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Regioselective C–S bond formation accomplished by copper-catalyzed regioselective C–F substitution of perfluoroarenes with aryl thioacetates or benzyl thioacetate

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ABSTRACT

Practical and straightforward method for regioselective C–S bond formation accomplished by copper-catalyzed regioselective C–F substitution of electron-deficient perfluoroarenes with aryl thioacetates or benzyl thioacetate has been developed. Because of its high reaction efficiency, good chemoselectivity and regioselectivity, and excellent functional-group compatibility, this protocol provides a useful and operationally simple access to polyfluoroaryl thioethers used for drugs and material chemistry.

1. Introduction

Polyfluorobenzene derivatives are very useful and significant compounds, which were widely used in drugs and materials.[1]

Polyfluorobenzene attract much interest in C–H functionalizations catalyzed by various transition metals in modern organic synthesis. Fagnou,[2] Daugulis,[3] Hiyama,[4] Su,[5] Zhang,[6] Shi,[7] and Miura[8] et al. developed direct transition-metal-catalyzed C–H bond functionalization of perfluoroarenes.

Perutz reported that fluorinated organic derivatives could be synthesized by nickel mediated C–F activation of heteroaromatics.[9] Radius reported that C–F bond could be efficiently activated by a novel *N*-heterocyclic carbene–nickel(0) complex,[10a] and that catalytic C–C bond formation was accomplished by selective C–F activation of polyfluoroarenes using *N*-heterocyclic carbene-stabilized nickel complex as catalyst.[10b]

It was reported decades ago that several fluorine atoms of hexafluorobenzene and pentafluorobenzene could be replaced by thiophenol through nucleophilic aromatic substitution (S_NAr), which showing no regioselectivity.[11,12] However, the reaction gave monothiolation product in very low yield. We have found that the regioselective nucleophilic aromatic substitution reaction of pentafluorobenzene, methyl 2,3,4,5-tetrafluorobenzoic acid ester, and 1,2,4,5-tetrafluorobene with substituted thiophenols showed good regioselectivity while pentafluorobenzene gave high yields, but 1,2,4-trifluorobenzene, 1,3,5-tifluorobenzene and 1,3-difluorobenzene did not react with thiophenol.[13]

The direct use of thiols has intrinsic shortcomes due to their foul smell, which could lead to a severe environmental problem. In addition, they are sensitive to oxidation and are prone to undergo oxidative homocoupling to produce disulfides as byproducts.

Lee developed Pd-catalyzed cross-couplings of aryl halides and thioacetates.[14a] Daniels established Pd-catalyzed cross-coupling of benzyl thioacetates and aryl halides.[14b]

In this paper, we describe regioselective C–S bond formation in mild to high yield accomplished by copper-catalyzed selective C–F substitution of polyfluoroarenes with aryl thioacetates or benzyl thioacetate.

2. Results and discussion

Pentafluorobenzene (1 mmol), paramethyl phenyl thioacetate (1 mmol), silver carbonate (2 mmol), and potassium carbonate (2 mmol) were placed in anhydrous dimethoxyethane (DME). The reaction was stirred at reflux under nitrogen atmosphere for 24 h. After work up, we obtained compound **3a** in 17% yield (see Scheme 1 and entry 1, Table 2). Compound **3a** was confirmed by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, MS (EI), and HRMS.

We screened various kinds of solvents, such as MeOH, THF, CH_3CN, $ClCH_2CH_2Cl$, dioxane, toluene, DME, and DMF, as well as various kinds of bases, such as K_2CO_3, K_3PO_4, KOAc, Na_2CO_3, and Cs_2CO_3, as well as various copper catalyst, such as CuI, CuBr, CuCl, $Cu(OAc)_2$, and $CuSO_4$, and as well as some ligands, such as L-proline, Phen, DMEDA, Xantphos, and BINAP (see Table 1).

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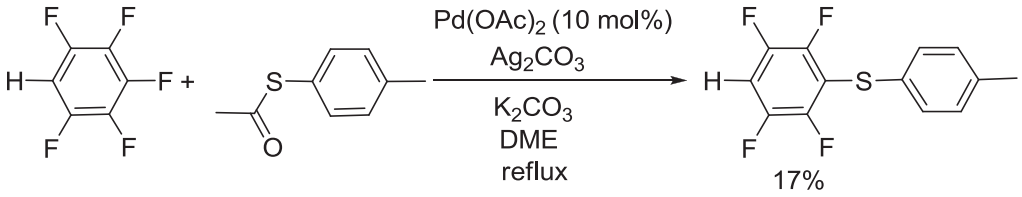


Scheme 1. Pd-catalyzed direct C–S bond formation by regioselective C–F substitution from pentafluorobenzene and paramethyl phenyl thioacetate.

Table 1
Optimization of the reaction conditions

Entry	Metal	Ligand	Base	Solvent	Temp	Yield%
1	$Pd(OAc)_2$		K_2CO_3 Ag_2CO_3	DME	Reflux	17
2	CuI	L-Proline	K_2CO_3	MeOH	Reflux	39
3	CuI	L-Proline	K_2CO_3	THF	Reflux	26
4	CuI	L-Proline	K_2CO_3	CH_3CN	Reflux	60
5	CuI	L-Proline	K_2CO_3	$ClCH_2CH_2Cl$	Reflux	9
6	CuI	L-Proline	K_2CO_3	Dioxane	Reflux	34
7	CuI	L-Proline	K_2CO_3	Toluene	110 °C	27
8	CuI	L-Proline	K_2CO_3	DMF	110 °C	79
9	CuI	L-Proline	K_2CO_3	DME	Reflux	25 (68[a])
10	CuI	L-Proline	K_3PO_4	DMF	110 °C	68
11	CuI	L-Proline	KOAc	DMF	110 °C	49
12	CuI	L-Proline	Na_2CO_3	DMF	110 °C	63
13	CuI	L-Proline	Cs_2CO_3	DMF	110 °C	77
14	**CuBr**	**L-Proline**	**K_2CO_3**	**DMF**	**110 °C**	**95**
15	CuCl	L-Proline	K_2CO_3	DMF	110 °C	86
16	$Cu(OAc)_2$	L-Proline	K_2CO_3	DMF	110 °C	82
17	$CuSO_4$	L-Proline	K_2CO_3	DMF	110 °C	94
18	CuBr	Phen	K_2CO_3	DMF	110 °C	84
19	CuBr	DMEDA	K_2CO_3	DMF	110 °C	89
20	**CuBr**	**Xantphos**	**K_2CO_3**	**DMF**	**110 °C**	**95**
21	CuBr	BINAP	K_2CO_3	DMF	110 °C	78
22	CuBr	Xantphos	K_2CO_3	DMF	110 °C	94[b]
23			K_2CO_3	DMF	110 °C	78

The values in bold indicate the best reaction conditions.
[a] DME (anhydrous) was distilled from sodium on benzophenone.
[b] DMF (anhydrous) was distilled from CaH_2.

Table 2
Substrate scope

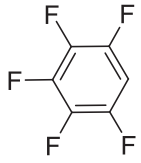
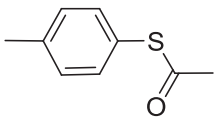
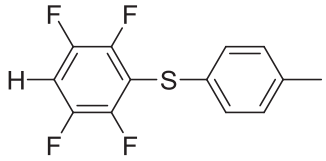
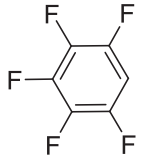
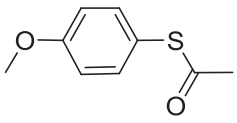
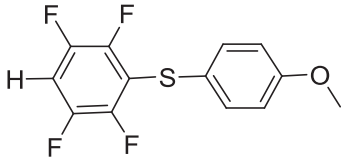
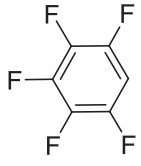
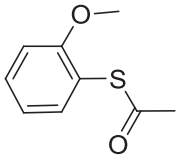
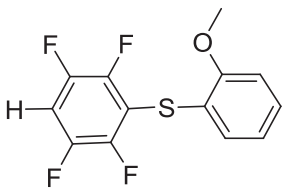
Entry	Fluoroarenes	Thioester	Product	Yield (%)
1			 **3a**	95
2			 **3b**	82
3			 **3c**	79

Table 2 (*continued*)

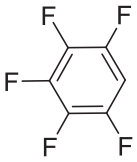
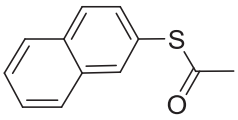
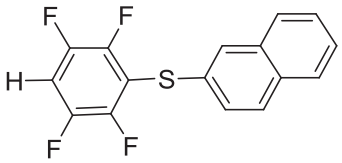
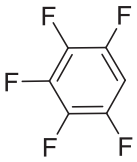
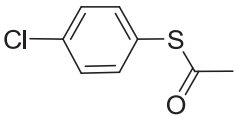
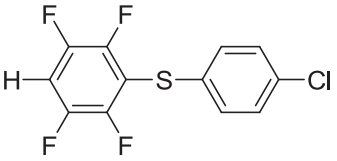
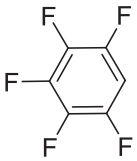
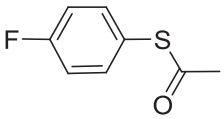
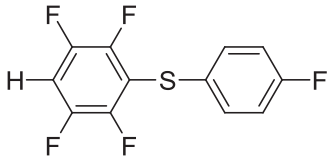
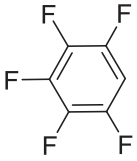
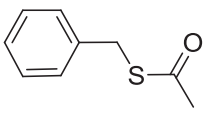
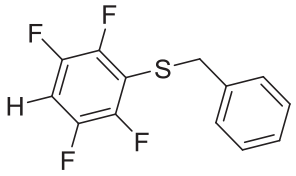
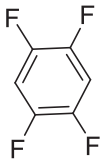
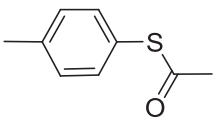
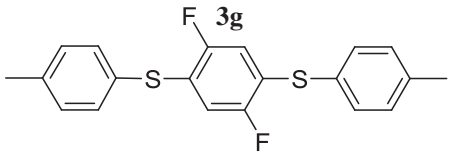
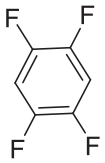
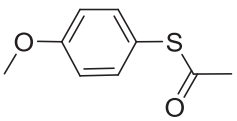
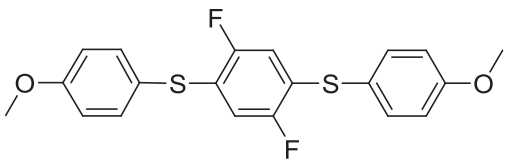
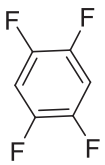
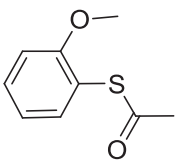
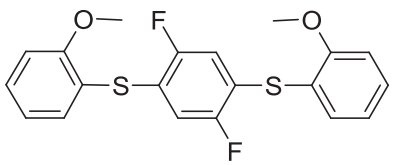
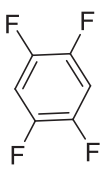
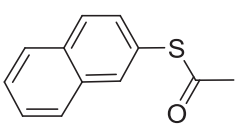
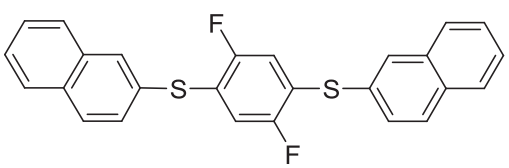
Entry	Fluoroarenes	Thioester	Product	Yield (%)
4			 **3d**	87
5			 **3e**	85
6			 **3f**	86
7			 **3g**	58
8			 **3h**	29 (14)[a]
9			 **3i**	24
10			 **3j**	24
11			 **3k**	32

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Table 2 (*continued*)

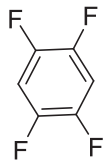
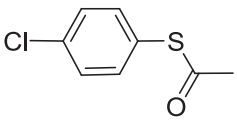
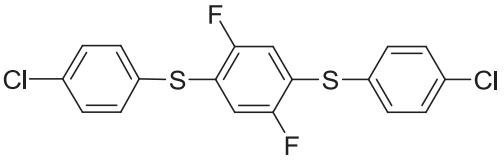
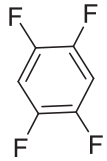
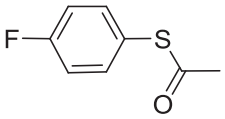
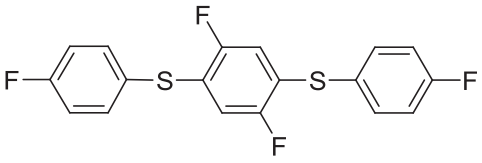
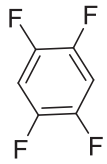
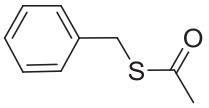
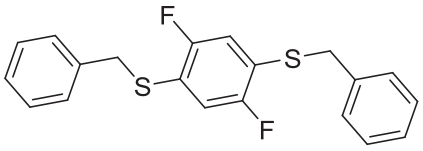
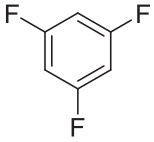
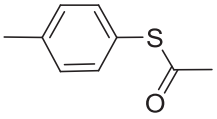
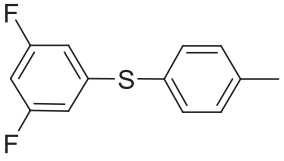
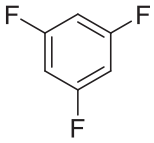
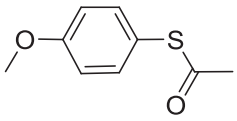
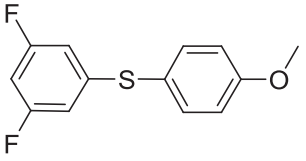
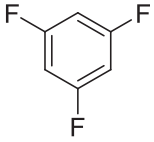
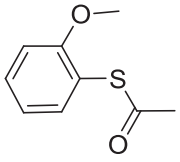
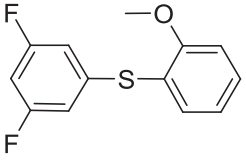
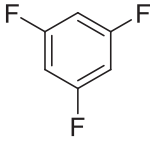
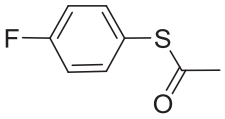
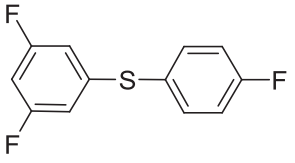
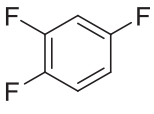
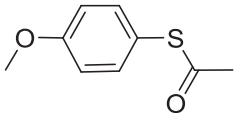
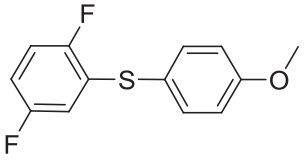
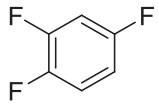
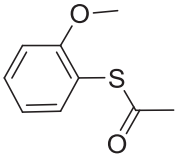
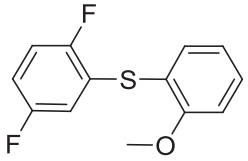
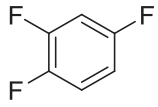
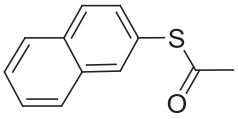
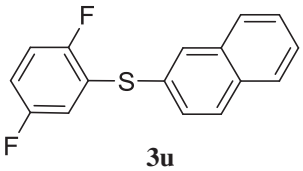
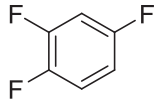
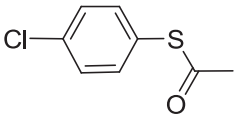
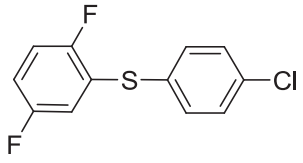
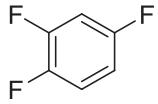
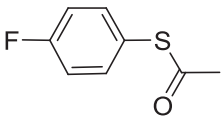
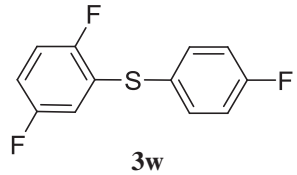
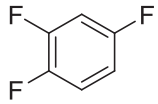
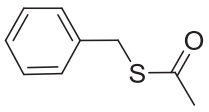
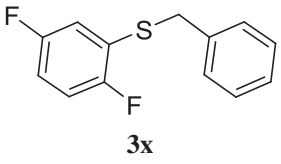
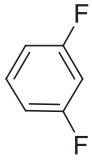
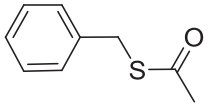
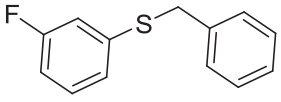
Entry	Fluoroarenes	Thioester	Product	Yield (%)
12			 **3l**	19
13			 **3m**	21
14			 **3n**	6
15			 **3o**	39
16			 **3p**	48
17			 **3q**	29
18			 **3r**	49
19			 **3s**	41

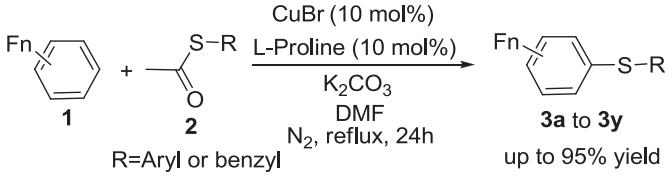
Table 2 (*continued*)

Entry	Fluoroarenes	Thioester	Product	Yield (%)
20			 **3t**	33
21			 **3u**	59
22			 **3v**	43
23			 **3w**	59
24			 **3x**	31
25			 **3y**	23

[a] 14% yield was obtained from reaction of 1,2,4,5-tetrafluorobenzene (1 mmol) and paramethyl phenyl thioacetate (2 mmol).

On the basis of these results, the optimal reaction condition involved the following parameters: CuBr as catalyst, L-proline (cheaper than Xantphos) as ligand, potassium carbonate as base, DMF as solvent, and reaction temperature at 110 °C under nitrogen atmosphere (see entry 14, Table 1).

Under the optimal reaction condition in hand, a study on the substrate scope was carried out, and the results are summarized in Table 2 (see Scheme 2 and Table 2).



Scheme 2. Synthesis of various polyfluoroaryl aryl thioethers.

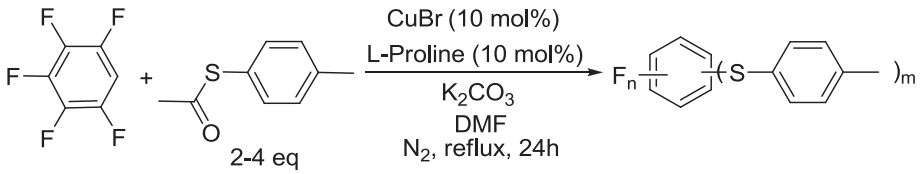
When pentafluorobenzene and aryl thioacetates bearing electron donating group as well as electron withdrawing group were used as starting materials, all products were obtained in high yield (79–95%, see entries 1–6, Table 2). All the aryl thioacetates bearing electron donating group as well as electron withdrawing group replaced the third F atom of pentafluorobenzene and showed similar reactivity to generate the corresponding product in high yields. The reaction showed good regioselectivity. Aryl thioacetates or benzyl thioacetate replaced the first and the forth F atoms of 1,2,4,5-tetrafluorobenzene in mild yields, which show regioselectivity (see entries 8–14, Table 2). Aryl thioacetates replaced the first F atom of 1,3,5-trifluorobenzene in mild yields, which show good regioselectivity (see entries 15–18, Table 2). Aryl thioacetates or benzyl thioacetate replaced the second F atom of 1,2,4-trifluorobenzene in mild yields, which show good regioselectivity (see entries 19–24, Table 2). Benzyl thioacetate replaced the first F atom of 1,3-difluorobenzene, which show good regioselectivity (see entry 25, Table 2). Compared with the aryl thioacetates, benzyl

thioacetate gave lower yield. The reactivity of benzyl thioacetate was lower than the aryl thioacetates.

We have reported that thiophenol showed mild to high reactivity with pentfluorobenzene and tetrafluorobenzene. However, thiophenol showed no reactivity with trifluorobenzene and 1,3-difluorobenzene.[13] Under this reaction condition, aryl thioacetates showed mild reactivity with trifluorobenzene and 1,3-difluorobenzene.

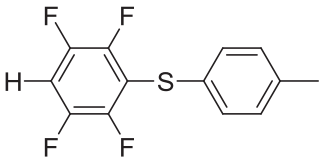
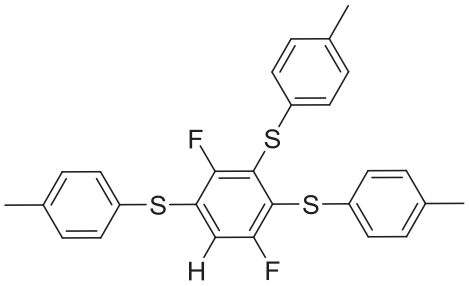
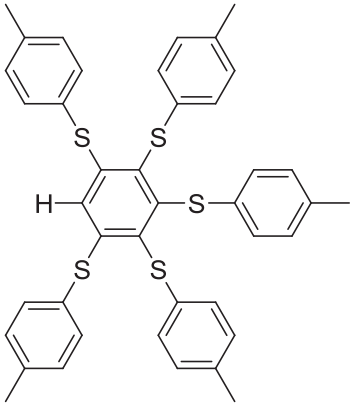
We have found that the reaction of pentafluorobenzene with more paramethyl phenyl thioacetate was very complex (see Scheme 3). Reaction of pentafluorobenzene with 2 equiv of paramethyl phenyl thioacetate provided compound **3a** in 29% yield and compound **4** in 47% yield (see entry 1, Table 3). Reaction of pentafluorobenzene with 3 equiv of paramethyl phenyl thioacetate provided compound **3a** in 2% yield and compound **4** in 80% yield (see entry 2, Table 3). Reaction of pentafluorobenzene with 4 equiv of paramethyl phenyl thioacetate provided compound **4** in 68% yield and compound **5** in 23% yield (see entry 3, Table 3).

Although aryl thioacetates could directly replace the fluorine atom via S_NAr mechanism, Herein, copper really can activate the C–F bond. It is reasonable to assume that the catalytic reaction proceeds by copper-promoted formation of fluoroarylcopper followed by the reaction of the copper species with paramethylphenylthio anion, affording the coupling product (Scheme 4).

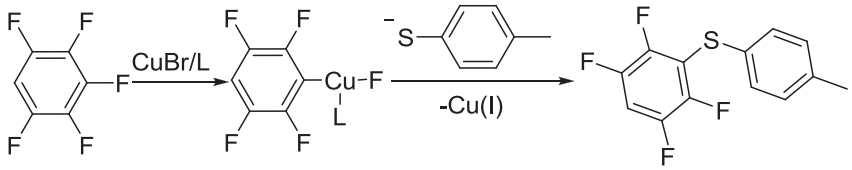


Scheme 3. Reaction of pentfluorobenzene with more paramethyl phenyl thioacetate.

Table 3
Control experiment: reaction of pentfluorobenzene with more paramethyl phenyl thioacetate

Entry	Product A	Product B	A: Yield (%)	B: Yield (%)
1[a]	 **3a**	 **4**	29	47
2[b]	**3a**	**4**	2	80
3[c]	**4**	 **5**	68	23

[a] Pentafluorobenzene (1 mmol), paramethyl phenyl thioacetates (2 mmol).
[b] Pentafluorobenzene (1 mmol), paramethyl phenyl thioacetates (3 mmol).
[c] Pentafluorobenzene (1 mmol), paramethyl phenyl thioacetates (4 mmol).



Scheme 4. Mechanistic considerations.

3. Conclusion

In summary, the copper-catalyzed coupling reaction of pentafluorobenzene with aryl thioacetates and benzyl thioacetate showed good regioselectivity and gave mild to high yields. Meanwhile, the copper-catalyzed coupling reaction of 1,2,3,4-tetrafluorobenzene, 1,3,5-trifluorobenzene, 1,2,4-trifluorobenzene, and 1,3-difluorobenzene with aryl thioacetates and benzyl thioacetate showed good regioselectivity and gave mild yields. The transition-metal-catalyzed cross-coupling reactivity of polyfluoroarene was on the progress.

4. Experimental section

4.1. General procedure for the copper-catalyzed coupling reaction of perfluoroarenes with aryl thioacetates and benzyl thioacetate

Pentafluorobenzene (0.168 g, 1 mmol), paramethyl phenyl thioacetates (0.166 g, 1 mmol), CuBr (14.3 mg, 0.1 mmol), L-proline (11.5 mg, 0.1 mmol), and potassium carbonate (0.276 g, 2 mmol) were placed in DMF (5 mL). The reaction was stirred at 110 °C under nitrogen atmosphere for 24 h. Till cooled, the reaction mixture was filtered. The organic solvent was evaporated. The mixture was dissolved with dichloromethane (10 mL). Then the mixture was washed with 10% NaOH (10 mL). The organic phase was dried over sodium sulfate. After evaporation of the solvent, the mixture was subjected column chromatography with petroleum ether as eluent.

*4.1.1. Compound **3a**.* Colorless gel; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.32–7.25 (m, 2H), 7.11–7.03 (m, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 148.0 (dm, J=69.0 Hz), 145.5 (dm, J=70.6 Hz), 138.6, 131.7, 130.4, 130.1, 129.6, 128.9, 116.0 (t, J=19.5 Hz), 106.9 (t, J=23.0 Hz), 21.4; ^{19}F NMR ($CDCl_3$, 300 MHz): −62.5 (m, 2F), −67.2 (m, 2F); MS (EI): 272; HRMS calcd for $C_{13}H_8F_4S$: 272.0283, found: 272.0281.

*4.1.2. Compound **3b**.* Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.44 (d, J=8.8 Hz, 2H), 6.97–7.05 (m, 1H), 6.82 (d, J=8.4 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 160.4, 147.8 (dm, J=44.7 Hz), 145.2 (dm, J=76.2 Hz), 134.8, 123.1, 116.9 (t, J=19.2 Hz), 115.2, 106.6 (t, J=22.4 Hz), 55.6; ^{19}F NMR ($CDCl_3$, 300 MHz): −61.4 (m, 2F), −65.7 (m, 2F); MS (EI): 288; HRMS calcd for $C_{13}H_8F_4OS$: 288.0232, found: 288.0234.

*4.1.3. Compound **3c**.* White solid; mp 44–45 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.22–7.26 (m, 1H), 7.04–7.11 (m, 2H), 6.85–6.88 (m, 2H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 157.8, 148.0 (dm, J=105.7 Hz), 145.5 (dm, J=107.6 Hz), 130.9, 129.3, 121.5, 121.3, 114.4 (t, J=19.2 Hz), 111.4, 106.8 (t, J=21.9 Hz), 56.2; ^{19}F NMR ($CDCl_3$, 300 MHz): −62.2 (m, 2F), −67.4 (m, 2F); MS (EI): 288; HRMS calcd for $C_{13}H_8F_4OS$: 288.0232, found: 288.0231.

*4.1.4. Compound **3d**.* White solid; mp 72–73 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.71–7.86 (m, 4H), 7.37–7.48 (m, 3H), 7.02–7.10 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 148.0 (dm, J=87.4 Hz), 145.5 (dm, J=89.7 Hz), 133.9, 132.8, 130.4, 130.1, 129.4, 128.0, 127.7, 127.1, 126.9, 115.2 (t, J=19.7 Hz), 107.3 (t, J=22.7 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −62.8 (d, J=10.2 Hz, 2F), −67.6 (d, J=6.6 Hz, 2F); MS (EI): 308; HRMS calcd for $C_{16}H_8F_4S$: 308.0283, found: 308.0281.

*4.1.5. Compound **3e**.* White solid; mp 60–62 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.32–7.25 (m, 4H), 7.13–7.08 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 148.0 (dm, J=75.3 Hz), 145.5 (dm, J=76.8 Hz), 134.5, 132.4, 131.7, 129.8, 114.9 (t, J=20.1 Hz), 107.5 (t, J=22.4 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −62.2 (m, 2F), −66.8 (m, 2F); MS (EI): 292; HRMS calcd for $C_{12}H_5ClF_4S$: 291.9737, found: 291.9734.

*4.1.6. Compound **3f**.* White solid; mp 56–58 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.46–7.42 (m, 2H), 7.12–6.98 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.3, 161.8, 147.9 (dm, J=67.7 Hz), 145.4 (dm, J=70.5 Hz), 134.2 (d, J=7.9 Hz), 131.6 (d, J=8.4 Hz), 128.1, 116.8 (d, J=21.6 Hz), 115.8 (t, J=20.4 Hz), 107.2 (t, J=22.6 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −62.8 (m, 2F), −67.1 (m, 2F), −87.9 (m, 1F); MS (EI): 276; HRMS calcd for $C_{12}H_5F_5S$: 276.0032, found: 276.0036.

*4.1.7. Compound **3g**.* White solid; mp 51–53 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.26 (s, 5H), 7.00–6.92 (m, 1H), 4.11 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 147.9 (dm, J=113.0 Hz), 145.4 (dm, J=115.2 Hz), 136.7, 129.1, 128.9, 128.0, 115.2 (t, J=20.4 Hz), 106.3 (t, J=22.5 Hz), 77.3 (t, J=32.5 Hz), 39.0 (t, J=2.8 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −133.91 (m, 2F), −138.84 (m, 2F); MS (EI): 272; HRMS calcd for $C_{13}H_8F_4S$: 272.0283, found: 272.0284.

*4.1.8. Compound **3h**.* White solid; mp 162–164 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.33 (d, J=8.0 Hz, 4H), 7.17 (d, J=8.0 Hz, 4H), 6.68 (t, J=7.6 Hz, 2H), 2.36 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): 157.4 (d, J=2.8 Hz), 155.0 (d, J=2.7 Hz), 139.2, 133.6, 130.8, 128.2, 125.0 (dd, J_1=12.6 Hz, J_2=11.4 Hz), 117.2 (m), 21.5; ^{19}F NMR ($CDCl_3$, 300 MHz): −84.3 (t, J=9.6 Hz, 2F); MS (EI): 358; HRMS calcd for $C_{20}H_{16}F_2S_2$: 358.0662, found: 358.0662.

*4.1.9. Compound **3i**.* White solid; mp 129.5–131.6 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.41 (d, J=8.8 Hz, 4H), 6.91 (d, J=8.8 Hz, 4H), 6.56 (t, J=8.0 Hz, 2H), 3.82 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): 160.8, 155.7 (dd, J_1=4.0 Hz, J_2=3.5 Hz), 136.3, 125.6 (q, J=11.7 Hz), 121.6, 116.2 (q, J=10.3 Hz), 115.7, 55.7; ^{19}F NMR ($CDCl_3$, 300 MHz): −83.6 (t, J=8.1 Hz, 2F); MS (EI): 390; HRMS calcd for $C_{20}H_{16}F_2O_2S_2$: 390.0560, found: 390.0557.

*4.1.10. Compound **3j**.* White solid; mp 132.5–134.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.35–7.24 (m, 4H), 6.94–6.91 (m, 4H), 6.73 (t, J=7.6 Hz, 2H), 3.87 (d, J=14.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): 158.7, 156.8 (dd, J_1=3.2 Hz, J_2=3.2 Hz), 133.9, 130.4, 123.3 (q, J=12.2 Hz), 121.8, 120.0, 117.8 (m), 111.6, 56.2; ^{19}F NMR ($CDCl_3$, 300 MHz): −84.6 (t, J=8.7 Hz, 2F); MS (EI): 390; HRMS calcd for $C_{20}H_{16}F_2O_2S_2$: 390.0560, found: 390.0564.

4.1.11. Compound ***3k***. White solid; mp 161.5–162.9 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.94 (s, 2H), 7.83–7.76 (m, 6H), 7.52–7.42 (m, 6H), 6.82 (t, J=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 156.6 (dd, J_1=3.4 Hz, J_2=3.4 Hz), 134.1, 133.2, 132.4, 129.8, 129.6, 129.4, 128.1, 127.9, 127.2 (d, 4C), 124.7 (q, J=12.0 Hz), 118.1 (m), 30.0; ^{19}F NMR ($CDCl_3$, 300 MHz): −85.5 (t, J=7.1 Hz, 2F); MS (EI): 430; HRMS calcd for $C_{26}H_{16}F_2S_2$: 430.0662, found: 430.0664.

4.1.12. Compound ***3l***. Colorless gel; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.33 (s, 8H), 6.80 (t, J=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 157.8 (d, J=3.1 Hz), 155.4 (d, J=3.6 Hz), 135.1, 134.0, 130.8, 130.2, 124.5 (dd, J_1=12.5 Hz, J_2=12.2 Hz), 118.3 (m); ^{19}F NMR ($CDCl_3$, 300 MHz): −86.0 (t, J=7.5 Hz, 2F); MS (EI): 398; HRMS calcd for $C_{18}H_{10}Cl_2F_2S_2$: 397.9569, found: 397.9566.

4.1.13. Compound ***3m***. White solid; mp 143–145 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.45–7.42 (m, 4H), 7.08 (t, J=8.4 Hz, 4H), 6.69 (t, J=7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 164.6, 162.2, 157.4, 155.0 (d, J=2.9 Hz), 135.7 (d, J=8.1 Hz), 127.0, 125.0 (dd, J_1=11.7 Hz, J_2=11.8 Hz), 117.4 (m); ^{19}F NMR ($CDCl_3$, 300 MHz): −112.1 (s, 2F), −115.9 (s, 2F); MS (EI): 366; HRMS calcd for $C_{18}H_{10}F_4S_2$: 366.0160, found: 366.0158.

4.1.14. Compound ***3n***. White solid; mp 109–111 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.29–7.21 (m, 10H), 6.92 (t, J=8.0 Hz, 2H), 4.05 (s, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): 157.3 (dd, J_1=3.7 Hz, J_2=3.2 Hz), 136.7, 129.1, 128.9, 127.8, 123.4 (q, J=12.2 Hz), 118.5 (m), 38.4; ^{19}F NMR ($CDCl_3$, 300 MHz): −85.5 (t, J=7.2 Hz, 2F); MS (EI): 358; HRMS calcd for $C_{20}H_{16}F_2S_2$: 358.0662, found: 358.0663.

4.1.15. Compound ***3o***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.39 (d, J=8.0 Hz, 2H), 7.21 (d, J=7.6 Hz, 2H), 6.64–6.51 (m, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 163.4 (dd, J_1=13.3 Hz, J_2=13.0 Hz), 143.3 (t, J=9.5 Hz), 139.8, 134.8, 130.9, 128.0, 110.3 (q, J=7.8 Hz), 101.3 (t, J 25.4 Hz), 21.5; ^{19}F NMR ($CDCl_3$, 300 MHz): −90.9 (t, J=8.4 Hz, 2F); MS (EI): 236; HRMS calcd for $C_{13}H_{10}F_2S$: 236.0471, found: 236.0470.

4.1.16. Compound ***3p***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.46 (d, J=8.8 Hz, 2H), 6.95 (d, J=8.8 Hz, 2H), 6.58–6.48 (m, 3H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 163.4 (dd, J_1=13.0 Hz, J_2=13.2 Hz), 161.1, 144.3 (t, J=9.3 Hz), 137.2, 121.6, 115.7, 109.5 (q, J=7.7 Hz), 100.9 (t, J=25.3 Hz), 55.7; ^{19}F NMR ($CDCl_3$, 300 MHz): −110.0 (t, J=8.4 Hz, 2F); MS (EI): 252; HRMS calcd for $C_{13}H_{10}F_2OS$: 252.0420, found: 252.0417.

4.1.17. Compound ***3q***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.43–7.38 (m, 2H), 6.98 (t, J=6.4 Hz, 2H), 6.67–6.53 (m, 3H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 163.3 (dd, J_1=13.0 Hz, J_2=13.3 Hz), 159.5, 114.7 (t, J=9.3 Hz), 136.1, 131.4, 121.8, 119.6, 111.9, 110.7 (q, J=7.1 Hz), 101.4 (t, J=25.6 Hz), 56.2; ^{19}F NMR ($CDCl_3$, 300 MHz): −110.2 (t, J=6.9 Hz, 2F); MS (EI): 252; HRMS calcd for $C_{13}H_{10}F_2OS$: 252.0420, found: 252.0422.

4.1.18. Compound ***3r***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.51–7.47 (m, 2H), 7.11 (t, J=8.8 Hz, 2H), 6.64–6.55 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 163.5 (dt, J_1=16.9 Hz, J_2=17.2 Hz), 142.6 (t, J=10.0 Hz), 136.8 (d, J=9.2 Hz), 131.6 (d, J=7.8 Hz), 127.0 (d, J=3.1 Hz), 117.3 (d, J=22.0 Hz), 110.6 (q, J=7.1 Hz), 101.7 (t, J=25.8 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −89.3 (m, 1F), −91.3 (t, J=7.8 Hz, 2F); MS (EI): 240; HRMS calcd for $C_{12}H_7F_3S$: 240.0221, found: 240.0216.

4.1.19. Compound ***3s***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.47–7.44 (m, 2H), 6.99–6.92 (m, 3H), 6.79–6.73 (m, 1H), 6.53–6.49 (m, 1H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 161.0, 159.2 (d, J=239.8 Hz), 155.4 (d, J=238.3 Hz), 136.8, 129.0 (q, J=8.4 Hz), 121.0, 116.3 (q, J=8.9 Hz), 115.7 (m, 3C), 113.4 (q, J=8.3 Hz), 55.7; ^{19}F NMR ($CDCl_3$, 300 MHz): −118.5 (m, 1F), −119.2 (m, 1F); MS (EI): 252; HRMS calcd for $C_{13}H_{10}F_2OS$: 252.0420, found: 252.0424.

4.1.20. Compound ***3t***. White solid; mp 67–69 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.37–7.28 (m, 2H), 7.03–6.92 (m, 3H), 6.86–6.82 (m, 1H), 6.71–6.66 (m, 1H), 3.84 (d, J=2.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 159.0 (dm, J=236.4 Hz), 159.0, 155.6 (d, J=1.5 Hz), 134.5, 130.6, 125.7 (q, J=7.9 Hz), 121.8, 119.8, 117.6 (d, J=25.2 Hz), 116.5 (q, J=8.7 Hz), 114.5 (q, J=7.9 Hz), 111.7, 56.2; ^{19}F NMR ($CDCl_3$, 300 MHz): −117.4 (m, 1F), −118.8 (m, 1F); MS (EI): 252; HRMS calcd for $C_{13}H_{10}F_2OS$: 252.0420, found: 252.0419.

4.1.21. Compound ***3u***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.95 (s, 1H), 7.84–7.75 (m, 3H), 7.52–7.43 (m, 3H), 7.05–7.00 (m, 1H), 6.89–6.76 (m, 2H), ^{13}C NMR ($CDCl_3$, 100 MHz): 158.8 (dd, J_1=2.1 Hz, J_2=2.8 Hz), 155.2 (d, J=2.5 Hz), 133.9, 132.9, 132.3, 129.6, 129.4, 129.2, 127.9, 127.7, 126.9 (d, J=4.2 Hz), 126.2 (q, J=8.0 Hz), 117.7 (d, J=15.9 Hz), 116.5 (q, J=8.8 Hz), 114.7 (q, J=7.7 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −117.0 (m, 1F), −118.2 (m, 1F); MS (EI): 272; HRMS calcd for $C_{16}H_{10}F_2S$: 272.0471, found: 272.0469.

4.1.22. Compound ***3v***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.34 (s, 4H), 7.06–7.01 (m, 1H), 6.93–6.87 (m, 1H), 6.83–6.79 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): ^{13}C NMR ($CDCl_3$, 100 MHz): 159.0 (dd, J_1=2.4 Hz, J_2=2.7 Hz), 156.9 (dd, J_1=2.9 Hz, J_2=2.9 Hz), 134.9, 133.9, 131.2, 130.1, 125.5 (q, J=8.7 Hz), 118.4 (d, J=25.5 Hz), 116.9 (q, J=8.0 Hz), 115.6 (q, J=7.8 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −116.4 (m, 1F), −117.9 (m, 1F); MS (EI): 256; HRMS calcd for $C_{12}H_7ClF_2S$: 255.9925, found: 255.9927.

4.1.23. Compound ***3w***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.48–7.25 (m, 2H), 7.10–6.98 (m, 3H), 6.87–6.82 (m, 1H), 6.70–6.65 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 163.4 (d, J=248.9 Hz), 159.1 (dd, J_1=2.3 Hz, J_2=2.4 Hz), 156.3 (dd, J_1=1.9 Hz, J_2=2.7 Hz), 135.9 (d, J=8.4 Hz), 131.6 (d, J=8.2 Hz), 126.9 (q, J=8.0 Hz), 116.9 (m), 114.7 (q, J=7.7 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −112.2 (m, 1F), −117.6 (m, 1F), −118.1 (m, 1F); MS (EI): 240; HRMS calcd for $C_{12}H_7F_3S$: 240.0221, found: 240.0222.

4.1.24. Compound ***3x***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.28–7.22 (m, 5H), 7.00–6.93 (m, 2H), 6.87–6.82 (m, 1H); 4.10 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 158.7 (dd, J_1=2.5 Hz, J_2=2.5 Hz), 157.6 (dd, J_1=2.7 Hz, J_2=2.7 Hz), 136.8, 129.1, 128.9, 127.8, 125.3 (q, J=8.2 Hz), 118.4 (d, J=25.3 Hz), 116.5 (q, J=8.9 Hz), 114.8 (q, J=8.1 Hz), 38.2 (d, J=2.4 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −116.4 (m, 1F), −118.7 (m, 1F); MS (EI): 236; HRMS calcd for $C_{13}H_{10}F_2S$: 236.0471, found: 236.0470.

4.1.25. Compound ***3y***. Colorless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.30–7.16 (m, 6H), 7.06–6.97 (m, 2H), 6.87–6.82 (m, 1H), 4.11 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 163.0 (d, J=246.7 Hz), 139.2 (d, J=7.4 Hz), 137.1, 130.3 (d, J=8.0 Hz), 129.1, 128.9, 127.7, 125.0 (d, J=2.9 Hz), 116.2 (d, J=22.8 Hz), 113.3 (d, J=21.0 Hz), 38.8; ^{19}F NMR ($CDCl_3$, 300 MHz): −88.0 (m, 1F); MS (EI): 218; HRMS calcd for $C_{13}H_{11}FS$: 218.0566, found: 218.0561.

4.1.26. Compound ***4***. White solid; mp 129–130.2 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.39 (d, J=8.0 Hz, 2H), 7.23 (t, J=6.4 Hz, 2H), 7.15 (d, J=8.0 Hz, 2H), 7.00–7.09 (m, 6H), 6.49 (dd, J_1=6.4 Hz, J_2=6.4 Hz, 1H), 2.38 (s, 3H), 2.28 (d, J=9.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): 159.5 (dd, J_1=2.5 Hz, J_2=3.3 Hz), 155.4 (d, J=242.7 Hz), 140.3, 137.3, 136.9, 135.2, 132.4, 131.8, 130.9, 130.4, 130.0 (d, J=6.9 Hz), 129.7, 128.9, 128.7, 126.1, 124.2, 124.0, 115.6 (dd, J_1=2.9 Hz, J_2=4.2 Hz), 21.6, 21.3 (d, J=4.9 Hz); ^{19}F NMR ($CDCl_3$, 300 MHz): −104.63 (m, 1F), −105.55 (m, 1F); MALDI (480.1); HRMS (MALDI) calcd for $C_{27}H_{22}F_2S_3$: 480.0837, found: 480.0846.

4.1.27. Compound ***5***. White solid; mp 168–170 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): 7.09 (d, *J*=8.4 Hz, 4H), 6.94–7.00 (m, 12H), 6.91 (s, 4H), 6.22 (s, 1H), 2.36 (s, 6H), 2.27 (s, 6H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 152.0, 149.1, 139.3, 135.6 (t, *J*=4.0 Hz), 134.8, 133.7, 130.9, 130.5, 129.9, 128.8, 128.0, 127.5, 123.8, 21.7, 21.3; MALDI (688.1); HRMS (MALDI) calcd for $C_{41}H_{362}S_5$: 688.1408, found: 688.1415.

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