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Oxidative nucleophilic substitution of hydrogen in nitro(pentafluorosulfanyl)benzenes with alkyl Grignard and lithium reagents

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Dedicated to Professor David O'Hagan on the occasion of receiving the ACS award for creative work in fluorine chemistry.

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ABSTRACT

Alkyl Grignard and lithium reagents underwent nucleophilic addition to *para*- and *meta*-nitro(pentafluorosulfanyl)benzenes in ether solvents to form σ^H adducts, which were oxidized with potassium permanganate in liquid ammonia to yield products of oxidative nucleophilic substitution of hydrogen in moderate to good yields.

1. Introduction

The pentafluorosulfanyl (SF_5) group is beginning to attract attention of medicinal and material chemists. This rather unusual group bears much similarity to the widely used trifluoromethyl group but is even more electronegative, lipophilic and sterically demanding. Apart from high chemical and thermal stability a special feature of the SF_5 group is the tetragonal bipyramid geometry as opposed to tetrahedral geometry of the CF_3 group. There is a steady growth of literature reports (mostly patents) dealing with SF_5-organics which points out to potential high importance of these compounds in applications ranging from bioactive compounds to liquid crystals, explosives or polymers [1]. However, a lack of availability of key building blocks is currently the main obstacle to the exploration of chemistry and the development of applications of SF_5-containing compounds.

In aromatic SF_5 compounds, *para*- and *meta*-nitro(pentafluorosufanyl)benzenes (**1** and **2**) are available by direct fluorination of the corresponding bis(nitrophenyl)disulfides [2]. Additionally, a patent literature described a two-step conversion of diaryl disulfides to SF_5-aromatics [3]. While S_EAr of **1** or **2** is very limited (nitration of **2** to give 3,5-dinitro(pentafluorosulfanyl)benzene in 33% yield was reported) [4], we have recently described S_NAr of the nitro group in compounds **1** and **2** with alkoxides and thiolates [5] and vicarious nucleophilic substitution (VNS) of the hydrogen with carbon [6], oxygen [7] and nitrogen [8] nucleophiles. Reduction of the nitro group in **1** or **2** to (pentafluorosulfanyl)anilines followed by acylation, S_EAr halogenation or diazotation (with follow-up reactions) provided number of SF_5-benzene derivatives [2b,9].

The first step in the reaction of nucleophiles with nitrobenzenes is usually reversible addition in the unsubstituted *ortho*- or *para*-positions to result in the anionic σ^H adducts (Meisenheimer complexes) [10]. These complexes are often formed under mild conditions (low temperature) and can react further in a variety of ways: (a) dissociate to the starting reagent and under forced conditions (excess of nucleophile, higher temperature) the nucleophile can attack the *ipso*-position followed by the departure of NO_2^- giving the product of S_NAr of the nitro group, (b) in the presence of base undergo elimination of HX, where X is a leaving group attached on the nucleophile; this process is called vicarious nucleophilic substitution (VNS) [10d,10e], (c) the hydride ion can be removed by oxidation, which results in oxidative nucleophilic substitution of hydrogen (ONSH) [11,12]. The success of the last process is mainly dependent on the presence of σ^H adducts in high concentration and resistance of nucleophiles toward oxidation.

In this paper, we present our findings on ONSH of *para*- and *meta*-nitro(pentafluorosufanyl)benzenes (**1** and **2**) with alkyl Grignard and organolithium reagents leading to alkylated nitro(-pentafluorosulfanyl)benzenes. This process allows direct introduction of alkyl group to the aromatic ring and gives access to substituted SF_5-nitrobenzenes.

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2. Results and discussion

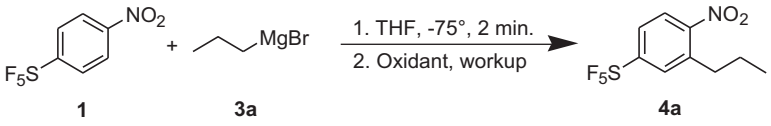
Preliminary experiments revealed that addition of 1.0–1.5 equiv. of MeLi, *n*-BuLi or freshly prepared *n*-PrMgBr solutions to 1-nitro-4-(pentafluorosulfanyl)benzene (**1**) in THF or Et_2O at temperatures below −50 °C and quenching the reaction mixture with saturated aqueous solution of NH_4Cl provided 2-alkyl-1-nitro-4-(pentafluorosulfanyl)benzenes in 10–25% yields. GCMS analyses of the crude product mixtures also showed the formation of small amounts of 2,6-dialkyl-1-nitro-4-(pentafluorosulfanyl)benzenes. When excess of *n*-BuLi (2 equiv.) was used at 0 °C, the ratio of **1**:butyl:dibutyl products was 12:51:37 by GCMS analysis and the combined yield of the butyl and dibutyl products was 30%. Attempts to improve the efficiency of monoalkylation by changing the reaction conditions (temperature, time, solvent, amount of the nucleophilic reagent) were not successful; however, it was found that the reactions are fast (<5 min at −75 °C). A more detailed optimization study was conducted to address the efficiency of oxidation of the formed σ^H intermediates. Freshly prepared *n*-PrMgBr (**3a**) was added to **1** in THF at −75 °C and the yield of **4a** was monitored by quantitative GCMS (Table 1). Addition of potassium permanganate to the reaction mixture before the final quench with sat. NH_4Cl solution improved the yield of **4a**, especially when liquid ammonia was added to solubilize $KMnO_4$. These conditions were described by Makosza and Surowiec in ONSH alkylation of nitroarenes with Grignard reagents [12]. An increase of the yield of **4a** and better conversion of **1** was observed when the excess of **3a** and $KMnO_4$ was used. Further improvement of efficiency was observed upon dilution of starting **1** or **3a** and the highest yield of **4a** (64% GCMS, 56% isolated) was achieved using conditions shown in Table 1, entry 10.

Several other experiments were performed (modifications of conditions shown in entry 10), but no further significant improvement was observed: (a) the use of Et_2O instead of THF gave 62% of **4a**, (b) reverse addition (**1** to the solution of **3a**) gave 35% of **4a**, (c) the use of 2.5 equiv. of **3a** yielded 62% of **4a**, showing that excess of the Grignard reagent does not have a significant effect on the yield (dialkylated product are formed only in trace amounts), (d) the use of $Na_2Cr_2O_7$ instead of $KMnO_4$ gave only 25% of **4a** (entry 11). It is known that the nature of the solvent has a dramatic effect on the structure of Grignard reagents. For example, in solvents such as 1,4-dioxane or DME the Shlenk equilibrium shifts toward the formation of dialkylmagnesium and insoluble magnesium halide [13]. When freshly prepared **3a** in THF was diluted with DME, white precipitate formed. Addition of the solution above this precipitate to **1** in THF/DME (1:1) under otherwise identical conditions to entry 10 gave only 14% of **4a**, concluding that dialkylmagnesium species are not suitable nucleophiles in our reaction.

The optimized conditions were used to study the scope of ONSH of **1** with Grignard and organolithium reagents (Table 2). Good isolated yields of alkyl products were observed with simple alkyl Grignard reagents **3a** and **3b**. On the other hand, benzyl-substituted product **4c** was obtained in reduced yield. Secondary alkyl Grignard reagent **3d** can be added in good yield; however, **3e** did not provide any biphenyl-containing product (**4e**). The later result is not surprising since Bertoli has found that σ^H adducts are not formed from nitroarenes and aryl or vinyl magnesium halides [14]. It seems that the nature of the halide in Grignard reagents did not play any role in all these reactions. Reactions with methyllithium or *n*-butyllithium under optimized conditions provided good yields of alkylated products (**4f** and **4b**, respectively). Here, Et_2O was used as a solvent because it is more resistant toward attack than THF [15]. Slight excess of alkyllithium reagents (1.3 equiv.) was sufficient for complete conversion of **1** and under these conditions only about 2% of dialkylated products were formed. Search for better oxidation system than $KMnO_4$/liquid NH_3 was not successful. For example in the reaction of **1** with *n*-BuLi the use of DDQ (1.3 equiv.) in THF, oxygen (1 atm) or air in *t*-BuOMe instead of THF to avoid the formation of potentially explosive peroxides gave 26%, 24%, and 20% of **4b**, respectively. Similarly, in the reaction of **1** with MeLi the use of ICl (6 equiv.) in THF gave 45% of **4f**. The reaction with PhLi provided phenol instead of **4e** (Table 2, entry 8).

Analogous ONSH reaction of Grignard and organolithium reagents with the *meta*-derivative **2** revealed rather non-selective addition to both activated positions (*ortho* and *para* relative to the nitro group) giving alkylated products **5** and **6**, respectively (Table 3). The structure of the products was established by NMR spectroscopy. The combined yields were good and the products were separated by column chromatography. The regioselectivity of the nucleophilic addition (**5**:**6** ratio) ranged from 1:1 for *i*-PrMgBr to 2:1 for MeLi, which is much lower than in previously described VNS reactions with more stabilized (less reactive) carbon or oxygen nucleophiles to **2** [6,7]. VNS amination of **2** with $Me_3N^+NH_2I^-$ proceeds exclusively

Table 1
Optimization of *n*-propylmagnesium bromide (**3a**) addition to 1-nitro-4-(pentafluorosulfanyl)benzene (**1**).[a]

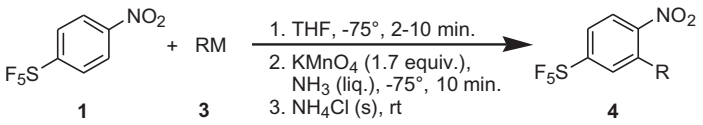


1 **3a** **4a**

Entry	c_1 (M)	c_{3a} (M) (equiv.)	Oxidant (equiv.)	Workup[b]	Yield of **4a** (%)[c]	Unreacted **1** (%)[c]
1	0.25	0.25 (1.0)	None	A	19	23
2	0.25	0.25 (1.0)	$KMnO_4$ (1.0)	B	22	24
3	0.25	0.25 (1.0)	$KMnO_4$ (1.0)	C	36	22
4	0.25	0.33 (1.3)	$KMnO_4$ (1.3)	C	36	n/d
5	0.25	0.38 (1.5)	$KMnO_4$ (1.5)	C	50	5
6	0.20	0.35 (1.5)	$KMnO_4$ (1.7)	C	51	Trace
7	0.10	0.35 (1.5)	$KMnO_4$ (1.7)	C	54	Trace
8	0.05	0.35 (1.5)	$KMnO_4$ (1.7)	C	59	5
9	0.25	0.50 (1.7)	$KMnO_4$ (1.7)	C	56	Trace
10	0.25	0.20 (1.7)	$KMnO_4$ (1.7)	C	64 (56)	Trace
11	0.25	0.20 (1.7)	$Na_2Cr_2O_7$ (1.7)	C	25	n/d

[a] Reactions were performed by addition of freshly prepared solution of **3a** in THF to a solution of **1** (0.25 mmol) in THF at −75° under Ar, followed by addition of oxidant and workup.
[b] Workup conditions were as follows: (A) aqueous NH_4Cl; (B) oxidant at −75° for 10 min, then aqueous NH_4Cl; and (C) liquid NH_3 and oxidant at −75° for 10 min, then solid NH_4Cl.
[c] Yields were determined by quantitative GCMS analysis using standard addition of 1-fluoro-4-nitrobenzene and isolated yield is shown in brackets.

Table 2
ONSH of 1-nitro-4-(pentafluorosulfanyl)benzene (**1**) with Grignard and organolithium reagents.[a]

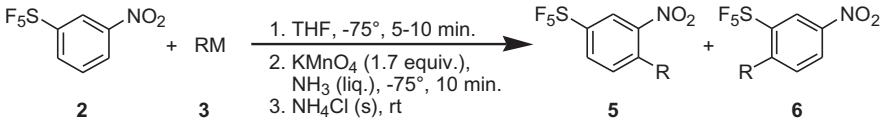


1 3 4

Entry	**3**, RM (equiv.)	**4**, yield (%)[b]
1	**3a**, *n*-PrMgBr (1.7)	**4a**, 56
2	**3b**, *n*-BuMgCl (1.7)	**4b**, 65
3	**3c**, $PhCH_2MgCl$ (1.7)	**4c**, 31
4	**3d**, *i*-PrMgBr (1.7)	**4d**, 49
5	**3e**, PhMgCl (1.7)	**4e**, 0
6	**3f**, MeLi (1.3)[c]	**4f**, 64
7	**3g**, *n*-BuLi (1.3)[c]	**4b**, 61
8	**3h**, PhLi (1.3)[c]	**4e**, 0[d]

[a] Reactions were performed by addition of **3** in THF (0.2 M) to a solution of **1** (0.60 mmol) in THF at −75° under Ar, followed by addition of $KMnO_4$ (1.7 equiv.), NH_3 (7 mL) (−75°, 10 min), followed by addition of solid NH_4Cl.
[b] Isolated yields.
[c] Et_2O was used instead of THF.
[d] Phenol was detected by GCMS analysis as the main product.

Table 3
ONSH of 1-nitro-3-(pentafluorosulfanyl)benzene (**2**) with Grignard and organolithium reagents.[a]



2 3 5 6

Entry	**3**, RM (equiv.)	**5**, yield (%)[b]	**6**, yield (%)[b]
1	**3a**, *n*-PrMgBr (1.7)	**5a**, 33	**6a**, 23
2	**3b**, *n*-BuMgCl (1.7)	**5b**, 30	**6b**, 20
3	**3d**, *i*-PrMgBr (1.7)	**5d**, 18	**6d**, 18
4	**3f**, MeLi (1.3)[c]	**5f**, 30	**6f**, 15
5	**3g**, *n*-BuLi (1.3)[c]	**5b**, 34	**6b**, 26

[a] Reactions were performed by addition of **3** in THF (0.2 M) over 5–10 min to a solution of **2** (0.60 mmol) in THF at −75° under Ar, followed by addition of $KMnO_4$ (1.7 equiv.), NH_3 (7 mL) (−75°, 10 min), followed by addition of solid NH_4Cl.
[b] Isolated yields.
[c] Et_2O was used instead of THF.

in position *ortho* relative to the nitro group [8]. This selectivity was attributed to steric reasons, where the SF_5 is a little more sterically demanding than the nitro group. The results presented here suggest that for highly reactive organolithium and Grignard reagents the steric factors do not play a significant role [16].

3. Conclusion

1-Nitro-4-(pentafluorosulfanyl)benzene underwent fast oxidative nucleophilic substitution of hydrogen with alkyl Grignard or alkyllithium reagents in ether solvent at −75 °C to provide good yields of 2-alkyl-1-nitro-4-(pentafluorosulfanyl)benzenes after oxidative workup (potassium permanganate in liquid ammonia). Analogous alkylation of 1-nitro-3-(pentafluorosulfanyl)benzene gave a separable mixture of products alkylated in *ortho*- and *para*-positions relative to the nitro group in 1:1–2:1 ratio and good combined yields.

4. Experimental

NMR spectra were recorded on $CDCl_3$ on a Bruker 400, 500 or 600 MHz instruments at ambient temperature. Chemical shifts (δ) are reported in ppm relative to Me_4Si (0 ppm for ^1H NMR), residual $CHCl_3$ (7.26 ppm for ^1H NMR), $CDCl_3$ (77.0 ppm for ^{13}C NMR), and internal $CFCl_3$ (0 ppm for ^{19}F NMR). GCMS spectra were recorded on an Agilent 7890A gas chromatograph coupled with 5975C quadrupole mass selective electron impact (EI) detector (70 eV). High resolution mass spectra (HRMS) were recorded on an Agilent 7890A gas chromatograph coupled with a Waters GCT Premier orthogonal acceleration time-of-flight detector using electron impact (EI) or chemical (CI) ionizations. Solvents (Et_2O, THF and DME) were dried by distillation with sodium/benzophenone before the use. Reactions were performed under dry argon atmosphere and the cooling bath (−75 °C) was prepared by the addition of solid CO_2 to EtOH. Commercial PhMgCl (2 M) solution in THF, MeLi (1.6 M) solution in Et_2O, *n*-BuLi (2.5 M or 1 M) solutions in hexane and PhLi (1.9 M) solution in *n*-Bu_2O were used and the concentration of organolithium reagents was determined by titration with diphenylacetic acid. The other Grignard reagents were freshly prepared from Mg turnings (1.1 equiv.) and alkyl halogenide in THF or Et_2O at 40 °C or under reflux. Concentration of Grignard solutions was not determined (the amount used does not have a significant effect on yields of alkylated products **4**–**6**).

4.1. General procedure for the preparation of compounds 4–6

Commercial or freshly prepared solution of **3** (0.78–1.02 mmol, 1.3–1.7 equiv.) diluted with THF or Et_2O to 0.2 M was added

dropwise (over 2–8 min) to a solution of **1** or **2** (150 mg, 0.60 mmol) in THF or Et_2O (7 mL) at −75 °C. After 2 min of stirring at this temperature, powdered $KMnO_4$ (158 mg, 1 mmol, 1.7 equiv.) followed by liquid NH_3 (7 mL) were added. After 10 min of stirring solid NH_4Cl (0.1 g) was carefully added and the mixture was warmed to rt. Aqueous solution of oxalic acid was added to decompose MnO_2 and the crude product was extracted into EtOAc (3 × 15 mL). The combined organic phase was washed with water (15 mL), aqueous $NaHCO_3$ (15 mL) and brine (15 mL), dried ($MgSO_4$), and solvent was removed under reduced pressure. Pure product was obtained by column chromatography using silica gel 60 and hexane as an eluent.

*4.1.1. 1-Nitro-4-(pentafluorosulfanyl)-2-n-propylbenzene (**4a**)*

An orange oil (98 mg, 56% yield); R_f 0.13 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.02 (t, 3H, $^3J_{HH}$ = 7.4 Hz), 1.71 (m, 2H), 2.90 (m, 2H) 7.72–7.77 (m, 2H), 7.90–7.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 13.8, 23.8, 34.7, 124.8, 124.9 (quin, $^3J_{CF}$ = 4.7 Hz), 129.6 (quin, $^3J_{CF}$ = 4.7 Hz), 138.4, 150.7, 155.8 (quin, $^2J_{CF}$ = 18.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 62.0 (d, 4F, $^2J_{FF}$ = 150.6 Hz), 80.5–82.1 (m, 1F); MS (EI) *m*/*z* (rel. int.) 291 (3) $[M]^+$, 274 (87), 246 (24), 218 (19), 147 (100), 115 (34), 89 (37), 77 (22), 63 (28); HRMS (EI) *m*/*z* calcd for $C_9H_{10}F_5NO_2S$ $[M]^+$ 291.0352, found 291.0349.

*4.1.2. 2-n-Butyl-1-nitro-4-(pentafluorosulfanyl)benzene (**4b**)*

An orange oil (120 mg, 65% yield); R_f 0.15 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.96 (t, 3H, $^3J_{HH}$ = 7.3 Hz), 1.38–1.48 (m, 2H), 1.58–1.70 (m, 2H), 2.89–2.95 (m, 2H) 7.73–7.77 (m, 2H), 7.89–7.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 13.6, 22.5, 32.5, 32.6, 124.7–124.9 (m, 2C), 129.4–129.6 (m), 138.7, 150.6, 155.8 (quin, $^2J_{CF}$ = 18.6 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F 62.1 (d, 4F, $^2J_{FF}$ = 150.4 Hz), 80.7–82.0 (m, 1F); MS (EI) *m*/*z* (rel. int.) 305 (4) $[M]^+$, 288 (100), 246 (74), 218 (20), 161 (57), 143 (23), 119 (24), 89 (32), 77 (20); HRMS (CI) *m*/*z* calcd for $C_{10}H_{13}$ F_5NO_2S $[MH]^+$ 306.0587, found 306.0581.

*4.1.3. 2-Benzyl-1-nitro-4-(pentafluorosulfanyl)benzene (**4c**)*

An orange oil (64 mg, 31% yield); R_f 0.28 (hexane:EtOAc, 97:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 4.33 (s, 2H), 7.11–7.15 (m, 2H), 7.23–7.28 (m, 1H), 7.29–7.35 (m, 2H), 7.69 (d, 1H, $^4J_{HH}$ = 2.4 Hz), 7.77 (dd, 1H, $^3J_{HH}$ = 8.9 Hz, $^4J_{HH}$ = 2.4 Hz), 7.96 (d, 1H, $^3J_{HH}$ = 8.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 38.3, 125.1, 125.3–125.5 (m), 127.2, 128.9 (2C), 128.9 (2C), 129.9–130.2 (m), 136.9, 137.1, 150.5, 155.5–156.4 (m); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F 62.0 (d, 4F, $^2J_{FF}$ = 150.7 Hz), 80.4–81.7 (m, 1F); MS (EI) *m*/*z* (rel. int.) 339 (12) $[M]^+$, 338 (11), 305 (20), 195 (45), 183 (15), 165 (53), 105 (17), 77 (19); HRMS (CI) *m*/*z* calcd for $C_{13}H_{11}F_5NO_2S$ $[MH]^+$ 340.0431, found 340.0425.

*4.1.4. 1-Nitro-4-(pentafluorosulfanyl)-2-isopropylbenzene (**4d**)*

An orange oil (86 mg, 49% yield); R_f 0.32 (hexane:EtOAc, 97:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.34 (d, 6H, $^3J_{HH}$ = 6.8 Hz), 3.42 (sept, 1H, $^3J_{HH}$ = 6.8 Hz), 7.70–7.78 (m, 2H), 7.84–7.86 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ_C 23.3 (2C), 29.0, 124.1, 124.7 (quin, $^3J_{CF}$ = 4.6 Hz), 125.8 (quin, $^3J_{CF}$ = 4.7 Hz), 143.5, 150.8, 156.1 (quin, $^2J_{CF}$ = 18.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 61.9 (d, 4F, $^2J_{FF}$ = 150.4 Hz), 80.7–82.3 (m, 1F); MS (EI) *m*/*z* (rel. int.) 291 (2) $[M]^+$, 276 (38), 247 (42), 231 (52), 147 (100), 130 (20), 115 (60), 102 (31), 89 (53), 77 (41); HRMS (CI) *m*/*z* calcd for $C_9H_{11}F_5NO_2S$ $[MH]^+$ 292.0431, found 292.0426.

*4.1.5. 2-Methyl-1-nitro-4-(pentafluorosulfanyl)benzene (**4f**)*

A yellow oil (103 mg, 64% yield); R_f 0.26 (hexane:EtOAc, 97:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.67 (s, 1H), 7.73–7.79 (m, 2H), 8.00-8.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 20.2, 124.8–125.0 (m, 2C), 130.4 (quin, $^3J_{CF}$ = 4.7 Hz), 134.5, 150.5, 155.5–156.3 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 62.1 (d, 4F, $^2J_{FF}$ = 150.6 Hz), 80.4–82.0 (m, 1F); MS (EI) *m*/*z* (rel. int.) 263 (15) $[M]^+$, 246 (100), 119 (57), 109 (30), 89 (54), 63 (30); HRMS (EI) *m*/*z* calcd for $C_7H_6F_5NO_2S$ $[M]^+$ 263.0039, found 263.0034.

*4.1.6. 2-Nitro-4-(pentafluorosulfanyl)-1-n-propylbenzene (**5a**)*

An orange oil (58 mg, 33% yield); R_f 0.19 (hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 1.02 (t, 3H, $^3J_{HH}$ = 7.5 Hz), 1.71 (m, 2H), 2.92 (m, 2H), 7.49 (d, 1H, $^3J_{HH}$ = 8.5 Hz), 7.89 (dd, 1H, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.4 Hz), 8.29 (d, 1H, $^4J_{HH}$ = 2.4 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ_C 13.9, 23.7, 34.7, 122.8 (quin, $^3J_{CF}$ = 4.9 Hz), 129.7 (quin, $^3J_{CF}$ = 4.4 Hz), 132.4, 141.5, 148.7, 151.5 (quin, $^2J_{CF}$ = 19.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 62.7 (d, 4F, $^2J_{FF}$ = 151.0 Hz), 80.5–82.2 (m, 1F); MS (EI) *m*/*z* (rel. int.) 291 (3) $[M]^+$, 274 (100), 246 (20), 147 (98), 115 (38), 89 (37), 77 (22), 63 (24); HRMS (CI) *m*/*z* calcd for $C_9H_{11}F_5NO_2S$ $[MH]^+$ 292.0431, found 292.0424.

*4.1.7. 4-Nitro-2-(pentafluorosulfanyl)-1-n-propylbenzene (**6a**)*

A yellow oil (42 mg, 23% yield); R_f 0.26 (hexane:EtOAc, 97:3); ^{1}H NMR (600 MHz, $CDCl_3$) δ_H 1.06 (t, 3H, $^3J_{HH}$ = 7.5 Hz), 1.66 (m, 2H), 3.00 (m, 2H) 7.57 (d, 1H, $^3J_{HH}$ = 8.6 Hz), 8.27 (dd, 1H, $^3J_{HH}$ = 8.6 Hz, $^4J_{HH}$ = 2.3 Hz), 8.67 (d, 1H, $^4J_{HH}$ = 2.3 Hz); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ_C 14.3, 25.3, 36.8 (quin, $^3J_{CF}$ = 3.4 Hz), 123.9 (quin, $^3J_{CF}$ = 5.9 Hz), 125.6, 133.7, 145.5, 147.2, 153.0 (quin, $^2J_{CF}$ = 17.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 66.6 (d, 4F, $^2J_{FF}$ = 149.6 Hz), 82.5–84.2 (m, 1F); MS (EI) *m*/*z* (rel. int.) 291 (100) $[M]^+$, 263 (17), 155 (52), 135 (30), 117 (33), 108 (53), 89 (86), 77 (22), 63 (24); HRMS (CI) *m*/*z* calcd for $C_9H_{11}F_5NO_2S$ $[MH]^+$ 292.0431, found 292.0430.

*4.1.8. 1-n-Butyl-2-nitro-4-(pentafluorosulfanyl)benzene (**5b**)*

An orange oil (62 mg, 34% yield); R_f 0.15 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.96 (t, 3H, $^3J_{HH}$ = 7.3 Hz), 1.38–1.48 (m, 2H), 1.60–1.69 (m, 2H), 2.92–2.97 (m, 2H) 7.49 (d, 1H, $^3J_{HH}$ = 8.5 Hz), 7.88 (dd, 1H, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.3 Hz), 8.29 (d, 1H, $^4J_{HH}$ = 2.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 13.7, 22.6, 32.5, 32.5, 122.6–122.9 (m), 129.6 (quin, $^3J_{CF}$ = 4.5 Hz), 132.4, 141.7, 148.7, 151.3–151.8 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 62.6 (d, 4F, $^2J_{FF}$ = 150.9 Hz), 80.5–82.2 (m, 1F); MS (EI) *m*/*z* (rel. int.) 305 (3) $[M]^+$, 288 (100), 246 (62), 161 (51), 143 (25), 89 (33), 77 (19), 63 (19); HRMS (CI) *m*/*z* calcd for $C_{10}H_{13}F_5NO_2S$ $[MH]^+$ 306.0587, found 306.0576.

*4.1.9. 1-n-Butyl-4-nitro-2-(pentafluorosulfanyl)benzene (**6b**)*

A yellow oil (45 mg, 26% yield); R_f 0.26 (hexane:EtOAc, 97:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.98 (t, 3H, $^3J_{HH}$ = 7.3 Hz), 1.48 (m, 2H), 1.60 (m, 2H), 3.03 (m, 2H) 7.56 (d, 1H, $^3J_{HH}$ = 8.6 Hz), 8.27 (dd, 1H, $^3J_{HH}$ = 8.6 Hz, $^4J_{HH}$ = 2.3 Hz), 8.66 (d, 1H, $^4J_{HH}$ = 2.3 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ_C 13.7, 22.9, 34.2, 34.6 (quin, $^3J_{CF}$ = 3.6 Hz), 123.9 (quin, $^3J_{CF}$ = 6.0 Hz), 125.6, 133.8, 145.4, 147.5, 152.9 (quin, $^2J_{CF}$ = 17.1 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F 66.6 (d, 4F, $^2J_{FF}$ = 149.7 Hz), 82.5–84.2 (m, 1F); MS (EI) *m*/*z* (rel. int.) 305 (13) $[M]^+$, 263 (43), 178 (15), 155 (70), 132 (51), 108 (30), 89 (30), 77 (15), 63 (15), 43 (100); HRMS (CI) *m*/*z* calcd for $C_{10}H_{13}F_5NO_2S$ $[MH]^+$ 306.0587, found 306.0586.

*4.1.10. 2-Nitro-4-(pentafluorosulfanyl)-1-isopropylbenzene (**5d**)*

An orange oil (31 mg, 18% yield); R_f 0.31 (hexane:EtOAc, 97:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.33 (d, 6H, $^3J_{HH}$ = 6.8 Hz), 3.46 (sept, 1H, $^3J_{HH}$ = 6.8 Hz), 7.61 (d, 1H, $^3J_{HH}$ = 8.7 Hz), 7.92 (dd, 1H, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.4 Hz), 8.12 (d, 1H, $^3J_{HH}$ = 2.4 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ_C 23.3, 28.8, 122.0 (quin, $^3J_{CF}$ = 4.9 Hz), 128.4, 129.6 (quin, $^3J_{CF}$ = 4.6 Hz), 146.5, 148.9, 151.3 (quin, $^2J_{CF}$ = 20.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 62.6 (d, 4F, $^2J_{FF}$ = 151.1 Hz), 80.5–82.2 (m, 1F); MS (EI) *m*/*z* (rel. int.) 291 (2) $[M]^+$, 274 (49), 256 (15), 247 (37), 231 (47), 147 (100), 130 (20), 115 (68), 102 (29), 89 (52), 77

(41); HRMS (CI) *m*/*z* calcd for $C_9H_{11}F_5NO_2S$ $[MH]^+$ 292.0431, found 292.0421.

*4.1.11. 4-Nitro-2-(pentafluorosulfanyl)-1-isopropylbenzene (**6d**)*

A yellow solid film (33 mg, 18% yield); R_f 0.26 (hexane:EtOAc, 97:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.32 (d, 6H, $^3J_{HH}$ = 6.8 Hz), 3.87 (sept, 1H, $^3J_{HH}$ = 6.8 Hz), 7.71 (d, 1H, $^3J_{HH}$ = 8.8 Hz), 8.31 (dd, 1H, $^3J_{HH}$ = 8.8 Hz, $^4J_{HH}$ = 2.3 Hz), 8.65 (d, 1H, $^3J_{HH}$ = 2.3 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ_C 24.0, 30.9 (quin, $^3J_{CF}$ = 4.4 Hz), 123.7 (quin, $^3J_{CF}$ = 6.1 Hz), 125.9, 130.2, 145.3, 152.2 (quin, $^2J_{CF}$ = 17.6 Hz), 153.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 67.5 (d, 4F, $^2J_{FF}$ = 149.7 Hz), 82.9–84.5 (m, 1F); MS (EI) *m*/*z* (rel. int.) 291 (84) $[M]^+$, 276 (100), 256 (53), 236 (27), 138 (20), 122 (72), 109 (51), 101 (30), 89 (95), 77 (26); HRMS (CI) *m*/*z* calcd for $C_9H_{11}F_5NO_2S$ $[MH]^+$ 292.0431, found 292.0421.

*4.1.12. 1-Methyl-2-nitro-4-(pentafluorosulfanyl)benzene (**5f**)*

A yellow oil (48 mg, 30% yield); R_f 0.23 (hexane:EtOAc, 97:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.7 (m, 3H), 7.50 (d, 1H, $^3J_{HH}$ = 8.5 Hz), 7.89 (dd, 1H, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.4 Hz), 8.39 (d, 1H, $^4J_{HH}$ = 2.4 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ_C 20.4, 122.9 (quin, $^3J_{CF}$ = 4.9 Hz), 129.9 (quin, $^3J_{CF}$ = 4.5 Hz), 133.3, 137.7, 148.5, 151.7 (quin, $^2J_{CF}$ = 20.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 62.5 (d, 4F, $^2J_{FF}$ = 150.9 Hz), 80.4–82.1 (m, 1F); MS (EI) *m*/*z* (rel. int.) 263 (12) $[M]^+$, 246 (100), 119 (35), 109 (26), 89 (47), 63 (23); HRMS (CI) *m*/*z* calcd for $C_7H_7F_5NO_2S$ $[MH]^+$ 264.0118, found 264.0114.

*4.1.13. 1-Methyl-4-nitro-2-(pentafluorosulfanyl)benzene (**6f**)*

A yellow oil (25 mg, 15% yield); R_f 0.35 (hexane:EtOAc, 95:5); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.75 (quin, 3H, $^4J_{HH}$ = 2.0 Hz), 7.52 (d, 1H, $^3J_{HH}$ = 8.5 Hz), 8.25 (dd, 1H, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.3 Hz), 8.68 (d, 1H, $^3J_{HH}$ = 2.3 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ_C 22.9 (quin, $^3J_{CF}$ = 4.4 Hz), 123.9 (quin, $^3J_{CF}$ = 6.0 Hz), 125.7, 134.5, 142.3, 145.7, 153.9 (quin, $^2J_{CF}$ = 17.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 64.6 (d, 4F, $^2J_{FF}$ = 149.3 Hz), 81.9–83.5 (m, 1F); MS (EI) *m*/*z* (rel. int.) 263 (100) $[M]^+$, 217 (11), 135 (22), 109 (45), 89 (82), 77 (19), 63 (28); HRMS (CI) *m*/*z* calcd for $C_7H_7F_5NO_2S$ $[MH]^+$ 264.0118, found 264.0120.

*4.2. Alkylation of **1** with excess of n-BuLi*

A solution of *n*-BuLi (1.2 mL, 1.2 mmol, 2 equiv.) in hexanes was added to a solution of **1** (150 mg, 0.6 mmol) in Et_2O (7 mL) at 0 °C. After 1 h of stirring at this temperature, saturated aqueous solution of NH_4Cl (20 mL) was added and the product was extracted into Et_2O (3 × 15 mL). The combined organic phase was washed with water (15 mL), brine (15 mL), dried ($MgSO_4$), and solvent was removed under reduced pressure giving a mixture of **1**, **4b** and 2,6-di-*n*-butyl-1-nitro-4-(pentafluorosulfanyl)benzene (**7b**) in 12:51:37 ratio (by GCMS). Flash chromatography using silica gel 60 and hexane as eluent gave a mixture of **4b** and **7b** (56 mg, ca. 30%). **7b**: R_f 0.20 (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.93 (t, 6H, $^3J_{HH}$ = 7.3 Hz), 1.32–1.42 (m, 4H), 1.56–1.65 (m, 4H), 2.56–2.62 (m, 4H) 7.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 13.7, 22.4, 31.3, 32.6, 125.6–125.8 (m), 135.1, 152.5, 153.8–154.4 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F 62.2 (d, 4F, $^2J_{FF}$ = 150.2 Hz), 81.5–83.2 (m, 1F); MS (EI) *m*/*z* (rel. int.) 361 (32) $[M]^+$, 344 (72), 302 (60), 286 (43), 274 (20), 260 (66), 232 (24), 217 (42), 202 (50), 189 (26), 174 (30), 158 (25), 146 (40), 130 (31), 115 (39), 104 (22), 89 (29), 71 (100).

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[16] Alkyllithium reagents are known to form aggregates in solution, which effectively increase their bulkiness. This might be the reason why with MeLi the **5**:**6** ratio was 2:1 and with *i*-PrMgBr the ratio was 1:1.