HETEROCYCLES, Vol. 103, No. 1, 2021, pp. 392 - 402. © 2021 The Japan Institute of Heterocyclic Chemistry
Received, 22nd June, 2020, Accepted, 29th July, 2020, Published online, 16th September, 2020
DOI: 10.3987/COM-20-S(K)23

SYNTHESIS OF (TRIFLUOROMETHYLDIAZIRINYL)PHENYLBORONIC ACID DERIVATIVES FOR PHOTOAFFINITY LABELING

Manami Hashinoki,[a] Natsumi Kurokawa,[a] Yuta Murai,[a,b] Zetryana Puteri Tachrim,[a,c] Yasuko Sakihama,[a] Takeyuki Suzuki,[d] and Makoto Hashimoto [a]*

[a]Division of Applied Bioscience, Graduate School of Agriculture, Hokkaido University, Kita 9, Nishi 9, Kita-ku, Sapporo, Hokkaido, Japan. [b]Faculty of Advanced Life Science, Frontier Research Center for Post-Genome Science and Technology, Hokkaido University, Kita 21, Nishi 11, Kita-ku, Sapporo, Hokkaido, Japan. [c]Program Study of Chemistry, Faculty of Mathematics and Natural Sciences, Institut Teknologi Bandung, Jalan Ganesha 10, Bandung, Indonesia. [d]Division of Applied Science, The Institute of Scientific and Industrial Research, Osaka University, Mihogaoka, Ibaraki-shi, Osaka 567-0047, Japan.
*Correspondence: hasimoto@abs.agr.hokudai.ac.jp; Tel./Fax: +81-11-706-3849

This paper is dedicated to Prof. Dr. Yasuyuki Kita on the occasion of his 77th birthday.

Abstract – Trifluoromethylphenyldiazirine is one of the most reliable photophores for photoaffinity labeling during functional analysis of biologically active compounds. Phenylboronic acid derivatives containing trifluoromethyldiazirinyl moiety have not yet been reported. The construction of the photophore was achieved using (3-formylphenyl)boronic acid and (4-formylphenyl)boronic acid pinacol esters effectively.

INTRODUCTION

Photoaffinity labeling is a useful biochemical method in the exploration of the structural and functional relationships between low molecular weight biologically active compounds and biomolecules.[1] This method is suitable for the analysis of biological interactions as it is based on the affinity of bioactive compounds for biomolecules using various photophores, such as phenyldiazirine, arylazide, and benzophenone. Although comparative irradiation studies of these three photophores in living cells indicated that a carbene precursor, trifluoromethylphenyldiazirine, is the most promising photophore,[2] the relatively complicated synthesis of the trifluoromethyldiazirinyl ring has resulted in fewer applications compared to other photophores in biomolecular studies. Phenylboronic acid derivatives were shown to be useful in Suzuki–Miyaura cross-coupling reagents,[3] stable complex formation with carbohydrates,[4] and chemical tools for boron transport in plants.[5] To the best of our knowledge, (trifluoromethyldiazirinyl)-phenylboronic acid derivative synthesis has not yet been reported. In this report, we describe the novel synthesis of phenylboronic acid derivatives with trifluoromethyldiazirinyl photophores at 3- and 4-positions (Figure 1).

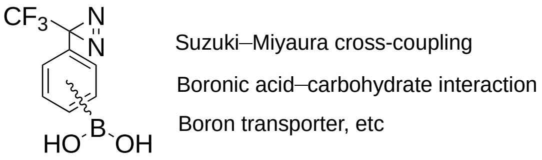


Figure 1. Structures of trifluoromethyldiazirine containing phenylboronic acid derivatives and their applications

RESULTS AND DISCUSSION

The construction of the boronic acid moiety in trifluoromethylphenyldiazirine derivatives is one way to synthesize the desired compounds: however it was reported that a three-membered diazirinyl ring, which acts as a leaving group, can be reacted with phenylboronic acid derivatives over 110 °C to produce 1,1-diphenylethylene skeletons.[6] Furthermore, it was reported that the reaction between diazirinyl halobenzenes and an arylboronic acid pinacol ester using a Pd catalyst afforded biaryl skeletons in lower yield.[7] Therefore, based on the stability of diazirine, we selected the synthetic pathway to construct the trifluoromethyldiazirinyl moiety in the phenylboronic acid derivatives. Preparations of trifluoroacetyl-substituted phenylboronic acid derivatives were essential for this synthetic pathway.

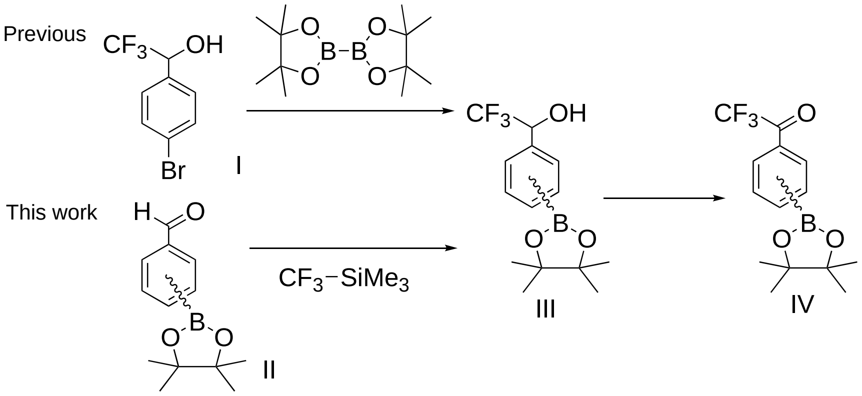
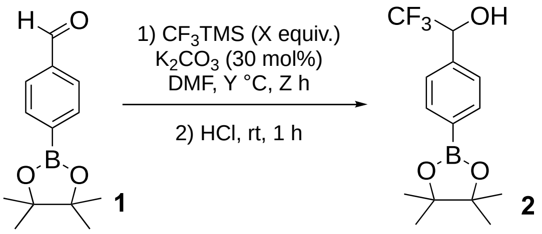


Figure 2. Synthetic strategy for the preparation of trifluoroacetylphenylboronic acid derivatives

Several patents reported the synthesis of trifluoroacetyl-substituted phenylpinacolborane from corresponding halogenated trifluoroacetophenone using a Pd catalysts, but the chemical yields were not high.[8] A few original reports exist regarding the preparation of trifluoroacetyl-substituted phenylboronic acid pinacol ester; the major synthetic route began from 2,2,2-trifluoroethan-1-ol derivatives of phenyl halide (Figure 2, I), which were reacted with bis(pinacolato)diboron to construct alcohol derivative III, followed by oxidation to produce the trifluoroacetyl derivatives (IV).[9] The trifluoroethanol-substituted phenyl halide derivative I (especially with a halogen at the 3-position) were very expensive, therefore, we selected formylphenylboronic acid pinacol esters II as the starting materials, which were reacted with (trifluoromethyl)trimethylsilane, followed by oxidation to form trifluoroacetophenone derivatives IV (Figure 2).

(4-Formylphenyl)boronic acid pinacol ester **1** was treated with 1.5 equivalents of CF_3TMS in the presence of K_2CO_3 (30 mol%) in DMF at room temperature, with slightly larger amounts of reagent and catalyst to construct the 2,2,2-trifluoro-1-phenylethan-1-ol derivative,[10] followed by acid hydrolysis to afford a low yield of **2** (Figure 3, entry 1). Excess CF_3TMS improved the chemical yield slightly (entries 2 and 3). The reaction times were reduced drastically in high temperature conditions, producing satisfactory yield (entries 4–7).



Entry	CF_3TMS X (equiv.)	Temp. Y (°C)	Time Z (h)	Yield (%)
1	1.5	rt	48	20
2	2	rt	48	40
3	3	rt	48	64
4	2	60	1	71
5	2	80	1	80
6	3	80	1	90
7	4	80	1	96

Figure 3. Trifluoromethylation of (4-formylphenyl)boronic acid pinacol ester **1** with CF_3TMS

(4- and 3-Formylphenyl)boronic acid pinacol esters (**1** and **3**) were subjected to gram-scale synthesis under the established conditions. There were no problems with large scale preparations of compounds **2** and **4**, with both producing satisfactory yields (Figure 4).

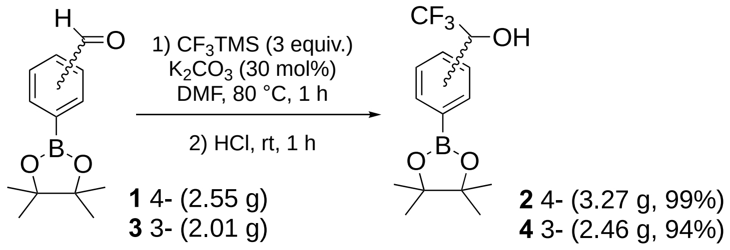
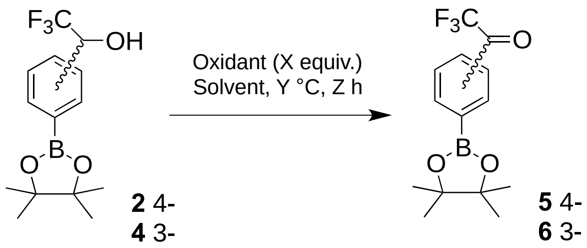


Figure 4. Gram-scale synthesis for the trifluoromethylation of (4- and 3-formylphenyl)boronic acid pinacol esters **1** and **3** with CF_3TMS



Entry	substrate	Oxidant	X (equiv.)	Solvent	Temp Y (°C)	Time Z (h)	Yield (%)
1	**2**	MnO_2	5	$ClCH_2CH_2Cl$	110	7	20
2	**2**	MnO_2	5	$ClCH_2CH_2Cl$	110	12	42
3	**2**	MnO_2	5	$ClCH_2CH_2Cl$	110	12	-[a]
4	**2**	MnO_2	15	$ClCH_2CH_2Cl$	110	6	42
5	**2**	MnO_2	15	$ClCH_2CH_2Cl$	110	12	70
6	**2**	Dess–Martin	1	CH_2Cl_2	rt	9	44
7	**2**	Dess–Martin	1.5	CH_2Cl_2	rt	9	75
8	**2**	Dess–Martin	2	CH_2Cl_2	rt	9	64
9	**4**	Dess–Martin	1.5	CH_2Cl_2	rt	9	77

Figure 5. Oxidation of 2,2,2-trifluoro-1-phenylethan-1-ol derivatives of phenylboronic acid pinacol esters **2** and **4** via oxidation

[a] The reaction was conducted in portable reactor (Taiatsu Techno) and afforded complex mixture.

Oxidations of 2,2,2-trifluoromethyl-1-phenylethan-1-ol skeleton have become of interest in recent years. Several oxidants (MnO_2, Dess-Martin periodinane, AcNH-TEMPO, and keto-ABNO etc) are subjected for the purpose. Kanai et al. only reported that the oxidation of phenylboronic acid pinacol ester derivative **2** with catalytic amounts of keto-ABNO, which can be oxidized other α-fluoroalkyl alcohols with excellent yields, afforded in 75% yield. MnO_2 (activated) and Dess-Martin periodinane were subjected to oxidations of boronic acid pinacol ester derivative **2**. Trifluoroacetyl-substituted compound **5** were afforded in low yields with 5 equivalents of activated MnO_2 at high temperature (Figure 5 entries 1-3).

Moderate yields were observed with 15 equivalents of activated MnO_2 at 110 °C for 12 h (entries 4 and 5). The same degree of oxidation in **2** was found when slight excess of Dess–Martin periodinane at room temperature was used (entries 6-8). The regioisomer **4** was also oxidized using Dess–Martin periodinane in an identical manner, producing 77% yield (entry 9), which experienced the same degree of oxidation as keto-AIBO.[9]

Trifluoroacetylphenylboronic acid pinacol ester derivatives were subjected to construction of a three-membered diazirine ring.[11] Compounds **5** and **6** were treated with hydroxylamine hydrochloride in ethanol and pyridine at 60 °C for 12 h to afford oximes **7** and **8**, then treated with tosyl chloride to convert them to tosyl oximes **9** and **10**. Diaziridine (**11** and **12**) formations from tosyl oximes were achieved with liquid ammonia treatment at room temperature in a shield tube. Oxidation of the diaziridines was conducted using activated MnO_2 at room temperature to construct diazirinyl moieties **13** and **14**.

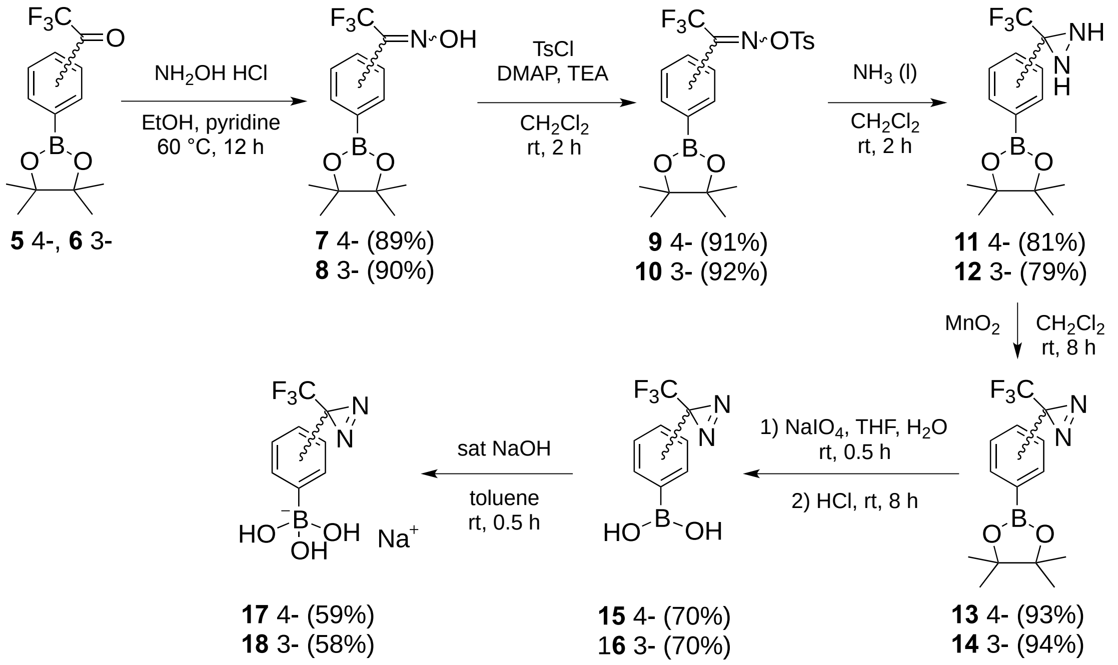


Figure 6. Synthesis of diazirinylphenylboronic acid derivatives

The tosyl oximes were subjected to one-pot conversion to diazirines in an identical manner to our previous reports.[12] The diaziridines were found to be the sole product of this the reaction in the presence of lithium amide at room temperature, with the chemical yields for diazirdine formation being almost same without the lithium amide. Diazirines were detected from the reaction mixture, which was conducted at 80 °C for 8 h, but byproducts were also detected, coparising up to 30% of the total products. Stepwise synthesis is therefore preferred for the synthesis of diazirinylated phenylboronic acid pinacol ester derivatives. Pinacol ester was deprotected with sodium periodate, which afforded unprotected diazirinylphenylboronic acid derivatives **15** and **16**, proving to be suitable compounds for the elucidation of interactions with carbohydrates. It was reported the phenylboronic acid produced a monomer and boroxine (a trimer) according to the $CDCl_3$ NMR spectrum.[13] Diazirinylphenylboronic acid derivatives **15** and **16** also resulted in a mixture of the monomer and the trimer when $CDCl_3$ was used. The monomer was only detected when the DMSO-d_6 solvent was used (Supporting Information). Sodium (trihydroxy)phenylborate derivatives **17** and **18**, which were suitable for the Suzuki–Miyaura coupling in aqueous media,[14] were also prepared from saturated sodium hydroxide treatment in toluene. It is difficult to measure mass spectrum of diazirine derivatives **13-18** due to instability of diazirinyl moiety.

In this work, the first synthesis of diazirinylphenylboronic acid derivatives was reported. The biological functions of these synthetic compounds as boron transporters are still under elucidations.

EXPERIMENTAL

General Remarks. All reagents used were of analytical grade. Dess–Martin periodinane was purchased from Chem-Impex International.[15] NMR spectra were measured using an EX 270 spectrometer (JEOL, Tokyo, Japan). HRMS-ESI spectra were obtained using a Waters UPLC ESI-TOF mass spectrometer (Waters, Milford, CT, USA).

2,2,2-Trifluoro-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-ol (2). Potassium carbonate (0.456 g, 3.3 mmol) was suspended in (4-formylphenyl)boronic acid pinacol ester (2.550 g, 11.0 mmol) and TMS-CF_3 (4.88 mL, 33.0 mmol) was dissolved in DMF (37 mL). The reaction mixture was stirred at 80 °C for 1 h, treated with 6M HCl (7.7 mL, 46.2 mmol) at rt for 1 h, then partitioned between AcOEt (160 mL) and H_2O (160 mL). The organic layer was washed with water and saturated aq .NaCl, dried over $MgSO_4$, filtrated and concentrated to afford **2** as yellow oil (3.274 g, 99%). ^{1}H-NMR ($CDCl_3$) δ: 7.81 (2H, d, J = 8.2 Hz), 7.42 (2H, d, J = 8.2 Hz), 4.97 (1H, q, J = 6.7 Hz), 1.33 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 136.9, 134.9, 133.8, 126.7, 124.2 (q, $^1J_{CF}$ = 282.0 Hz), 84.2, 72.7 (q, $^2J_{CF}$ = 32.0 Hz), 24.7. ^{19}F-NMR ($CDCl_3$) δ: -78.04, -78.06. HRMS-ESI (m/z) $[M+H]^+$ calcd for $C_{14}H_{19}BF_3O_3$ 303.1374, found 303.1359.

2,2,2-Trifluoro-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-ol (4). (3-Formylphenyl)boronic acid pinacol ester (2.028 g, 8.97 mmol) was treated in the manner described above to afford **4** as yellow oil (2.393 g, 88%). ^{1}H-NMR ($CDCl_3$) δ: 7.83 (1H, s), 7.81 (1H, d, J = 7.6 Hz), 7.55 (1H, d, J = 7.6 Hz), 7.37 (1H, t, J = 7.6 Hz), 4.92 (1H, q, J = 6.7 Hz), 1.32 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 135.8 133.8, 130.3, 128.0, 124.3 (q, $^1J_{CF}$ = 282.1 Hz), 84.2, 72.5 (q, $^2J_{CF}$ = 31.7 Hz), 24.6. ^{19}F-NMR ($CDCl_3$) δ: -78.0, -78.1. HRMS-ESI (m/z) $[M+H]^+$ calcd for $C_{14}H_{19}BF_3O_3$ 303.1374, found 303.1374.

2,2,2-Trifluoro-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (5). Alcohol **2** (0.253 g, 0.84 mmol) was dissolved in CH_2Cl_2 (3.8 mL). Dess–Martin periodinane (0.533 g, 1.26 mmol) was added at rt. The reaction mixture was stirred at rt for 9 h and diluted with CH_2Cl_2 (16 mL). The organic layer was stirred with sodium thiosulfate (1.00 g) in saturated sodium hydrogen carbonate (20 ml) at rt for 10 min, washed with aq. NaCl, dried over $MgSO_4$, filtrated and concentrated to afford **5** as yellow oil (0.188 g, 75%). ^{1}H-NMR ($CDCl_3$) δ: 8.05 (2H, d, J = 8.2 Hz), 7.97 (2H, d, J = 8.2 Hz), 1.38 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 180.6 (q, $^2J_{CF}$ = 34.8 Hz), 135.1, 134.8, 131.6, 128.8, 116.6 (q, $^1J_{CF}$ = 291.3 Hz), 84.4, 24.7. ^{19}F-NMR ($CDCl_3$) δ: -71.6. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{14}H_{17}BF_3O_3$ 301.1217, found 301.1211.

2,2,2-Trifluoro-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one (6). Compound **4** (0.915 g, 3.03 mmol) was treated in the manner described above to afford **6** as orange oil (0.699 g, 77%). ^{1}H-NMR ($CDCl_3$) δ: 8.50 (1H, s), 8.13 (2H, d, J = 7.6 Hz), 7.55 (1H, t, J = 7.6 Hz), 1.36 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 180.7 (q, $^2J_{CF}$ = 34.8 Hz), 141.6, 136.4, 132.4, 129.4, 129.0, 128.4, 116.7 (q, $^1J_{CF}$ = 290.5 Hz), 84.4, 24.8. ^{19}F-NMR ($CDCl_3$) δ: -78.0, -78.1. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{14}H_{17}BF_3O_3$ 301.1217, found 301.1232.

2,2,2-Trifluoro-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one oxime (7). 4-Trifluoroacetylphenylboronic acid pinacol ester **5** (0.755 g, 2.52 mmol) and hydroxylamine hydrochloride (0.175 g, 2.52 mmol) were dissolved in EtOH (1.4 mL) and pyridine (2.7 mL). The reaction mixture was heated at 60 °C for 8 h and partitioned between Et_2O (50 mL) and H_2O (50 mL) The organic layer was washed with saturated aq. $NaHCO_3$ and saturated aq. NaCl, dried over $MgSO_4$, filtrated and concentrated to afford **7** as yellow oil (0.708 g, 89%). ^{1}H-NMR ($CDCl_3$) δ: 7.92 and 7.86 (2H, d, J = 8.2 Hz), 7.49 and 7.48 (2H, d, J = 8.2 Hz), 1.36 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 147.6 and 147.5 (q, $^2J_{CF}$ = 30.2 Hz), 134.8, 132.8 and 132.7, 128.8 and 127.7, 127.5 and 127.5, 120.6 and 118.3 (q, $^1J_{CF}$ = 274.9 Hz), 84.3, 24.8. ^{19}F-NMR ($CDCl_3$) δ: -62.4, -66.6. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{14}H_{18}BF_3NO_3$ 316.1326, found 316.1302.

2,2,2-Trifluoro-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one oxime (8). Compound **6** (0.890 g, 2.96 mmol) was treated in the manner described above to afford **8** as orange oil (0.838 g, 90%). ^{1}H-NMR ($CDCl_3$) δ: 7.97-7.93 (2H, m), 7.58-7.40 (2H, m), 1.37 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 147.7 and 147.6 (q, $^2J_{CF}$ = 30.2 Hz), 136.8 and 136.5, 134.9 and 134.7, 131.1, 129.7 and 129.0, 127.9 and 127.8, 125.9 and 125.4, 120.7 and 118.4 (d, $^1J_{CF}$ = 276.5 Hz), 84.4 and 84.3, 24.75. ^{19}F-NMR ($CDCl_3$) δ: -62.4, -66.7. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{14}H_{18}BF_3NO_3$ 316.1326, found 316.1333.

2,2,2-Trifluoro-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one *O*-tosyl oxime (9). Oxime **7** (0.506 g, 1.61 mmol), tosyl chloride (0.306 g, 1.61 mmol) and DMAP (9.8 mg, 0.08 mmol) were suspended in TEA (0.6 mL) and CH_2Cl_2 (3 mL). The reaction mixture was stirred at rt for 8 h and partitioned between CH_2Cl_2 (50 mL) and H_2O (50 mL). The organic layer was washed with 1M HCl, saturated aq. $NaHCO_3$ andsaturaed aq. NaCl, dried over $MgSO_4$, filtrated and concentrated to afford tosyl oxime **9** as pale yellow oil (0.684 g, 91%). ^{1}H-NMR ($CDCl_3$) δ: 7.90-7.85 (4H, m), 7.41-7.36 (4H, m), 2.47 and 2.45 (3H, each s), 1.35 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 154.2 and 153.9 (q, $^2J_{CF}$ = 33.0 Hz), 146.1 and 146.0, 134.9 and 134.8, 131.3 and 131.2, 130.0 and 129.9, 129.2 and 129.1, 127.9 and 127.6, 127.3 and 126.9, 121.4 and 119.5 (q, $^1J_{CF}$ = 275.4 Hz), 84.3, 24.8, 21.7. ^{19}F-NMR ($CDCl_3$) δ: -61.5, -66.9. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{21}H_{24}BF_3NO_5S$ 470.1415, found 470.1441.

2,2,2-Trifluoro-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethan-1-one *O*-tosyl oxime (10). Compound **8** (0.472 g, 1.50 mmol) was treated in the manner described above to afford **10** as orange oil (0.650 g, 92%). ^{1}H-NMR ($CDCl_3$) δ: 7.96-7.73 (4H, m), 7.49-7.36 (4H, m), 2.48 (3H, s), 2.46 (3H, s), 1.36 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 153.9 and 153.7 (q, $^2J_{CF}$ = 30.4 Hz), 146.1 and 146.0, 137.9 and 137.6, 134.8 and 133.8, 131.1 and 131.0, 130.6, 129.7, 128.9, 128.0 and 127.9, 126.9, 124.0, 119.4 and 117.1 (q, $^1J_{CF}$ = 282.1 Hz), 84.1 and 84.0, 24.5, 21.3. ^{19}F-NMR ($CDCl_3$) δ: -61.8, -67.1. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{21}H_{24}BF_3NO_5S$ 470.1415, found 470.1392.

3-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)diaziridine (11). Tosyl oxime **9** (0.130 g, 0.28 mmol) was dissolved in Et_2O (2 mL) and the solution in the shield tube was cooled at -78 °C, then liquid ammonia (3 mL) was added to the solution. The reaction mixture was warmed at rt and stirred for 1 h. After evaporated ammonia gas, the residue was partitioned between Et_2O and H_2O. The organic layer was dried over $MgSO_4$, filtrated and concentrated to afford **11** as pale yellow oil (0.080 g, 91%). ^{1}H-NMR ($CDCl_3$) δ: 7.86 (2H, d, *J* = 7.9 Hz), 7.61 (2H, d, *J* = 7.9 Hz), 2.80 (1H, d, *J* = 8.6 Hz), 2.23 (1H, d, *J* = 8.6 Hz), 1.35 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 135.0, 134.2, 127.5, 127.3, 123.5 (q, $^1J_{CF}$ = 276.5 Hz), 84.01, 58.1 (q, $^2J_{CF}$ = 36.1 Hz), 24.78. ^{19}F-NMR ($CDCl_3$) δ:-75.4. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{14}H_{19}BF_3N_2O_2$ 315.1486, found 315.1502.

3-(3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)diaziridine (12). Compound **10** (0.621 g, 1.32 mmol) was treated in the manner described above to afford **12** as yellow oil (0.327 g, 79%). ^{1}H-NMR ($CDCl_3$) δ: 8.04 (1H, s), 7.87 (1H, d, *J* = 7.6 Hz), 7.67 (1H, d, *J* = 7.6 Hz), 7.40 (1H, t, *J* = 7.6 Hz), 2.87 (1H, d, *J* = 8.9 Hz), 2.42 (1H, d, *J* = 8.9 Hz), 1.32 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 136.3, 134.2, 131.0, 130.9, 127.9, 123.5 (q, $^1J_{CF}$ = 277.7 Hz), 84.0, 58.0 (q, $^2J_{CF}$ = 35.9 Hz), 24.6. ^{19}F-NMR ($CDCl_3$) δ: -75.61. HRMS-ESI (*m*/*z*) $[M+H]^+$ calcd for $C_{14}H_{19}BF_3N_2O_2$ 315.1486, found 315.1489.

3-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)-3*H*-diazirine (13). Activated MnO_2 (0.330 g, 3.80 mmol) was suspended in diaziridine derivative **11** (0.234 g, 0.75 mmol) in CH_2Cl_2 (7 mL). The reaction mixture was stirred at rt for 8 h and filrated by Celite pad, then the filtrate was concentrated to afford diazirine **13** as yellow oil (0.217 g, 93%). ^{1}H-NMR ($CDCl_3$) δ: 7.82 (2H, d, *J*

= 8.6 Hz), 7.17 (2H, d, J = 8.6 Hz), 1.34 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 135.0, 131.8, 126.5, 125.5 122.1 (q, $^{1}J_{CF}$ = 274.9 Hz), 84.2, 28.5 (q, $^{2}J_{CF}$ = 40.6 Hz), 24.82. ^{19}F-NMR ($CDCl_3$) δ: -65.1. UV ($CHCl_3$) λ_{max} (ε): 273 (1820), 350 (330).

3-(3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)-3*H*-diazirine (14). Compound **12** (0.272 g, 0.87 mmol) was treated in the manner described above to afford **14** as orange oil (0.254 g, 94%). ^{1}H-NMR ($CDCl_3$) δ: 7.85 (1H, t, J = 7.2 Hz), 7.54 (1H, s), 7.42 (1H, m), 7.41 (1H, d, J = 7.2 Hz), 1.34 (12H, s). ^{13}C-NMR ($CDCl_3$) δ: 136.0, 132.5, 129.4, 128.4, 128.1, 122.2 (q, $^{1}J_{CF}$ = 274.3 Hz), 84.2, 28.4 (q, $^{2}J_{CF}$ = 40.4 Hz), 24.7. ^{19}F-NMR ($CDCl_3$) δ: -65.3. UV ($CHCl_3$) λ_{max} (ε): 280 (755), 353 (278).

(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)boronic acid (15). Sodium periodinate (0.158 g, 0.74 mmol) was added to the solution of pinacol ester **11** (0.077 g, 0.25 mmol) in THF (1.3 mL) and H_2O (0.3 mL). The reaction mixture was stirred at room temperature for 1 h and treated with 1 M HCl (0.25 mL) for 8 h, then partitioned between Et_2O (30 mL) and H_2O (15 mL). The organic layer was washed with H_2O and saturated NaCl, dried over $MgSO_4$, filtrated and evaporated to afford **15** as pale yellow amorphous mass (0.040 g, 70%). ^{1}H-NMR (DMSO-d_6) δ: 8.25 (2H, s), 7.87 (2H, d, J = 7.6 Hz), 7.21 (2H, d, J = 7.6 Hz). ^{13}C-NMR (DMSO-d_6) δ: 178.7, 134.8, 129.1, 125.2, 121.9 (q, $^{1}J_{CF}$ = 274.3 Hz), 28.2 (q, $^{2}J_{CF}$ = 39.7 Hz). ^{19}F-NMR ($CDCl_3$) δ: -64.5. UV ($CHCl_3$) λ_{max} (ε): 272 (1100), 350 (278).

(3-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)boronic acid (16). Compound **14** (0.219 g, 0.70 mmol) was treated in the manner described above to afford **16** as pale yellow amorphous mass (0.113 g, 70%). ^{1}H-NMR (DMSO-d_6) δ: 8.29 (2H, s), 7.90 (1H, d, J = 7.6 Hz), 7.61 (1H, s), 7.47 (1H, t, J = 7.6 Hz), 7.34 (1H, d, J = 7.6 Hz).^{13}C-NMR (DMSO-d_6) δ: 135.9, 131.7, 128.5, 128.1, 126.7, 122.0 (q, $^{1}J_{CF}$ = 272.1 Hz), 28.2 (q, $^{2}J_{CF}$ = 39.7 Hz). ^{19}F-NMR (DMSO-d_6) δ: -68.8. UV ($CHCl_3$) λ_{max} (ε): 271 (1390), 353 (343).

Sodium trihydroxy(4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)borate (17). Saturated aq. sodium hydroxide (0.7 mL) was added to diazirinylphenylboronic acid **15** (0.022 g, 0.10 mmol) in toluene (1 mL). The suspension was stirred at rt for 0.5 h. Insoluble material was washed with Et_2O and MeCN to afford **17** as pale yellow amorphous mass (0.016 g, 59%). ^{1}H-NMR (CD_3OD) δ: 7.47 (2H, d, J = 8.2 Hz), 6.89 (2H, d, J = 7.6 Hz). ^{13}C-NMR (CD_3OD) δ: 134.7, 126.0, 125.2,124.0 (q, $^{1}J_{CF}$ = 273.8 Hz), 29.7 (q, $^{2}J_{CF}$ = 39.1 Hz).^{19}F-NMR (CD_3OD) δ: -67.1. UV (MeOH) λ_{max} (ε): 280 (700), 350 (136).

Sodium trihydroxy(3-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)borate (18). Compound **16** (0.041 g, 0.18 mmol) was treated in the manner described above to afford **18** as pale yellow amorphous mass (0.028 g, 58%). ^{1}H-NMR (CD_3OD) δ: 7.50 (1H, d, J = 7.6 Hz), 7.21 (1H, s), 7.12 (1H, t, J = 7.6 Hz), 6.90 (1H, d, J = 7.6 Hz). ^{13}C-NMR (CD_3OD) δ: 133.7, 129.7, 125.6, 125.2, 121.9, 121.9 (q, $^{1}J_{CF}$ = 272.1 Hz), 27.8 (q, ${}^2J_{CF}$ = 39.1 Hz). ^{19}F-NMR (CD_3OD) δ: -70.3. UV (MeOH) λ_{max} (ε): 263 (925), 350 (254).

ACKNOWLEDGEMENTS

Part of this work was performed under the Cooperative Research Program of the Network Joint Research Center for Materials and Devices. This research was partially supported by Hokkaido University Research and Education Center for the Robust Agriculture, Forestry and Fisheries Industry.

REFERENCES AND NOTES

1. J. Brunner, *Annu. Rev. Biochem.*, 1993, **62**, 483; Y. Xia and L. Peng, *Chem. Rev.*, 2013, **113**, 7880; Y. Hatanaka, *Chem. Pharm. Bull.*, 2015, **63**, 1; J. R. Hill and A. A. B. Robertson, *J. Med. Chem.*, 2018, **61**, 6945.
2. T. Tomohiro, M. Hashimoto, and Y. Hatanaka, *Chem. Records*, 2005, **5**, 385; M. Hashimoto and Y. Hatanaka, *Eur. J. Org. Chem.*, 2008, 2513; M. Hashimoto, 'Photoaffinity Labeling for Structural Probing Within Protein', ed. by Y. Hatanaka and M. Hashimoto, Springer, Tokyo, 2017.
3. N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457; S. E. Hooshmand, B. Heidari, R. Sedghi, and R. S. Varma, *Green Chem.*, 2019, **21**, 381.
4. J. Yan, H. Fang, and B. Wang, *Med. Res. Rev.*, 2005, **25**, 490; G. Chen, J. Qiu, J. Xu, X. Fang, Y. Liu, S. Liu, S. Wei, R. Jiang, T. Luan, F. Zeng, F. Zhu, and G. Ouyang, *Chem. Sci.*, 2016, **7**, 1487.
5. J. Takano, K. Noguchi, M. Yasumori, M. Kobayashi, Z. Gajdos, K. Miwa, H. Hayashi, T. Yoneyama, and T. Fujiwara, *Nature*, 2002, **420**, 337; J. Takano, K. Miwa, L. Yuan, N. von Wirén, and T. Fujiwara, *Proc. Natl. Acad. Sci. USA*, 2005, **102**, 12276.
6. G. Wu, X. Zhao, W. Ji, Y. Zhang, and J. Wang, *Chem. Commun.*, 2016, **52**, 1961.
7. N. Ichiishi, K. P. Moore, A. M. Wassermann, S. E. Wolkenberg, and S. W. Krska, *ACS Med. Chem. Lett.*, 2019, **10**, 56.
8. N. Subasinghe, E. Khalil, K. Leonard, F. Ali, H. R. Hufnagel, J. M. Travins, S. K. Ballentine, K. T. Wilson, M. D. Cummings, W. Pan, J. Gushue, S. Meegalla, M. Wall, J. Chen, M. J. Rudolph, and H. Huang, WO2003099805, 2003; S. Hadida-Ruah, M. Hamilton, M. Miller, P. D. J. Grootenhuis, B. Bear, J. McCartney, J. Zhou, and F. Van Goor, US20080019915, 2008; D. Chen, C. L. Franklin, P. R. Guzzo, L. S. Lin, M. M. C. Lo, R. P. Nargund, and I. K. Sebhat, WO2008051406, 2008; Miller, P. D. J. Grootenhuis, B. Bear, J. McCartney, J. Zhou, and F. Van Goor, US20080019915, 2008; J. Chen, S. Liu, and S. Ying, CN108912020, 2018.
9. Y. Kadoh, M. Tashiro, K. Oisaki, and M. Kanai, *Adv. Synth. Catal.*, 2015, **357**, 2193.
10. S. Crotti, N. Di Iorio, A. Mazzanti, P. Righi, and G. Bencivenni, *J. Org. Chem.*, 2018, **83**, 12440.
11. Y. Hatanaka, M. Hashimoto, H. Kurihara, H. Nakayama, and Y. Kanaoka, *J. Org. Chem.*, 1994, **59**, 383; Y. Murai, K. Masuda, Y. Sakihama, Y. Hashidoko, Y. Hatanaka, and M. Hashimoto, *J. Org.*

Chem., 2012, **77**, 8581; L. Wang, T. Yoshida, Y. Muto, Y. Murai, Z. P. Tachrim, A. Ishida, S. Nakagawa, Y. Sakihama, Y. Hashidoko, K. Masuda, Y. Hatanaka, and M. Hashimoto, *Eur. J. Org. Chem.*, 2015, 3129; T. Nakakita, A. Ishida, Z. P. Tachrim, L. Wang, T. Misaka, and M. Hashimoto, *Molecules*, 2020, **25**, 2790.

12. L. Wang, Y. Murai, T. Yoshida, A. Ishida, K. Masuda, Y. Sakihama, Y. Hashidoko, Y. Hatanaka, and M. Hashimoto, *Org. Lett.*, 2015, **17**, 616; A. Ishida, L. Wang, Z. P. Tachrim, T. Suzuki, Y. Sakihama, Y. Hashidoko, and M. Hashimoto, *ChemistrySelect*, 2017, **2**, 160.
13. R. Chaudhari, *Chem. Phys. Lett.*, 2015, **634**, 95.
14. A. N. Cammidge, V. H. M. Goddard, H. Gopee, N. L. Harrison, D. L. Hughes, C. J. Schubert, B. M. Sutton, G. L. Watts, and A. J. Whitehead, *Org. Lett.*, 2006, **8**, 4071.
15. It was sometimes found that excess amounts of Dess-Martin periodinane from other suppliers was needed to oxidation of 2,2,2-trifluoromethyl-1-phenylethan-1-ol skeleton completely.