Nucleophilic Pentafluorophenylation of Nitroalkenes

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Abstract: The interaction of pentafluorophenylmagnesium bromide with conjugate nitroalkenes is described. The optimized conditions involve performing the reaction either in diethyl ether in the presence of chlorotrimethylsilane or in a tetrahydrofuran–diethyl ether solvent mixture. The addition products can be transformed into 4,5,6,7-tetrafluoroindolines by means of a reduction and cyclization sequence.

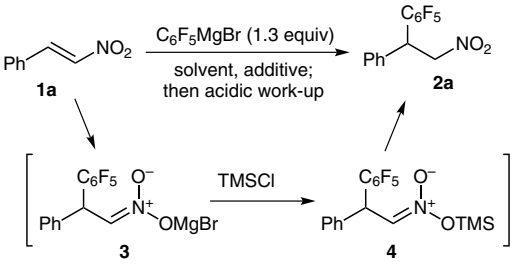
Key words: alkenes, nucleophilic addition, fluorine, nitro compounds, pentafluorophenyl

Fluorinated aromatic compounds have attracted considerable attention as a result of their applications in various fields.[1] Having the highest number of fluorine atoms, the pentafluorophenyl group possesses unique properties in terms of steric requirements and electronic effects, as well as its ability to engage in stacking interactions. As a result, substances bearing the C_6F_5-substituent have been investigated in medicinal chemistry,[2] supramolecular chemistry,[3] and in surface and materials sciences.[4] As an additional synthetic benefit, the *para*- and *ortho*-positions display enhanced reactivity towards nucleophilic substitution of fluorine, which allows for the synthesis of a wide array of fluorinated aromatics.[5]

Among several methods used for the direct introduction of the C_6F_5-group,[6] processes involving nucleophilic pentafluorophenylation appear to be most attractive. Whereas the addition of the C_6F_5-carbanion to C=O and C=N bonds is well-developed,[7] the addition to electron-deficient alkenes is rare.[8–10] Within the framework of our studies of fluoroalkylation of various Michael acceptors,[8] we turned our attention to conjugate nitroalkenes.

Recently, we have shown that highly electrophilic α-nitrocinnamates undergo nucleophilic fluoroalkylation with fluorinated silicon reagents activated by Lewis base.[8d] Using a similar methodology, 4-nitroisoxazoles formally containing a nitroalkene fragment were successfully fluoroalkylated.[11] However, under these conditions, conventional nitroalkenes do not afford any product. Herein, we describe an efficient method for nucleophilic pentafluorophenylation of nitroalkenes.

Pentafluorophenylmagnesium bromide was selected as a nucleophilic reagent because it can be readily prepared from pentafluorophenyl bromide and magnesium in diethyl ether. It is stable at room temperature and is commercially available. When the Grignard reagent was added to a suspension of nitrostyrene (**1a**) in diethyl ether at –78 °C followed by warming and stirring overnight at room temperature, product **2a** was isolated in 43% yield (Scheme 1, Table 1, entry 1). Given the complete consumption of nitrostyrene (**1a**), we propose that initially formed magnesium nitronate **3** can react with **1a**, thereby leading to oligomerization of the Michael acceptor. Indeed, poorly soluble polymeric material was observed during the work-up. Based on our earlier observation that chlorosilanes do not react with C_6F_5MgBr in diethyl ether,[12] we performed the reaction in the presence of chlorotrimethylsilane (TMSCl). Rewardingly, product **2a** was obtained in 84% yield. We believe that the role of chlorosilane is to rapidly trap magnesium nitronate **3** to generate silyl nitronate **4**, which is hydrolyzed on work-up.[13] As an alternative procedure, we used a tetrahydrofuran–ether (3:1) solvent mixture, and obtained **2a** in 80% yield (entry 4).



Scheme 1 Pentafluorophenylation of nitrostyrene (**1a**)

Table 1 Pentafluorophenylation of Nitrostyrene (**1a**)

Entry	Solvent	Additive	Time (h)[a]	Yield (%)[b]
1	Et_2O	–	18	43
2	Et_2O	TMSCl (1.1 equiv)	18	83
3	Et_2O	TMSCl (1.2 equiv)	2	84
4	THF–Et_2O	–	2	80

[a] Reagents were combined at –78 °C, then the mixture was stirred at r.t. for the specified time.
[b] Isolated yield.

The protocol involving the use of TMSCl (Method A) was selected for further studies, and a series of nitroalkenes were subjected to the pentafluorophenylation reaction (Table 2). Aromatic and heteroaromatic substrates gave nitro-containing compounds **2** in high yields (entries 1–7).

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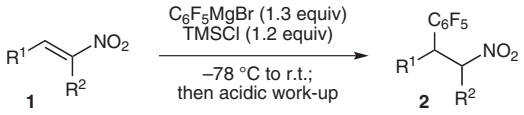
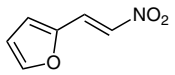
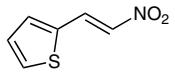
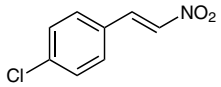
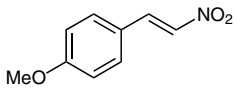
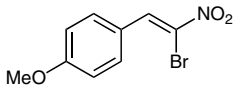
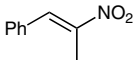
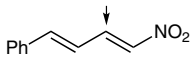
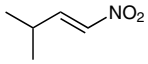
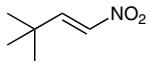
However, nitroalkenes **1i** and **1j**, bearing isopropyl and *tert*-butyl groups, respectively, reacted poorly under the standard conditions. In these cases, performing the reaction in a THF–diethyl ether solvent mixture without TMSCl for 18 hours at room temperature afforded the desired products in good yields (entries 9 and 11).

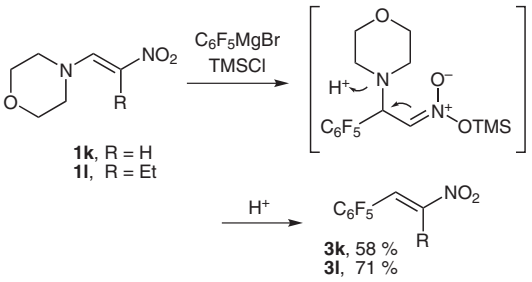
Table 2 Pentafluorophenylation of Nitroalkenes **1**



Entry	Substrate	Product	Method[a]	Yield (%)[b]
1	 **1b**	**2b**	A	83
2	 **1c**	**2c**	A	88
3	 **1d**	**2d**	A	87
4	 **1e**	**2e**	A	90
5	 **1f**	**2f**	A	92[c]
6	 **1g**	**2g**	A	82[d]
7	 **1h**	**2h**	A	75
8	 **1i**	**2i**	A	–[e]
9			B	76
10	 **1j**	**2j**	A	n.r
11			B	78

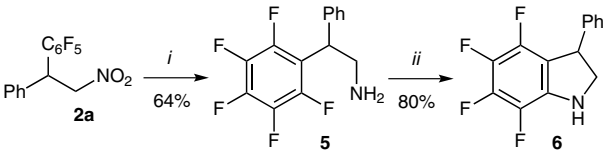
[a] Method A: C_6F_5MgBr, TMSCl, Et_2O, –78 °C to r.t., 2 h; Method B: C_6F_5MgBr, THF–Et_2O (3:1), –78 °C to r.t., 18 h at r.t.
[b] Yield of isolated product.
[c] Mixture of isomers (dr = 1.2:1).
[d] Mixture of isomers (dr = 1.8:1).
[e] Approximately 50% conversion along with formation of byproducts.

When β-morpholino-substituted nitroalkenes **1k** and **1l** were reacted with the C_6F_5MgBr and TMSCl system, nitroalkenes **3k** and **3l** were obtained, respectively (Scheme 2). Presumably, the initially formed silyl nitronates underwent elimination of morpholine upon acidic work-up.



Scheme 2 Reaction of β-morpholino-substituted enamines

We demonstrated that C_6F_5-substituted nitroalkanes can be transformed into 4,5,6,7-tetrafluoroindolines (Scheme 3). Thus, reduction of the nitro group of product **2a** under an atmospheric pressure of hydrogen furnished amine **5**. Subsequent heating of the latter in *N*,*N*-dimethylformamide (DMF) in the presence of potassium fluoride effected substitution of *ortho*-fluorine leading to the formation of 4,5,6,7-tetrafluoroindoline **6**. It should be pointed out that this approach to the synthesis of tetrafluoroindolines, which starts from nitroalkene and C_6F_5 nucleophile, is more general and efficient than previously reported methods.[14]



Scheme 3 Synthesis of 4,5,6,7-tetrafluoroindoline **6**. *Reagents and conditions*: (i) H_2 (1 atm), Pd/C; (ii) KF, DMF, 150 °C, 4 h.

In summary, a convenient protocol for the addition of pentafluorophenylmagnesium bromide to conjugate nitroalkenes has been elaborated. The addition products, C_6F_5-substituted nitro compounds, can be readily converted into fluorinated indolines.

All reactions were performed under an argon atmosphere. Column chromatography was carried out with Merck silica gel (Kieselgel 60, 230–400 mesh). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography; visualizing under UV light and/or dipping in acidic aq $KMnO_4$ solution. NMR spectra were recorded with a Bruker AM-300 instrument. Microanalyses were performed with a KarloErba 1106 instrument. Nitroalkenes **1a**, **1c**–**e**, and **1h**,[15] **1f**,[16] **1g**,[17] **1i**,[18] **1j**,[19] and **1l**,[20] were obtained according to literature procedures.

2-[(*E*)-2-Nitrovinyl]furan (1b)[21]

A solution of MeONa [prepared by dissolving of sodium (0.96 g, 41.0 mmol) in MeOH (10 mL)] was added to a mixture of nitromethane (2.14 mL, 39 mmol) and 2-furaldehyde (3.45 mL, 41.0 mmol) at 0 °C. After stirring for 10 min at 0 °C, the mixture was

treated with H_2O (5 mL), and then with cold HCl (prepared from 15 mL of conc. HCl and 25 mL of H_2O). The precipitate was filtered, washed with H_2O (3 × 20 mL), dried, and recrystallized from MeOH to give nitroalkene **1b**.

Yield: 2.0 g (37%); brown crystals; mp 72–73 °C.

4-[(*E*)-2-Nitrovinyl]morpholine (1k)[22]
p-Toluenesulfonic acid (162 mg, 0.85 mmol) was added to a mixture of morpholine (2.46 mL, 28.5 mmol), trimethyl orthoformate (8.73 mL, 78.9 mmol) and nitromethane (7.76 mL, 142.5 mmol). The mixture was heated at reflux for 7 h, then concentrated under reduced pressure and the residue was recrystallized from MeOH to give nitroalkene **1k**.

Yield: 1.58 g (35%); dark-green crystals; mp 140–141 °C.

Preparation of C_6F_5MgBr
Bromopentafluorobenzene (6.2 mL, 50 mmol) was added dropwise to a suspension of magnesium turnings (1.28 g, 52.5 mmol) in Et_2O (20 mL) at a rate that was sufficient to maintain gentle reflux. After complete addition, the mixture was heated to reflux for an additional 1 h. The concentration of the Grignard reagent was determined by ^{19}F NMR spectroscopy using $PhCF_3$ as internal standard to be 1.92 M.

Reactions of Nitroalkenes with C_6F_5MgBr; General Procedure

Method A
A Schlenk flask was evacuated, filled with argon, charged with nitroalkene (1.0 mmol), Et_2O (1 mL) and TMSCl (152 μL, 1.2 mmol), and the flask was cooled to –78 °C. A solution of C_6F_5MgBr (1.3 mmol) was added dropwise, then the temperature was allowed to rise to r.t. during 1 h and the mixture was stirred for an additional 1 h. The mixture was quenched with AcOH (86 μL, 1.5 mmol), diluted with H_2O (5 mL), and extracted with Et_2O (3 × 5 mL). The organic phase was dried over Na_2SO_4, concentrated under vacuum, and the residue was purified by chromatography.

Method B
A Schlenk flask was evacuated, filled with argon, charged with nitroalkene (1.0 mmol) and THF (2 mL), and the flask was cooled to –78 °C. A solution of C_6F_5MgBr (1.3 mmol) was added dropwise, then the temperature was allowed to rise to r.t. during 1 h, and the mixture stirred for an additional 18 h (reaction monitored by TLC analysis). The mixture was quenched with aq HCl (0.5 M, 5.2 mL), diluted with H_2O (5 mL), and extracted with Et_2O (3 × 5 mL). The organic phase was dried over Na_2SO_4, concentrated under vacuum, and the residue was purified by chromatography.

1,2,3,4,5-Pentafluoro-6-(2-nitro-1-phenylethyl)benzene (2a)
Yield: 266 mg (84%); colorless oil; R_f = 0.24 (hexane–EtOAc, 20:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.07–5.37 (m, 1 H, CHC_6F_5), 5.22 (dd, *J* = 46.7, 13.3 Hz, 2 H, CH_2), 7.25–7.44 (m, 5 H, PhH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.2, 76.3 (t, *J* = 4.3 Hz), 113.3 (m), 127.4 (t, *J* = 1.5 Hz), 128.6, 129.5, 136.1, 137.7 (dm, *J* = 241.3 Hz), 140.9 (dm, *J* = 240.7 Hz), 145.1 (dm, *J* = 251.1 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.4 (ddd, *J* = 21.2, 21.2, 7.4 Hz, 2 F, *meta*), –154.8 (t, *J* = 21.21 Hz, 1 F, *para*), –145.5 (dd, *J* = 21.2, 7.4 Hz, *ortho*).

Anal. Calcd for $C_{14}H_8F_5NO_2$ (317.21): C, 53.01; H, 2.54; N, 4.42. Found: C, 53.11; H, 2.47; N, 4.29.

2-[2-Nitro-1-(perfluorophenyl)ethyl]furan (2b)
Yield: 255 mg (83%); pale-yellow oil; R_f = 0.21 (hexane–EtOAc, 15:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.04 (dd, *J* = 13.7, 8.7 Hz, 1 H, $CH_AH_BNO_2$), 5.15 (dd, *J* = 13.7, 6.8 Hz, 1 H, $CH_AH_BNO_2$), 5.41 (dd, *J* = 8.7, 6.8 Hz, 1 H, CHPh), 6.21 (d, *J* = 2.8 Hz, 1 H, C=CH), 6.35 (dd, *J* = 2.8, 1.7 Hz, 1 H, OCH=C*H*), 7.38 (s, 1 H, OCH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 33.1, 74.7 (t, *J* = 3.5 Hz), 107.9, 110.7 (m), 110.8, 137.7 (dm, *J* = 250.0 Hz), 141.2 (dm, *J* = 252.2 Hz), 143.0, 145.2 (dm, *J* = 250.0 Hz), 148.2.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.4 (ddd, *J* = 20.7, 20.3, 5.7 Hz, 2 F, *meta*), –154.0 (t, *J* = 20.7 Hz, 1 F, *para*), –142.1 (dd, *J* = 20.3, 5.7 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{12}H_6F_5NO_3$ (307.17): C, 46.92; H, 1.97; N, 4.56. Found: C, 46.84; H, 1.98; N, 4.47.

2-[2-Nitro-1-(perfluorophenyl)ethyl]thiophene (2c)
Yield: 284 mg (88%); pale-yellow oil; R_f = 0.26 (hexane–EtOAc, 15:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.11 (dd, *J* = 13.6, 7.9 Hz, 1 H, $CH_AH_BNO_2$), 5.19 (dd, *J* = 13.6, 8.6 Hz, 1 H, $CH_AH_BNO_2$), 5.57 (dd, *J* = 8.6, 7.9 Hz, 1 H, CHAr), 6.92–7.07 (m, 2 H, C=C*H*-C*H*), 7.28 (dd, *J* = 4.9, 0.7 Hz, 1 H, SCH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.5, 76.8 (t, *J* = 4.3 Hz), 112.9 (m), 126.0, 126.3, 127.4, 137.9 (dm, *J* = 242.0 Hz), 138.0, 141.3 (dm, *J* = 243.1 Hz), 145.2 (dm, *J* = 248.1 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.1 (ddd, *J* = 21.0, 20.7, 5.7 Hz, 2 F, *meta*), –154.1 (t, *J* = 20.7 Hz, 1 F, *para*), –142.2 (dd, *J* = 21.0, 5.7 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{12}H_6F_5NO_2S$ (323.24): C, 44.59; H, 1.87; N, 4.33. Found: C, 44.64; H, 1.86; N, 4.23.

1-[1-(4-Chlorophenyl)-2-nitroethyl]-2,3,4,5,6-pentafluorobenzene (2d)
Yield: 306 mg (87%); colorless oil; R_f = 0.26 (hexane–EtOAc, 15:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 5.08–5.22 (m, 2 H, CH_2NO_2), 5.29 (dd, *J* = 8.0, 7.9 Hz, 1 H, CHPh), 7.26 (d, *J* = 7.4 Hz, 2 H, ArH), 7.35 (d, *J* = 7.4 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.6, 76.1 (t, *J* = 4.3 Hz), 112.9 (m), 128.8 (t, *J* = 1.6), 129.7, 134.6, 134.7, 138.0 (dm, *J* = 254.9 Hz), 141.0 (dm, *J* = 255.8 Hz), 145.2 (dm, *J* = 249.7 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.1 (dt, *J* = 20.9, 6.2 Hz, 2 F, *meta*), –154.2 (t, *J* = 20.9 Hz, 1 F, *para*), –142.4 (dd, *J* = 20.9, 6.2 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{14}H_7ClF_5NO_2$ (351.66): C, 47.82; H, 2.01; N, 3.98. Found: C, 47.71; H, 1.94; N, 3.92.

1,2,3,4,5-Pentafluoro-6-[1-(4-methoxyphenyl)-2-nitroethyl]benzene (2e)
Yield: 313 mg (90%); colorless oil; R_f = 0.20 (hexane–EtOAc, 10:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 5.08 (dd, *J* = 12.4, 6.5 Hz, 1 H, CHPh), 5.13–5.30 (m, 2 H, CH_2NO_2), 6.89 (d, *J* = 8.5 Hz, 2 H, ArH), 7.24 (d, *J* = 8.5 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.6, 55.3, 76.5 (t, *J* = 4.3 Hz), 113.6 (m), 114.8, 128.0, 128.6, 137.9 (dm, *J* = 254.0 Hz), 140.7 (dm, *J* = 254.6 Hz), 145.1 (dm, *J* = 247.0 Hz), 159.7.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.4 (ddd, *J* = 21.2, 20.8, 6.2 Hz, 2 F, *meta*), –155.0 (t, *J* = 20.8 Hz, 1 F, *para*), –142.6 (dd, *J* = 21.2, 6.2 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{15}H_{10}F_5NO_3$ (347.24): C, 51.88; H, 2.90; N, 4.03. Found: C, 51.87; H, 2.76; N, 3.89.

1-[2-Bromo-1-(4-methoxyphenyl)-2-nitroethyl]-2,3,4,5,6-pentafluorobenzene (2f)
Obtained as a mixture of isomers 1.2:1.

Yield: 392 mg (92%); colorless crystals; mp 64–65 °C; R_f = 0.27 (hexane–EtOAc, 15:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ (major) = 3.78 (s, 3 H, OCH_3), 5.30 (d, J = 11.9 Hz, 1 H, $CHNO_2$), 6.83 (d, J = 11.9 Hz, 1 H, CHAr), 6.87 (d, J = 8.9 Hz, 2 H, ArH), 7.30 (d, J = 8.9 Hz, 2 H, ArH); δ (minor) = 3.82 (s, 3 H, OCH_3), 5.23 (d, J = 11.4 Hz, 1 H, $CHNO_2$), 6.83 (d, J = 11.4 Hz, 1 H, CHAr), 6.93 (d, J = 8.9 Hz, 2 H, ArH), 7.33 (d, J = 8.9 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major) = 47.8, 55.2, 78.5 (t, J = 5.0 Hz), 113.2 (m), 115.0, 126.1, 129.1, 137.7 (dm, J = 249.3 Hz), 141.1 (dm, J = 249.9 Hz), 144.5 (dm, J = 249.9 Hz), 160.3; δ (minor) = 47.3, 55.3, 78.8 (t, J = 5.0 Hz), 112.2 (m), 114.8, 126.6, 129.5, 137.7 (dm, J = 249.3 Hz), 141.1 (dm, J = 249.9 Hz), 144.5 (dm, J = 249.9 Hz), 160.0.

^{19}F NMR (282 MHz, $CDCl_3$): δ (major) = –160.9 (ddd, J = 21.8, 21.2, 6.0 Hz, 2 F, *meta*), –154.1 (t, J = 21.2 Hz, 1 F, *para*), –141.9 (dd, J = 21.8, 6.0 Hz, 2 F, *ortho*); δ (minor) = –160.5 (ddd, J = 20.6, 20.5, 5.2 Hz, 2 F, *meta*), –153.6 (t, J = 20.5 Hz, 1 F, *para*), –141.9 (dd, J = 20.6, 5.2 Hz, 1 F, *ortho*).

Anal. Calcd for $C_{15}H_9BrF_5NO_3$ (426.13): C, 42.28; H, 2.13; N, 3.29. Found: C, 42.14; H, 2.07; N, 3.19.

1,2,3,4,5-Pentafluoro-6-(2-nitro-1-phenylpropyl)benzene (2g)
Obtained as a mixture of isomers 1.8:1.

Yield: 272 mg (82%); colorless crystals; mp 67–76 °C; R_f = 0.20 (hexane–EtOAc, 25:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62 (d, J = 6.7 Hz, 3 H, CH_3), 5.01 (d, J = 11.7 Hz, 1 H, CHPh), 5.66–5.81 [m, 1 H, C*H*(CH_3)NO_2], 7.22–7.54 (m, 5 H, PhH); δ (minor) = 1.57 (d, J = 6.7 Hz, 3 H, CH_3), 4.86 (d, J = 11.7 Hz, 1 H, CHPh), 5.66–5.81 [m, 1 H, C*H*(CH_3)NO_2], 7.22–7.54 (m, 5 H, PhH).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major) = 19.3, 45.7, 84.1 (dd, J = 4.3, 4.0 Hz); δ (minor) = 19.4, 46.4, 83.7 (dd, J = 3.6, 3.9 Hz); δ (both isomers) = 113.4 (m), 127.5 (t, J = 1.8 Hz), 128.2 (t, J = 2.1 Hz), 128.5 (d, J = 8.4 Hz), 128.6, 129.3, 129.6, 136.0, 136.5, 137.9 (dm, J = 249.9), 140.7 (dm, J = 257.0), 144.9 (dm, J = 247.7).

^{19}F NMR (282 MHz, $CDCl_3$): δ (major) = –160.9 (dt, J = 21.2, 6.7 Hz, 2 F, *meta*), –154.6 (t, J = 21.2 Hz, 1 F, *para*), –142.2 (dd, J = 21.2, 6.7 Hz, 1 F, *ortho*); δ (minor) = –161.6 (dt, J = 21.2, 6.4 Hz, 2 F, *meta*), –155.3 (t, J = 21.2 Hz, 1 F, *para*), –141.4 (dd, J = 21.2, 6.4 Hz, 1 F, *ortho*).

Anal. Calcd for $C_{15}H_{10}F_5NO_2$ (331.24): C, 54.39; H, 3.04; N, 4.23. Found: C, 54.27; H, 2.91; N, 4.11.

(*E*)-1,2,3,4,5-Pentafluoro-6-(1-nitro-4-phenylbut-3-en-2-yl)benzene (2h)
Yield: 257 mg (75%); pale-yellow crystals; mp 99–101 °C; R_f = 0.28 (hexane–EtOAc, 15:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.78–4.95 (m, 3 H, C*H*C*H*$_2$$NO_2$), 6.28 (dd, J = 16.0, 6.4 Hz, 1 H, PhCH=C*H*), 6.67 (d, J = 16.0 Hz, 1 H, PhC*H*=CH), 7.27–7.39 (m, 5 H, PhH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 37.8, 76.7, 112.3 (m), 122.2, 126.7, 128.7, 128.8, 135.5, 135.6, 138.0 (dm, J = 249.8 Hz), 144.5 (dm, J = 262.2 Hz), 145.1 (dm, J = 247.8 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.3 (ddd, J = 21.0, 20.7, 6.2 Hz, 2 F, *meta*), –154.6 (t, J = 20.7 Hz, 1 F, *para*), –142.6 (dd, J = 21.0, 6.2 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{16}H_{10}F_5NO_2$ (343.25): C, 55.99; H, 2.94; N, 4.08. Found: C, 55.84; H, 2.90; N, 4.01.

1,2,3,4,5-Pentafluoro-6-(3-methyl-1-nitrobutan-2-yl)benzene (2i)
Yield: 215 mg (76%); colorless oil; R_f = 0.28 (hexane–EtOAc, 15:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 [d, J = 6.6 Hz, 3 H, C(CH_3)$_A$(CH_3)$_B$], 1.10 [d, J = 6.6 Hz, 3 H, C(CH_3)$_A$(CH_3)$_B$], 2.02–2.20 [m, 1 H, C*H*(CH_3)$_2$], 3.99 (dt, J = 8.2, 8.2 Hz, 1 H, CHPh), 4.82 (d, J = 7.9 Hz, 2 H, CH_2NO_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 20.7, 30.0, 41.6, 76.2 (t, J = 3.5 Hz), 112.8 (tm, J = 16.2 Hz), 137.7 (dm, J = 254.0 Hz), 140.5 (dm, J = 253.0 Hz), 145.4 (dm, J = 247.6).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –162.2 (dt, J = 21.2, 6.4 Hz, 2 F, *meta*) –155.4 (t, J = 21.2 Hz, 1 F, *para*), –141.8 (dd, J = 21.2, 6.3 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{11}H_{10}F_5NO_2$ (283.19): C, 46.65; H, 3.56; N, 4.95. Found: C, 46.54; H, 3.56; N, 4.97.

1-(3,3-Dimethyl-1-nitrobutan-2-yl)-2,3,4,5,6-pentafluorobenzene (2j)
Yield: 232 mg (78%); colorless oil; R_f = 0.31 (hexane–EtOAc, 15:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 [s, 9 H, C(CH_3)$_3$], 3.89 (dd, J = 10.9, 4.8 Hz, 1 H, CHC_6F_5), 4.82 (dd, J = 13.3, 4.8 Hz, 1 H, C*H*$_A$H$_B$), 5.00 (dd, J = 13.3, 10.9 Hz, 1 H, CH$_A$C*H*$_B$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.9 (d, J = 2.9 Hz), 35.2, 44.8 (dd, J = 1.5, 1.4 Hz), 74.5 (d, J = 8.1 Hz).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –162.3 (ddd, J = 21.8, 21.5, 7.1 Hz, 1 F, *meta*), –162.0 (ddd, J = 21.5, 21.4, 7.4 Hz, 1 F, *meta*), –155.1 (t, J = 20.8 Hz, 1 F, *para*), –139.0 (d, J = 21.8 Hz, 2 F, *ortho*), –138.3 (dm, J = 21.5 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{12}H_{12}F_5NO_2$ (297.22): C, 48.49; H, 4.07; N, 4.71. Found: C, 48.29; H, 3.82; N, 4.54.

(*E*)-1,2,3,4,5-Pentafluoro-6-(2-nitrovinyl)benzene (3k)
Yield: 139 mg (58%); colorless oil; R_f = 0.24 (hexane–EtOAc, 25:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81 (d, J = 14.0 Hz, 1 H, NO_2HC=C*H*), 8.02 (d, J = 14.0 Hz, 1 H, PhCH=C*H*).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 106.2 (ddd, J = 13.9, 14.1, 4.3 Hz), 123.0, 137.9 (dm, J = 253.7 Hz), 142.3 (dd, J = 9.8, 9.9 Hz), 143.2 (dm, J = 261.8 Hz), 146.0 (dm, J = 256.7).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.0 (ddd, J = 20.4, 19.3, 5.8 Hz, 2 F, *meta*), –148.0 (dd, J = 20.4, 19.3 Hz, 1 F, *para*), –136.8 (m, 2 F, *ortho*).

Anal. Calcd for $C_8H_2F_5NO_2$ (239.10): C, 40.19; H, 0.84; N, 5.86. Found: C, 40.33; H, 0.83; N, 5.88.

(*E*)-1,2,3,4,5-Pentafluoro-6-(2-nitrobut-1-en-1-yl)benzene (3l)
Yield: 190 mg (71%); colorless oil; R_f = 0.36 (hexane–EtOAc, 25:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.17 (t, J = 7.3 Hz, 3 H, CH_2CH_3), 2.61 (q, J = 7.3 Hz, 2 H, CH_2CH_3), 7.55 (s, 1 H, PhCH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.3 (t, J = 1.5 Hz), 22.2 (t, J = 1.8 Hz), 107.7 (td, J = 17.9, 4.0 Hz), 117.1, 138.1 (dm, J = 257.4 Hz), 142.1 (dm, J = 258.7 Hz), 144.2 (dm, J = 249.5 Hz), 158.9.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –161.2 (ddd, J = 20.9, 20.6, 6.2 Hz, 2 F, *meta*), –151.7 (t, J = 20.6 Hz, 1 F, *para*), –137.9 (dd, J = 20.9, 6.2 Hz, 2 F, *ortho*).

Anal. Calcd for $C_{10}H_6F_5NO_2$ (267.15): C, 44.96; H, 2.26; N, 5.24. Found: C, 44.79; H, 2.24; N, 5.13.

4,5,6,7-Tetrafluoro-3-phenylindoline (6)
Palladium on carbon (20 mg, 10% palladium content) and AcOH (144 μL, 2.52 mmol) were added to a solution of **2a** (533 mg, 1.68 mmol) in MeOH (3 mL). The flask was flushed with hydrogen and connected to a hydrogen balloon (atmospheric pressure), and the mixture was vigorously stirred for 24 h. After consumption of starting compound (reaction monitored by TLC), the mixture was filtered through the pad of Celite and concentrated. The residue was

dissolved in EtOAc (5 mL), washed with sat. aq $NaHCO_3$ (3 × 5 mL), and the aqueous phase was washed with EtOAc (3 × 5 mL). The combined organic phase was dried over Na_2SO_4 and concentrated under vacuum. The residue was passed through a short silica gel pad (eluting with hexane–EtOAc, 1:1 containing 2 vol% Et_3N), to give amine **5** (307 mg), which was used without further purification.

Anhydrous KF (93 mg, 1.6 mmol) was added to a solution of amine **5** (307 mg) in DMF (2 mL), and the suspension was heated at 150 °C for 5 h. The mixture was cooled to r.t., quenched with aq HCl (5 M, 4 mL), and washed with hexane–EtOAc (1:1, 3 × 5 mL). The combined organic phase was dried over Na_2SO_4, concentrated under vacuum, and the residue was purified by chromatography on silica gel (hexane–EtOAc, 10:1) to give indoline **6**.

Yield: 228 mg (80% based on **5**, 51% based on **2a**); colorless oil; R_f = 0.23 (hexane–EtOAc, 10:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (ddd, J = 9.2, 7.3, 2.0 Hz, 2 H, CH_AH$_B$), 3.96 (br, 1 H, NH), 4.09 (ddd, J = 9.2, 7.3, 2.0 Hz, 1 H, CH$_A$$H_B$), 4.69 (dd, J = 9.2, 7.3 Hz, 1 H, CHPh), 7.25–7.41 (m, 5 H, PhH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.9, 57.0, 114.6, 114.8, 126.8, 127.1, 128.6, 133.5 (dm, J = 249.3 Hz), 133.7 (dm, J = 250.1 Hz), 140.7 (dm, J = 250.7 Hz), 141.3, 143.9 (dm, J = 250.4 Hz).

^{19}F (282 MHz, $CDCl_3$): δ = –171.2 (ddd, J = 21.2, 21.2, 6.7 Hz, 1 F), –162.8 (ddd, J = 21.2, 21.2, 14.8 Hz, 1 F), –158.6 (dd, J = 21.2, 21.2 Hz, 1 F), –164.8 (dd, J = 21.2, 14.8 Hz, 1 F).

Anal. Calcd for $C_{14}H_9F_4N$ (267.22): C, 62.93; H, 3.39; N, 5.24. Found: C, 62.74; H, 3.35; N, 5.17.

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