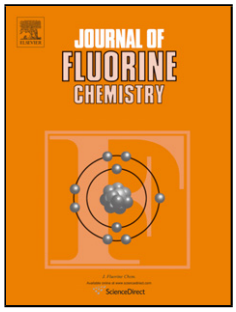

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Coupling of *gem*-difluorinated organozinc reagents with S-electrophiles

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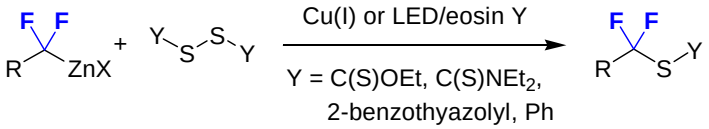
GRAPHICAL ABSTRACT



Copper-catalyzed or light-promoted coupling of *gem*-difluorinated organozinc reagents with disulfides is described.

HIGHLIGHT

Reactions of fluorinated organozinc reagents.

Copper-catalyzed copper-sulfur bond coupling.

Light-promoted reactions of disulfides.

Abstract *gem*-Difluorinated organozinc reagents, which were prepared by insertion of CF_2-fragment into C-Zn bond, couple with diethyl dixanthogen, di(benzothiazolyl) disulfide, and tetraethylthiuram disulfide. The reaction is promoted either by a copper(I) catalyst or by irradiation with blue light in the presence of Eosin Y disodium salt.

Keywords: Organozinc reagents, Difluorinated compounds, Difluorocarbene, Disulfides

1. Introduction

Fluorinated organometallics constitute important class of reagents for the introduction fluorine-containing fragment into organic molecules [1]. In contrast to lithium and magnesium reagents, which frequently possess limited stability, less polar organozincs [2] are notably more robust that offers wider scope of possible reagents. On the other hand, decreased reactivity of carbon-zinc bond narrows the scope of suitable electrophiles. Typically, fluorinated organozincs are prepared from

fluorinated bromides or iodides either by reaction with elemental zinc [3] or by halogen/zinc exchange [4]. In some cases, direct zincation of C-H bonds by zinc amides is possible [5].

Recently, we proposed a concept for the generation of reagents **1** by insertion of CF_2-fragment into carbon-zinc bond [6]. These reagents were coupled with carbon [7], halogen [6,8] and nitrogen [9] electrophiles. Herein we report our studies on the interaction of species **1** with S-electrophiles.

2. Results and discussion

Sulfenyl chlorides were first considered as typical sulfur electrophiles [10]. When reagent **1a** was treated with phenyl sulfenyl chloride, compound **2** bearing bromodifluoromethyl group was observed, whereas no desired sulfenylation product was detected (Scheme 2). At the same time, organozinc **1a** was absolutely unreactive towards diphenyl disulfide. Correspondingly, we proposed to employ thio-electrophiles of intermediate electrophilic activity, such as dixanthogens.

Reaction of organozinc **1a** obtained in acetonitrile with 1.1 equivalent of diethyl dixanthogen **3a** provided product **4a** in 24% yield (Table 1, entry 1). Addition of 2.5 mol % of copper chloride/triphenylphosphine complex doubled the product yield (entry 2). Subsequent optimization revealed that increase of amount of catalyst to 5 mol % and use of DMF as a co-solvent allowed to obtain sulfenylation product **4a** in 64% isolated yield (entry 4). Further variation of reaction conditions did not lead to increase of yield. The accelerating role of copper in this process is likely to generate fluorinated organocopper species, which undergoes oxidative addition into S-S bond of the disulfide followed by reductive elimination from copper(III) intermediate.

Under optimized conditions a series of conventional organozinc reagents were subjected to the difluoromethylene insertion using (bromodifluoromethyl)trimethylsilane followed by coupling with disulfides (Table 2). Besides dixanthogene, di(benzothiazolyl) disulfide (**3b**) was also employed, which typically gave slightly higher yields of products compared to those of dixanthogene. The scalability of the reaction was demonstrated by coupling of 10 mmol of benzylzinc bromide with disulfide **3b** affording product **4b** in 50% yield.

Surprisingly, when difluorinated reagents **1** were coupled with thiuram disulfide **3c** under typical conditions involving a copper catalyst, no sulfenylation products were formed. Extensive screening of conditions demonstrated that irradiation of the mixture of **1** and **3c** with blue light (strip of light emitting diodes) in the presence of 2 mol % of Eosin Y disodium salt led to desired products **4l-n** (Table 3). No products were formed when the reaction was performed in the dark.

Concerning mechanism, we may propose that the reaction starts from the generation of thiyl radical **5** by one electron reduction of disulfide **3c** with light activated Eosin Y [11] (Schem 3). Then, thiyl radical **5** may attack at the zinc of reagent **1** to effect radical substitution [12,13] with the formation of fluorinated radical **6**. The latter species reacts at the C=S bond of disulfide **3c** in a typical way [14] leading to the product with the regeneration of radical **5**.

The key point of this mechanism is the intermediacy of thiyl radical **5**. In fact, it is known that the S-S bond can be homolytically cleaved under photochemical conditions [15]. Accordingly, when reactions of **1** with disulfide **3c** were performed without Eosin Y but with blue light irradiation, expected products **4** were also formed in similar yields as with Eosin (for example, for product **4l**, 50% yield).

Encouraged by these results, we tested diphenyl disulfide under light mediated conditions (Scheme 4). Thus, the reaction of organozinc **1a** proceeded smoothly, and expected product **4o** was isolated in 53% yield, while in reaction without Eosin, the product was formed in 51% yield.

3. Conclusions

In summary, various disufide reagents were demonstrated to behave as competent electrophiles towards *gem*-difluorinated organozinc reagents. The reactions were promoted either by copper(I) catalyst or visible light in the presence of Eosin Y.

4. Experimental

4.1 General Experimental Procedures

All reactions were performed under an argon atmosphere. DMF and MeCN were distilled under vacuum from P_2O_5 and stored over MS 4Å. 1,2-Dimethoxyethane (DME) was distilled from $LiAlH_4$. As light source, a strip of diodes SMD 2835 120 LED/m Blue was used. NMR spectra were recorded on a Bruker AM-300 instrument. Starting organozinc reagents [6], Me_3SiCF_2Br [16] were obtained according to literature procedures. Diphenyl disulfide was commercial.

4.2. Preparation of disulfides.

*4.2.1. Dixanthogen (**3a**)* [17].

Iodine (7 g, 27.5 mmol) was slowly added to a solution of potassium ethyl xanthogenate (8.8 g, 55 mmol) in water at room temperature, and the mixture was stirred for 2 hours. The mixture was extracted with hexane (3×15 mL), the combined extracts were filtered through Na_2SO_4, concentrated under vacuum, and the residue was recrystallized from petrol ether with cooling to –12 °C. Yield 4.7 g (70%). Mp 29–30 °C.

*4.2.2. 2-(1,3-Benzothiazol-2-yldithio)-1,3-benzothiazole (**3b**)* [18].

Hydrogen peroxide (5 mL of 12M aqueous solution, 60 mmol) was added to a solution of 2-mercaptobenzothiazole (10 g, 60 mmol) in ethanol (100 mL). Then, iodine (20 mg) was added at room temperature, and the mixture was heated at 55 °C for 30 min. The heating bath was removed, and the mixture was allowed to stand overnight without stirring. The precipitate was filtered, washed with ethanol, and dried under vacuum. Yield 10 g (98%). Mp 176–178 °C.

*4.2.3. Tetraethylthiuram disulfide (**3c**)* [19].

To a solution of diethylamine (7 mL, 67 mmol) in methanol (50 mL) upon cooling with room temperature water bath was added dropwise CS_2 (4.3 mL, 71 mmol), and then hydrogen peroxide (3.1 mL of 12M aqueous solution, 37 mmol) which caused the formation of the precipitate. The mixture was heated until dissolution of the precipitate. The mixture was allowed cool slowly to 5 °C. The crystals was filtered, washed with methanol, and dried under vacuum. Yield 5.5 g (55%). Mp 69–71 °C.

*4.3. Synthesis of compounds **4a-k** (General Procedure).*

A solution of organozinc reagent in THF (1 mmol) was concentrated under vacuum, the residue was dissolved in DME (1.5 mL), and sodium acetate (99 mg, 1.2 mmol) was added at room temperature. The mixture was cooled to –25 °C, Me_3SiCF_2Br (244 mg, 1.2 mmol) was added dropwise, and the mixture was stirred for at –25 °C for 18 h. Then, DMF (0.5 mL) was added. Disulfide (1.1 mmol) was added [dixanthogen **3a** was added in one portion; for dibenzothiazolyl disulfide **3b**, half of the amount was added, the mixture was stirred for 30 min followed by addition of the second half]. The reaction mixture was allowed to warm to room temperature during 6 h, and stirred for additional 12 h. For the work-up, water (7 mL) was added, the mixture was extracted with methyl *tert*-butyl ether/hexane, 1/1 (for **4a-j**) or methyl *tert*-butyl ether (for **4k**) (3×5 mL). The combined organic layers were filtered through Na_2SO_4, concentrated under vacuum, and the residue was purified by column chromatography.

*4.3.1. S-(1,1-Difluoro-2-phenylethyl) O-ethyl (dithiocarbonate) (**4a**).*

Yield 168 mg (64%). Yellow oil. R_f 0.23 (Hexanes/CH_2Cl_2, 10/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.54 (t, 3H, *J* = 7.3 Hz), 3.62 (t, 2H, *J* = 16.0 Hz), 4.75 (q, 2H, *J* = 7.3 Hz), 7.31–7.44 (m, 5H). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –73.8 (t, *J* = 16.0 Hz). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 13.7, 45.0 (t, *J* = 23.2 Hz), 70.6, 127.6 (t, *J* = 285.3 Hz), 128.1, 128.7, 130.7, 131.3 (t, *J* = 3.3 Hz), 205.9 (t, *J* = 2.9 Hz). HRMS (ESI): calcd for $C_{11}H_{12}F_2OS_2Na$ [M+Na] 285.0190, found 285.0191.

*4.3.2. 2-[(1,1-Difluoro-2-phenylethyl)thio]-1,3-benzothiazole (**4b**).*

Yield 169 mg (55%). For the reaction performed on 10 mmol of benzylzinc bromide, the yield was 1.58 g (50%). Colorless solid. Mp 57–60 °C. R_f 0.29 (Hexanes/EtOAc, 15/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.68 (t, 3H, *J* = 15.4 Hz), 7.34–7.56 (m, 1H), 7.87 (d, 1H, *J* = 8.1 Hz), 8.12 (d, 1H, *J* = 8.1 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 45.4 (t, *J* = 23.2 Hz), 121.2, 123.6, 126.0, 126.6, 128.2, 128.7, 128.8 (t, *J* = 284.7 Hz), 130.8, 131.2 (t, *J* = 3.3 Hz), 137.6, 153.2, 156.0 (t, *J* = 2.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –70.0 (t, *J* = 14.1 Hz). HRMS (ESI): calcd for $C_{15}H_{12}F_2NS_2$ [M+H] 308.0374, found 308.0368.

*4.3.3. S-(1,1-Difluoro-2-methylpropyl) O-ethyl (dithiocarbonate) (**4c**).*

Yield 107 mg (50%). Yellow oil. R_f 0.29 (Hexanes/CH_2Cl_2, 30/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.13 (d, 6H, *J* = 3.0 Hz), 1.48 (t, 3H, *J* = 7.3 Hz), 2.35–2.57 (m, 1H), 4.72(q, 2H, *J* = 7.3 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 13.6, 16.1 (t, *J* = 3.8 Hz), 37.0 (t, *J* = 21.1 Hz), 70.5, 131.2 (t, *J* = 287.5 Hz), 206.5 (t, *J* = 2.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –81.9 (d, *J* = 11.3 Hz). HRMS (ESI): calcd for $C_7H_{13}F_2OS_2$ [M+H] 215.0370, found 215.0373.

*4.3.4. 2-[(1,1-Difluoro-2-methylpropyl)thio]-1,3-benzothiazole (**4d**).*

Yield 155 mg (60%). Colorless oil. R_f 0.33(Hexanes/EtOAc, 12/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.22 (d, 6H, *J* = 6.9 Hz), 2.52 (sept, 1H, *J* = 6.9 Hz), 7.45 (m, 2H), 7.86 (d, 1H, *J* = 7.8 Hz), 8.08 (d, 1H, *J* = 7.8 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 16.5 (t, *J* = 3.4 Hz), 37.6 (t, *J* = 21.5 Hz), 121.0, 123.6, 126.0, 126.5, 132.4 (t, *J* = 286.0 Hz), 137.8, 153.1, 155.9 (t, *J* = 2.3 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –77.5 (d, *J* = 12.7 Hz). HRMS (ESI): calcd for $C_{11}H_{12}F_2NS_2$ [M+H] 260.0374, found 260.0375.

*4.3.5. S-(1,1-Difluoro-3-methylbutyl) O-ethyl (dithiocarbonate) (**4e**).*

Yield 91 mg (40%). Yellow oil. R_f 0.33 (Hexanes/CH_2Cl_2, 40/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.03 (d, 6H, *J* = 6.5 Hz), 1.48 (t, 3H, *J* = 7.3 Hz), 1.96–2.12 (m, 1H), 2.18 (td, 2H, *J* = 17.0, 6.5 Hz), 4.71 (q, 2H, *J* = 7.3 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 13.6, 23.2, 24.1 (t, *J* = 2.3 Hz), 47.0 (t, *J* = 21.9 Hz), 70.4, 129.0 (t, *J* = 284.5 Hz), 206.4 (t, *J* = 3.8 Hz). ^{19}F NMR (282 MHz,

$CDCl_3$), δ: –72.0 (t, *J* = 17.0 Hz). Calcd for $C_8H_{14}F_2OS_2$ (228.32): C 42.09, H 6.18 Found: C 42.04, H 6.28.

*4.3.6. 2-[(1,1-Difluoro-3-methylbutyl)thio]-1,3-benzothiazole (**4f**).*

Yield 128 mg (47%). Colorless oil. R_f 0.33 (Hexanes/CH_2Cl_2, 25/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.05 (d, 6H, *J* = 6.4 Hz), 2.10–2.29(m, 3H Hz), 7.40–7.53(m, 2H), 7.86 (d, 1H, *J* = 8.2 Hz), 8.08 (d, 1H, *J* = 8.2 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 23.2, 24.2 (t, *J* = 2.3 Hz), 47.2 (t, *J* = 21.1 Hz), 121.2 , 123.6, 126.0, 126.6, 130.0 (t, *J* = 284.0 Hz), 137.7, 153.1, 156.0 (t, *J* = 3.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –68.3(t, *J* = 15.5 Hz). HRMS (ESI): calcd for $C_{12}H_{14}F_2NS_2$ [M+H] 274.0530, found 274.0536.

*4.3.7. 2-[(1,1-Difluoroethyl)thio]-1,3-benzothiazole (**4g**).*

Yield 160 mg (61%). Colorless liquid. R_f 0.27 (Hexanes/EtOAc, 12/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.13(t, 3H, *J* = 16.5 Hz), 7.38–7.52(m, 2H Hz), 7.83(d, 1H, *J* = 8.2 Hz), 8.07(d, 1H, *J* = 8.2 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 26.6 (t, *J* = 24.9 Hz), 121.1, 123.6, 126.0, 126.6, 128.0 (t, *J* = 280 Hz), 137.6, 153.1, 156.0 (t, *J* = 3.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –64.6 (q, *J* = 16.9 Hz). HRMS (ESI): calcd for $C_9H_8F_2NS_2$ [M+H] 232.0061, found 232.0067.

*4.3.8. S-[4-(Benzyloxy)-1,1-difluorobutyl] O-ethyl (dithiocarbonate) (**4h**).*

Yield 112 mg (35%). Colorless oil. R_f 0.23 (Hexanes/EtOAc, 15/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.46 (t, 3H, *J* = 7.3 Hz), 1.85–1.95 (m, 2H), 2.36–2.52(m, 2H), 3.56 (t, 2H, *J* = 5.9 Hz), 4.53 (s, 2H), 4.70 (q, 2H, *J* = 7.3 Hz), 7.27–7.42 (m, 5H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 13.5, 23.1 (t, *J* = 3.8 Hz), 35.8 (t, *J* = 22.6 Hz), 68.8, 70.5, 73.0, 127.7, 127.8, 128.5, 128.9 (t, *J* = 284.5 Hz), 138.3, 206.1 (t, *J* = 3.8 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –74.4 (t, *J* = 14.1 Hz). HRMS (ESI): calcd for $C_{14}H_{19}F_2O_2S_2$ [M+H] 321.0789, found 321.0797.

*4.3.9. 2-{[4-(Benzyloxy)-1,1-difluorobutyl]thio}-1,3-benzothiazole (**4i**).*

Yield 190 mg (52%). Colorless oil. R_f 0.23 (Hexanes/EtOAc, 4/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.96–2.05 (m, 2H), 2.42–2.58 (m, 2H), 3.56 (t, 2H, *J* = 5.5 Hz), 4.52 (s, 2H), 7.29–7.54 (m, 7H), 7.84 (d, 1H, *J* = 8.2 Hz), 8.10 (d, 1H, *J* = 8.2 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 23.6 (t, *J* =

3.4 Hz), 36.2 (t, *J* = 22.6 Hz), 68.7, 73.0, 121.2, 123.7, 126.0, 126.6, 127.7, 127.8, 128.5, 130.0 (t, *J* = 283.0 Hz), 137.3, 138.4, 153.2, 155.6 (t, *J* = 2.3 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ:–68.3(t, *J* = 15.3 Hz). HRMS (ESI): calcd for $C_{18}H_{18}F_2NOS_2$ [M+H] 366.0792, found 366.0795.

*4.3.10. Ethyl 5-(1,3-benzothiazol-2-ylthio)-5,5-difluoropentanoate (**4j**).*

Yield 142 mg (43%). Colorless oil. R_f 0.28 (Hexanes/EtOAc, 4/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.24 (t, 3H, *J* = 7.3 Hz), 1.95–2.05 (m, 2H), 2.32–2.47 (m, 4H), 4.13 (q, 2H, *J* = 7.3 Hz), 7.40–7.53 (m, 2H), 7.85(d, 1H, *J* = 8.1 Hz), 8.10 (d, 1H, *J* = 8.1 Hz). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 14.0, 18.4 (t, *J* = 3.5 Hz), 32.9, 38.0 (t, *J* = 22.6 Hz), 60.3, 121.0, 123.4, 125.8, 126.4, 129.3 (t, *J* = 283.3 Hz), 137.4, 152.9, 155.4 (t, *J* = 3.0 Hz), 172.2. ^{19}F NMR (282 MHz, $CDCl_3$), δ: –70.9 (t, *J* = 14.1 Hz). HRMS (ESI): calcd for $C_{14}H_{16}F_2NO_2S_2$ [M+H] 332.0585, found 332.0572.

*4.3.11. Diethyl 3-(1,3-benzothiazol-2-ylthio)-3,3-difluoropropylphosphonate (**4k**).*

Yield 187 mg (49%). Colorless oil. R_f 0.33 (Hexanes/*i*-PrOH, 5/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.26 (t, 6H, *J* = 7.2 Hz), 1.98–2.10 (m, 2H), 2.48–2.68 (m, 2H), 4.01–4.17 (m, 4H), 7.37–7.49 (m, 2H), 7.81 (d, 1H, *J* = 8.2 Hz), 8.02 (d, 1H, *J* = 8.2 Hz). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 16.4 (d, *J* = 5.3 Hz), 19.9 (dt, *J* = 145.3, 3.2 Hz), 32.9 (td, *J* = 24.1, 3.0 Hz), 62.1 (d, *J* = 6.8 Hz), 121.2, 123.7, 126.2, 126.7, 129.1 (t, *J* = 283.8 Hz), 137.6, 153.2, 155.0 (t, *J* = 3.0 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –72.8 (t, *J* = 14.1 Hz). HRMS (ESI): calcd for $C_{14}H_{19}F_2NO_3PS_2$ [M+H] 382.0507, found 382.0502.

*4.4. Synthesis of compounds **4l-n** (General Procedure).*

A solution of organozinc reagent in THF (1 mmol) was concentrated under vacuum, the residue was dissolved in DME (1.5 mL), and sodium acetate (99 mg, 1.2 mmol) was added at room temperature. The mixture was cooled to –25 °C, Me_3SiCF_2Br (244 mg, 1.2 mmol) was added dropwise, and the mixture was stirred for at –25 °C for 18 h. Then, DMF (0.5 mL) was added. To the resulting mixture were successively added disulfide **3c** (311 mg, 1.05 mmol) and Eosin Y disodium salt (15 mg, 0.02 mmol). The cooling bath was removed, and the reaction flask was irradiated with blue LED at room temperature during 4 h. For the work-up, water (7 mL) was

added, the mixture was extracted with methyl *tert*-butyl ether/hexane (1/1, 3×5 mL). The combined organic layers were filtered through Na_2SO_4, concentrated under vacuum, and the residue was purified by column chromatography.

*4.3.1. 1,1-Difluoro-2-phenylethyl diethyl-(dithiocarbamate) (**4l**).*

Yield 147 mg (51%). Yellow oil. R_f 0.22 (Hexanes/EtOAc, 20/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.21 (t, 3H, *J* = 6.9 Hz), 1.32 (t, 3H, *J* = 6.9 Hz), 3.62 (q, 2H, *J* = 6.9 Hz), 4.01 (q, 2H, *J* = 6.9 Hz), 4.10 (t, 2H, *J* = 15.5 Hz), 7.28–7.41(m, 5H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 11.2, 12.7, 43.4(t, *J* = 22.1 Hz), 47.9, 48.3, 127.5, 128.1, 129.1 (t, *J* = 280.3 Hz), 130.6, 132.4 (t, *J* = 3.5 Hz), 186.7(t, *J* = 5.5 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –71.1 (t, *J* = 15.5 Hz). HRMS (ESI): calcd for $C_{13}H_{18}F_2NS_2$ [M+H] 290.0843, found 290.0847.

*4.3.2. Methyl 4-(2-{[(diethylamino)carbonothioyl]thio}-2,2-difluoroethyl)benzoate (**4m**).*

Yield 187 mg (54%). Yellow oil. R_f 0.28 (Hexanes/EtOAc, 6/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.22 (t, 3H, *J* = 7.2 Hz), 1.30 (t, 3H, *J* = 7.2 Hz), 3.61 (q, 2H, *J* = 7.2 Hz), 3.90 (s, 3H), 3.98 (q, 2H, *J* = 7.2 Hz), 4.16 (t, 2H, *J* = 16.5 Hz), 7.42 (d, 2H, *J* = 8.1 Hz), 7.98 (d, 2H, *J* = 8.1 Hz). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 11.4, 13.0, 43.5 (t, *J* = 22.7 Hz), 48.1, 48.6, 52.1, 128.9 (t, *J* = 280.6 Hz), 129.6, 130.9, 137.9 (t, *J* = 3.2 Hz), 166.9, 186.6 (t, *J* = 5.4 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –70.9 (t, *J* = 16.4 Hz). HRMS (ESI): calcd for $C_{15}H_{20}F_2NO_2S_2$ [M+H] 348.0898, found 348.0890.

*4.3.3. 1,1-Difluoro-2-methylpropyl diethyl-(dithiocarbamate) (**4n**).*

Yield 77 mg (32%). Yellow oil. R_f 0.28 (Hexanes/EtOAc, 20/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.12 (d, 6H, *J* = 6.9 Hz), 1.22–1.34 (m, 6H), 3.11–3.35 (m, 1H), 3.76 (q, 2H, *J* = 6.9 Hz), 3.97 (q, 2H, *J* = 6.9 Hz). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$), δ: 11.4, 13.1, 16.1 (t, *J* = 4.1 Hz), 36.0 (t, *J* = 21.3 Hz), 48.4, 132.3 (t, *J* = 284.6 Hz), 186.2 (t, *J* = 3.9 Hz). ^{19}F NMR (282 MHz, $CDCl_3$), δ: –81.7 (d, *J* = 15.0 Hz). HRMS (ESI): calcd for $C_9H_{18}F_2NS_2$ [M+H] 242.0843, found 242.0838.

*4.4. [(1,1-Difluoro-2-phenylethyl)thio]benzene (**4o**)* [20].

A solution of reagent **1a** (4.2 mL of 0.45 M in DMF, 1.88 mmol, 1 equiv, prepared according to a literature procedure [7c]) was treated diphenyl disulfide (436 mg, 2 mmol, 1.05 eqiuv) and Eosin

Y disodium salt (26 mg, 0.0375 mmol, 0.02 equiv) at room temperature. Then, the reaction flask was irradiated with blue LED at room temperature during 4 h. For the work-up, water (7 mL) was added, the mixture was extracted with methyl *tert*-butyl ether/hexane (1/1, 3×5 mL). The combined organic layers were filtered through Na_2SO_4, concentrated under vacuum, and the residue was purified by column chromatography. Yield 248 mg (53%). Colorless oil. R_f 0.10 (Hexanes/EtOAc, 40/1). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.50 (t, 2H, J = 15 Hz), 7.39–7.49 (m, 8H), 7.66 (d, J = 2.4 Hz). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$), δ: 45.3 (t, J = 24.4 Hz), 127.2, 127.9, 128.6, 128.9(t, J = 282.2 Hz), 129.2, 129.8, 130.7, 132.2 (t, J = 3.2 Hz), 136.3. ^{19}F NMR (282 MHz, $CDCl_3$), δ: –72.2(t, J = 14.7 Hz). Calcd for $C_{14}H_{12}F_2S$ (250.31): C 67.18, H 4.83. Found: C 67.15, H 4.98.

Acknowledgments

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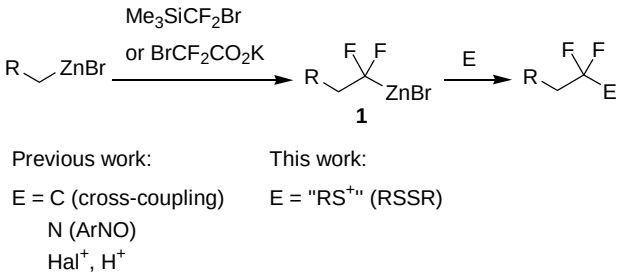
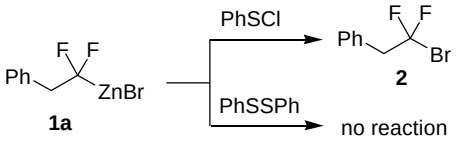
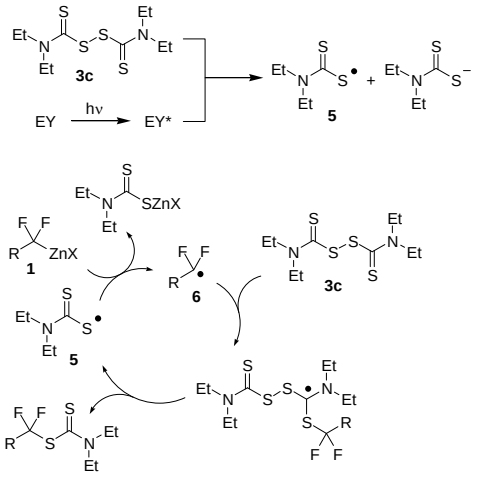


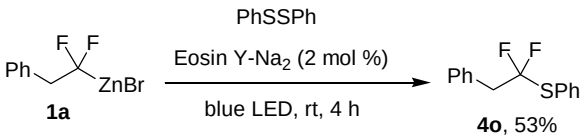
Scheme 1. Preparation of reagents **1**.



Scheme 2. Attempted sufenylation reactions.



Scheme 3. Proposed mechanism.

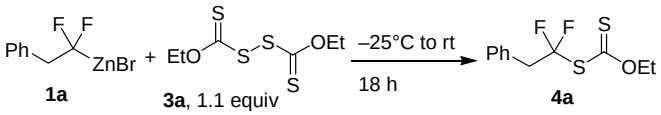


1a

4o, 53%

Scheme 4. Synthesis of sulfide **4o**.

Table 1. Reaction of organozinc **1a**.



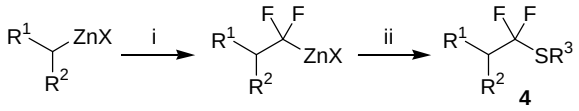
Entry	Solv.	Cat. (mol %)	Yield of **4a**, %[a]
1	MeCN	–	24
2	MeCN	$CuCl \cdot 1.5PPh_3$ (2.5)	52
3	DME	$CuCl \cdot 1.5PPh_3$ (2.5)	60
4[b]	DME	$CuCl \cdot 1.5PPh_3$ (5)	65 (64[c])
5	DME	CuCN (2.5)	53
6	DME	CuI·IMes (2.5)	61

[a] Determined by ^{19}F NMR of crude material with 4-fluorotoluene as an internal standard.

[b] DMF was used as a co-solvent.

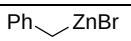
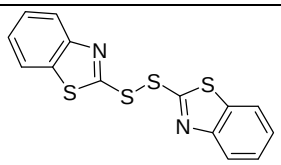
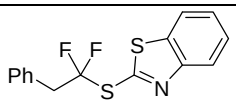
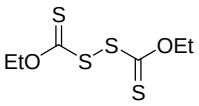
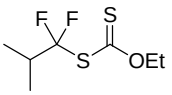
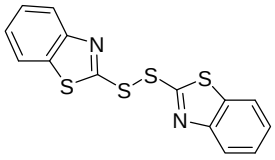
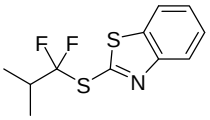
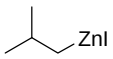
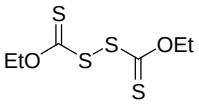
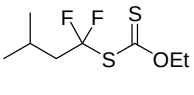
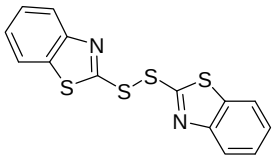
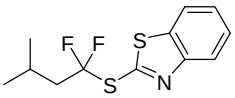
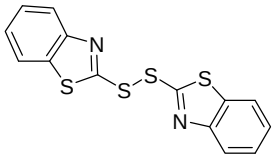
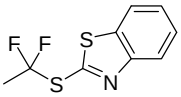
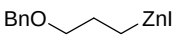
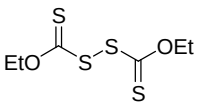
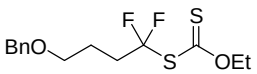
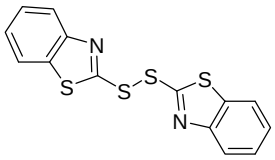
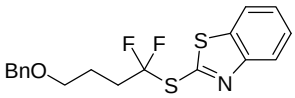
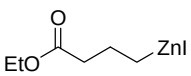
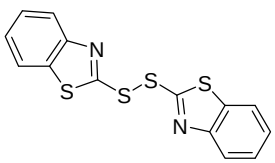
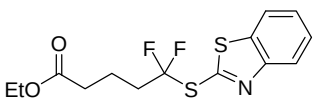
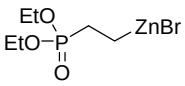
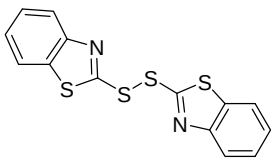
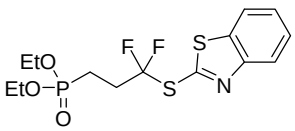
[c] Isolated yield.

Table 2. Synthesis of sulfides **4**.



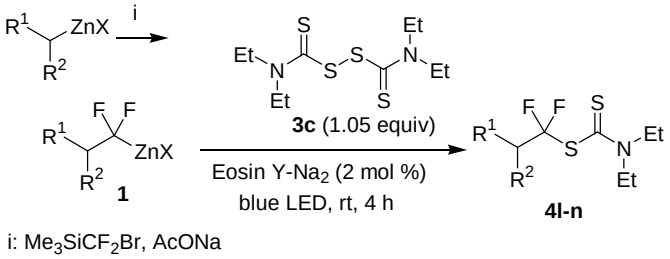
i: Me_3SiCF_2Br (1.2 equiv)
AcONa (1.2 equiv)
DME, –25 °C, 18 h

ii: R^3SSR^3 (1.1 equiv)
$CuCl{\cdot}PPh_3$ (5 mol %)
DME/DMF, –25 °C to rt

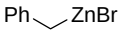
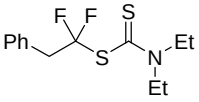
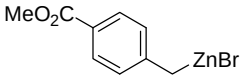
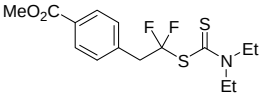
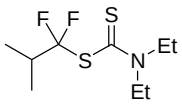
Entry	Reagent	R^3SSR^3	Product		Yield of **4**, %[a]
				**4b**	55
				**4c**	50
				**4d**	60
				**4e**	40
				**4f**	47
	Me—ZnI			**4g**	61
				**4h**	35
				**4i**	52
				**4j**	43
				**4k**	49

[a] Isolated yield.

Table 3. Light mediated reactions.



i: Me_3SiCF_2Br, AcONa

Reagent	Product		Yield of **4**, %[a]
		**4l**	51
		**4m**	54
		**4n**	32

[a] Isolated yield.