temperature using 1.1 eq of BrF_3-KHF_2 to **5**.

[b]Isolated yield based on **5**. In parentheses, ^{19}F NMR yield.

[c] 1.5 eq of BrF_3-KHF_2 to **5** was used.

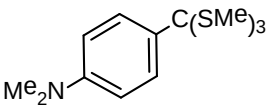
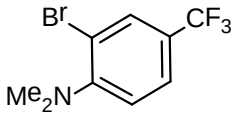
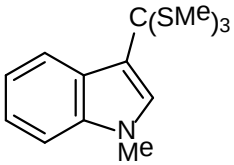
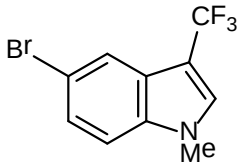
[d] The reaction was carried out at 0 °C.

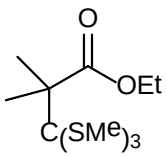
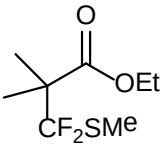
*2.4. Reaction of trimethyl trithioorthocarboxylates **7** with BrF_3-KHF_2*

A tris(methylthio)methyl group can be introduced to the electron rich aromatic ring and α-position of the ester group by a reaction with tris(methylthio)methyl cation species generated from dimethyl trithiocarbonate [12]. The reaction of *N*,*N*-dimethyl-4-[tris(methylthio)methyl]aniline (**7a**) with BrF_3-KHF_2 was completed in 15 min at 0 °C, and the tris(methylthio)methyl group was converted to the trifluoromethyl group. However, bromination at the aromatic ring took place concurrently and 2-bromo-*N*,*N*-dimethyl-4-(trifluoromethyl)aniline (**8a**) was formed in moderate yield (Entry 1 in Table 5). Similarly, in the reaction of *N*-methyl-3-tris(methylthio)methylindole (**7b**), 5-bromo-1-methyl-3-(trifluoromethyl)-1*H*-indole (**8b**) was obtained selectively (Entry 2). On the other hand, in the reaction of ethyl 2,2-dimethyl-3,3,3-tris(methylthio)propanoate (**7c**) with BrF_3-KHF_2, only two fluorine atoms were introduced and one methylthio group remained (Entry 3).

Table 5.

Reaction of trimethyl trithioorthocarboxylates **7** with BrF_3-KHF_2 [a]

Entry	Substrate **7**	Reacion time	Product **8**	Yield (%)[b]
1	 **7a**	15 min	 **8a**	52 (62)
2	 **7b**	15 min	 **8b**	76 (83)

3	 **7c**	1 h	 **8c**	81

[a]The reaction was carried out in CH_2Cl_2 at 0 °C using 3.2 eq of BrF_3-KHF_2 to **7**.

[b]Isolated yield based on **7**. In parentheses, ^{19}F NMR yield.

3. Conclusion

A new air-stable fluorinating reagent, BrF_3-KHF_2, was prepared by the reaction of BrF_3 with KHF_2. The reagent was shown to be more reactive than the previously reported IF_5-pyridine-HF in desulfurizing difluorination reaction of the benzylic sulfide. The reagent was successively applied to desulfurizing fluorination reactions of dithioacetals, (phenylthio)glycosides, and trimethyl trithioorthocarboxylates.

4. Experimental

4.1. General

The melting points were measured with a Yanagimoto micro melting-point apparatus. The IR spectra were recorded using a JASCO FT/IR-410. The ^1H NMR (400 MHz) spectra, ^{19}F NMR (376 MHz) spectra, and ^{13}C NMR (100 MHz) were recorded in $CDCl_3$ on a JEOL JNM-A400II FT NMR and the chemical shift, δ, is referred to TMS (^1H, ^{13}C) and $CFCl_3$ (^{19}F), respectively. BrF_3 in a cylinder was purchased from Galaxy Chemicals, LLC and used without purification. BrF_3 was transferred from cylinder to a Teflon™ bottle through a Teflon™ tube using nitrogen pressure. BrF_3 decomposes in air

by humidity under emitting HF fume, and should be handled in a bench hood with rubber-gloved hands under nitrogen atmosphere. BrF_3 reacts violently with most of organic solvents at room temperature and a special care is required for its use.

4.2. Preparation of BrF_3-KHF_2

To a suspension of KHF_2 (3.4 g, 44 mmol) in CH_2Cl_2 (10 mL) in a Teflon™ bottle, BrF_3 (3.0g, 22 mmol) was slowly added through a Teflon™ tube at –78 °C. The resulting mixture was stirred at –78 °C for 30 min, and the cooling bath was removed and temperature was allowed to reach room temperature. A slightly reddish supernatant was removed using a Teflon™ pipette, and the remaining solid was washed with CH_2Cl_2 (10 mL) several times, until CH_2Cl_2 became almost colorless. The remaining solvent was removed by stirring under nitrogen stream for a few hours. The resulting pale yellow solid (5.4 g) was stored in a Teflon™ bottle in the refrigerator. It is slightly hygroscopic, and therefore, it should be used as quickly as possible to minimize contact with moisture.

*4.2. Desulfurizing difluorination of benzylic sulfides **1** with BrF_3-KHF_2*

*4.2.1. 2,2-Difluoro-1,2-diphenylethanone (**2a**)*

To a suspension of BrF_3-KHF_2 (129 mg) in CH_2Cl_2 (2.4 mL) in Teflon™ bottle, **1a** (101 mg, 0.3 mmol) in CH_2Cl_2 (1.0 mL) was added at room temperature, and the mixture was stirred at room temperature for 15 min. Then, H_2O (5 mL) was added to the reaction mixture and the resulting product was extracted with CH_2Cl_2 (5 mL X 3). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (5 mL) and

saturated aqueous $Na_2S_2O_3$ (5 mL), and dried over $MgSO_4$. After concentration under reduced pressure, **2a** was isolated by column chromatography (silica gel, hexane-ether) in 89% yield. IR (neat) 1703 (C=O), 1450, 1256, 1135 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 7.43-7.61 (m, 8H), 8.02-8.04 (m, 2H); ^{19}F NMR (376MHz, $CDCl_3$) δ –98.12 (s, 2F); ^{13}C NMR (100MHz, $CDCl_3$) δ 188.9 (t, $^2J_{C-F}$ = 30.7 Hz), 134.2, 133.1 (t, $^2J_{C-F}$ = 24.9 Hz), 132.1, 130.9, 130.3 (t, $^4J_{C-F}$ = 2.9 Hz, 2C), 128.8 (2C), 128.6 (2C), 125.6 (t, $^3J_{C-F}$ = 5.8 Hz, 2C), 116.9 (t, $^1J_{C-F}$ = 253.9 Hz); HRMS (EI) calcd for $C_{14}H_{10}F_2O$ 232.0700, found 232.0683.

*4.2.2. Butyl 2,2-difluoro-2-phenylacetate (**2b**)*

IR (neat) 2963, 1764 (C=O), 1265, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62-7.60 (m, 2H), 7.49-7.45 (m, 3H), 4.24 (t, *J* = 6.6 Hz, 2H), 1.68-1.60 (m, 2H), 1.37-1.28 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ –104.65 (s, 2F); ^{13}C NMR (100 MHz) δ 164.3 (t, $^2J_{C-F}$ = 35.7 Hz), 132.8 (t, $^2J_{C-F}$ = 25.8 Hz), 130.9, 128.6 (2C), 125.4 (t, $^3J_{C-F}$ = 6.2 Hz, 2C), 113.4 (t, $^1J_{C-F}$ =251.9 Hz), 66.8, 30.2, 18.9, 13.5; HRMS (EI) calcd for $C_{12}H_{14}F_2O_2$ 228.0962, found 228.0956.

*4.2.3. N,N-Diethyl-2,2-difluoro-2-phenylacetamide (**2c**)*

IR (neat) 2979, 1669 (C=O), 1452, 1364, 1260, 1093 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.0 Hz, 2H), 7.44-7.49 (m, 3H), 3.42 (q, *J* = 7.2 Hz, 2H), 3.25 (q, *J* = 7.2 Hz, 2H), 1.17 (t, *J* = 7.2Hz, 3H), 1.03 (t, *J* = 7.0 Hz, 3H); ^{19}F NMR (376MHz, $CDCl_3$) δ –95.41 (s, 2F); ^{13}C NMR (100MHz, $CDCl_3$) δ 162.7 (t, $^2J_{C-F}$ = 29.7 Hz), 133.9 (t, $^2J_{C-F}$ = 23.6 Hz), 130.7 (t, $^4J_{C-F}$ = 1.9 Hz, 2C), 128.7, 125.1 (t, $^3J_{C-F}$ = 5.8 Hz, 2C),

115.5 (t, $^{1}J_{C\text{-}F}$ = 251.5 Hz), 42.0 (t, $^{4}J_{C\text{-}F}$ = 3.8 Hz), 41.4, 13.7, 12.2; HRMS(EI) calcd for $C_{12}H_{15}F_2NO$ 227.1122, found 227.1128.

*4.3. The reaction of aldehyde and ketone thioacetals **3** with BrF_3-KHF_2*

*4.3.1. 1-(Difluoromethyl)naphthalene (**4a**)*

The reaction was carried out as in the case of **2a** using 2.2 eq of BrF_3-KHF_2 to **3a**, and yield of **4a** was determined to be 91 % by ^{19}F NMR using fluorobenzene as an internal standard. IR (neat) 1514, 1349, 1242 cm^{-1}; ^{1}H NMR δ 8.19-7.49 (m, 7H), 7.14 (t, *J* = 55.8 Hz, 1H); ^{19}F NMR δ -111.48 (d, *J* = 56.0 Hz, 2F) (lit.[13] –111.38 (d, *J* = 55.2 Hz)); ^{13}C NMR δ 133.7, 131.5, 129.7, 129.5 (t, $^{2}J_{C\text{-}F}$ = 21.1 Hz), 128.7, 127.1, 126.4, 124.8 (t, $^{3}J_{C\text{-}F}$ = 8.6 Hz), 124.6, 123.5, 115.4 (t, $^{1}J_{C\text{-}F}$ = 239.5 Hz).

*4.3.2. 4-(Difluoromethyl)-1,1'-biphenyl (**4b**)*

White solid. mp 71-72 °C (lit.[14] 77.0-77.5 °C); IR (KBr) 1414, 1380, 1226, 1077, 1024, 767 cm^{-1}; ^{1}H NMR δ 7.69-7.39 (m, 9H), 6.70 (t, *J* = 56.5 Hz, 1H); ^{19}F NMR δ –110.98 (d, *J* = 57.3 Hz, 2F); ^{13}C NMR δ 143.7 (t, $^{5}J_{C\text{-}F}$ = 1.9 Hz), 140.2, 133.2 (t, $^{2}J_{C\text{-}F}$ = 22.1 Hz), 128.9 (2C), 127.9, 127.4 (2C), 127.2 (2C), 126.0 (t, $^{3}J_{C\text{-}F}$ = 6.2 Hz, 2C), 114.7 (t, $^{1}J_{C\text{-}F}$ = 238.5 Hz).

*4.3.3. Methyl 4-(difluoromethyl)benzoate (**4c**)*

White solid. mp 38 °C (lit.[15] 36.5-37.0 °C); IR (KBr) 1724 (C=O), 1442, 1281 cm^{-1}; ^{1}H NMR δ 8.13 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 8.1 Hz, 2H), 6.70 (t, *J* = 56.7 Hz,

1H), 3.95 (s, 3H); ^{19}F NMR δ –112.86 (d, *J* = 57.9 Hz, 2F); ^{13}C NMR δ 166.2, 138.4 (t, $^{2}J_{C\text{-}F}$ = 22.5 Hz), 132.3, 129.9 (2C), 125.6 (t, $^{3}J_{C\text{-}F}$ = 6.3 Hz, 2C), 114.0 (t, $^{1}J_{C\text{-}F}$ = 240.9 Hz), 52.3.

*4.3.4. 9,9-Difluoro-9H-fluorene (**4d**)*

White solid. mp 46-48 °C (lit.[16] 47-48 °C). IR (KBr) 1918, 1454, 1261 cm^{-1}; ^{1}H NMR δ 7.62 (d, *J* = 7.0 Hz, 2H), 7.56 (d, *J* = 7.3 Hz, 2H), 7.45 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.33 (dd, *J* = 7.6, 7.6 Hz, 2H); ^{19}F NMR δ –112.12 (s, 2F); ^{13}C NMR δ 139.4 (t, $^{3}J_{C\text{-}F}$ = 5.3 Hz, 2C), 137.9 (t, $^{2}J_{C\text{-}F}$ = 25.1 Hz, 2C), 132.0 (2C), 128.7 (2C), 123.7 (2C), 123.2 (t, $^{1}J_{C\text{-}F}$ = 244.0 Hz), 120.3 (2C).

*4.3.5. 2,2-Difluoroadamantane (**4e**)*

White solid. mp 102-103 °C (lit.[17] 104-105 °C); IR (KBr) 2938, 2917, 1389, 1121 cm^{-1}; ^{1}H NMR δ 2.18 (brs, 2H), 1.97 (brs, 2H), 1.94 (brs, 2H), 1.86 (brs, 2H), 1.78-1.72 (m, 6H); ^{19}F NMR δ –100.41 (s, 2F); ^{13}C NMR δ 125.5 (t, $^{1}J_{C\text{-}F}$ = 248.2 Hz), 36.6 (2C), 35.8 (t, $^{2}J_{C\text{-}F}$ = 4.0 Hz, 2C), 34.0 (t, $^{3}J_{C\text{-}F}$ = 4.0 Hz, 4C), 26.4.

*4.4. The reaction of phenylthioglycosides **5** with BrF_3-KHF_2*

*4.4.1. 2,3,4,5-Tetra-O-acetyl-D-glucopyranosyl fluoride (**6a**)*

The reaction was carried out as in the case of **2a** using 1.5 eq of BrF_3-KHF_2 to **5a**, and **6a** was isolated in 83% yield. The ratio of α-isomer : β-isomer was determined to be 63:37 from ^{1}H NMR spectra. (**6a-α**) mp 104-106 °C. IR (neat) 2958, 1748 (C=O),

1379, 1230, 1038 cm^{-1}. ^{1}H NMR δ = 5.76 (dd, *J* = 53.4, 2.76 Hz, 1H), 5.50 (dd, *J* = 9.9, 9.9 Hz, 1H), 5.16 (dd, *J* = 9.9, 9.9 Hz, 1H), 4.96 (ddd, *J* = 24.6, 10.4, 2.8 Hz, 1H), 4.29 (dd, *J* = 12.2, 3.8 Hz, 1H), 4.21-4.13 (m, 2H), 2.14 (s, 3H), 2.11 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H); ^{19}F NMR δ –150.34 (dd, *J* = 52.5, 25.3 Hz, 1F); ^{13}C NMR δ = 170.5, 169.9, 169.8, 169.4, 103.7 (d, $^{1}J_{C-F}$ = 228.8 Hz), 70.1 (d, $^{2}J_{C-F}$ = 24.8 Hz), 69.7 (d,$^{3}J_{C-F}$ = 4.1Hz), 69.3, 67.2, 61.1, 20.6, 20.5, 20.4 (2C). (**6a-β**) mp 77-78 °C. IR (neat) 2942, 1761, 1439, 1378, 1227, 1109, 1042 cm^{-1}; ^{1}H NMR δ 5.37 (dd, *J* = 52.0, 6.1 Hz, 1H), 5.22-5.20 (m, 2H), 5.18-5.08 (brs, 1H), 4.29-4.20 (m, 2H), 3.93-3.88 (s, 1H), 2.11 (s, 6H), 2.05 (s, 6H); ^{19}F NMR δ –137.83 (1F, dd, *J* = 51.9, 10.4 Hz); ^{13}C NMR δ 170.5, 170.0, 169.2, 169.1, 106.1 (d, $^{1}J_{C-F}$ = 219.2 Hz), 72.0 (d, $^{3}J_{C-F}$ = 4.1 Hz), 71.7 (d, $^{3}J_{C-F}$ = 8.3 Hz), 71.1 (d, $^{2}J_{C-F}$ = 28.9 Hz), 67.4, 61.7, 20.6-20.5 (4C); HRMS (EI) calcd for $C_{14}H_{20}O_9F$ (M^{+}+H) 351.1091, found 351.1115.

*2,3;5,6-di-O-Isopropylidene-α-D-mannofuranosyl fluoride (**6b-α**)*

IR (neat) 2989, 1374, 1212, 1130, 1070, 972, 849 cm^{-1}; ^{1}H NMR δ 5.69 (d, *J* = 59.5 Hz, 1H), 4.77-4.43 (m, 2H), 4.43-4.38 (m, 1H), 4.18-4.05 (m, 3H), 1.46 (s, 6H), 1.39 (s, 3H), 1.35 (s, 3H); ^{19}F NMR δ –129.25 (dd, *J* = 59.5, 6.7 Hz, 1F); ^{13}C NMR δ 113.6 (d, $^{1}J_{C-F}$ = 221.6 Hz), 113.2, 109.4, 84.7, (d, $^{2}J_{C-F}$ = 42.2 Hz), 82.6, 78.6, 72.7, 66.6, 26.9, 25.8, 25.1, 24.5; HRMS (EI) calcd for $C_{12}H_{19}O_5F$ (M^{+}+H) 263.1295, found 263.1317.

*4.4.4. 2,3-O-Isopropylidene-5-O-benzoyl-β-D-ribofuranosiyl fluoride (**6c**)*

IR (neat) 2990, 1725, 1273, 1094, 977, 714 cm^{-1}; ^{1}H NMR δ 8.07 (d, *J* = 8.2 Hz, 2H), 7.61-7.56 (m, 1H), 7.48-7.42 (m, 2H), 5.83 (d, *J* = 61.8 Hz, 1H), 4.88-4.85 (m, 2H), 4.71-4.67 (m, 1H), 4.45-4.37 (m, 2H), 1.50 (s, 3H), 1.35 (s, 3H); ^{19}F NMR δ –116.44 (d,

J = 60.9 Hz, 1F){ lit.[18] –115.85 (dq, J = 61.6, 4.0 Hz, 1F)}; ^{13}C NMR δ = 166.1, 133.4, 129.9 (2C), 129.6, 128.5(2C),115.4 (d, $^{1}J_{C\text{-}F}$ = 223.1 Hz), 113.3, 86.5 (d, $^{3}J_{C\text{-}F}$ = 3.2 Hz), 85.1 (d, $^{2}J_{C\text{-}F}$ = 40.8 Hz), 81.0, 64.7, 26.4, 25.0.

*4.4.5. 2,3,5-Tri-O-benzyl-β-D-arabinofuranosyl fluoride (**6d**)*

White solid. mp 78-79 °C (lit.[19] 77-78 °C); IR (KBr) 3062, 3030, 2865, 1454, 1115, 1028, 738, 698 cm^{-1}; ^{1}H NMR δ 7.30-7.17 (m, 15H), 5.79 (d, J = 61.5 Hz, 1H), 4.73-4.45 (m, 7H), 4.17 (dd, J = 9.3, 2.2 Hz, 1H), 3.96 (dd, J = 5.1, 2.0 Hz, 1H), 3.64-3.57 (m, 2H); ^{19}F NMR δ –121.23 (dd, J = 61.6, 9.2 Hz, 1F); ^{13}C NMR δ 137.9, 137.7, 137.2, 127.7-128.5 (15C), 108.3 (d, $^{1}J_{C\text{-}F}$ = 229.9 Hz), 84.5 (d, $^{2}J_{C\text{-}F}$ = 21.5 Hz), 82.4, 81.5, 73.5, 72.6, 72.4, 71.5.

*4.5. Reaction of trimethyl trithioorthocarboxylates **7** with BrF_3-KHF_2*

*4.5.1. 2-Bromo-N,N-dimethyl-4-(trifluoromethyl)aniline (**8a**)*

The reaction was carried out as in the case of **2a** at 0 °C using 3.2 eq of BrF_3-KHF_2 to **7a**, and **8a** was isolated in 52% yield. IR (neat) 2952, 2874, 2842, 2791, 1608, 1324, 1123 cm^{-1}; ^{1}H NMR δ 7.79 (s, 1H), 7.49 (d, J = 7.5 Hz, 1H), 7.09 (d, J = 7.5 Hz, 1H), 2.87 (s, 6H); ^{19}F NMR δ –62.52(s, 3F); ^{13}C NMR δ 154.9, 131.3, (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 125.3 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 125.2 (q, $^{2}J_{C\text{-}F}$ = 34.3 Hz), 123.7 (t, $^{1}J_{C\text{-}F}$ = 276.0 Hz), 120.3, 117.9, 43.8 (2C); HRMS (EI) calcd for $C_9H_8BrF_3N$ (M^+-1) 265.9791, found 265.9792.

*4.5.2. 5-Bromo-1-methyl-3-(trifluoromethyl)-1H-indole (**8b**)*

White solid. mp 60 °C (lit.[20] 58-60 °C); IR (KBr) 1558, 1473, 1235, 1095 cm^{-1}; ^{1}H

NMR (DMSO-d_6) δ 8.08 (s, 1H), 7.72 (s, 1H), 7.60 (d, *J* = 8.9 Hz, 1H), 7.46 (dd, *J* = 8.9, 1.9 Hz, 1H), 3.86 (s, 3H); ^{19}F NMR (DMSO-d_6) δ –54.8 (s, 3F); ^{13}C NMR (DMSO-d_6) δ 135.4, 131.8 (q, $^3J_{C\text{-}F}$ = 4.9 Hz), 125.4, 124.8 (q, $^3J_{C\text{-}F}$ = 2.2 Hz), 124.3 (q, $^1J_{C\text{-}F}$ = 270.0 Hz), 120.4, 113.9, 113.3, 120.6 (q, $^2J_{C\text{-}F}$ = 37.2 Hz), 33.2.

*4.5.3. Ethyl 3,3-difluoro-2,2-dimethyl-3-(methylthio)propanoate (**8c**)*

IR (neat) 2988, 2938, 1737, 1274, 1175, 1034 cm^{-1}; ^{1}H NMR δ 4.20 (q, *J* = 7.3 Hz, 2H), 2.29 (s, 3H), 1.40 (s, 6H), 1.28 (t, *J* = 7.3 Hz, 3H); ^{19}F NMR δ –84.67 (s, 2F); ^{13}C NMR δ 171.7 (t, $^3J_{C\text{-}F}$ = 2.8 Hz), 131.5 (t, $^1J_{C\text{-}F}$ = 289 Hz), 61.5, 51.6 (t, $^3J_{C\text{-}F}$ = 22.0 Hz), 20.7 (t, $^3J_{C\text{-}F}$ = 3.1 Hz, 2C), 13.9, 9.9 (t, $^2J_{C\text{-}F}$ = 5.3 Hz); HRMS (EI) calcd for $C_8H_{14}F_2O_2S$ 212.0683, found 262.0682.

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