ELSEVIER

Journal of Fluorine Chemistry 99 (1996) 87–92

JOURNAL OF FLUORINE CHEMISTRY

Reaction of pentafluoropyridine with lithium hydrazonides; competing monosubstitution at the 2- and 4-positions

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Received 11 September 1995; accepted 18 December 1995

Abstract

Treatment of pentafluoropyridine (**1**) in diethyl ether with approximately 1 M equiv. of the hydrazonides $Ph_2C{=}NNHLi$ (**3a**) and $Ph_2C{=}NNLiPh$ (**3b**) under mild conditions gives good yields (62% and 83%) of 4- and 2-$(Ph_2C{=}NH)C_5F_4N$ (**5a** and **6a**) and 4- and 2-$(Ph_2C{=}NPh)C_5F_4N$ (**5b** and **6b**), respectively, containing unusually large amounts of 2-substituted products (**5a**/**6a** = 50:50; **5b**/**6b** = 65:35). The increased ease of displacement of a 2-F substituent from **1** (→**6a** and **6b**) in these cases is ascribed to chelation of the lithium cation in the transition state involved in the rate-determining step leading to formation of an *ortho*-quinonoidal σ-complex. Catalytic hydrogenation of a 1:1 mixture of hydrazones **5a** and **6a** affords the corresponding hydrazines, 4- and 2-$H_2NNHC_5F_4N$ (**7** and **8**) in good yield (78%); acidic hydrolysis (hot HCl aq.) of the **5a**/**6a** mixture yields tetrafluoro-4-hydrazinopyridine (**9**) and, depending on the conditions, tetrafluoro-2-hydrazinopyridine (**10**) or 2-aminotetrafluoropyridine (**11**).

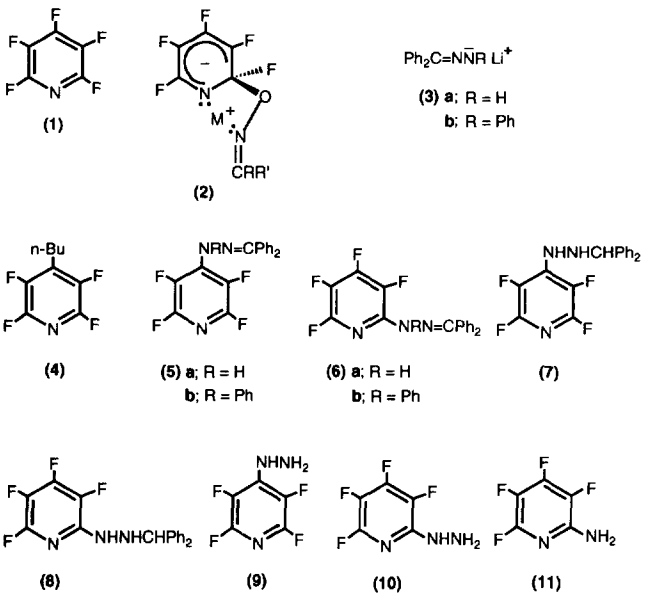
Keywords: S_NAr substitution; Pentafluoropyridine; Lithium hydrazonides; NMR spectroscopy; Mass spectrometry

1. Introduction

In 1989, we reported that treatment of pentafluoropyridine (**1**) with alkali-metal oximates $RR'C{=}NO^-M^+$ (R = R′ = Me or Ph; R = Me, R′ = Ph; R = H, R′ = Ph; $M^+ = Li^+$, Na^+, K^+) in low polarity suspending agents/solvents (Et_2O, THF or C_6H_6) gave unprecedented results in that S_NAr attack at C-2 competes strongly and often successfully with the 4-substitution normally observed [1]. For example, a 2-/4-substitution ratio of 74:26 was obtained using a slurry of the salt (*E*)-MeCPh=NO^-Na^+ in benzene. The crux of the mechanistic interpretation proposed [1] is coordination of the oximate anion–metal cation ion pair with pentafluoropyridine (**1**) in the rate-determining step, with participation of the metal cation; this can occur only during attack at the 2-position, leading to a σ-complex of the *ortho*-quinonoid type (**2**). This paper reports an extension of this work to S_NAr attack on **1** by lithium salts of hydrazones, which are structural and electronic analogues of oximates.

2. Results and discussion

Details of monosubstitution reactions carried out between pentafluoropyridine (**1**) and lithium hydrazonides **3a** and **3b** in diethyl ether are given in Table 1, together with those of chemical conversions of the product (**5a** + **6a**) derived from **3a**.



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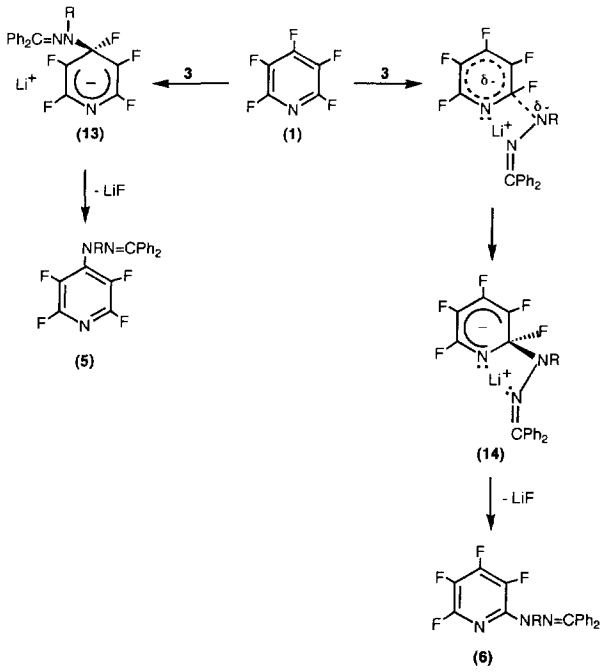
SSDI 0022-1139(96)03394-5



Scheme 1.

2.1. Reaction of the lithium hydrazonides 3a and 3b with pentafluoropyridine (1)

As found for alkali-metal oximate attack on pentafluoropyridine [1,2], competing 4- and 2-substitution also took place with the lithium hydrazonides **3a** and **3b** to afford the corresponding tetrafluoro-4- and -2-pyridylhydrazones **5** and **6**, respectively. The observed 4-/2-substitution ratios for reaction under heterogeneous conditions of lithium salts **3a** and **3b** were 50:50 and 65:35, respectively, as compared to 67:33 found for heterogeneous reaction of the corresponding sodium ketoximate $Ph_2C{=}NO^-Na^+$ (**12**) with **1** under identical conditions (ca. 20 °C in Et_2O). In pentafluoropyridine-oximate ($RR'C{=}NO^-M^+$) reactions, 4-/2-substitution ratios vary according to which alkali-metal cation M^+ is employed, with 2-substitution favoured in the order Na > K > Li, e.g. 4-/2-substitution ratios for attack by (*E*)-MeCPh=NO^-M^+ in Et_2O are: M = Na, 65:35 (−35 °C), 40:60 (+36 °C); M = K, 83:17 (−35 °C); M = Li, 87:13 (+36 °C) [1,2].

The bimolecular two-step fluorine displacement [3] involving a resonance-stabilized σ-complex (**13**) accounts for the products **5a** and **5b**. The severe loss of the usual regiospecificity for Nu^-/C_5F_5N reactions revealed by the production of **6a** and **6b** is ascribed to a stabilizing interaction involving lithium cation and the lone-pair electrons of the ring nitrogen (Scheme 1).

Since pentafluoropyridine is virtually non-basic [1], the lithium cation clearly cannot begin to play its role in lowering the activation energy for formation of a resonance-stabilized σ-complex (**14**) until an incipient bond arises between C-2 and the attacking terminal nitrogen of the hydrazonide **3**.

Differences in bond lengths and bond angles between the oximates and hydrazonides can explain why effective chelation is achieved by the sodium cation in 2-substitution by oximates and the smaller lithium cation in 2-substitution by hydrazonides {C=N ca. 1.28 Å (oximes) and ca. 1.31 Å (hydrazones); N–O ca. 1.43 Å; N–N ca. 1.38 Å; C=N–O ca. 109°; C=N–N ca. 112° [2].

The different 2-/4-substitution ratios observed for attack by **3a** and **3b** seem unlikely to arise directly from steric effects, because replacement of H (**3a**) by Ph (**3b**) would be expected to increase the activation energy for 4-attack more than that for 2-attack and result in less 4-substitution, contrary to what is observed [attack at the 4-position is more sterically hindered (two *ortho*-fluorines) than attack at the 2-position (one *ortho*-fluorine)]. It is considered more probable that substitution of H by Ph results in small bond length and bond angle changes which render chelation of the lithium

[1] Pentafluoropyridine forms salts only with superacids [4].

[2] QUEST3D was used to search the Cambridge Database (CSD) with VISTA (Visualisation of Statistics) used to analyse the molecular parameters; both programs are the property of the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CD2 1EZ, UK.

Table 1
Reaction of lithium hydrazonides **3a** and **3b** with pentafluoropyridine (**1**) (ca. 1:1 molar ratio) and conversion of the products from **3a**

Substrate	Reactant	Conditions		Products (%) [b]
		Temp. (°C)	Time (h)	
1	**3a** [a]	−35	1	**4** (10); **5a** (31); **6a** (31) [c]
		ca. 20	4	
1	**3b** [a]	−78	1	**5b** (54); **6b** (29)
		ca. 20	24	
5a/6a	H_2/Pt–C	ca. 20	24	**7** (39); **8** (39) [d]
5a/6a	HCl (15% w/w)	ca. 100	2	**9** (trace); **10** (26)
5a/6a	HCl (24% w/w)	ca. 100	3	**9** (7); **11** (43)

[a] The salts **3a** and **3b** were prepared by treatment of the parent hydrazones with n-butyl-lithium.

[b] Product yields are based on substrate reacted.

[c] Separation was achieved by dry column flash chromatography (DCFC), giving pure **5a** (9%), pure **6a** (9%) and a 1:1 mixture of these compounds (44%).

[d] Unchanged **5a/6a** (1:1 mixture; 20% recovery) was also obtained.

cation less effective, and hence raise the activation energy for 2-substitution.

The mixture of hydrazones **5a** and **6a** could not be separated completely by DCFC, although small amounts of pure materials were isolated to enable elemental analyses and spectral data to be obtained. By contrast, the mixture of hydrazones **5b** and **6b** was separated readily by DCFC. 4-n-Butyltetrafluoropyridine (**4**), isolated from the reaction involving **3a**, must have arisen from attack on the heteroaromatic substrate **1** by the n-butyl-lithium present in the reaction mixture due to incomplete formation of salt **3a**.

2.2. Reactions of hydrazones 5a and 6a

Catalytic hydrogenation (H_2/Pt–C) of a 1:1 mixture of these hydrazones in ethanol at room temperature afforded equal amounts (78% yield based on 80% conversion) of the corresponding 4-pyridylhydrazine (**7**) and 2-pyridylhydrazine (**8**) (separated successfully by DCFC).

Hydrolysis of the hydrazone mixture with aqueous hydrochloric acid (15% w/w) under reflux (2 h) gave only low yields of the 4- and 2-hydrazinotetrafluoropyridines **9** (trace) and **10** (26%), respectively. No attempt was made to isolate the unchanged reactants **5a**/**6a** or the hydrolysis product benzophenone. Compound **9** was identified by a comparison of its ^{19}F NMR spectrum with that reported for a sample prepared previously by the reaction of hydrazine hydrate with **1** in ethanol [5].

The yield of **9** was increased to 7% by the use of stronger hydrochloric acid (24% w/w) and a longer reflux period (3 h); under these conditions, however, the 2-hydrazino compound **10** was deaminated to 2-aminotetrafluoropyridine (**11**), isolated in 43% yield by DCFC. Deamination of **9** to 4-aminotetrafluoropyridine (54%) proceeded with hydriodic acid (54% w/w) under reflux (2 h) [6], but this amine was not detected in our reaction products.

The results indicate that both hydrolysis of the 2-pyridylhydrazone (**6a**) and deamination of the hydrolysis product **10** are more facile than the corresponding reactions of the 4-substituted compounds **5a** and **9**. Although no attempts were made to optimise the yields of compounds **10** and **11**, the initial results show that they can be prepared from hydrazone **6a** and isolated by DCFC.

Hydrazine **10** was stable when pure and dry, and could be stored unchanged in glass for several weeks under air. In solution ($CDCl_3$), however, a brown precipitate was observed after 2 d. By contrast, the amine **11** was stable only for a short period of time in air after DCFC isolation; thus, although it gave clean IR and ^1H and ^{19}F NMR spectra directly after separation, elemental analyses (for C, H, N) were incorrect when obtained after 3 d, and the ^1H and ^{19}F NMR spectra of a sample stored for 7 d were complex.

The new 2-substituted tetrafluoropyridines **6a**, **6b**, **8**, **10** and **11** were readily distinguished from their 4-substituted analogues **5a**, **5b**, **7** and **9** by ^{19}F NMR spectroscopy (four peaks of equal relative intensity versus two peaks) [7], and all the compounds except **11** gave satisfactory elemental analyses and consistent molecular ion peaks in their mass spectra. NMR data are recorded in Table 2; mass spectra are summarised in Table 3.

3. Experimental details

3.1. Starting materials

Pentafluoropyridine (**1**) was prepared by heating pentachloropyridine with potassium fluoride [8] and its purity checked by ^{19}F NMR spectroscopy. Reaction of benzophenone with (i) N_2H_4 in AcOH/Et_2O heated under reflux (3 h) gave benzophenone hydrazone (32%) {m.p. 95 °C; lit. value [9], m.p. 98 °C} and (ii) $PhNH\overset{+}{N}H_3Cl^-$/AcONa in EtOH/$H_2O$ heated under reflux (1 h) afforded benzophenone phenylhydrazone (40%) {m.p. 136–137 °C; lit. value [10], m.p. 137 °C}. The hydrazones were then converted into their lithium salts **3a** and **3b** by treatment at −35 °C with n-butyl-lithium (1.6 M in hexane) in anhydrous diethyl ether under nitrogen; the resulting mixtures were stirred at −35 °C (1 h), then at room temperature (15 min) and finally recooled to the desired temperature (see text) before being used in situ.

3.2. General techniques

Product mixtures were examined by thin-layer chromatography (TLC) using silica gel (Merck 60 GF_{254}) and ^{19}F NMR spectroscopy, and were separated into their components by dry column flash chromatography (DCFC) using silica gel (Fluka 60 GF_{254}) and the eluants stated in the text. Pure components were examined by IR spectroscopy (Perkin-Elmer DE 783 instrument), ^1H NMR spectroscopy [Perkin-Elmer R34 (220 MHz) spectrometer, external reference Me_4Si], ^{19}F NMR spectroscopy [Perkin-Elmer R32 (84.6 MHz) instrument; external reference CF_3CO_2H], ^{13}C NMR spectroscopy [Bruker AC300 (75.0 MHz) spectrometer with broad-band proton decoupling and D_2O as the deuterium lock signal; external reference Me_4Si] and mass spectrometry [Kratos MS45 spectrometer operating with an electron beam energy of 70 eV under electron impact (EI) conditions]. The NMR spectra were run on solutions in $CDCl_3$, and chemical shifts to low field of reference are designated positive.

Melting points are uncorrected.

3.3. Reactions of lithium salts of hydrazones with pentafluoropyridine (1)

(a) Lithium benzophenone hydrazonide (3a)

Pentafluoropyridine (**1**) (3.90 g, 23.1 mmol) in diethyl ether (ca. 10 cm^3) was slowly added to a cold (−35 °C) stirred slurry of lithium benzophenone hydrazonide (**3a**) [prepared from n-butyl-lithium in hexane (12.6 cm^3, 1.6 M,

Table 2
NMR data

Compound	δ (ppm) (assignment)
5a	δ_H: 7.80 (br., 1H, NH); 7.50 (mult., 5H, C_6H_5); 7.23 (mult., 5H, C_6H_5). δ_F: −14.0 (mult., 2F, F-2/6); −81.2 (mult., F-3/5). δ_C: 153.1 (s, C=N); 144.8 (d, C-2/6, ^1J=238 Hz); 137.0/131.0/130.9/130.6/130.3/129.0/128.9/127.8 (8s, 2 C_6H_5); 134.3 (dd, C-4, ^2J=13.1 Hz, ^3J=6.1 Hz); 131.8 (d, C-3/5, ^1J=255 Hz).
5b	δ_H: 7.70–7.00 (complex, 3 C_6H_5). δ_F: −13.0 (mult., F-2/6); −62.8 (mult., F-3/5). δ_C: 163.3 (s, C=N); 144.3/137.4/134.9/130.6/129.5/129.1/128.9/128.5/128.3/127.8/124.3/118.1 (12s, 3 C_6H_5); 142.8 (d, C-2/6, ^1J=243 Hz); 136.4 (d, C-3/5, ^1J=262 Hz); 133.8 (dd, C-4, ^2J=10.3 Hz, ^3J=4.5 Hz).
6a	δ_H: 7.95 (br., 1H, NH); 7.60 (mult., 5H, C_6H_5); 7.35 (mult., 5H, C_6H_5). δ_F: −8.0 (ddd, F-6, J_{3-6}=25.0 Hz, J_{5-6}=23.9 Hz, J_{4-6}=15.8 Hz); −60.5 (td, F-4, $J_{3-4}=J_{5-4}$=18.6 Hz, J_{6-4}=15.8 Hz); −83.5 (ddd, F-3, J_{6-3}=25.0 Hz, J_{4-3}=18.6 Hz, J_{5-3}=4.0 Hz); −92.5 (ddd, F-5, J_{6-5}=23.0 Hz, J_{4-5}=18.6 Hz, J_{3-5}=4.0 Hz). δ_C: 151.6 (s, C=N); 148.7 (dtd, C-4, ^1J=262.4 Hz, ^2J=12.2 Hz, ^3J=6.6 Hz); 146.4 (dddd, C-6, ^1J=234.9 Hz, ^2J=11.7 Hz, ^3J=6.2 Hz, ^4J=3.1 Hz); 138.5 (ddd, C-2, ^2J=15.7 Hz, ^3J=7.2 and 4.2 Hz); 137.7/132.2/130.7/130.6/130.1/129.2/128.9/127.9 (7s, 2 C_6H_5); 133.4 (ddd, C-3, ^1J=250 Hz, ^2J=10.5 Hz, ^3J=7.5 Hz); 128.0 (d mult., C-5, ^1J=257 Hz).
6b	δ_H: 7.70–6.95 (complex, 3 C_6H_5). δ_F: −6.0 (td, F-6, $J_{3-6}=J_{5-6}$=25.0 Hz, J_{4-6}=14.4 Hz); −59.8 (td, F-4, $J_{3-4}=J_{5-4}$=19.0 Hz, J_{6-4}=14.4 Hz); −65.2 (dd, F-3, J_{6-3}=25.0 Hz, J_{4-3}=19.0 Hz); −85.0 (dd, F-5, J_{6-5}=25.0 Hz, J_{4-5}=19.0 Hz).
7	δ_H: 7.35 (mult., 10H, 2 C_6H_5); 5.85 (br., 1H, NH); 5.12 (s, 1H, C*H*Ph_2); 4.52 (br., 1H, NH). δ_F: −15.8 (mult., 2F, F-2/6); −83.5 (mult., 2F, F-3/5). δ_C: 143.9 (d mult., C-2/6, ^1J=238 Hz); 139.8/128.8/128.0/127.6 (4s, C_6H_5); 137.9 (mult., C-4); 131.0 (d mult., C-3/5, ^1J=250 Hz); 69.2 (s, *C*HPh_2).
8	δ_H: 7.45 (mult., 4H, 4 *o*-C_6H_5); 7.30 (mult., 6H, 6 *m/p*-C_6H_5); 6.20 (br., 1H, NH); 5.32 (s, 1H, C*H*Ph_2); 4.80 (br., 1H, NH). δ_F: −10.2 (ddd, F-6, J_{3-6}=27.0 Hz, J_{5-6}=21.3 Hz, J_{4-6}=13.6 Hz); −62.6 (ddd, F-4, J_{3-4}=19.0 Hz, J_{5-4}=17.0 Hz, J_{6-4}=13.6 Hz); −87.0 (ddd, F-3, J_{6-3}=27.0 Hz, J_{4-3}=19.0 Hz, J_{5-3}=5.1 Hz); −95.0 (ddd, F-5, J_{6-5}=21.3 Hz, J_{4-5}=17.0 Hz, J_{3-5}=5.1 Hz). δ_C: 147.8 (d mult., C-4, ^1J=263 Hz); 146.2 (d mult, C-6, ^1J=246 Hz); 141.7 (mult., C-2); 141.0/128.6/127.8/127.6 (4s, C_6H_5); 131.3 (d mult., C-3, ^1J=239 Hz); 126.8 (dddd, C-5, ^1J=241 Hz, ^2J=8.0 Hz, ^2J=3.5 Hz, ^3J=ca. 1 Hz); 67.6 (s, *C*HPh_2).
10	δ_H: 6.84 (br., 1H, NH); 3.86 (br., 2H, NH_2). δ_F: −11.2 (mult., F-2); −64.5 (mult., F-4); −89.8 (mult., F-3); −98.5 (mult., F-5). δ_C: 146.5 (dtd, C-4, ^1J=263 Hz, ^2J=12.4 Hz, ^3J=7.1 Hz); 146.1 (dddd, C-6, ^1J=234 Hz, ^2J=11.6 Hz, ^3J=6.2 Hz, ^4J=3.2 Hz); 143.4 (dddd, C-2, ^2J=17.7 Hz, ^3J=10.7 Hz, ^3J=4.0 Hz, ^4J=2.1 Hz); 131.7 (dddd, C-3, ^1J=253 Hz, ^2J=11.9 Hz, ^3J=6.7 Hz, ^4J=2.4 Hz); 126.9 (dddd, C-5, ^1J=255 Hz, ^2J=34.3 Hz, ^2J=14.4 Hz, ^3J=1.8 Hz).
11	δ_H: 7.20 (br., NH_2); δ_F: −10.0 (mult., 1F, F-6); −64.0 (mult., 1F, F-4); −84.8 (mult., 1F, F-3); −96.5 (mult., 1F, F-5).

20.2 mmol) and benzophenone hydrazone (4.00 g, 20.4 mmol) in diethyl ether (ca. 50 cm^3)] and the resulting bright yellow mixture was stirred at −35 °C (1 h) and then at room temperature (4 h). The product mixture was shown by TLC (eluant: CH_2Cl_2/n-C_6H_{14} 2:5 v/v) to contain two major components (R_F=0.52 and 0.48) and ^{19}F NMR spectroscopy showed the components were present in the ratio 50:50). The mixture was filtered to afford a yellow solid (3.0 g) [NMR (acetone-d_6). δ_F: −17.0 (mult., 2F); −20.0 (mult., 1F); −71.0 (mult., 2F); −84.0 (mult., 1F); −87.5 (mult., 2F) ppm. δ_H: 8.30–7.70 (complex) ppm] and a pink filtrate from which the solvent was removed in vacuo to give a pink residue (5.40 g). The residue was shown by TLC (eluant CH_2Cl_2/n-C_6H_{14} 2:5 v/v) to contain three components (R_F=0.90, 0.52 and 0.48) which on separation by DCFC afforded the following compounds: (i) 4-n-butyltetrafluoropyridine (**4**) (0.40 g, 2.0 mmol, 10%) (eluant n-C_6H_{14}) [δ_H: 4.55 (t, 2H, CH_2^nPr, J=7 Hz); 1.85 (pentet, 2H, CH_2CH_2Et, J=7 Hz); 1.55 (sextet, 2H, $CH_2CH_2CH_2Me$, J=7 Hz); 1.05 (t, 3H, CH_3, J=7 Hz) ppm. δ_F: −12.5 (mult., 2F, F-2/6); −80.5 (mult., 2F, F-3/5) ppm]; (ii) benzophenone *N*-(tetrafluoro-4-pyridyl)hydrazone (**5a**) (nc) (0.60 g, 1.8 mmol, 9%)

Table 3
Mass spectral data [a]

Compound	MS: *m/z* (%, assignment) [b]
5a	345 (100, M^+); 344 [11, $(M-H)^+$]; 267 [2, $(M-C_6H_6)^+$]; 180 (90, Ph_2CN^+); 166 (46, $C_5H_2F_4N_2^+$); 165 (14, $C_5HF_4N_2^+$); 138 (11, $C_4F_4N^+$); 103 (49, $C_7H_5N^+$); 77 (88, $C_6H_5^+$).
5b	421 (13, M^+); 242 (5, $C_{11}H_6F_4N_2^+$); 241 [1, $(M-Ph_2CN)^+$]; 222 [4, $(M-Ph_2CN-F)^+$]; 180 (100); 165 (2); 77 (49).
6a	345 (100, M^+); 344 (10); 180 (93); 166 (28); 165 (19); 139 (10, $C_4HF_4N^+$); 138 (8); 104 (14, $C_7H_6N^+$); 103 (24); 77 (62).
6b	421 (27, M^+); 242 (11); 241 (12); 222 (4); 194 (2, $Ph_2CN_2^+$); 180 (100); 165 (5); 77 (84).
7	347 (15, M^+); 346 [7, $(M-H)^+$]; 345 [10, $(M-2H)^+$]; 328 [8, $(M-F)^+$]; 327 [12, $(M-HF)^+$]; 270 [2, $(M-C_6H_5)^+$]; 182 (20, Ph_2CHNH^+); 181 (26, Ph_2CNH^+); 180 (40); 167 (100, Ph_2CH^+); 166 (40, Ph_2C^+); 165 (59, $C_5HF_4N_2^+$); 77 (27).
8	347 (9, M^+); 346 (3); 345 (4); 328 (3); 327 (5); 270 (2); 182 (18); 181 (20); 180 (27); 167 (100); 166 (33); 165 (58); 77 (25).
10	181 (100, M^+); 166 [7, $(M-NH)^+$]; 164 [4, $(M-NH_3)^+$]; 151 [12, $(M-N_2H_2)^+$]; 138 (15); 132 (10, $C_5HF_3N^+$); 119 (12, $C_4F_3N^+$); 100 (8, $C_4F_2N^+$).

[a] Electron impact (EI) spectra.
[b] Expressed as a percentage of the base peak.

(Analysis: Found: C, 62.4; H, 3.1; F, 22.1; N, 12.0%; M^+, 345. $C_{18}H_{11}F_4N_3$ requires: C, 62.6; H, 3.2; F, 22.0; N, 12.2%; M, 345) (eluant: CH_2Cl_2/n-C_6H_{14} 1:1 v/v), m.p. 128–130 °C; (iii) a mixture (3.0 g) of compound **5a** (1.50 g, 4.5 mmol, 22%) and its 2-pyridyl isomer **6a** (1.50 g, 4.5 mmol, 22%) (eluant: CH_2Cl_2/n-C_6H_{14} 1:1 v/v) in the ratio 50:50 (^{19}F NMR spectroscopy); and (iv) benzophenone *N*-(tetrafluoro-2-pyridyl)hydrazone (**6a**) (nc) (0.60 g, 1.8 mmol, 9%) (Analysis: Found: C, 62.5; H, 3.2; F, 22.0; N, 11.9%; M^+, 345. $C_{18}H_{11}F_4N_3$ requires: C, 62.6; H, 3.2; F, 22.0; N, 12.2%; M, 345) (eluant: CH_2Cl_2/n-C_6H_{14} 1:1 v/v), m.p. 147–149 °C.

(b) Lithium benzophenone phenylhydrazonide (3b)

Pentafluoropyridine (**1**) (1.88 g, 11.1 mmol) in diethyl ether (ca. 5 cm^3) was added slowly to a cold (−78 °C) stirred slurry of lithium benzophenone phenylhydrazonide (**3b**) [prepared from n-butyl-lithium in hexane (7.0 cm^3, 1.6 M, 11.2 mmol) and benzophenone phenylhydrazone (2.72 g, 10.0 mmol) in diethyl ether (ca. 50 cm^3)] and the resulting deep red mixture stirred at −78 °C (1 h) and then at room temperature (24 h). Examination of the product mixture by TLC (eluant: CH_2Cl_2/n-C_6H_{14} 1:3 v/v) and ^{19}F NMR spectroscopy showed the presence of two major components (R_f = 0.45 and 0.35) in the ratio 65:35 which were separated by DCFC to afford the following products: (i) benzophenone *N*-phenyl-*N*-(tetrafluoro-4-pyridyl)hydrazone (**5b**) (nc) (2.52 g, 6.0 mmol, 54%) (Analysis: Found: C, 68.7; H, 3.6; F, 18.0; N, 10.0%; M^+, 421. $C_{24}H_{15}F_4N_3$ requires: C, 68.4; H, 3.6; F, 18.1; N, 10.0%; M, 421) (eluant: CH_2Cl_2/n-C_6H_{14} 1:3 v/v), m.p. 157–159 °C, and (ii) benzophenone *N*-phenyl-*N*-(tetrafluoro-2-pyridyl)hydrazone (**6b**) (nc) (1.35 g, 3.2 mmol, 29%) (Analysis: Found: C, 68.7; H, 3.5; F, 18.1; N, 9.7%; M^+, 421. $C_{24}H_{15}F_4N_3$ requires: C, 68.4; H, 3.6; F, 18.1; N, 10.0%; M, 421) (eluant: CH_2Cl_2/n-C_6H_{14} 1:2 v/v), m.p. 144–145 °C.

3.4. Reactions of a 1:1 mixture of the benzophenone-N-(tetrafluoropyridyl)hydrazones 5a and 6a

(a) Hydrogenation

A stirred 1:1 mixture of compounds **5a** and **6a** (1.00 g, 2.9 mmol) and platinum on carbon (5% w/w, 1.00 g) in ethanol (ca. 40 cm^3) was hydrogenated in a standard apparatus (24 h) and the resulting material was filtered through silica gel (TLC grade, ca. 10 g). The residue was washed with ethanol (ca. 50 cm^3) and the washings were added to the filtrate from which the ethanol was removed in vacuo to afford a solid residue (0.98 g) which was shown by TLC (eluant: $CHCl_3$/n-C_6H_{14} 1:1 v/v) to contain four components (R_f = 0.85, 0.80, 0.63 and 0.50). The mixture was separated by DCFC to afford the following compounds: (i) a mixture (0.20 g) of unchanged **5a** (0.10 g, 0.30 mmol, 10% recovered) and **6a** (0.10 g, 0.30 mmol, 10% recovered) (eluant: $CHCl_3$/n-C_6H_{14} 1:1 v/v) in the ratio 1:1 (^{19}F NMR spectroscopy); (ii) *N*-(diphenylmethyl)-*N'*-(tetrafluoro-2-pyridyl)-hydrazine (**8**) (0.30 g, 0.90 mmol, 39%) (Analysis: Found: C, 62.3; H, 3.8; F, 22.1; N, 11.8%; M^+, 347. $C_{18}H_{13}F_4N_3$ requires: C, 62.2; H, 3.7; F, 21.9; N, 12.1%; M, 347) (eluant: Et_2O/n-C_6H_{14} 1:1 v/v), m.p. 86–88 °C; IR (ν_{max}) (cm^{-1}): 3390/3360 (s, N–H str.); and (iii) *N*-(diphenyl)-*N'*-(tetrafluoro-4-pyridyl)hydrazine (**7**) (nc) (0.30 g, 0.90 mmol, 39%) (Analysis: Found: C, 62.5; H, 3.9; F, 21.6; N, 12.1%; M^+, 347. $C_{18}H_{13}F_4N_3$ requires: C, 62.2; H, 3.7; F, 21.9; N, 12.1%; M, 347) (eluant: Et_2O/n-C_6H_{14} 1:1 v/v), m.p. 75–77 °C; IR (ν_{max}) (cm^{-1}): 3410/3350 (s, N–H str.).

(b) With hydrochloric acid (15% w/w)

A 1:1 mixture of compounds **5a** and **6a** (5.00 g, 14.4 mmol) and hydrochloric acid (15% w/w, 100 cm^3) was heated under reflux (2 h) and the resulting heterogeneous mixture extracted with dichloromethane (3 × 100 cm^3) to remove unreacted **5a** and **6a** and the hydrolysis product benzophenone. The aqueous layer was made basic (pH 8–9) with solid sodium carbonate and then extracted with dichloromethane (3 × 50 cm^3). The extract was dried ($MgSO_4$) and the solvent removed in vacuo to afford a solid residue (0.42 g) which was shown by TLC (eluant: CH_2Cl_2) and ^{19}F NMR spectroscopy to contain two components (R_f = 0.55 and 0.25) in the ratio 17:83. These were separated by DCFC (same eluant) to give the following products: (i) 4-hydrazinotetrafluorpyridine (**9**) (trace), which was characterised by a comparison of its ^{19}F NMR spectrum [δ_F: −16.5 (mult., 2F, F-2/6); −88.2 (mult., 2F, F-3/5) ppm] with that reported values [δ_F: −19.0 (F-2/6); −86.1 (F-3/5) ppm] [6] and (ii) 2-hydrazinotetrafluoropyridine (**10**) (nc) (0.35 g, 1.9 mmol, 26%) (Analysis: Found: C, 33.4; H, 1.6; F, 42.0; N, 23.2%; M^+, 181. $C_5H_3F_4N_3$ requires: C, 33.1; H, 1.7; F, 42.0; N, 23.2%; M, 181), m.p. 62–63 °C; IR ($\nu_{max.}$) (cm^{-1}): 3350/3230 (s, N–H str.).

(c) With hydrochloric acid (24% w/w)

A 1:1 mixture of compounds **5a** and **6a** (6.00 g, 17.4 mmol) and hydrochloric acid (24% w/w, 150 cm^3) heated under reflux (3 h) and then worked-up in the previous experiment gave a solid residue (0.80 g) which was shown by TLC (eluant: CH_2Cl_2) and ^{19}F NMR spectroscopy to contain two components (R_f = 0.55 and 0.40) in the ratio 13:87. These were separated by DCFC (same eluant) to afford the following compounds: (i) 4-hydrazinotetrafluoropyridine (**9**) (0.10 g, 0.60 mmol, 7%) and (ii) 2-aminotetrafluoropyridine (**11**) (nc) (0.62 g, 3.7 mmol, 43%), an unstable compound: IR ($\nu_{max.}$) (cm^{-1}): 3280 (broad, NH str.).

Acknowledgements

We thank the UK Committee of Vice-Chancellors and Principals for an overseas research studentship (ORS) (to W.J.J.).

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