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Journal of Fluorine Chemistry 128 (2007) 1439–1443
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Continuous flow glassware reactors for the laboratory Synthesis of 2-alkoxy-4-aminotrifluoropyridine derivatives from pentafluoropyridine

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Received 20 June 2007; received in revised form 10 July 2007; accepted 12 July 2007
Available online 1 August 2007

Dedicated to our good friend Professor Neil Bartlett on the occasion of his 75th birthday.

Abstract

Simple, general use continuous flow glassware reactors that are constructed by standard glass blowing techniques have been designed and used for various nucleophilic aromatic substitution reactions. The glassware flow reactors, consisting of a reaction channel that is 0.5 mm in diameter and may possess a range of inlet and outlet ports, provide the opportunity for research scientists to use inexpensive, conveniently operated continuous flow methodology in the laboratory environment. A short series of 2-alkoxy-4-aminotrifluoropyridine derivatives was prepared from pentafluoropyridine in a single continuous flow process by sequential nucleophilic aromatic substitution.

Keywords: Continuous flow reactor; Microreactor; Heterocycles; Perfluoroheteroaromatic

1. Introduction

Continuous flow processes are the methods of choice for the synthesis of many industrial products on both the pilot-plant and manufacturing scales for many reasons, including increased control, lack of downtime, quality control and improved safety. In stark contrast, many research laboratories do not possess equipment that may be used for performing exploratory reactions by a continuous flow technique and chemists have continued to use 'batch' methodology in standard glassware reaction vessels for many years with, of course, great success. Consequently, subsequent development of novel reaction methodology and synthetic strategies that are established in the laboratory are sometimes difficult to scale-up. In many cases, synthetic sequences must be adapted, and sometimes completely changed, when taking a process from laboratory through to pilot-plant and manufacturing scale to accommodate the limitations and different operating requirements of the batch-wise and continuous flow reaction procedures.

The recent developments in microreactor technology [1–8] and the use of such devices as continuous flow reactor systems may help to persuade research chemists to use continuous flow procedures as a laboratory technique for synthesis. However, sometimes very complex fabrication procedures and associated difficult, expensive engineering that is required for the production of many microreactor devices, as well as the lack of general availability of such apparatus to laboratories that do not have access to the necessary engineering skills, has made general adoption of these potentially very useful reaction systems relatively slow.

In an attempt to alleviate the problem of general availability of continuous flow reactors to research scientists, we describe here a design for continuous flow reaction apparatus that may be constructed from glass by standard scientific glass blowing techniques. The design is simple and easily constructed glassware and in this paper we demonstrate the use of the apparatus for various nucleophilic aromatic substitution processes, with the ultimate aim of changing chemists' attitudes towards using continuous flow processes in the laboratory.

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doi:10.1016/j.jfluchem.2007.07.010

2. Results and discussion

We have designed and constructed simple continuous flow reactors using borosilicate glass and common scientific glassblowing techniques and an example is shown in Fig. 1.

Essentially, a T-piece of glass tubing, with 0.5 mm internal diameter, is first constructed and forms the reaction microchannel of the device. The T-piece is then enclosed in a larger outer glass tube, rather like a simple reflux condenser fitted with a very small bore inner tube, and ground glass joints attached to the ends of each piece of tubing. Fluid inlet and outlet ports to the outer glass tube that allows the circulation of cooling or heating fluid around the microchannel tubing completes the design. The reactor channel is approximately 130 mm long in this case, but, of course, this may be varied according to a particular application.

Reagents are introduced simultaneously into the reactor channel by standard syringe pumps that are attached to the glass joint by appropriate Swagelok^{TM} fittings and product mixtures are collected from the outlet. The whole apparatus may be constructed by a scientific glassblower in 10–15 min and no special techniques or fittings are required. Of course, this simple design may be adapted easily to provide multiple inlet ports as appropriate for specific reactions.

As part of a wider project in the development of the chemistry of perfluorinated heterocyclic systems [9] for applications in the synthesis of scaffolds for drug discovery [10,11], multi-functional heterocyclic derivatives [12], macrocycles, heteraryl glycosyl donors and polyfunctional ring-fused systems [13], we have used a continuous flow reactor, such as that illustrated in Fig. 1, as a reaction vessel for a short series of simple chemical transformations involving reactions of pentafluoropyridine **1** and a series of amines **2** to give the corresponding 4-aminopyridine derivatives **3** (Table 1). In all cases, two equivalents of amine are used so that one equivalent is available to neutralise the HF byproduct, maximising yields.

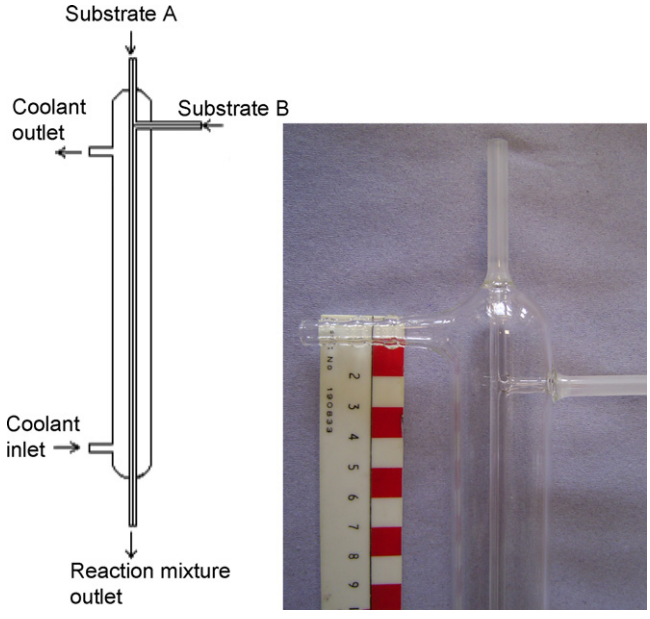
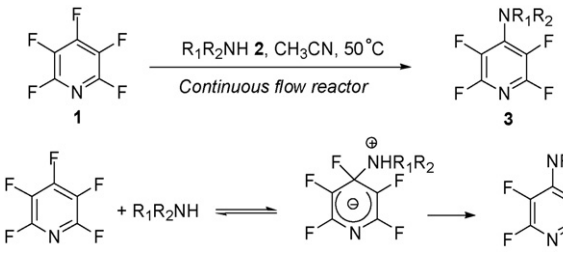
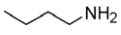
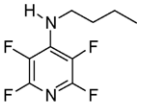
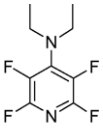
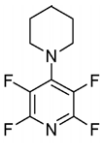
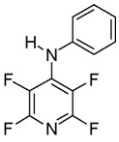


Fig. 1. Continuous flow glassware reactor.

Table 1
Synthesis of 4-dialkylamino tetrafluoropyridine derivatives using a continuous flow glassware reactor

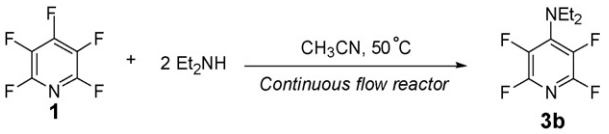


R_1R_2NH	Product	Yield (%)
	 **3a**	72
	 **3b**	59
	 **3c**	68
	 **3d**	54

Each reaction proceeds by nucleophilic aromatic substitution, as shown in Table 1, providing examples of what may be achieved using this simple technology. In each case, reagents were added simultaneously by syringe pump drive into the two inlet ports and, after passage down the glass channel, collected from the outlet into a vessel that contained water or aqueous base solution, thus quenching the reaction immediately after exiting from the flow reactor. Heating fluid was circulated at 50 °C through the outer glass jacket by a cryostat.

One of the key benefits of using continuous flow methodology is the very efficient way in which reactions may be optimised [3] by simple adjustment of flow rates and operating temperature and scale is simply time dependent. Reaction of pentafluoropyridine with diethylamine is only required to be carried out until just 0.5 ml of product mixture has been collected and analysis of the small sample by ^{19}F NMR provides a very rapid indication of conversion and yield. Adjustments of flow rate and the temperature of the circulating liquid around the microreactor channel and subsequent analysis allows the simple optimisation of the reaction within a few

Table 2
Reaction optimisation



T (°C)	Flow rate pentafluoropyridine (ml h^{-1})	Flow rate diethylamine (ml h^{-1})	Conv. (%)
24	4.5	4.5	59
24	4.5	9 (4 equiv.)	86
35	0.5	0.5	67
42	0.25	0.25	69
47	0.25	0.25	78
53	0.25	0.25	100

hours. An example of such a process is shown in Table 2, in which reaction of pentafluoropyridine with diethylamine is optimised to 100% conversion as determined by ^{19}F NMR of the crude product mixture. We find that lowering the flow rate of each component, thus increasing the residence time of the reagents in the microchannels, coupled with heating the reaction to 50 °C gives very clean reaction to a single product in 100% conversion. As the boiling point of acetonitrile is 80 °C, reaction temperatures above 50 °C were not assessed.

Above, we established that, using a continuous flow glassware reactor (130 mm in length), conversion of pentafluoropyridine into the corresponding 4-monosubsituted product is quantitative. The 4-substituted product is, of course, susceptible towards further nucleophilic attack and we were interested in exploring the possibility of performing two nucleophilic substitution reactions in series using pentafluoropyridine as the starting material without the need for work-up after the first step. Consequently, we constructed a continuous flow reactor that possesses three inlet ports, with the third inlet located approximately 130 mm along the reactor channels as shown in Fig. 2.

Solutions of one equivalent of pentafluoropyridine **1** and two equivalents of an amine **2** in dry acetonitrile were simultaneously injected into the reactor via inlets A and B, respectively, at a flow rate of 1 ml h^{-1}. Furthermore, excess sodium alkoxide **4** in the corresponding alcohol was introduced into the reactor via inlet C, half way along the reactor, using the same flow rate (1 ml h^{-1}). Products arising from two sequential nucleophilic substitution reactions were collected from the single flow reactor, isolated and purified. A range of disubstituted trifluoropyridine derivatives **5** were prepared from pentafluoroyridine and these are collated in Table 3.

In summary, simple glassware continuous flow reactors are now available that may be constructed very inexpensively and used for the study of chemical transformations using flow systems by all research chemists. We have demonstrated the use of the glass reactors in processes involving nucleophilic aromatic substitution reactions of pentafluoropyridine, providing an indication of the possibilities offered by this simple technology.

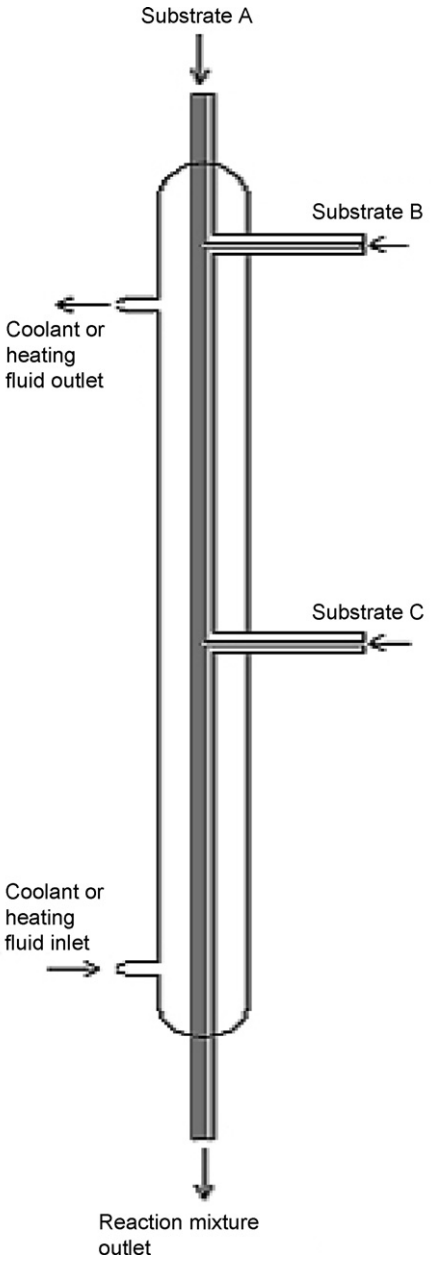


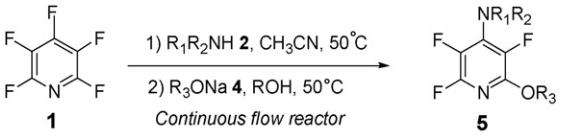
Fig. 2. Continuous flow glassware reactor for sequential chemical transformations.

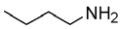
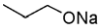
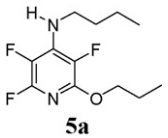
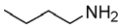
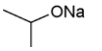
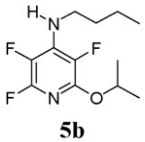
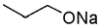
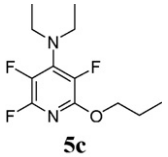
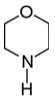
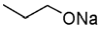
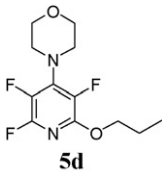
3. Experimental

3.1. General

All starting materials were obtained commercially (Aldrich, Lancaster or Fluorochem) All solvents were dried using literature procedures. NMR spectra were recorded in deuteriochloroform, unless otherwise stated, on a Varian VXR 400S NMR spectrometer operating at 400 MHz (^{1}H NMR), 376 MHz (^{19}F NMR) and 100 MHz (^{13}C NMR) with tetramethylsilane and trichlorofluoromethane as internal standards. Mass spectra were recorded on a Fisons VG-Trio 1000 Spectrometer coupled with a Hewlett-Packard 5890 series II gas chromatograph using a 25 m HP1 (methyl-silicone) column. Elemental analyses were

Table 3
Synthesis of 2-alkoxy-4-dialkylamino pyridine derivatives using two-step continuous flow glassware reactor



R_1R_2NH	R_3ONa	Product	Yield (%)
		 **5a**	76
		 **5b**	75
		 **5c**	78
		 **5d**	86

obtained on an Exeter Analytical CE-440 elemental analyser. Melting points and boiling points were recorded at atmospheric pressure unless otherwise stated and are uncorrected. Column chromatography was carried out on silica gel (Merck no. 109385, particle size 0.040–0.063 mm) and TLC analysis was performed on silica gel TLC plates (Merck).

3.2. One step reactor—general procedure

A solution of the amine **2** in acetonitrile and a solution of pentafluoropyridine **1** in acetonitrile were passed simultaneously at RT through the reactor via inlets 1 and 2, respectively (Fig. 1) at a prescribed flow rate controlled by a syringe pump. The product mixture was collected upon emerging from the reactor in a receiving vessel that contained water (50 ml). The aqueous phase was extracted with dichloromethane (3×20 ml). The organic extracts were dried ($MgSO_4$) and evaporated to give the crude product **3** which could be purified by either column chromatography on silica gel using hexane/dichloromethane as the eluant.

3.2.1. *N*-Butyl-2,3,5,6-tetrafluoropyridin-4-amine **3a**

N-Butyl amine (0.52 g, 7.5 mmol) in acetonitrile (5 ml, 0.5 ml h^{-1}) and pentafluoropyridine (0.63 g, 3.75 mmol) in acetonitrile (5 ml, 0.5 ml h^{-1}) gave *N-butyl-2,3,5,6-tetrafluoropyridin-4-amine* **3a** (0.60g, 72%) as a colourless oil; (found C, 48.4; H, 4.4; N, 12.4. $C_9H_{10}F_4N_2$ requires C, 48.6; H, 4.5; N, 12.6%); δ_F −95.4 (2F, m, F-2), −165.2 (m, F-3); δ_H 0.94 (3H, t, $^3J_{HH}$ 7.2, CH_3), 1.39 (2H, sextet, $^3J_{HH}$ 6.5, CH_2CH_3), 1.62 (2H, m, $^3J_{HH}$ 7.6, $NHCH_2CH_2$), 3.54 (2H, t, $^3J_{HH}$ 6.6, $NHCH_2$), 4.65 (2H, s, NH); δ_C 13.7 (s, CH_3), 19.8 (s, CH_2CH_3), 32.9 (s, $NHCH_2CH_2$), 44.8 (s, $NHCH_2$), 132.3 (dm, $^1J_{CF}$ 246.9, C-3); 138.0 (m, C-4), 144.5 (dm, $^1J_{CF}$ 236.2, C-2); *m/z* (EI^+) 222 ($[M]^+$, 20%), 179 (100).

3.2.2. *N,N*-Diethyl-2,3,5,6-tetrafluoropyridin-4-amine **3b**

N,N-Diethylamine (1.09 g, 15 mmol) in acetonitrile (5 ml, 4.5 ml h^{-1}) and pentafluoropyridine (1.26 g, 7.5 mmol) in acetonitrile (5 ml, 4.5 ml h^{-1}) gave *N,N-diethyl-2,3,5,6-tetrafluoropyridin-4-amine* **3b** (1.79 g, 59%) as a yellow oil; (found C, 48.6; H, 4.3; N, 12.3. $C_{10}H_{10}F_4N_2$ requires C, 48.6; H, 4.5; N, 12.6%); δ_F −96.6 (2F, m, F-2), −157.3 (2F, m, F-3); δ_H 1.17 (3H, t, $^3J_{HH}$ 6.8, CH_3), 3.44 (2H, q, $^3J_{HH}$ 7.1, CH_2); δ_c 13.9 (s, CH_3), 46.8 (s, CH_2), 134.0 (dm, $^1J_{CF}$ 249.0, C-3), 139.6 (dm, $^2J_{CF}$ 12.4, C-4), 145.7 (dm, $^1J_{CF}$ 239.3, C-2); *m/z* (EI^+) 222 ($[M]^+$, 80%), 207 (85), 179 (100).

3.2.3. 2,3,5,6-Tetrafluoro-4-(piperidin-1-yl)-pyridine **3c**

Piperidine (0.63 g, 7.5 mmol) in acetonitrile (5 ml, 0.5 ml h^{-1}) and pentafluoropyridine (0.63 g, 3.75 mmol) in acetonitrile (5 ml, 0.5 ml h^{-1}) gave *2,3,5,6-tetrafluoro-4-(piperidin-1-yl)-pyridine* **3c** (0.63 g, 68%) as a yellow oil; (found C, 51.2; H, 4.0; N, 11.6. $C_{10}H_{10}F_4N_2$ requires C, 51.3; H, 4.3; N, 12.0%); δ_F −94.7 (1F, m, F-2), −155.5 (1F, m, F-3); δ_H 1.6–1.9 (6H, m, CH_2), 3.5 (4H, m, N-CH_2); δ_C 24.1 (s, C-4′), 26.5 (s, C-3′), 51.6 (s, –NCH_2), 134.2 (dm, $^1J_{CF}$ 253.6, C-3), 140.9 (m, C-4), 145.4 (dm, $^1J_{CF}$ 240.0, C-2); *m/z* (EI^+) 246 ($[M]^+$, 40%), 233 (100), 177 (75).

3.2.4. 2,3,5,6-Tetrafluoro-*N*-phenylpyridin-4-amine **3d**

Aniline (0.75 g, 7.5 mmol) in acetonitile (5 ml, 0.5 ml h^{-1}) and pentafluoropyridine (0.63 g, 3.75 mmol) in acetonitrile (5 ml, 0.5 ml h^{-1}) gave *2,3,5,6-tetrafluoro-N-phenylpyridin-4-amine* **3d** (0.49 g, 54%) as an off-white solid; (found C, 54.4; H, 2.4; N, 11.8. $C_{11}H_6F_4N_2$ requires C, 54.6; H, 2.5; N, 11.6%); δ_F −92.7 (1F, m, F-2), −155.9 (1F, m, F-3); δ_H 6.32 (1H, m, N-H), 7.0–7.4 (5H, m, ArH); δ_C 121.9 (s, C-2′), 125.6 (s, C-4′), 129.1 (s, C-3′), 132.2 (dm, $^1J_{CF}$ 252.2, C-3), 138.1 (s, C-1′), 140.2 (m, C-4), 144.4 (dm, $^1J_{CF}$ 223.8, C-2); *m/z* (EI^+) 242 ($[M]^+$, 73%), 222 (90), 51 (100).

3.3. Sequential nucleophilic substitution reactions—general procedure

These reactions were performed using the three-inlet reactor (Fig. 2). A solution of the amine **2** in acetonitrile, a solution of pentafluoropyridine **1** in acetonitrile and a solution of the alkoxide **4** in the corresponding alcohol were passed simultaneously through the reactor via inlets A, B and C, respectively (Fig. 2) at a prescribed flow rate controlled by a syringe pump. Heating fluid was circulated by a cryostat at 50 °C through the apparatus. The product mixture was collected

in a receiving vessel that contained water (50 ml). The aqueous phase was extracted with dichloromethane (3 × 20 ml). The organic extracts were dried ($MgSO_4$) and evaporated to give the crude product **5** which could be purified by either column chromatography on silica gel using hexane/dichloromethane as the eluant.

3.3.1. *N*-Butyl-2,3,5-trifluoro-6-propoxypyridin-4-amine ***5a***

n-Butylamine (0.58 g, 8 mmol, 0.5 ml h^{-1}) in acetonitrile (5 ml), pentafluoropyridine (0.59 g, 3.5 mmol, 0.5 ml h^{-1}) in acetonitrile (5 ml) and sodium *n*-propoxide (4 mmol, 0.5 ml h^{-1}) in propanol (10 ml) gave *N-butyl-2,3,5-trifluoro-6-propoxypyridin-4-amine* **5a** (0.70 g, 76%) as a yellow oil; (found C, 54.7; H, 6.8; N, 10.9. $C_{12}H_{17}N_2F_3O$ requires C, 54.9; H, 6.5; N, 10.7%); δ_F −99.3 (1F, m, F-2), −166.0 (1F, m, F-3), −171.5 (1F, m, F-5); δ_H 0.87 (3H, t, $^3J_{HH}$ 7.7, CH_3), 0.94 (3H, t, $^3J_{HH}$ 8.4, CH_3), 1.32 (2H, m, $NCH_2CH_2CH_2$), 1.51 (2H, m, NCH_2CH_2), 1.73 (2H, m, OCH_2CH_2), 3.52 (2H, m, NCH_2), 4.13 (2H, t, $^3J_{HH}$ 6.5, OCH_2), 4.32 (1H, br s, NH); δ_C 10.4 (s, $OCH_2CH_2CH_3$) 13.8 (s, $NCH_2CH_2CH_2CH_3$), 20.1 (s, $NCH_2CH_2CH_2CH_3$), 22.4 (s, $OCH_2CH_2CH_3$), 33.1 (s, $NCH_2CH_2CH_2CH_3$), 44.7 (s, $NCH_2CH_2CH_2CH_3$), 68.7 (s, $OCH_2CH_2CH_3$), 129.3 (dd, $^1J_{CF}$ 242.5, $^2J_{CF}$ 32.1, C-3), 132.2 (dd, $^1J_{CF}$ 243.5, $^3J_{CF}$ 6.2, C-5), 136.3 (m, C-4), 145.2 (dd, $^1J_{CF}$ 228.3, $^2J_{CF}$ 13.9, C-2), 145.9 (dd, $^2J_{CF}$ 16.1, $^4J_{CF}$ 12.3, C-6); *m/z* (EI^+) 262 ($[M]^+$, 44%), 219 (82), 177 (100).

3.3.2. *N*-Butyl-2,3,5-trifluoro-6-isopropoxypyridin-4-amine ***5b***

n-Butylamine (0.58 g, 8 mmol, 0.5 ml h^{-1}) in acetonitrile (5 ml), pentafluoropyridine (0.59 g, 3.5 mmol, 0.5 ml h^{-1}) in acetonitrile (5 ml) and sodium *iso*-propoxide (4 mmol, 0.5 ml h^{-1}) in *iso*-propanol (5 ml) gave *N-butyl-2,3,5-trifluoro-6-isopropoxypyridin-4-amine* **5b** (0.69 g, 75%) as a yellow oil; (found C, 54.4; H, 6. 8; N, 10.9. $C_{12}H_{17}N_2F_3O$ requires C, 54.9; H, 6.5; N, 10.7%); δ_F −97.1 (1F, m, F-2), −165.0 (1F, m, F-3), −171.4 (1F, m, F-5); δ_H 0.94 (3H, t, $^3J_{HH}$ 7.3, CH_2CH_3), 1.32 (6H, d, $^3J_{HH}$ 7.6, $CHCH_3$), 1.35 (2H, m, $NCH_2CH_2CH_2$), 1.59 (2H, m, NCH_2CH_2), 3.45 (2H, m, NCH_2), 4.29 (1H, br s, NH), 5.13 (1H, sept, $^3J_{HH}$ 5.8, OCH); δ_C 14.1 (s, CH_2CH_3), 20.1 (s, CH_2CH_3), 22.1 (s, $CHCH_3$), 33.1 (s, NCH_2CH_2), 44.8 (s, NCH_2), 69.8 (s, OCH), 128.3 (dd, $^1J_{CF}$ 244.5, $^2J_{CF}$ 31.4, C-3), 133.5 (dd, $^1J_{CF}$ 241.2, $^3J_{CF}$ 5.6, C-5), 136.3 (m, C-4); 143.5 (dd, $^1J_{CF}$ 218.8, $^2J_{CF}$ 13.7, C-2), 147.8 (dd, $^2J_{CF}$ 14.6, $^3J_{CF}$ 13.1, C-2); *m/z* (EI^+) 262 ($[M]^+$, 40%), 220 (43), 177 (100).

3.3.3. *N,N*-Diethyl-2,3,5-trifluoro-6-propoxypyridin-4-amine ***5c***

N,N-Diethylamine (0.58 g, 8 mmol, 0.5 ml h^{-1}) in acetonitrile (5 ml), pentafluoropyridine (0.59 g, 3.5 mmol, 0.5 ml h^{-1}) in acetonitrile (5 ml) and sodium *n*-propoxide (4 mmol, 0.5 ml h^{-1}) in propanol (10 ml) gave *N,N-diethyl-2,3,5-trifluoro-6-propoxypyridin-4-amine* **5c** (0.71 g, 78%) as an orange oil; (found C, 54.8; H, 6.6; N, 10.6. $C_{12}H_{17}N_2F_3O$ requires C, 54.9; H, 6.5; N, 10.7%); δ_F −97.2 (1F, m, F-2), −155.4 (1F, m, F-3), 162.8 (1F, m, F-5); δ_H 0.98 (3H, t, $^3J_{HH}$ 7.4, CH_2CH_3), 1.14 (6H, t, $^3J_{HH}$ 6.7, NCH_2CH_3), 1.81 (2H, sextet, $^3J_{HH}$ 7.2, CH_2CH_3), 3.35 (4H, q, $^3J_{HH}$ 6.9, NCH_2), 4.18 (2H, t, $^3J_{HH}$ 6.8, OCH_2); δ_C 10.5 (s, $OCH_2CH_2CH_3$), 13.8 (s, NCH_2CH_3), 22.5 (s, $OCH_3CH_2CH_3$), 46.7 (s, NCH_2), 68.6 (s, OCH_2), 133.3 (dd, $^1J_{CF}$ 245.7, $^2J_{CF}$ 28.5, C-3), 136.1 (dd, $^1J_{CF}$ 248.0, $^3J_{CF}$ 4.6, C-5), 137.9 (m, C-4), 146.1 (dd, $^1J_{CF}$ 232.9, $^2J_{CF}$ 13.3, C-2), 146.4 (dd, $^2J_{CF}$ 15.9, $^3J_{CF}$ 13.4, C-6); *m/z* (EI^+) 262 ($[M]^+$, 75%), 247 (97), 205 (98), 176.7 (100).

3.3.4. 4-(2,3,5-Trifluoro-6-propoxypyridin-4-yl) morpholine ***5d***

Morpholine (0.70 g, 8 mmol, 1 ml h^{-1}) in acetonitrile (5 ml), pentafluoropyridine (0.59 g, 3.5 mmol, 1 ml h^{-1}) in acetonitrile (5 ml) and sodium *n*-propoxide (4 mmol, 1 ml h^{-1}) in propanol (5 ml) gave *4-(2,3,5-trifluoro-6-propoxypyridin-4-yl) morpholine* **5d** (0.83 g, 86%) as a colourless liquid: (found C, 52.0; H, 5.4; N, 9.9. $C_{12}H_{15}F_3N_2O_2$ requires C, 52.2; H, 5.4; N, 10.1%); δ_F −96.0 (1F, m, F-2), −154.6 (1F, m, F-3), −161.9 (1F, m, F-5); δ_H 0.98 (3H, t, $^3J_{HH}$ 6.2, CH_3), 1.76 (2H, m, CH_2CH_3), 3.37 (4H, t, $^3J_{HH}$ 4.8, CH_2N), 3.69 (4H, m, CH_2-O), 4.19 (2H, t, $^3J_{HH}$ 7.0, CH_2O); δ_C 10.6 (s, CH_3), 22.4 (s, CH_2CH_3), 50.8 (s, CH_2N), 67.4 (s, CH_2O), 68.7 (s, OCH_2), 132.2 (dd, $^1J_{CF}$ 248.5, $^2J_{CF}$ 30.9, C-3), 136.8 (dd, $^1J_{CF}$ 245.4, $^3J_{CF}$ 6.1, C-5), 138.3 (m, C-4), 145.4 (dd, $^1J_{CF}$ 235.3, $^2J_{CF}$ 15.3, C-2), 146.6 (dd, $^2J_{CF}$ 15.3, $^3J_{CF}$ 2.2, C-6); *m/z* (EI^+) 276 ($[M]^+$, 19%), 234 (72), 176 (100).

Acknowledgments

We thank the EPSRC Crystal Faraday Partnership for funding and Mr. Peter Coyne for scientific glassblowing.

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