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POLYFLUOROARENE-CAPPED THIOPHENE DERIVATIVES VIA FLUORIDE-CATALYZED NUCLEOPHILIC AROMATIC SUBSTITUTION

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Abstract – Arylthiophene derivatives are potential components of functional materials, including organic electronics. Herein, we describe a nucleophilic aromatic substitution reaction of polyfluoroarenes using silylthiophenes as nucleophiles in the presence of a catalytic amount of a fluoride salt. Various polyfluoroarene-capped thiophene derivatives were synthesized via double arylation under transition metal-free conditions. A fluoride ion activates a silylthiophene to trigger a nucleophilic aromatic substitution, subsequently affording the coupling product along with elimination of the fluoride ion, which serves as a promoter of the catalytic reaction.

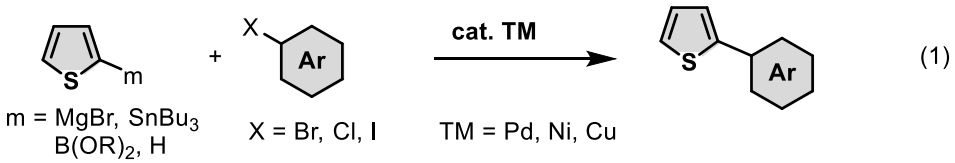
Dedicated to Professor Yasuyuki Kita on the occasion of his 77th birthday

INTRODUCTION

Thiophene derivatives can be found in functional organic materials, naturally occurring compounds, and pharmaceuticals.[1,2] Poly- and oligothiophenes can be potentially employed to develop organic electronics, such as organic light-emitting diodes (OLEDs), organic field-effect transistors (OFETs), organic solar cells (OSCs), and chemical/biological sensors. The functionalization of the thiophene core through the introduction of electronically tunable substituent groups and/or connection with other π-conjugated

molecules can be used to modify the chemical and physical properties of the resulting derivatives, thereby allowing for the development of novel functional molecules. 3,4-Ethylenedioxythiophene (EDOT) can be converted by oxidation to poly(3,4-ethylenedioxythiophene) (PEDOT),[3] which is one of the most attractive thiophene-based oligomers.[4] However, the preparation of arylthiophene derivatives, including functionalized oligothiophenes, generally relies on the use of transition metal reagents or catalysts (Eq. 1).[1b,5–7] Conventionally, the EDOT dimer is synthesized through α-lithiation of thiophene followed by copper- or iron-mediated coupling.[5] Trimerization has been carried out by nickel-catalyzed coupling of dibromo-EDOT with a thienomagnesium reagent prepared from α-lithiothiophene.[6a]

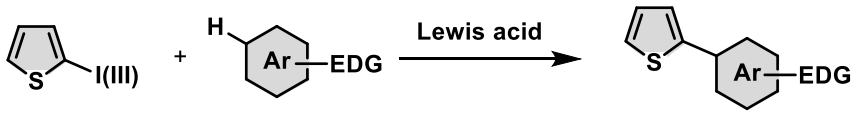
Typical method: Transition metal-catalyzed coupling



(1)

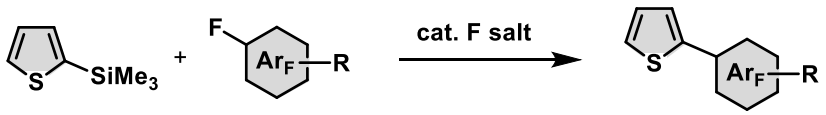
Alternative methods: Transition metal-free reactions

Hypervalent iodine(III)-mediated coupling (previous work)



(2)

Nucleophilic aromatic substitution of polyfluoroarene (this work)



(3)

As an alternative method to transition metal-catalyzed C-C bond formation to generate biaryl derivatives, the Kita group including us developed metal-free oxidative biaryl coupling reactions that proceeded through an aryliodonium(III) intermediate, while the direct Ar-H bond arylation occurred without pre-functionalization (Eq. 2).[8,9] Various arylthiophene derivatives were selectively obtained, although the coupling partners were limited to electron-rich arenes, such as thiophene and methoxybenzenes.[8b,8c,9] In the present study, we developed a transition metal-free coupling reaction of thiophene derivatives with electron-deficient arenes such as polyfluoroarenes, which are also key structural units for functional molecules including liquid crystals and electronic devices.[10]

Typically, the preparation of functionalized polyfluoroarenes has been accomplished by using transition metal-catalyzed coupling reactions, involving C-F or C-H bond activation.[11,12] Owing to the low electron density of the aromatic ring, polyfluoroarenes could react with nucleophiles in the absence of a transition metal to undergo a nucleophilic aromatic substitution (S_NAr) to afford substituted polyfluoroarenes.[13]

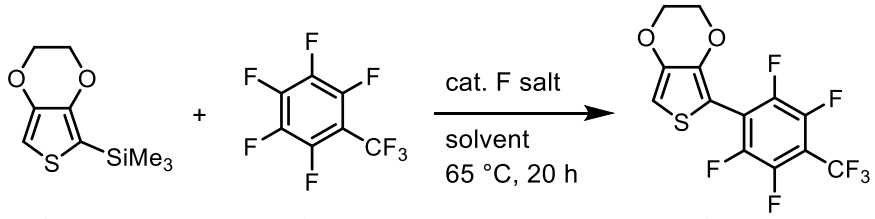
Recently, S_NAr reactions between an organosilicon compound and polyfluoroarene in the presence of a fluoride anion have been demonstrated to occur under mild conditions.[14–16] The hydrodefluorination of polyfluoroarenes proceeds upon reaction with a hydrosilane in the presence of a catalytic amount of fluoride salt.[14] In this reaction, a fluoride anion attacks the hydrosilane to generate a pentacoordinate silicate, which reacts with the polyfluoroarene to give a hydrodefluorination product along with the regeneration of the fluoride anion. Therefore, the reaction proceeds with a catalytic amount of fluoride source. The use of trimethylsilylthiophene enables the introduction of a thienyl group into a polyfluoroarene; examples of transition metal-free copolymerization of perfluoroarene with thiophene derivatives have been described.[15,16] The chemical and physical properties of the π-conjugated compounds depend on their lengths; therefore, a more concise synthetic approach is required for unified structures, which are difficult to access by polymerization reactions. The combination of silylthiophene with polyfluoroarene bearing a substituent group would suppress the multiple S_NAr reactions (Eq. 3). Herein, we describe a transition metal-free arylation of silylthiophene derivatives via the S_NAr reaction of polylfluoroarenes, which provides an efficient synthesis of polyfluroarene-capped thiophene derivatives.

RESULTS AND DISCUSSION

We first examined the synthesis of biaryl compounds using mono-silylated EDOT (**1a**) and octafluorotoluene (**2a**) in the presence of a catalytic amount of tetrabutylammonium difluorotriphenylsilicate (TBAT), which is a fluoride salt with a high solubility in organic solvents (Table 1). When 2-(trimethylsilyl)-EDOT (**1a**) was reacted in the presence of 10 mol% of TBAT in THF at room temperature, the coupling product **3aa** was obtained in 64% yield (entry 1). During the reaction, a fluorine atom at the *p*-position to the trifluoromethyl group was substituted by EDOT. The regioselectivity was accordant with that observed for the reported S_NAr reaction of octafluorotoluene,[14] which is determined by the electron density at the reacting carbons on the aromatic ring and the steric effect of trifluoromethyl group. For a mechanistic viewpoint, it can be assumed that the additional fluoride anion attacked the silyl group to generate a pentacoordinated silicate, which then underwent a nucleophilic aromatic substitution reaction to form the C-C bond. When the reaction was conducted under reflux conditions, the efficiency of the reaction improved leading to the product in a quantitative yield (entry 2). A screening of different solvents revealed that 1,2-dimethoxyethane, 1,4-dioxane, DMSO, and DMF could also be employed affording **3aa** in high yields (entries 3–6). On the other hand, acetonitrile, hexane, and 1,2-dichloroethane resulted in low yields or no reaction (entries 7–9). We next surveyed other fluoride salts. The use of tetrabutylammonium fluoride (TBAF, 1.0 M solution in THF, used as received) instead of TBAT led to a decreased reaction yield presumably due to the contamination of TBAF with trace amounts of water (entry 10), which could induce the hydrolysis of the pentacoordinated silicate intermediate stopping the

catalytic cycle. When TBAF was dried by treatment with 5Å molecular sieves prior to use, the resulting yield increased to 75% (entry 11). Metal fluorides, such as KF and CsF, combined with 18-crown-6 were ineffective for the present reaction (entries 12 and 13). Furthermore, the amount of TBAT could be successfully reduced to 2 mol% to afford **3aa** in 99% yield (entry 14).

Table 1. Reaction of mono-silylated EDOT with octafluorotoluene in the presence of TBAT



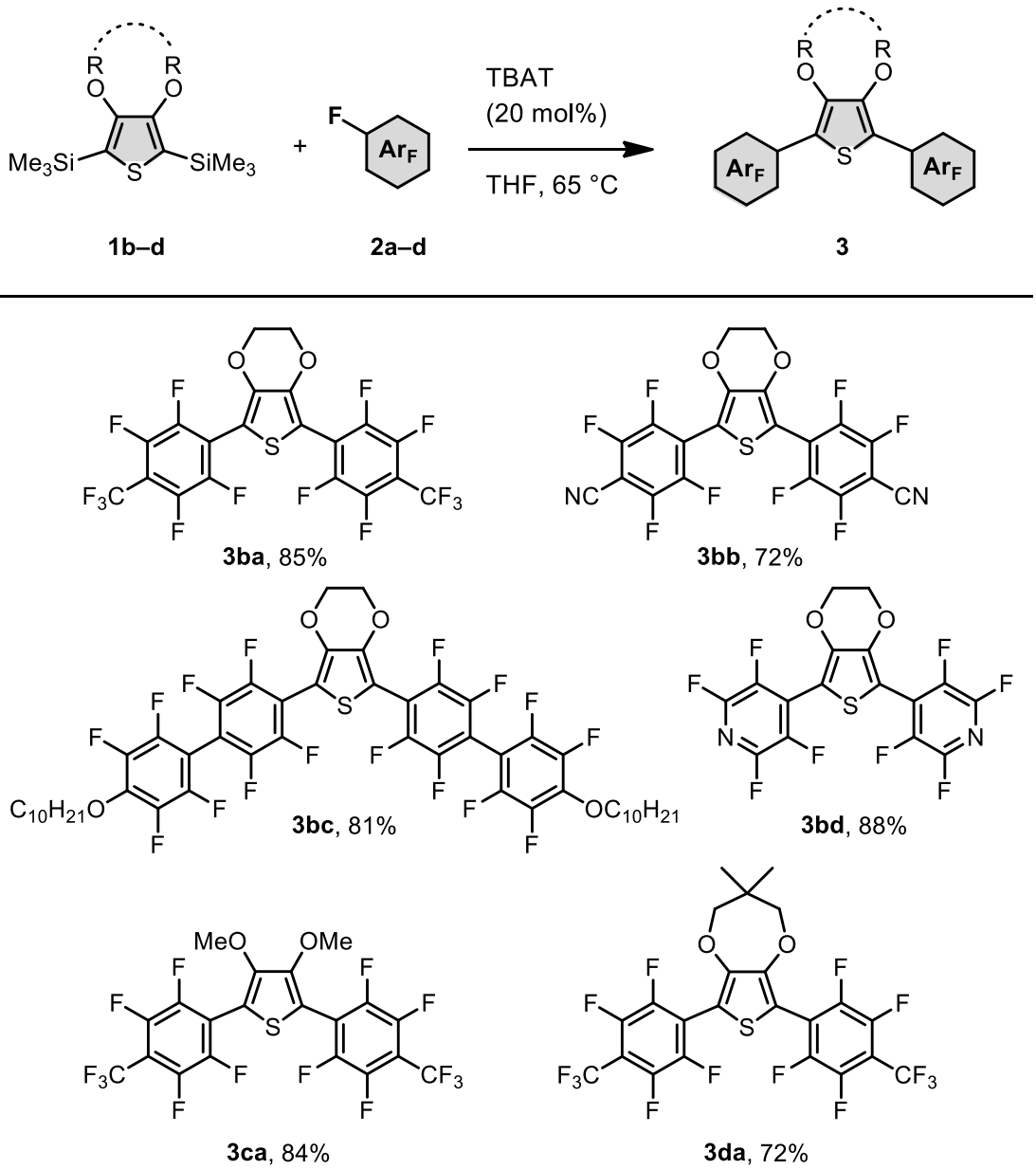
1a **2a** **3aa**

entry	solvent	F salt		yield
1	THF	TBAT	10 mol%	64%[a]
2	THF	TBAT	10 mol%	99%
3	DME	TBAT	10 mol%	93%
4	1,4-dioxane	TBAT	10 mol%	84%
5	DMSO	TBAT	10 mol%	82%
6	DMF	TBAT	10 mol%	88%
7	MeCN	TBAT	10 mol%	11%
8	hexane	TBAT	10 mol%	17%
9	DCE	TBAT	10 mol%	0%
10	THF	TBAF[b]	10 mol%	10%
11	THF	TBAF[c]	10 mol%	75%
12	THF	KF[d]	10 mol%	0%
13	THF	CsF[d]	10 mol%	0%
14	THF	TBAT	2 mol%	99%

[a] Conducted at room temperature. [b] Used as received.
[c] Dried over MS 5Å prior to use. [d] With 18-crown-6.

Concomitantly to the optimization of the reaction conditions, we investigated a double fluoroarylation using bis-silylated EDOT derivatives (Scheme 1). The reaction of 2,5-bis(trimethylsilyl)-EDOT (**1b**) with octafluorotoluene (**2a**) in the presence of 20 mol% of TBAT afforded the corresponding product **3ba** in 85% yield. The reaction yield was slightly drooped in contrast with mono-substitution using **1a** and **2a**. The first S_NAr reaction occurs to introduce the polyfluoroarene, which possibly serves as an electron-deficient group to decrease the rate of second S_NAr reaction. Various polyfluoroarenes can be employed for achieving a double fluoroarylation. Pentafluorobenzonitrile (**2b**) underwent the S_NAr reaction to give **3bb** in 72%, wherein the cyano group remained intact. As with reaction of **2a**, the fluorine atom at the *p*-position to the cyano group was substituted with thiophene nucleophile. A

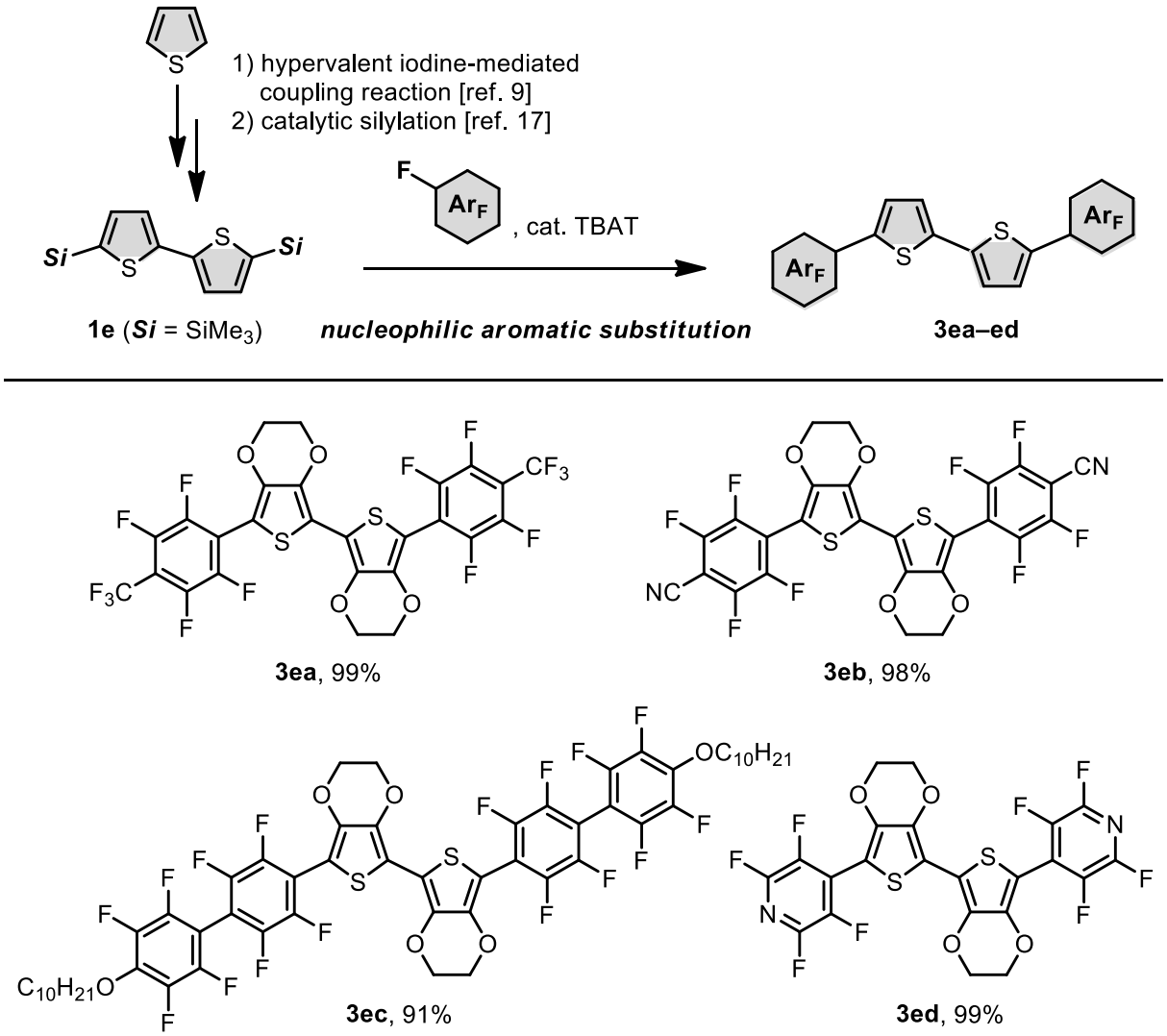
polyfluorobiphenyl bearing a long alkoxy chain (**2c**) reacted with **1b** to give the corresponding product **3bc** in 81% yield. The S_NAr reaction of pentafluoropyridine (**2d**) also proceeded smoothly, and the coupling product **3bd** was obtained in 88% yield. In these cases, the observed *p*-selectivities can also be explained by inductive and/or steric effects. In addition to the EDOT derivatives, dialkoxythiophene derivatives, such as **1c** and **1d**, were also shown to participate in the S_NAr reaction to afford the corresponding compounds **3ca** and **3da**, respectively.



Scheme 1. Reaction of bis-silylated thiophenes with polyfluoroarenes

The polyfluoroarylation of bis-EDOT derivatives was next carried out (Scheme 2). The starting material, bis-siliylated bis-EDOT, can be prepared by the hypervalent iodine-mediated dimerization of EDOT[9] followed by catalytic C-H silylation.[17] The combination of these reactions and the present S_NAr reaction

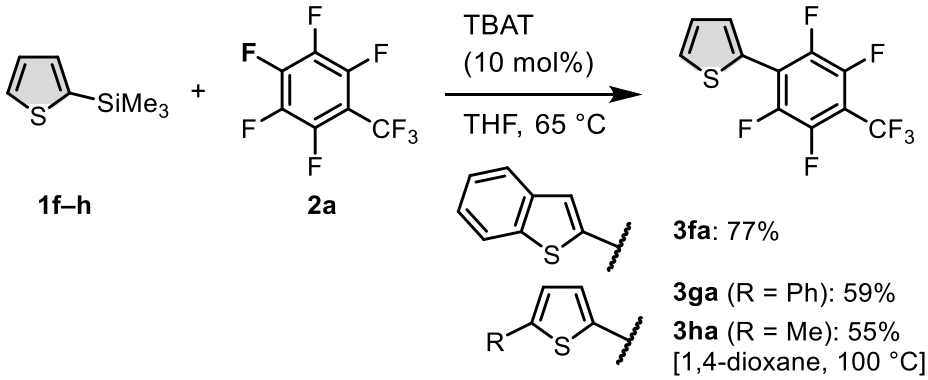
offers an opportunity to synthesize various π-conjugated arylthiophenes with polyfluoroarenes starting from thiophenes under transition metal-free conditions. The reaction of bis(trimethylsilyl) bis-EDOT (**1e**) with **2a** exhibited high efficacy and afforded the desired compound **3ea** quantitatively. Various bis-EDOT derivatives bearing polyfluoroarenes (**3eb**–**3ed**) were synthesized in high yields. These oligoaromatic compounds containing EDOT, which have an attractive thiophene core based on their high electron density, could be synthesized in three steps via transition metal-free methods.



Scheme 2. Access to polyfluoroarene-capped bis-EDOT without transition metals

We also examined the use of other silylated thiophenes without alkoxy groups at the 3,4-positions (Scheme 3). 2-Trimethylsilylbenzothiophene (**1f**) underwent an S_NAr reaction with **2a** to afford the corresponding product **3fa** in 77% yield. The observed reactivity was slightly decreased, probably due to the lower electron density of the benzothiophene compared to the EDOT derivative. 2-Silylthiopehene

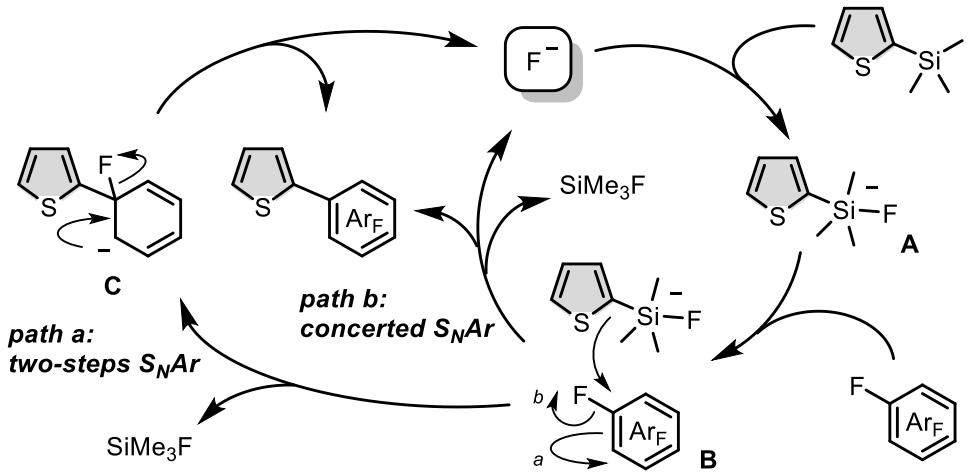
bearing a phenyl group at the 5-position (**1g**) could also be employed for this transformation to give teraryl **3ga**, albeit in moderate yield. On the other hand, the reaction of 2-silylthiophene bearing a methyl group (**1h**) resulted in a low yield under standard conditions. In this case, an elevated temperature of 100 °C in 1,4-dioxane afforded **3ha** in 55% yield.



Scheme 3. Reaction of 2-(trimethylsilyl)thiophenes with octafluorotoluene

The proposed mechanism of the present reaction is shown in Scheme 4. A fluoride ion reacts with a silylthiophene to generate pentacoordinated silicate **A**, which undergoes a nucleophilic aromatic substitution with a polyfluoroarene. Typically, a nucleophilic aromatic substitution proceeds in two steps via the generation of Meisenheimer-type complex **C** as the reaction intermediate (path a). However, a concerted nucleophilic aromatic substitution involving one-step direct substitution through path b is also possible.[14,18] The eliminated fluoride ion activates the silylthiophene again, and the reaction proceeds with a catalytic amount of fluoride salt. The high electron density of the thiophene core probably enhances the stability of the pentacoordinated silicate **A** and/or the reactivity for the nucleophilic aromatic substitution (step **B**). Thus, the reaction of EDOT and bis-EDOT derivatives exhibited higher yields than those of thiophene derivatives without alkoxy groups.

In conclusion, we have demonstrated a transition metal-free synthesis of arylthiophene derivatives via nucleophilic aromatic substitution of polyfluoroarenes in the presence of a catalytic amount of tetrabutylammonium difluorotriphenylsilicate. Various polyfluoroarene-capped EDOT and bis-EDOT derivatives were synthesized in high yields, which could be potentially employed for the preparation of functional organic materials. Further investigation of the physical properties of these products, including their optical characteristics is currently in progress.



Scheme 4. Proposed reaction mechanism for the nucleophilic aromatic substitution

EXPERIMENTAL

General. All manipulations were conducted under a nitrogen atmosphere using standard Schlenk techniques. ^{1}H, ^{13}C, and ^{19}F nuclear magnetic resonance (NMR) spectra were recorded on JEOL JMN-400 spectrometers at 25 °C unless otherwise noted. The chemical shifts in ^{1}H NMR spectra were recorded relative to residual solvent peaks ($CDCl_3$: δ 7.26). The chemical shifts in ^{13}C NMR spectrum were recorded relative to residual solvent peaks ($CDCl_3$: δ 77.0). The chemical shifts in ^{19}F NMR spectrum were recorded relative to internal standards (4-fluorotoluene: δ -121.0). High resolution mass spectra (HRMS) were measured with a Thermo Scientific Exactive Plus Orbitrap (Thermo Fisher Scientific., Inc., Waltham, MA, USA). All commercially available reagents were used as received unless otherwise noted. DMSO, DMF, MeCN, and DCE were distilled over CaH_2 prior to use. THF, DME, 1,4-dioxane, and hexane were distilled from sodium benzophenone ketyl prior to use. TBAF was dried by treatment with 5Å molecular sieves prior to use. Silylthiophene derivatives were prepared according to the reported methods.[17a,19]

General procedure A for the optimization of the reaction conditions (Table 1)

[Entry 2] TBAT (10.8 mg, 0.02 mmol, 10 mol%) was placed in a J. Young NMR tube and dried under vacuum for 1 h. After backfilling with N_2, THF (0.40 mL), silylthiophene **1a** (42.9 mg, 0.20 mmol), and octafluorotoluene (30 μL, 0.21 mmol, 1.05 eq) were added in this order. The reaction mixture was stored at 65 °C for 20 h. $CDCl_3$ (0.20 mL) and 4-fluorotoluene (11 μL, 0.10 mmol; as an internal standard for ^{19}F NMR) were added to the mixture. ^{19}F NMR analysis revealed that the desired compound was formed in 99% yield. According to this procedure, the reaction conditions were optimized, and the reaction mixture was analyzed by ^{19}F NMR spectroscopy to determine the yield. The reaction in entry 1 was conducted at room temperature. When TBAF was employed as a fluoride source, TBAF was added to all reagents (entries 10 and 11).

General procedure B for the polyfluoroarylation of mono-silylated thiophenes

In a well-dried screw-capped test tube, TBAT (27.0 mg, 0.05 mmol, 10 mol%) and silylthiophene (0.50 mmol) were added and dried under vacuum for 1 h. After backfilling with N_2, THF (2.5 mL) and octafluorotoluene (75 μL, 0.525 mmol, 1.05 eq) were added to the mixture in this order. The test tube was sealed with a cap, and the reaction mixture was stirred at 65 °C for 16 h. The reaction was quenched with water (20 mL) and the mixture was then transferred to a separatory funnel with AcOEt (20 mL). The organic layer was separated, and the aqueous layer was extracted with AcOEt (2 × 10 mL). The combined organic fractions were washed with brine (20 mL) and then dried over Na_2SO_4. After removal of all the volatiles under vacuum, the residue was purified by flash column chromatography (SiO_2).

General procedure C for the polyfluoroarylation of bis-silylated thiophenes

In a well-dried screw-capped test tube, TBAT (54.0 mg, 0.1 mmol, 20 mol%) and silylthiophene (0.50 mmol) were added and dried under vacuum for 1 h. After backfilling with N_2, THF (2.5 mL) and octafluorotoluene (150 μL, 1.05 mmol, 2.1 eq) were added to the mixture in this order. The test tube was sealed with a cap, and the reaction mixture was stirred at 65 °C for 16 h. The reaction was quenched with water (20 mL) and the mixture was then transferred to a separatory funnel with AcOEt (20 mL). The organic layer was separated, and the aqueous layer was extracted with AcOEt (2 × 10 mL). The combined organic fractions were washed with brine (20 mL) and then dried over Na_2SO_4. After removal of all the volatiles under vacuum, the residue was purified by flash column chromatography (SiO_2).

5-(2,3,5,6-Tetrafluoro-4-(trifluoromethyl)phenyl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (3aa)

The title compound **3aa** was synthesized according to general procedure B with (2,3-dihydrothieno[3,4-*b*][1,4]dioxin-5-yl)trimethylsilane (**1a**) (107.2 mg, 0.50 mmol), octafluorotoluene (**2a**) (75 μL, 0.525 mmol, 1.05 eq), and TBAT (27.0 mg, 0.05 mmol, 10 mol%). The product was isolated (168.2 mg, 94%) as a colorless oil after preparative TLC (SiO_2, hexane). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 6.65 (s, 1H), 4.28–4.26 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 144.3 (dm, J = 254 Hz), 144.1 (dm, J = 254 Hz), 141.6, 141.4, 120.9 (q, J = 275 Hz), 116.7 (t, J = 17.2 Hz), 108.9–107.7 (m), 103.6, 99.6, 64.9, 64.3. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.6 (t, J = 23.0 Hz, 3F), -138.8 – -138.9 (m, 4F), -143.4 – -143.5 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{13}H_6F_7O_2S^+$ 358.9971; Found 358.9971.

5,7-Bis(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (3ba)

The title compound **3ba** was synthesized according to general procedure C with 5,7-bis(trimethylsilyl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (**1b**) (143.3 mg, 0.50 mmol), octafluorotoluene (**2a**) (150 μL, 1.05 mmol, 2.1 eq), and TBAT (54.0 mg, 0.1 mmol, 20 mol%). The product was isolated (244 mg, 85%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.35 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm):

144.3 (dm, *J* = 260 Hz), 144.1 (dm, *J* = 260 Hz), 141.1, 120.7 (q, *J* = 276 Hz), 115.4 (t, *J* = 17.2 Hz), 109.9–108.6 (m), 103.2, 64.6. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.6 (t, *J* = 23.0 Hz, 3F), -137.9 – -138.0 (m, 4F), -142.6 – -142.8 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{20}H_5F_{14}O_2S^+$ 574.9781; Found 574.9781.

4,4'-(2,3-Dihydrothieno[3,4-*b*][1,4]dioxine-5,7-diyl)bis(2,3,5,6-tetrafluorobenzonitrile) (3bb)

The title compound **3bb** was synthesized according to general procedure C with 5,7-bis(trimethylsilyl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (**1b**) (143.3 mg, 0.50 mmol), pentafluorobenzonitrile (**2b**) (303 μL, 2.4 mmol, 4.8 eq), and TBAT (54.0 mg, 0.1 mmol, 20 mol%). The product was isolated (175 mg, 72%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.36 (s, 4H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -134.5 – -134.6 (m, 4F), -136.5 – -136.7 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{20}H_5F_8N_2O_2S^+$ 488.9939; Found 488.9936.

5,7-Bis(4'-(decyloxy)-2,2',3,3',5,5',6,6'-octafluoro-[1,1'-biphenyl]-4-yl)-2,3-dihydrothieno[3,4-*b*][1,4]-dioxine (3bc)

The title compound **3bc** was synthesized according to general procedure C with 5,7-bis(trimethylsilyl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (**1b**) (143.3 mg, 0.50 mmol), 4-decyloxynonafluorobiphenyl (**2c**) (520 mg, 1.1 mmol, 2.2 eq), and TBAT (54.0 mg, 0.1 mmol, 20 mol%). The product was isolated (424 mg, 81%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/20). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.38 (s, 4H), 4.34 (t, *J* = 6.8 Hz, 4H), 1.83 (tt, *J* = 6.8, 7.6 Hz, 4H), 1.51 – 1.45 (m, 4H), 1.40 – 1.27 (m, 24 H), 0.89 (t, *J* = 6.4 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -139.6 – -139.7 (m, 4F), -140.7 – -140.8 (m, 4F), -141.8 – -141.8 (m, 4F), -158.7 – -158.7 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{50}H_{47}F_{16}O_4S^+$ 1047.2934; Found 1047.2931.

5,7-Bis(perfluoropyridin-4-yl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (3bd)

The title compound **3bd** was synthesized according to general procedure C with 5,7-bis(trimethylsilyl)-2,3-dihydrothieno[3,4-*b*][1,4]dioxine (**1b**) (143.3 mg, 0.50 mmol), pentafluoropyridine (**2d**) (115 μL, 1.05 mmol, 2.1 eq), and TBAT (54.0 mg, 0.1 mmol, 20 mol%). The product was isolated (194 mg, 88%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.39 (s, 4H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -92.5 – -92.6 (m, 4F), -141.3 – -141.5 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{16}H_5F_8N_2O_2S^+$ 440.9939; Found 440.9937.

3,4-Dimethoxy-2,5-bis(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)thiophene (3ca)

The title compound **3ca** was synthesized according to general procedure C with (3,4-dimethoxythiophene-2,5-diyl)bis(trimethylsilane) (**1c**) (144.1 mg, 0.50 mmol), octafluorotoluene

(**2a**) (150 μL, 1.05 mmol, 2.1 eq), and TBAT (54.0 mg, 0.1 mmol, 20 mol%). The product was isolated (242 mg, 84%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.92 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.6 (t, *J* = 23.0 Hz, 3F), -138.2 – -138.3 (m, 2F), -142.2 – -142.4 (m, 2F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{20}H_7F_{14}O_2S^+$ 576.9938 Found 576.9940.

3,3-Dimethyl-6,8-bis(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-3,4-dihydro-2*H*-thieno[3,4-*b*]-[1,4]dioxepine (3da)

The title compound **3da** was synthesized according to general procedure C with (3,3-dimethyl-3,4-dihydro-2*H*-thieno[3,4-*b*][1,4]dioxepine-6,8-diyl)bis(trimethylsilane) (**1d**) (164.3 mg, 0.50 mmol), octafluorotoluene (**2a**) (150 μL, 1.05 mmol, 2.1 eq), and TBAT (54.0 mg, 0.1 mmol, 20 mol%). The product was isolated (222 mg, 72%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.90 (s, 4H), 1.06 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.6 (t, *J* = 23.0 Hz, 3F), -138.6 – -138.7 (m, 2F), -142.5 – -142.8 (m, 2F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{23}H_{11}F_{14}O_2S^+$ 617.0251 Found 617.0250.

7,7'-Bis(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-2,2',3,3'-tetrahydro-5,5'-bithieno[3,4-*b*][1,4]-dioxine (3ea)

The title compound **3ea** was synthesized according to general procedure C with 7,7′-bis(trimethylsilyl)-2,2′,3,3′-tetrahydro-5,5′-bithieno[3,4-*b*][1,4]dioxine (**1e**) (128.0 mg, 0.30 mmol), octafluorotoluene (**2a**) (300 μL, 2.1 mmol, 4.2 eq), and TBAT (32.4 mg, 0.06 mmol, 20 mol%). The product was isolated (212 mg, 99%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/2). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.45 – 4.42 (m, 4 H), 4.36 – 4.33 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 144.3 (dm, *J* = 260 Hz), 144.1 (dm, *J* = 260 Hz), 141.1, 137.3, 121.0 (q, *J* = 274 Hz), 116.5 (t, *J* = 17.2 Hz), 108.8–107.6 (m), 99.4, 98.8, 65.0, 65.0. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.5 (t, *J* = 23.0 Hz, 3F), -138.4 – -138.5 (m, 4F), -143.3 – -143.5 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{26}H_9F_{14}O_4S_2^+$ 714.9713; Found 714.9711.

4,4'-(2,2',3,3'-Tetrahydro-[5,5'-bithieno[3,4-*b*][1,4]dioxine]-7,7'-diyl)bis(2,3,5,6-tetrafluorobenzo-nitrile) (3eb)

The title compound **3eb** was synthesized according to general procedure C with 7,7′-bis(trimethylsilyl)-2,2′,3,3′-tetrahydro-5,5′-bithieno[3,4-*b*][1,4]dioxine (**1e**) (128.0 mg, 0.30 mmol), pentafluorobenzonitrile (**2b**) (303 μL, 2.4 mmol, 8.0 eq), and TBAT (32.4 mg, 0.06 mmol, 20 mol%). The product was isolated (184 mg, 98%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/2). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.46–4.42 (m, 4 H), 4.37–4.33 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -135.2 – -135.4 (m, 4F), -137.1 – -137.2 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{26}H_9F_8N_2O_4S^+$ 628.9871; Found 628.9871.

7,7'-Bis(4'-(decyloxy)-2,2',3,3',5,5',6,6'-octafluoro-[1,1'-biphenyl]-4-yl)-2,2',3,3'-tetrahydro-5,5'-bithieno[3,4-*b*][1,4]dioxine (3ec)

The title compound **3ec** was synthesized according to general procedure C with 7,7′-bis(trimethylsilyl)-2,2′,3,3′-tetrahydro-5,5′-bithieno[3,4-*b*][1,4]dioxine (**1e**) (128.0 mg, 0.30 mmol), 4-decyloxy-nonafluorobiphenyl (**2c**) (330 mg, 0.70 mmol, 2.3 eq), and TBAT (32.4 mg, 0.06 mmol, 20 mol%). The product was isolated (324 mg, 91%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/4). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.44 – 4.41 (m, 4 H), 4.37 – 4.35 (m, 4H), 4.33 (t, *J* = 7.3 Hz, 4H), 1.83 (tt, *J* = 6.9, 7.3 Hz, 4H), 1.51 – 1.45 (m, 4H), 1.39 – 1.26 (m, 24 H), 0.89 (t, *J* = 6.4 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -140.0 – -140.1 (m, 4F), -141.2 – -141.3 (m, 4F), -141.8 – -141.9 (m, 4F), -158.8 – -158.9 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{56}H_{51}F_{16}O_6S^+$ 1187.2866; Found 1187.2861.

7,7'-Bis(perfluoropyridin-4-yl)-2,2',3,3'-tetrahydro-5,5'-bithieno[3,4-*b*][1,4]dioxine (3ed)

The title compound **3ed** was synthesized according to general procedure C with 7,7′-bis(trimethylsilyl)-2,2′,3,3′-tetrahydro-5,5′-bithieno[3,4-*b*][1,4]dioxine (**1e**) (128.0 mg, 0.30 mmol), pentafluoropyridine (**2d**) (263 μL, 2.4 mmol, 8.0 eq), and TBAT (32.4 mg, 0.06 mmol, 20 mol%). The product was isolated (324 mg, 91%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/2). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.47–4.44 (m, 4 H), 4.39–4.36 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -93.5 – -93.7 (m, 4F), -141.9 – -142.1 (m, 4F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{22}H_9F_8N_2O_4S^+$ 580.9871; Found 580.9866.

2-(2,3,5,6-Tetrafluoro-4-(trifluoromethyl)phenyl)benzo[*b*]thiophene (3fa)

The title compound **3fa** was synthesized according to general procedure B with benzo[*b*]thiophen-2-yltrimethylsilane (**1f**) (103.2 mg, 0.50 mmol), octafluorotoluene (**2a**) (75 μL, 0.525 mmol, 1.05 eq), and TBAT (27.0 mg, 0.05 mmol, 10 mol%). The product was isolated (134.6 mg, 77%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.93–7.91 (m, 2H), 7.90 (s, 1H), 7.46–7.43 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.5 (t, *J* = 23.0 Hz, 3F), -139.8 – -139.9 (m, 2F), -142.7 – -142.9 (m, 2F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{15}H_6F_7S^+$ 351.0073; Found 351.0071.

2-Phenyl-5-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)thiophene (3ga)

The title compound **3ga** was synthesized according to general procedure B with trimethyl(5-phenylthiophen-2-yl)silane (**1g**) (116.2 mg, 0.50 mmol), octafluorotoluene (**2a**) (75 μL, 0.525 mmol, 1.05 eq), and TBAT (27.0 mg, 0.05 mmol, 10 mol%). The product was isolated (111.2 mg, 59%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.74 (d, *J* = 4.1 Hz, 1H), 7.69–7.66 (m, 2H), 7.46–7.42 (m, 2H), 7.41 (m, 1H), 7.39–7.34 (m,

1H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.4 (t, *J* = 23.0 Hz, 3F), -140.5 – -140.6 (m, 2F), -143.3 – -143.5 (m, 2F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{17}H_8F_7S^+$ 377.0229; Found 377.0230.

2-Methyl-5-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)thiophene (3ha)

The title compound **3ha** was synthesized according to general procedure B with trimethyl(5-methylthiophen-2-yl)silane (**1h**) (85.2 mg, 0.50 mmol), octafluorotoluene (**2a**) (75 μL, 0.525 mmol, 1.05 eq), and TBAT (27.0 mg, 0.05 mmol, 10 mol%) in 1,4-dioxane at 100 °C. The product was isolated (86.3 mg, 55%) as a white solid after column chromatography (SiO_2, AcOEt/hexane = 1/10). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.74 (d, *J* = 4.1 Hz, 1H), 7.69–7.66 (m, 2H), 7.46–7.42 (m, 2H), 7.41 (m, 1H), 7.39–7.34 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): -58.4 (t, *J* = 23.0 Hz, 3F), -140.5 – -140.6 (m, 2F), -143.3 – -143.5 (m, 2F). HRMS (DART) *m/z*: ($[M+H]^+$) Calcd for $C_{17}H_8F_7S^+$ 377.0229; Found 377.0230.

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