*Journal of Fluorine Chemistry*
Elsevier Sequoia S.A., Lausanne – Printed in Switzerland

# POLYFLUORO-HETEROCYCLIC COMPOUNDS
# PART XIX*. RELATIVE BASE STRENGTHS OF SOME POLYFLUOROARYL–NITROGEN HETEROCYCLIC SYSTEMS

S. L. BELL, R. D. CHAMBERS, W. K. R. MUSGRAVE AND J. G. THORPE

*Department of Chemistry, University Science Laboratories, South Road, Durham City (Gt. Britain)*

(Received March 9th, 1971)

---

## SUMMARY

A series of hexafluoroantimonate salts of perfluoro-pyridine, -quinoline, -isoquinoline, and -pyrazine and of 3,5-dichlorofluoropyridine have been isolated. A relative order of base strength has been obtained from $^{19}F$ NMR measurements on mixtures of bases with acid which indicates that a dominant factor affecting base strength is the number of fluorine atoms *ortho* to the nitrogen.

---

## INTRODUCTION

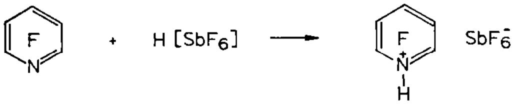
We have previously reported syntheses of a variety of polyfluorinated aromatic nitrogen heterocycles including the pyridine, quinoline, isoquinoline and monocyclic diazine[2] systems, and early experiments with pentafluoropyridine[3] suggested that the system is effectively non-basic, since attempts to isolate salts were unsuccessful. Later observations, however, showed that acid-induced reactions of the quinoline and, to a lesser extent, the isoquinoline systems occur[2b], and tetrafluoropyridazine was subsequently shown to be particularly susceptible to this type of reaction[4]. Indeed, the only salt of this series which has hitherto been successfully isolated[4] is an *N*-alkyl salt of tetrafluoropyridazine. These, and other observations, only suggest an order of base-strength for these systems but no definitive comparison has so far been reported.

---

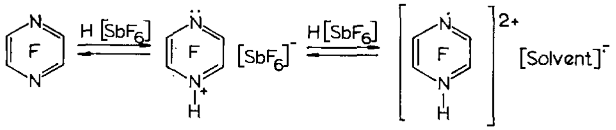
[*] For Part XVIII see ref. 1.

## RESULTS AND DISCUSSION

Mixtures of ethereal solutions of hydrogen chloride or hydrogen bromide with pentafluoropyridine gave no isolatable salts, and pentafluoropyridine was recovered, whereas with heptafluoro-quinoline and -isoquinoline exchange of fluorine for other halogen occurred[1], and the reaction proceeds very rapidly with tetrafluoropyridazine[4]. Mixtures of the protonic acids with the corresponding boron or aluminium trihalides gave solid products on mixing, but only exchange products were actually isolated[5]. However, we have now successfully isolated a series of salts using super acids, *e.g.*, mixtures of hydrogen fluoride with antimony pentafluoride or boron trifluoride. The salts were made using sulphur dioxide as solvent, in which the salts are very soluble but can still be recrystallised.



Since pentafluoropyridine, in particular, is such a weak base it was necessary to confirm that the salts are produced by *N*-protonation, and this is indeed indicated by the following variety of spectral changes, observed on reaction of the heterocycles with acid. The salts all gave bands in the infrared spectrum which may be attributed to N–H stretch and, for example, the hexafluoroantimonate salts had bands in common, attributable to $SbF_6^-$[6]; the shifts induced on the ultraviolet spectra by solution in sulphuric acid are comparable with shifts observed on protonation of the corresponding hydrocarbon heterocyclic systems[2b]; and, finally, the $^{19}F$ NMR spectra are only consistent with *N*-protonation and these data are discussed later. Hexafluorobenzene dissolves in super acids to give radical cations[7], but this type of process, even with the least basic of these heterocycles, is not consistent with the generally well-resolved $^{19}F$ NMR spectra obtained. However, the situation may be more complicated with tetrafluoropyrazine; a sharp $^{19}F$ resonance is obtained up to addition of one molecular equivalent of acid, but when this is exceeded the signal disappears. Further addition of base leads to return of the signal when only one molecular equivalent of acid, or less, is present. The production of a radical di-cation, which destroys the signal, is the most likely explanation of these observations.



The salts were obtained as white crystalline solids, after recrystallisation, but they are all extremely moisture-sensitive. Stability appears to vary significantly with the counter-ion because the hexafluoroantimonates were successfully stored for extensive periods in a dry-box, while the tetrafluoroborates were found to be much less stable.

The $^{19}F$ NMR data for the salts, dissolved in $SO_2$, are given in Table 1, where a comparison is made with the free bases in the same solvent. A naive approach would anticipate that fluorine atoms at all positions would be de-shielded on protonation. Substantial down-field shifts are indeed observed for positions

TABLE 1

$^{19}F$ DATA OF THE HEXAFLUOROANTIMONATE SALTS OF SOME PERFLUORO-HETEROCYCLIC COMPOUNDS AND OF THE BASES DISSOLVED IN VARIOUS STRONG ACIDS[a]

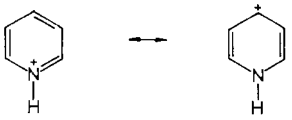
| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *Pyrazine* | | | | | | | | |
| Base in $SO_2$ | 95.9 | | | | | | | |
| Salt in $SO_2$ | 90.9 | $\delta = 5.0$ | | | | | | |
| Base in $H_2SO_4$ | 93.7 | $\delta = 2.2$ | | | | | | |
| Base in $FSO_3H$ | 92.6 | $\delta = 3.3$ | | | | | | |
| Base in $FSO_3H/SbF_5$ | No peak | | | | | | | |
| *Pentafluoropyridine* | | | | | | | | |
| | (2,6) | (4) | (3,5) | | | | | |
| Base in $SO_2$ | 89.5 | 135.0 | 163.5 | | | | | |
| | m | $J = 13.8$; 18.0 Hz | m | | | | | |
| Salt in $SO_2$ | 97.8 | 107.1 | 156.4 | | | | | |
| | m | $J = 21.6$; 27.3 Hz | m | | | | | |
| $\delta =$ | +8.3 | −28.9 | −7.1 | | | | | |
| Base in conc. $H_2SO_4$ | 91.8 | 126.0 | 160.0 | | | | | |
| $\delta =$ | +2.3 | −9.0 | −3.5 | | | | | |
| Base in $FSO_3H$ | 97.4 | 109.4 | 156.7 | | | | | |
| $\delta =$ | +7.9 | −25.6 | −6.8 | | | | | |
| Base in $FSO_3H/SbF_5$ | 96.4 | 102.8 | 154.5 | | | | | |
| $\delta =$ | +6.9 | −32.2 | −9.0 | | | | | |
| *3,5-Dichlorotrifluoropyridine* | | | | | | | | |
| | (2,6) | (4) | | | | | | |
| Base in $SO_2$ | 71.1 | 96.8 | | | | | | |
| | $J_{2,4} = 14$ Hz | $J_{4,2} = 14$ Hz | | | | | | |
| Salt in $SO_2$ | 79.1 | 68.1 | | | | | | |
| | $J_{2,4} = 25.3$ Hz | $J_{4,2} = 25.3$ Hz | | | | | | |
| $\delta =$ | +8.0 | −28.7 | | | | | | |
| *Heptafluoroquinoline* | | | | | | | | |
| | (2) | (4) | | (5) | | | | |
| Base in $SO_2$ | 75.0 | 126.5 | | 148.5 | 151.0 | 154.2 | 157.5 | 163.7 |
| Salt in $SO_2$ | 78.1 | 95.2 | 138.1 | 140.0 | 147.7 | 150.7 | 159.4 | |
| $\delta =$ | +3.1 | −31.3 | | −8.5 | | | | |
| Base in conc. $H_2SO_4$ | 86.1 | 92.1 | 134.1 | 136.3 | 144.9 | 146.5 | 156.2 | |
| $\delta =$ | +11.1 | −34.4 | | −12.2 | | | | |
| Base in $FSO_3H$ | 85.3 | 91.5 | 134.1 | 136.0 | 143.8 | 146.2 | 156.0 | |
| $\delta =$ | +10.3 | −35.0 | | −12.5 | | | | |
| Base in $FSO_3H/SbF_5$ | 77.3 | 90.5 | 135.0 | 137.7 | 145.5 | 151.2 | 158.2 | |
| $\delta =$ | +2.3 | −36.0 | | −10.8 | | | | |

[a] Shifts (in ppm) relative to $CFCl_3$ in capillary tube, assignments in parentheses, m = multiplet, $\delta$ = difference between chemical shift recorded and that of the free base.

TABLE 1 *(Continued)*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Heptafluoroisoquinoline* | | | | | | | |
| | (1) | (3) | | | | | |
| Base in $SO_2$ | 63.5 | 99.3 | 141.6 | 147.3 | 148.0 | 155.3 | 157.5 |
| Salt in $SO_2$ | 69.1 | 113.9 | 133.2 | 134.8(8) | 142.7 | 147.1 | 150.3 |
| $\delta =$ | +5.6 | +14.6 | | | | | |
| *Pyridazine* | | | | | | | |
| | (3,6) | (4,5) | | | | | |
| Base in $SO_2$ | 90.7 | 144.6 | | | | | |
| Base in $H_2SO_4$ | 80.2 | 121.4 | | | | | |
| $\delta =$ | —10.5 | —23.2 | | | | | |
| Base in $FSO_3H$ | 81.0 | 123.0 | | | | | |
| $\delta =$ | —9.7 | —21.6 | | | | | |
| Base in $FSO_3H/SbF_5$ | 80.3 | 122.0 | | | | | |
| | —10.4 | —22.6 | | | | | |

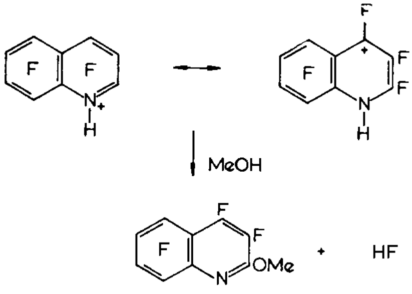
*para* to ring nitrogen, and smaller downfield shifts are observed for corresponding *meta* positions, but, in contrast, positions *ortho* to the nitrogen are shielded. Similar trends have been observed previously for $^{13}$C and $^{1}$H chemical shifts for the hydrocarbon heterocyclic systems[8,9], and the $^{13}$C data indicates that the electron density at carbon atoms *ortho* to nitrogen actually increases on protonation. It has been concluded, from calculations, that both mixing of ground states and low-lying excited states[10] and changes in bond orders occur[8] on protonation, but a qualitative model to account for the upfield shift could possibly be used which accepts that the charge lies principally on the carbon *para* to nitrogen, as represented below.



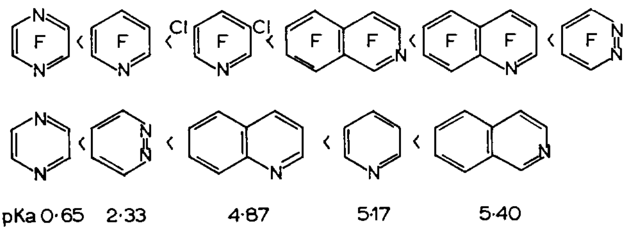
$^{13}$C and $^{19}$F chemical shifts are very large in comparison with those of $^{1}$H, and it is interesting that the values for $^{19}$F reported here parallel the $^{13}$C shifts reported for corresponding hydrocarbon systems[8]. It is probable, therefore, that $^{19}$F shifts can be used, at least qualitatively, to reflect electron distribution in charged systems in comparison with the neutral molecules.

It is interesting to note that, while protonation of heptafluoroquinoline appears to lead to the lowest charge density at the 4-position, nucleophilic substitution in the protonated species leads to, exclusively, 2-substitution[2b]. Quite clearly ground-state electron distribution gives no indication of the positions of maximum reactivity for these acid-induced processes, unless product formation is thermodynamically controlled[11].

Table 1 also contains $^{19}$F NMR data for some of the polyfluoroheterocycles dissolved in various strong acids. From the NMR shifts observed for heptafluoroquinoline and tetrafluoropyridazine, it is apparent that these bases exist largely in their protonated forms in all three acids, whereas pentafluoropyridine and tetrafluoropyrazine are not protonated to such a high degree. The shifts for pentafluoropyridine in concentrated sulphuric acid lie between those of the free base and the salt, indicating only partial protonation, whereas tetrafluoropyrazine is neither completely protonated in concentrated sulphuric nor fluorosulphuric acids. As the $H_0$ values for these acids are known ($H_2SO_4$ −11.0, $FSO_3H$ −12.8)[12], the p$K_a$ values of pentafluoropyridine and tetrafluoropyrazine may be estimated as near −11 and −13 respectively.



Mixtures of the salt of 3,5-dichlorotrifluoropyridine and its base in sulphur dioxide exhibited $^{19}F$ NMR spectra intermediate between those of the salt and the base, and were invariant down to the freezing point of the solvent (about −70°), indicating rapid exchange of the proton between nitrogen sites. Similarly, mixtures of other salts with different bases also exhibited rapid exchange and equilibration of the proton between the bases. Therefore, after assigning peaks in the spectrum of such a mixture it was possible to assess the relative proportions of protonated and unprotonated forms of each base from the $^{19}F$ NMR shifts, and so identify the stronger base. Measurement of the spectra of several pairs of bases mixed with a deficiency of acid, in sulphur dioxide, led to a consistent order of base strength for the series of bases shown above, in comparison with the corresponding hydrocarbon systems. It appears that the most important factor which changes the relative order of base strengths from the hydrocarbon- to the fluorocarbon-series is the number of fluorine atoms which flank the ring nitrogen in each system.



($H_2O$, 20–25°) (Ref. 13)

## EXPERIMENTAL

### *Preparation of pentafluoropyridinium hexafluoroantimonate*

Hexafluoroantimonic acid (14.15 g, 59.7 mmole) (prepared by shaking together equimolar quantities of anhydrous hydrogen fluoride and antimony pentafluoride in a polyfluoroethylene bottle) was added to (10.09 g, 59.7 mmole) pentafluoropyridine dissolved in 20 ml of sulphur dioxide in one limb of a dry, double-limbed Schlenk tube. The mixture was well stirred and allowed to warm up, when the sulphur dioxide boiled off leaving a quantitative yield of light brown crystals of pentafluoropyridinium hexafluoroantimonate (nc), which was recrystallised from sulphur dioxide, m.p. 98–102° (decomp.), (Found: C, 14.4; Sb, 30.2. $C_5HF_{11}NSb$ requires C, 14.7; Sb, 30.0 %). The infrared spectrum was recorded as a mull in dry Nujol, and some of the main peaks are listed as follows: $\nu_{max.}$ 2899 (broad), 1639, 1538, 1346, 1124, 1075, 1031, 980, 877 (broad), 735, 660 (broad), 546 (broad) and 478 $cm^{-1}$, (compare pentafluoropyridine, $\nu_{max.}$ (KBr) 1645, 1493, 1290 (w), 1075 and 978 $cm^{-1}$).

### *Other Salts*

The method described above was used for the isolation of other salts as indicated below, and the $^{19}F$ NMR data for these is shown in Table 1.

#### *3,5-Dichlorotrifluoropyridinium hexafluoroantimonate (nc)*

M.p. 95–98° (decomp.) (Found: C, 13.4. $C_5HCl_2F_9NSb$ requires C, 13.7 %). $\nu_{max.}$ (Nujol) 2915 (broad), 1653, 1560, 1330, 1099, 1062, 802, 667 (broad), 613, 580 and 561 $cm^{-1}$, (3,5-dichlorotrifluoropyridine $\nu_{max.}$ 1613, 1575, 1443, 1422, 1089, 1062, 792 and 741 $cm^{-1}$).

#### *Heptafluoroquinolinium hexafluoroantimonate (nc)*

M.p. 102–104° (decomp.) (Found: C, 22.2. $C_9HF_{13}NSb$ requires C, 22.0 %). $\nu_{max.}$ (Nujol) 2941 (broad), 1667 (broad), 1408 (broad), 952, 862, 797, 729, 658 and 550 $cm^{-1}$, (heptafluoroquinoline, $\nu_{max.}$ (KBr) 1667, 1471, 1389, 1351, 1205, 997, 812 and 800 $cm^{-1}$).

#### *Heptafluoroisoquinolinium hexafluoroantimonate (nc)*

M.p. 120–124° (decomp.) (Found: C, 22.3. $C_9HF_{13}NSb$ requires C, 22.0 %).

#### *Pyrazinium hexafluoroantimonate (nc)*

M.p. 101–103° (decomp.) (Found: C, 11.9. $C_4HF_{10}N_2Sb$ requires C, 12.1 %).

### *Preparation of NMR Samples*

In a typical case, the salt was transferred to an NMR tube in a dry box, then sulphur dioxide was condensed on to the salt from a vacuum line and the solution was stirred and left for about 10 min at −23° ($CCl_4$ bath). The $^{19}F$ spectrum was then recorded at −30° and small portions of base were added (directly in the case of a solid base, and by means of a dropping pipette in the case of liquids). The solution was stirred and left for several minutes at −23° before the spectrum was recorded; subsequent spectra were recorded after each addition of base.

An alternative procedure was also used; approximately equimolar portions of the two bases under study were dissolved in sulphur dioxide in an NMR tube at −23° and a deficiency of acid was added from a dropping pipette to the mixture, which was well stirred. The $^{19}$F NMR spectrum was then recorded at −30°, and again after each addition of acid.

In the case of pyrazine, either $HSO_3F$–$SbF_5$ or HF–$SbF_5$ was added drop by drop to a solution of the base in sulphur dioxide, the $^{19}$F NMR spectrum being recorded after each addition. The single sharp NMR signal shifted downfield after each addition, until a position (89.9 ppm) close to that of the salt, was reached. On further addition of acid the signal vanished, but returned on addition of base.

## ACKNOWLEDGEMENTS

We thank the Imperial Smelting Corporation and the University of Durham for maintenance grants (to J.G.T. and S.L.B.).

## REFERENCES

1 R. D. CHAMBERS, M. HOLE, W. K. R. MUSGRAVE, AND J. G. THORPE, *J. Chem. Soc. (C)*, (1970) 61.

2(a) R. D. CHAMBERS, J. HUTCHINSON, AND W. K. R. MUSGRAVE, *J. Chem. Soc.*, (1964) 3573.

(b) R. D. CHAMBERS, M. HOLE, B. IDDON, W. K. R. MUSGRAVE, AND R. A. STOREY, *J. Chem. Soc. (C)*, (1966) 2328.

(c) R. D. CHAMBERS, J. A. H. MACBRIDE, AND W. K. R. MUSGRAVE, *J. Chem. Soc. (C)*, (1968) 2116.

(d) C. G. ALLISON, R. D. CHAMBERS, J. A. H. MACBRIDE, AND W. K. R. MUSGRAVE, *J. Chem. Soc. (C)*, (1970) 1023.

3 R. D. CHAMBERS, J. HUTCHINSON, AND W. K. R. MUSGRAVE, *J. Chem. Soc. (C)*, (1964) 3736.

4 R. D. CHAMBERS, J. A. H. MACBRIDE, AND W. K. R. MUSGRAVE, *J. Chem. Soc. (C)*, (1968) 2989.

5 J. G. THORPE, *Ph. D. Thesis*, Durham, 1969.

6 G. A. OLAH, *J. Amer. Chem. Soc.*, *87* (1965) 1103.

7 N. M. BAZHIN, YU. V. POZDNYAKOVICH, V. D. SHLEINGARTS AND G. G. YAKOBSON, *Bull. Acad. Sci., U.S.S.R. (Engl. Trans.)*, *10* (1969) 2146.

8 W. ADAM, A. GRIMISON AND G. RODRIGUEZ, *Tetrahedron*, *23* (1961) 2513.

9 I. C. SMITH AND W. G. SCHNEIDER, *Canad. J. Chem.*, *39* (1961) 1158.

10 V. M. S. GIL AND J. N. MURRELL, *Trans. Faraday Soc.*, *60* (1964) 248.

11 R. E. LYLE AND G. J. GAUTHIER, *Tetrahedron Letters*, (1965) 4615.

12 G. A. OLAH, A. M. WHITE AND D. H. O'BRIEN, *Chem. Rev.*, *70* (1970) 561.

13 M. H. PALMER, *The Structure and Reactions of Heterocyclic Compounds*, Edward Arnold, London, 1967.