Journal of Fluorine Chemistry, *30* (1985) 211–226

Received: April 9, 1985; accepted: July 20, 1985

STUDIES IN AZIDE CHEMISTRY. PART 13 [1]. INTERMOLECULAR INSERTION OF AZIDE-DERIVED POLYFLUORINATED ARYL- AND HETEROARYL-NITRENES INTO RING C-H BONDS OF 1,3,5-TRIMETHYL- AND 1,3,5-TRIMETHOXY-BENZENE

RONALD E. BANKS* and ISMAIL M. MADANY

Chemistry Department, The University of Manchester
Institute of Science and Technology,
Manchester M60 1QD (U.K)

SUMMARY

Thermolysis of perfluoroazidobenzene, perfluoro-4-azidotoluene, perfluoro-4-azidopyridine, 4-azido-3-chlorotrifluoropyridine, and 4-azido-3,5-dichlorodifluoropyridine (Ar_FN_3) in the presence of a large excess (ca. 10 molar) of 1,3,5-trimethyl- or 1,3,5-trimethoxy-benzene (ArH) gave the diarylamines expected from nitrene 'insertions' at nuclear C-H bonds ($Ar_FN_3 + ArH \rightarrow Ar_FNHAr + N_2$); product yields in the cases of the perfluorinated azides are the highest ever recorded for this type of reaction. By contrast, no recognisable products were obtained when either perfluoro-(2-azido-4-isopropylpyridine) or 2-azido-4-chlorotrifluoropyridine were decomposed thermally in 1,3,5-trimethylbenzene.

INTRODUCTION

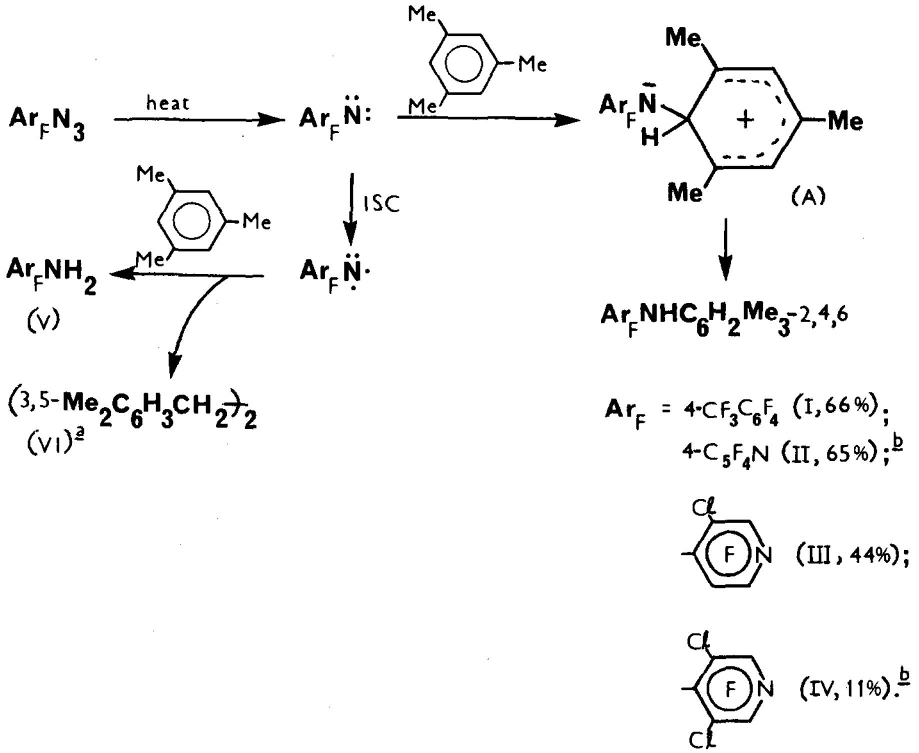
Singlet pentafluorophenylnitrene (from thermolysis of perfluoroazidobenzene [2,3] or deoxygenation of pentafluoronitrosobenzene [3]) and tetrafluoro-4-pyridylnitrene (from thermolysis of perfluoro-4-azidopyridine [4]) appear to be unique [5,6] amongst arylnitrenes in that they attack benzene to yield products of notional insertion into a C-H bond: $Ar_F\ddot{N}: + Ph\text{-}H \rightarrow Ar_FNHPh$ ($Ar_F = C_6F_5$, ca. 2% yield [2,3]; Ar_F = 4-C_5F_4N, 13% [4]); indeed, the yield of the diarylamine in the latter case has prompted one reviewer [5] to remark that tetrafluoro-4-pyridylnitrene is 'perhaps the most electrophilic arylnitrene yet generated'. Published information on insertion of polyfluoroarylnitrenes into aromatic C-H bonds belonging to traps with greater π-nucleophilicities than benzene is restricted to pentafluorophenylnitrene generated from pentafluoronitrosobenzene and triethyl phosphite [3]; 1,3,5-trimethylbenzene [→ 2,4,6-$Me_3C_6H_2NHC_6F_5$ (32%)] was the most successful of the traps investigated, being slightly better than 1,3-dimethylbenzene [→ 2,6- and 2,4-$Me_2C_6H_3NHC_6F_5$ (30.5%)].

RESULTS AND DISCUSSION

Zuberi [7] carried out the first reaction between 1,3,5-trimethylbenzene and a perfluorinated azidoarene when he was reinvestigating some of Bailey's work [8] on the thermal decomposition of perfluoro-2-azido-1-azacyclohexene;* he found that the known (see above) diarylamine 2,4,6-$Me_3C_6H_2NHC_6F_5$ is produced in ca. 80% yield when a solution of perfluoroazidobenzene in 1,3,5-trimethylbenzene (molar ratio $C_6F_5N_3:C_6H_3Me_3$ = ca. 1:12) was heated at 150 °C for 4 hours under nitrogen. Similar experiments now conducted with perfluoro-4-azidotoluene, perfluoro-4-azidopyridine, 4-azido-3-chlorotrifluoropyridine, and 4-azido-3,5-dichlorodifluoropyridine [azide:trap ratio = ca. 1:10 molar in each case] have provided the same type of circumstantial evidence for the generation of a singlet polyfluoroarylnitrene (see Scheme 1).

---

* Neither investigator encountered evidence for the generation of perfluoro-1-azacyclohexen-2-ylnitrene; the azide appears to undergo concerted loss of nitrogen and ring-expansion to yield the cyclic carbodi-imide $\overline{CF_2CF_2CF_2CF_2N{=}C{=}N}$, which then attacks 1,3,5-trimethylbenzene to give the 1:1 adduct $\overline{CF_2CF_2CF_2CF_2N{=}C(C_6H_2Me_3\text{-}2,4,6)N}H$.



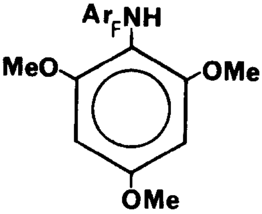
SCHEME 1

[a] To assist with the search for this diarylethane in crude reaction products, an authentic sample was procured by heating 1,3,5-trimethylbenzene with aqueous potassium persulphate [cf. ref. 20].

[b] Products (II)(58% yield) and(IV)(19%) were also prepared by heating pentafluoropyridine and 3,5-dichlorotrifluoropyridine, respectively, with sodium 2,4,6-trimethylphenylamide in tetrahydrofuran; the latter reaction was not regiospecific, displacement of fluorine from the 2-position also occurring to provide 3,5-dichloro-4,6-difluoro-2-(2,4,6-trimethylphenylamino)pyridine (29% yield).

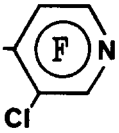
The yields quoted in the Scheme refer to purified products and include the highest (66% for I) yet reported for an aryl C-H insertion product derived from 1,3,5-trimethylbenzene and a thermally-generated arylnitrene [9,10]. That these yield values represent an underestimate of the efficiency of the trimethylarene as a trap for the putative singlet nitrenes involved here was revealed by carrying out NMR and HPLC analyses of crude reaction products derived from perfluoro-4-azidotoluene and perfluoro-4-azidopyridine; this revealed that the corresponding insertion products (I and II) had been formed in 88 and 81% yield, respectively, and also failed to provide evidence that the singlet nitrenes had enjoyed opportunities to undergo intersystem crossing to triplet species. By contrast, products (V + VI) indicative [5,6,11] of the incursion of triplet nitrenes *were* present in the crude products from reactions involving 4-azido-3-chlorotrifluoropyridine and 4-azido-3,5-dichlorodifluoropyridine; not unexpectedly, this was reflected in the decreased yields of isolated aryl C-H insertion products (III and IV, 44 and 11% respectively) compared with the experiment involving perfluoro-4-azidopyridine (II, 65%). Although work-up difficulties increased when 4-azidotetrafluoropyridine was replaced by its chloro-analogues owing to the greater complexities of the products and increases in 'tar' formation, this is judged not to have had an inordinate effect on the yields of isolated diarylamines (III and IV). Thus, the trappability by 1,3,5-trimethylbenzene of the 4-pyridylnitrenes (fully formed or incipient) clearly decreases in the order $NC_5F_4\ddot{N}: > NC_5F_3Cl\ddot{N}: > NC_5F_2Cl_2\ddot{N}:$, which is the decreasing order both of access to the reactive site and of the electrophilicity of that site based on *ortho* halogen electronegativities and any contribution by chlorine lone-pair electrons to intramolecular solvation of the nitrene [12].

1,3,5-Trimethoxybenzene, known [9] to be more efficient than 1,3,5-trimethylbenzene as a trap for singlet 4,6-dimethyl-2-pyrimidinylnitrene generated thermally from the corresponding azide (yields of aryl C-H insertion products 50 and



Ar_F = C_6F_5 (VII); 4-$CF_3C_6F_4$ (VIII);

(IX);

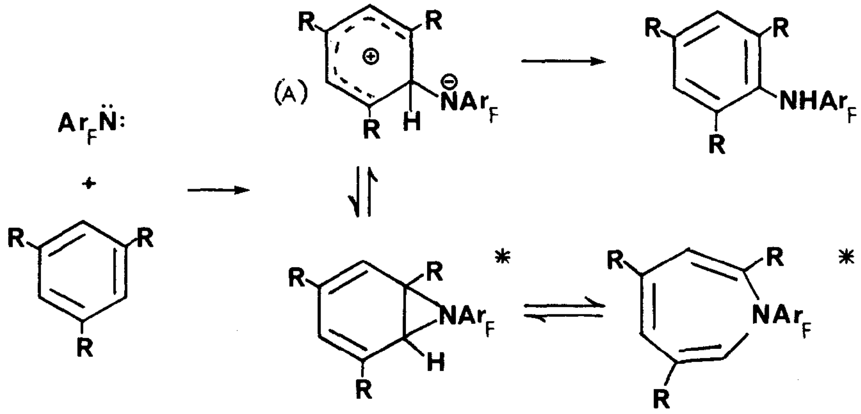


(X);

(XI).

34%, respectively), proved to be an excellent trap for putative singlet pentafluorophenylnitrene and its p-tolyl analogue. Thus, thermolysis of their azido-progenitors in the presence of a 10-molar excess of the trimethoxyarene at 170 °C under nitrogen gave (after work-up) C-H insertion products (VII) and (VIII) in 92 and 82% yield respectively. Similar experiments with the azidopyridines gave darker-coloured, more complex products from which the corresponding aryl C-H insertion products (IX), (X) and (XI) were isolated in 69.5, 53, and 45% yield, respectively. The 'super-trap' status of 1,3,5-trimethoxybenzene was confirmed by repeating the original experiment with perfluoro-4-azidotoluene using trap: azide ratios of 5:1 and then equimolar ; the yields of the insertion product (VIII) fell to only 76 and 38% (isolated material), respectively. No attempts were made to determine the fate(s) of perfluoro-4-azidotoluene not converted to the diarylamine (VIII) in these last experiments; with trap:azide (Ar_FN_3) molar ratios of 10:1, crude products were shown by HPLC analysis to contain primary polyfluoroarylamines (Ar_FNH_2) in every case except that of perfluoro-4-azidotoluene.

As with the azide thermolyses conducted in 1,3,5-trimethylbenzene, no N-arylazepines indicative of benzaziridine intermediates (see Scheme 2) were isolated from any of the crude products derived from 1,3,5-trimethoxybenzene {*cf.* [3] the formation of the azepinone $C_6F_5\overline{NCH{=}CHCH{=}CHCH_2C}{=}O$ (15.9% yield) and 2- and 4-$MeOC_6H_4NHC_6F_5$ (2.7 and 4.3%, respectively) *via* reaction of C_6F_5NO with $(EtO)_3P$ in methoxybenzene}.



R = Me or OMe

* Formation not detected.

SCHEME 2

Clearly, the electronic natures of the ring substituents in the nitrenes and their traps greatly favour formation of dipolar species (A, Schemes 1 and 2) of the type believed [3,9] to be involved in diarylamine formation from arylnitrenes and aromatic substrates. Note, however, that comparison of 1,3,5-trimethylbenzene with its methoxy-analogue as a trap for the highly electrophilic polyhalogenoarylnitrenes studied here cannot be restricted solely to cognizance of the relative abilities of a methyl and a methoxy group to encourage development of a positive charge on adjacent carbon: consideration must also be given to the stabilisation of developing singlet nitrenes *via* co-ordination involving oxygen lone-pair electrons in 1,3,5-trimethoxybenzene, a phenomenon which will decelerate singlet→triplet crossing [12,13], presumably retard ring-expansion [14] excursions, and assist in 'docking' of complexed nitrenes at adjacent =CH- sites. The influence of steric factors, particularly where the last type of event is concerned, is revealed by the progressive decrease in yield (69.5 → 53 → 45%) of 'insertion' product with stepwise replacement of the 3,5-fluorines in perfluoro-4-azidotetrafluoropyridine by chlorine.

In stark contrast to the work with mesitylene described above, attempts to obtain circumstantial evidence for the generation of nitrenes via thermal decomposition of two polyfluorinated pyridines carrying an azido function alpha to ring nitrogen, namely perfluoro-(2-azido-4-isopropylpyridine) and 2-azido-4-chlorotrifluoropyridine, proved fruitless: only black materials from which no identifiable materials could be isolated were produced. This is consistent with previous failures to intercept nitrenes from fluorinated pyridines {including perfluoro-(2-azido-4-isopropylpyridine) [15]} and pyrimidines [16] containing the $N{=}CN_3$ grouping. 2-Azido-4-chlorotrifluoropyridine, a new compound, was prepared by treating 4-chlorotetrafluoropyridine with sodium azide; 2,6-diazido-4-chlorodifluoropyridine was formed as a by-product.

EXPERIMENTAL

Spectroscopic Analysis

NMR spectra were obtained with a Perkin-Elmer R32 instrument operating at 84.6 (^{19}F; ext. CF_3CO_2H ref.) or 90 (^1H; ext. Me_4Si ref.) MHz; absorptions to low field of reference signals are assigned positive chemical shift values. Mass spectra were recorded on an AEI MS902 or Kratos MS45 spectrometer (electron beam energies 70 eV); data were processed by a Digital PDP 8/1 Interface System, and correct isotope peak intensities were found throughout for molecular ions and related fragments in the cases of chloro-compounds.

Synthesis of Azides

(a) Known azides

Perfluoroazidobenzene [17], perfluoro-4-azidotoluene [2], perfluoro-(2-azido-4-isopropylpyridine)[15] and the azidohalogenopyridines [4] were prepared as described previously.

(b) 2-Azido-4-chlorotrifluoropyridine

A yellow product obtained by heating a mixture of 4-chlorotetrafluoropyridine [18] (15.0 g, 81 mmol), sodium azide (5.2 g, 80 mmol), and acetonitrile (200 cm^3) at 70 °C for 12 days was poured into water (400 cm^3); the aqueous material was extracted with diethyl ether (3 x 150 cm^3), and the extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Low-pressure distillation of the residual oil in a semi-micro one-piece Vigreux unit provided 4-chlorotetrafluoropyridine (7.0 g, 37.8 mmol, 47% recovery), a *ca*. 1:6.5 molar mixture (by ^{19}F NMR analysis) of 4-chlorotetrafluoropyridine and 2-azido-4-chlorotrifluoropyridine (*ca*. 4 g), a pale yellow liquid (3.0 g), b.p. 27-28 °C at *ca*. 4.5 mmHg, that was shown by NMR analysis to be 95% pure (the contaminant was $4\text{-}ClC_5F_4N$) 2-azido-4-chloro-2,3,6-trifluoropyridine (nc), $\lambda_{max.}$ (film) 4.69 (N_3 asym. str.) μm, δ_F (neat) -10.5 (dd; 6-F, $J_{3,6}$ 27, $J_{5,6}$ 21 Hz), -57.7 (dd; 3-F, $J_{3,5}$ 2.5 Hz), -68.0 (dd; 5-F) p.p.m., and 2,6-diazido-4-chloro-3,5-difluoropyridine (nc)(1.0 g, 3.7 mmol, 5%) $\lambda_{max.}$ (film) 4.59 (sh.), 4.67 (N_3 asym. str.) μm, δ_F -59.2 (s; 3-,5-F) p.p.m., a yellow oil, b.p. 46 °C at *ca*. 4.5 mmHg, which solidified when stored at 6 °C. The yield of 2-azido-4-chloro-3,5,6-trifluoropyridine, based on 4-chlorotetrafluoropyridine converted, was estimated to be 36%.

Thermolysis Experiments

(a) General procedure

A solution of the fluorinated azide under investigation in one of the aromatic substrates was heated (oil bath) behind a stout blast screen at a temperature in the range 160-180 °C for ca. 5 hours under an atmosphere of nitrogen (i.e. until complete decomposition of the azide was assured, as revealed by i.r. analysis of samples of reaction mixtures) in a Pyrex flask equipped with a water-cooled condenser, a gas inlet tube, and a magnetic stirrer. The dark-coloured reaction product was distilled at reduced pressure to remove as much of the excess of aromatic substrate as possible, and the residue (usually dark brown in colour) was subjected to NMR (^{19}F and ^{1}H) and (except in the $C_6F_5N_3$-$C_6H_3Me_3$ reaction) HPLC analysis; compounds present in the residue were then isolated by standard techniques and their purities checked by HPLC. When 1,3,5-trimethoxybenzene (m.p. 54-55 °C) was involved as co-reactant, it was not melted prior to addition of an azide.

(b) Results

(i) Perfluoro-4-azidopyridine (1.0 g, 5.2 mmol) and 1,3,5-trimethylbenzene (6.3 g, 52.5 mmol) at 170 °C for 5 h gave [via sublimation (at 90-110 °C and ca. 4 mmHg) of the residue followed by recrystallization of the sublimate from aqueous ethanol] pale-yellow needles of 2,3,5,6-tetrafluoro-4-(2,4,6-trimethylphenylamino)pyridine (nc)(0.96 g, 3.4 mmol, 65%) [Found: C, 58.9; H, 4.5; F, 26.5; N, 9.9%; M (mass spec.), 284 (base peak, M^{+}). $C_{14}H_{12}F_4N_2$ requires C, 59.15; H, 4.2; F, 26.8; N, 9.9%; M, 284], m.p. 108-109 °C, $\lambda_{max.}$ (mull) 2.92 µm (N-H str.), δ_F ($CDCl_3$ soln.) -14.1 (m; 2-, 6-F) and -85.7 (m; 3-,5-F) p.p.m., δ_H (same soln) 2.15 (s; 2-,6-CH_3), 2.23 (s; 4-CH_3), 5.7 (br.s; NH), and 6.82 (s; 3-,5-H) p.p.m.

(ii) 4-Azido-3-chlorotrifluoropyridine (6.0 g, 29 mmol) and 1,3,5-trimethylbenzene (36.0 g, 300 mmol) at 160 °C for 4 h gave (via fractional sublimation in vacuo of the black tarry residue left after removal of 1,3,5-trimethylbenzene) 3-chloro-2,5,6-trifluoro-4-(2,4,6-trimethylphenylamino)pyridine (nc) [3.8 g (after recrystallization from aqueous ethanol),13 mmol, 44%] [Found: C, 55.8; H, 3.8; F, 19.2; N, 9.1%; M (mass spec.) 300.5. $C_{14}H_{12}ClF_3N_2$ requires C, 55.9; H, 4.0; F, 19.0; N, 9.3%; M, 300.5], as white needles, m.p. 90-91 °C,

$\lambda_{max.}$ (mull) 2.97 (N-H str.) μm, δ_F ($CDCl_3$ soln.) 2.5 (2-F; dd), -13.1 (6-F; dd), and -87.5 (5-F; td) p.p.m. ($J_{2,5} \approx J_{2,6} \approx 23$, $J_{5,6}$ 13, $J_{5,NH}$ 3 Hz), δ_H (same soln.) 2.20 (s; 2-, 6-CH_3), 2.30 (s; 4-CH_3), 6.25 (br.s; NH), and 6.92 (s; 3-, 5-H) p.p.m., and 4-amino-3-chloro-2,5,6-trifluoropyridine (0.5 g, 3 mmol, 10%), m.p. 117-118 °C (lit. [19], 117-118 °C) with a correct IR spectrum. The crude reaction product was shown to contain 1,2-bis(3,5-dimethylphenyl)ethane by HPLC analysis [an authentic sample of this hydrocarbon was synthesised from 1,3,5-trimethylbenzene (see later)]; NMR analysis of the crude reaction product also revealed the presence of this diarylethane.

(iii) *4-Azido-3,5-dichlorodifluoropyridine* (10.0 g, 44 mmol) and *1,3,5-trimethylbenzene* (48.0 g, 400 mmol) at 160 °C for 6 h gave [work-up as in experiment (ii)] 3,5-dichloro-2,6-difluoro- 4-(2,4,6-trimethylphenylamino)pyridine (nc) (1.5 g, 4.7 mmol, 11%), m.p. 90-92 °C, identical spectroscopically (IR and NMR) and by HPLC with a sample prepared as described below, and 4-amino-3,5-dichloro-2,6-difluoropyridine (0.9 g, 4.5 mmol, 10%) identified by comparison of its HPLC retention characteristics with those of an authentic sample. HPLC and NMR analysis of the crude reaction product revealed the presence of 1,2-bis(3,5-dimethylphenyl)ethane.

(iv) (WITH SHARIQUE S. ZUBERI) *Perfluoroazidobenzene* (2.5 g, 12 mmol) and *1,3,5-trimethylbenzene* (20 cm^3) at 150 °C for 4 h gave a dark-brown crude product (3 g) which was shown by ^{19}F NMR spectroscopy to be essentially 1,2,3,4,5-pentafluoro-6-(2,4,6-trimethylphenylamino)benzene (estimated crude yield 80%), a sample of which was purified by recrystallization (aqueous ethanol) to provide pale-brown needles with m.p. 125 °C (nc) {[Found: C, 59.9; H, 4.0; F, 31.9; N, 4.6%; M (mass spec.), 301 (base peak, $M^{+\cdot}$). Calc. for $C_{15}H_{12}F_5N$:C, 59.8; H, 4.0; F, 31.6; N, 4.65%; M, 301]; $\lambda_{max.}$ (mull) 2.97 (N-H str.) μm; δ_F (soln. in $CDCl_3$) -82.6 (m;1-,5-F), -86.0 (m;2-,4-F), and -94.1 (tt, $J_{3,2(4)}$ 23, $J_{3,1(5)}$ 6.5 Hz; 3-F) p.p.m. (rel. int. 2:2:1); δ_H (same soln.) 2.17 (s; 2-,6-CH_3), 2.26 (s; 4-CH_3), 4.9 (br.s; NH), and 6.89 (s; 3-,5-H) p.p.m.}.

(v) **Perfluoro-4-azidotoluene** (1.0 g, 3.9 mmol) and **1,3,5-trimethylbenzene** (4.6 g, 38.3 mmol) at 170 °C for 5 h gave [after sublimation (at 80-100 °C and *ca.* 4 mmHg) of the residue followed by recrystallization of the sublimate from aqueous ethanol] pale-yellow needles of 1,2,4,5-tetrafluoro-3-trifluoromethyl-6-(2,4,6-trimethylphenylamino)benzene (nc) (0.9 g, 2.6 mmol, 66%)[Found: C, 54.7; H, 3.1; F, 37.8; N, 3.8%; M (mass spec.), 351 (base peak, $M^{+\cdot}$). $C_{16}H_{12}F_7N$ requires C, 54.7; H, 3.4; F, 37.9; N, 4.0%; M, 351], m.p. 90-91 °C, $\lambda_{max.}$ (mull) 2.90 (N-H str.) µm, δ_F ($CDCl_3$ soln.) + 23.5 (t, J 21 Hz; CF_3), -65.2 (m; 2-,4-F), and -83.0 (m; 1-,5-F) p.p.m., δ_H (same soln.) 2.29 (s; 2-,6-CH_3), 2.37 (s; 4-CH_3),5.45 (br.s; NH), and 6.97 (s; 3-,5-H) p.p.m.

(vi) **Perfluoro-4-azidopyridine** (1.5 g, 7.8 mmol) and **1,3,5-trimethoxybenzene** (13.1 g, 78 mmol) at 170 °C for 5 h gave (*via* sublimation of the black residue and recrystallization of the sublimate from aqueous ethanol) white flakes of 2,3,5,6-tetrafluoro-4-(2,4,6-trimethoxyphenylamino)pyridine (nc) (1.8 g, 5.4 mmol, 69.5%)[Found: C, 50.6; H, 3.5; F, 23.2; N, 8.1%; M (mass spec.), 332 (base peak, $M^{+\cdot}$). $C_{14}H_{12}F_4N_2O_3$ requires C, 50.6; H, 3.6; F, 22.9; N, 8.4%; M, 332], m.p. 126-127 °C, $\lambda_{max.}$ (mull) 2.97 (N-H str.) µm, δ_F (soln. in $CDCl_3$) -17.1 (m; 2-,6-F) and -85.3 (m; 3-,5-F) p.p.m., δ_H (same soln.) 3.80 (s; 2-,6-OCH_3), 3.83 (s; 4-OCH_3), 5.8 (br.s; NH), and 6.17 (s; 3-,5-H) p.p.m. HPLC analysis revealed the presence of some 4-aminotetrafluoropyridine in the residue (crude product) together with another (unidentified) component.

(vii) **4-Azido-3-chlorotrifluoropyridine** (2.5 g, 12 mmol) and **1,3,5-trimethoxybenzene** (18.0 g, 107 mmol) at 160 °C for 4.5 h gave [work-up as in experiment (vi)] white flakes of 3-chloro-2,5,6-trifluoro-4-(2,4,6-trimethoxyphenylamino)pyridine (nc) (2.2 g, 6.3 mmol, 53%)[Found: C, 48.0; H, 3.4; F, 16.3; N, 7.9%; M (mass spec.), 348.5. $C_{14}H_{12}ClF_3N_2O_3$ requires C, 48.2; H, 3.4; F, 16.4; N, 8.0%; M 348.5], m.p. 118-119 °C, $\lambda_{max.}$ (KBr disc) 2.88 (N-H str.) µm, δ_F (soln. in

CDCl$_3$) 1.2 (dd; 2-F), -15.1 (dd; 6-F), -88.2 (dd; 5-F) p.p.m., δ_H (same soln.) 3.78 (s; 2-,6-OCH$_3$), 3.82 (s; 4-OCH$_3$), 6.1 (br.s; NH, checked by D$_2$O exchange technique), and 6.15 (s; 3-,5-H) p.p.m., *m/z* 348 [$M^{+\bullet}$ (^{35}Cl), 100%; correct *M*+2 peak observed]. HPLC analysis of the crude product revealed the presence of traces of 4-amino-3-chloro-2,5,6-trifluoropyridine (an authentic sample was available for comparison).

(viii) 4-Azido-3,5-dichloro-2,6-difluoropyridine (1.5 g, 6.7 mmol) and 1,3,5-trimethoxybenzene (11.2 g, 66 mmol) at 160 °C for 4 h gave [as in (vi)] pale-yellow needles of 3,5-dichloro-2,6-difluoro-4-(2,4,6-trimethoxyphenylamino)pyridine (nc) (1.1 g, 3.0 mmol, 45%) [Found: C, 46.0; H, 3.2; F, 10.4; N, 7.6%; *M* (mass spec.), 365. $C_{14}H_{12}Cl_2F_2N_2O_3$ requires C, 46.0; H, 3.3; F, 10.4; N, 7.7%; *M*, 365], m.p. 145-146 °C, $\lambda_{max.}$ (mull) 2.98 (N-H str.) µm, *m/z* 364 [$M^{+\bullet}$ (^{35}Cl), 100%; *M*+2 and *M*+4 isotope peaks of correct abundances observed], δ_F (soln. in CDCl$_3$) 4.0 (s; 3-,5-F) p.p.m., δ_H (same soln.) 3.78 (s; 2-,6-OCH$_3$), 3.85 (s; 4-OCH$_3$), 6.14 (s; 3-,5-H), and 6.37 (br.s; NH) p.p.m.

(ix) Perfluoro-4-azidotoluene (2.0 g, 7.7 mmol) and 1,3,5-trimethoxybenzene (13.0 g, 77 mmol) at 170 °C for 4 h gave [as in (vi)] white flakes (tinged with yellow) of 1,2,4,5-tetrafluoro-3-trifluoromethyl-6-(2,4,6-trimethoxyphenylamino)-benzene (nc) (2.5 g, 6.3 mmol, 82%) [Found: C, 47.8; H, 2.7; N, 3.5%: *M* (mass spec.), 399 (base peak, $M^{+\bullet}$). $C_{16}H_{12}F_7NO_3$ requires C, 48.1; H, 3.0; N, 3.5%; *M*, 399], m.p. 149 °C, $\lambda_{max.}$ (mull) 2.98 (N-H str.) µm, δ_F (soln. in CDCl$_3$) 23.9 (t, *J* 21 Hz; CF$_3$), -66.3 (m; 2-,4-F), and -82.0 (m; 1-,5-F) p.p.m., δ_H (same soln.) 3.80 (s; 2-,6-OCH$_3$), 3.83 (s; 4-OCH$_3$), 5.55 (br.s; NH), and 6.17 (s; 3-,5-H) p.p.m.

(x) Perfluoroazidobenzene (3.0 g, 14 mmol) and 1,3,5-trimethoxybenzene (24.0 g, 143 mmol) at 170 °C for 4 h gave [as in (vi)] white needles of 1,2,3,4,5-pentafluoro-6-(2,4,6-trimethoxyphenylamino)benzene (nc) (4.4 g, 13 mmol, 92%) [Found: C, 51.4; H, 3.6; N, 4.0%; *M* (mass spec.), 349 (base peak, $M^{+\bullet}$). $C_{15}H_{12}F_5NO_3$ requires C, 51.6; H, 3.4; N, 4.0%;

M, 349], m.p. 106-107 °C, $\lambda_{max.}$ (KBr disc) 2.92 (N-H str.) μm, δ_F (soln. in $CDCl_3$) -81.8 (m; 1-,5-F), -87.9 (m; 2-,4-F), -94.2 (tt, $J_{3,2(4)}$ 21, $J_{3,1(5)}$ 6.5 Hz; 3-F) p.p.m. (rel. int. 2:2:1), δ_H (same soln.) 3.78 (s; 2-,6-OCH_3), 3.81 (s; 4-OCH_3), 5.15 (br.s; NH), and 6.19 (s; 3-,5-H) p.p.m. HPLC analysis of the crude product revealed the presence of traces of pentafluoroaniline.

Independent Synthesis of 3,5-Dichloro-2,6-difluoro-4-(2,4,6-trimethylphenylamino)pyridine

3,5-Dichlorotrifluoropyridine (6.1 g, 30 mmol) was heated under reflux (22 h) with a mixture prepared by refluxing (2 h) oil-free sodium hydride (obtained by washing 3 g of commercial 50% w/w NaH-hydrocarbon oil dispersion with anhydrous light petroleum) in dry tetrahydrofuran (30 cm^3) containing 1-amino-2,4,6-trimethylbenzene (8.0 g, 59 mmol). The product was poured into 2M-hydrochloric acid (1.5 l), and the mixture was extracted with methylene chloride (3 x 150 cm^3). Evaporation of the extract followed by semi-preparative HPLC separation of the black residual solid [on Partisil 20 silica (30 cm x 8 mm) eluted with hexane] provided two white solids, namely 3,5-dichloro-4,6-difluoro-2-(2,4,6-trimethylphenylamino)pyridine (nc) (2.8 g, 8.8 mmol, 29%) [Found: C, 53.2; H, 3.8; N, 8.8%; *M* (mass spec.), 317. $C_{14}H_{12}Cl_2F_2N_2$ requires C, 53.0; H, 3.8; N, 8.8%], m.p. 136-137 °C, $\lambda_{max.}$ (KBr disc) 2.96 (N-H str.) μm, δ_F (soln. in $CDCl_3$) + 8.9 (d; 6-F), -22.9 (d; 4-F; $J_{4,6}$ 15 Hz) p.p.m., δ_H (same soln.) 2.18 (s; 2-,6-CH_3), 2.30 (s; 4-CH_3), 6.40 (br.s; NH), 7.00 (s; 3-,5-H) p.p.m., *m/z* 316 [$M^{+\cdot}$(^{35}Cl), 100%; *M*+2 and *M*+4 ions of correct abundances observed] and 3,5-dichloro-2,6-difluoro-4-(2,4,6-trimethylphenylamino)pyridine (nc) (1.8 g, 5.7 mmol, 19%) (Found: C, 52.8; H, 3.9; N, 8.6. $C_{14}H_{12}Cl_2F_2N_2$ requires C, 53.0; H, 3.8; N, 8.8%), m.p. 90-93 °C, $\lambda_{max.}$ 2.95 (N-H str.) μm, δ_F (soln. in $CDCl_3$) 5.4 (s; 2-,6-F) p.p.m., δ_H (same soln.) 2.18 (s; 2-,6-CH_3), 2.33 (s; 4-CH_3), 6.6 (br.s; NH), 6.96 (s; 3-,5-H) p.p.m., *m/z* 316 [$M^{+\cdot}$(^{35}Cl), 100%; correct *M*+2 and *M*+4 ions observed].

Independent Synthesis of Tetrafluoro-4-(2,4,6-trimethylphenylamino)pyridine

The last reaction described above was repeated, using pentafluoropyridine (8.1 g, 48 mmol), 1-amino-2,4,6-trimethylbenzene (11.0 g, 81.5 mmol), sodium hydride (from 2.2 g of a commercial dispersion), and tetrahydrofuran (110 cm^3), to give, after chromatographic purification [by dry-column flash method; silica eluted with petroleum ether (b.p. 40-60 °C)], tetrafluoro-4-(2,4,6-trimethylphenylamino)pyridine (8.0 g, 28 mmol, 58%), m.p. 108-109°C, with correct spectroscopic (IR, NMR) properties.

Synthesis of 1,2-Bis(3,5-dimethylphenyl)ethane [based on ref.20]

A stirred mixture of 1,3,5-trimethylbenzene (39.0 g, 32.5 mol) and potassium persulphate (44.0 g, 16.3 mol) in water (550 cm^3) was heated (98 °C) for 5 h. The organic layer was filtered to remove a small amount (*ca*. 1.0 g) of yellow (impure by ^1H NMR) 1,2-bis(3,5-dimethylphenyl)ethane, and the filtrate was evaporated to remove unchanged 1,3,5-trimethylbenzene (20.0 g, 51%)]; sublimation of the residue, followed by dry-column flash chromatographic purification of the sublimate [on silica, eluted with petroleum ether (b.p. 40-60 °C)] afforded, after a final recrystallization from aqueous ethanol, white plates of 1,2-bis(3,5-dimethylphenyl)ethane (6.0 g, 2.5 mol, 15% based on 1,3,5-$Me_3C_6H_3$ consumed) (Found: C, 90.8; H, 9.5. Calc. for $C_{18}H_{22}$: C, 90.75; H, 9.25%), m.p. 74-76 °C (lit. [20], 77-78 °C), δ_H (soln. in $CDCl_3$) 2.24 (s; 4 x CH_3), 277 (s; 2 x CH_2), 6.80 (s; 6 x aromatic CH) p.p.m., *m/z* 238 ($M^{+\cdot}$, 19%), 119 ($C_9H_{11}^+$, 100%).

REFERENCES

1 Part 12, R.E. Banks and I.M. Madany, J. Fluorine Chem., 28 (1985) 357.

2 R.E. Banks and A. Prakash, Tetrahedron Letters, (1973) 99; J. Chem. Soc., Perkin Trans. I, (1974) 1365.

3 R.A. Abramovitch, S.R. Challand and E.F.V. Scriven, J. Am. Chem. Soc., 94 (1972) 1374.

4 R.E. Banks and G.E. Sparkes, J. Chem. Soc., Perkin Trans. I, (1972) 2964.

5 E.F.V. Scriven, in 'Reactive Intermediates', ed. R.A. Abramovitch, Plenum Press, New York, 2 (1982) 1.

6 P.A.S. Smith, in 'Azides and Nitrenes', ed. E.F.V. Scriven, Academic Press, New York, (1984) 95.

7 S.S. Zuberi, Ph.D. Thesis, University of Manchester, 1983.

8 A.R. Bailey, Ph.D. Thesis, University of Manchester, 1981; A.R. Bailey and R.E. Banks, J. Fluorine Chem., 24 (1984) 117.

9 R. Huisgen and K.v. Fraunberg, Tetrahedron Letters, (1969) 2595.

10 R.A. Abramovitch, S.R. Challand and E.F.V. Scriven, J. Org. Chem., 37 (1972) 2705.

11 B. Iddon, O. Meth-Cohn, E.F.V. Scriven, H. Suschitzky, and P.T. Gallagher, Angew. Chem. Int. Edn. Engl., 18 (1979) 900.

12 R. Gleiter and R. Hoffmann, Tetrahedron, 24 (1968) 5899; L. D'Epifanio, L. Pellacani, and P.A. Tardella, J. Org. Chem., 44 (1979) 3606.

13 L. Horner, A. Christmann and A. Gross, Chem. Ber., 96 (1963) 399; G.R. Felt, S. Linke and W. Lwowski, Tetrahedron Letters, (1972) 2037; G.R. Felt and W. Lwowski, J. Org. Chem., 41 (1976) 96; H. Takeuchi, N. Murata, Y. Nakagawa, T. Tsuchida and K. Koyama, J. Chem. Soc., Perkin Trans. II, (1977) 80.

14 R.E. Banks, T.A. Hamor and N.D. Venayak, J. Chem. Soc., Chem. Commun., (1980) 900; R.E. Banks, M.G. Barlow, and I.M. Madany, J. Fluorine Chem., 28 (1985) 413.

15 R.E. Banks and A. Prakash, J. Chem. Soc., Perkin Trans. I, (1974) 2479.

16 R.E. Banks, A. Prakash and N.D. Venayak, J. Fluorine Chem., 16 (1980) 325.

17 J.M. Birchall, R.N. Haszeldine and A.R. Parkinson, J. Chem. Soc., (1962) 4966.

18 R.D. Bowden and R. Slater, B.P. 1 367 383 (1974).

19 R.D. Chambers, J. Hutchinson and W.K.R. Musgrave, J. Chem Soc., (1964) 5634.

20 C. Moritz and R. Wolffenstein, Ber., **32** (1899) 432.