Trifluoromethanethiolate Ion. Part 2.[1] Nucleophilic Substitution in Pentafluoropyridine. Synthesis and Characteristics of Trifluoromethylthio and Trifluoromethylsulphonyl Derivatives

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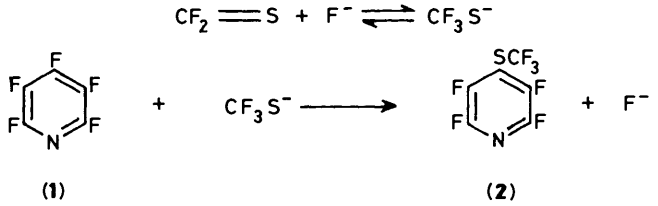
The CF_3S^- anion, generated from thiocarbonyl difluoride or its trimer and caesium fluoride, reacted with pentafluoropyridine (**1**) at −15 °C to give a high yield of 2,3,5,6-tetrafluoro-4-trifluoromethylthiopyridine (**2**). When the trimer was used as a precursor of the CF_3S^- anion, compound (**2**) reacted further at 20 °C to give a mixture of mono- (**2**), bis- (**3**) and (**4**), and tris-(trifluoromethylthio) (**5**) substituted fluoropyridines. At 100—110 °C, 2,4,6-trifluoro-3,5-bis(trifluoromethylthio)pyridine (**4**) was obtained as the only product. On oxidation with CrO_3 in conc. sulphuric acid compound (**2**) gave 2,3,5,6-tetrafluoro-4-trifluoromethylsulphonylpyridine (**12**), and the oxidation of compound (**4**) led to a mixture of 2,4,6-trifluoro-3,5-bis(trifluoromethylsulphonyl)pyridine (**13**) and two isomeric fluoro-3,5-bis(trifluoromethylsulphonyl)pyridinediols (**14a**) and (**14b**). The sulphone (**12**) reacted readily with monomeric CF_2S to yield a mixture of compounds (**3**), (**5**), and 2,4,5,6-tetrafluoro-3-trifluoromethylthiopyridine (**15**). The reaction of compound (**2**) with potassium thiophenolate and potassium phenolate also led to a substitution of fluorines and the CF_3S group with the PhS or PhO substituents to give compounds (**7**)—(**11**). The sulphone (**13**) readily reacts with methanol to yield 2,4,6-trimethoxy-3,5-bis(trifluoromethylsulphonyl)pyridine (**18**). The structures of the new pyridine derivatives (**2**)—(**5**), (**7**)—(**15**), and (**18**) have been elucidated from the m.s., ^{19}F n.m.r., and ^{13}C n.m.r. spectra. The *X*-ray molecular structure of derivative (**18**) has been obtained.

The direct introduction of trifluoromethylthio groups into sufficiently active substrates may be easily achieved *via* an electrophilic route by means of trifluoromethanesulphenyl chloride. Numerous reactions of this type, such as with substituted benzenes,[2] arylmagnesium halides,[3] pyrrole,[4] thiophene,[5] furan, selenophene, pyridine (as an organometallic),[6] and other compounds,[7] have been reported. This method, however, cannot be applied to the synthesis of trifluoromethylthio derivatives of highly electron-deficient substrates, *e.g.* perfluoroaromatics and perfluoroheterocycles. Trifluoromethylthio derivatives of some nitrogen heterocycles and nitrobenzenes were obtained from the corresponding halogen derivatives by nucleophilic substitution with trifluoromethylthiocopper.[8]

In the preliminary communication,[1] we briefly reported that the trifluoromethanethiolate ion, generated in a reversible addition of a fluoride ion to thiocarbonyl difluoride in an aprotic solvent, is stable enough to react with sufficiently electrophilic substrates, *e.g.* pentafluoropyridine (**1**) to give 2,3,5,6-tetrafluoro-4-trifluoromethylthiopyridine (**2**) (Scheme 1).



Scheme 1.

The present paper gives full details of this reaction and reports the introduction of further CF_3S groups into a fluoropyridine ring; it also describes some chemistry and properties of trifluoromethylthio-and trifluoromethylsulphonylfluoropyridines.

Both caesium and potassium fluoride were satisfactory sources of the fluoride ion, but the best results were obtained with the former. The reaction proceeded smoothly under mild conditions (−15 °C) but larger scale experiments have shown that vigorous stirring is the critical factor; otherwise, the yield of compound (**2**) was considerably diminished by the self-condensation of thiocarbonyl difluoride to form a brown-red polymeric material. It has been found that instead of gaseous thiocarbonyl difluoride its liquid trimer, *i.e.* bis(trifluoromethyl) trithiocarbonate, $(CF_3S)_2C{=}S$,[9] may be conveniently used as a precursor of the CF_3S^- anion, according to the equilibria:

$$(CF_3S)_2C{=}S + F^- \rightleftharpoons CF_3S{-}CF{=}S + CF_3S^-$$

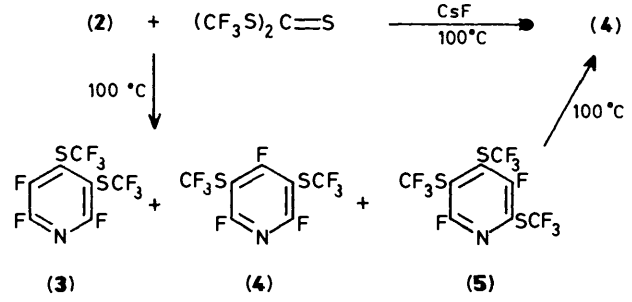
$$CF_3S{-}CF{=}S + F^- \rightleftharpoons CF_2{=}S + CF_3S^-$$

$$CF_2{=}S + F^- \rightleftharpoons CF_3S^-$$

However, the use of monomeric thiocarbonyl difluoride resulted in a higher yield and a higher purity of compound (**2**).

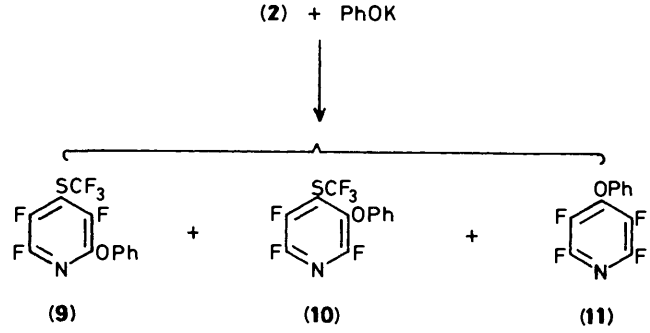
The attempted preparation of poly(trifluoromethylthio) substituted fluoropyridines by using an excess of thiocarbonyl difluoride failed; when CF_2S (> 1 mol equiv.) was introduced into the reaction mixture, it was immediately converted into a brown-red tar. Nevertheless, prolonged reaction of compound (**2**) with the trimer and caesium fluoride in sulpholane at 20 °C gave, in addition to unchanged (**2**) and tar, a mixture of 2,3,6-trifluoro-4,5-bis(trifluoromethylthio)pyridine (**3**), 2,4,6-trifluoro-3,5-bis(trifluoromethylthio)pyridine (**4**), and 2,5-difluoro-3,4,6-tris(trifluoromethylthio)pyridine (**5**) in the ratio of 4.5:2:1, respectively. When the reaction mixture was then heated at 100 °C both compounds (**3**) and (**5**) were fully converted into compound (**4**). Compound (**4**) was the only product (65%) of the reaction which was carried out at 100—110 °C (Scheme 2).

The formation of compounds (**2**) and (**5**) is entirely consistent



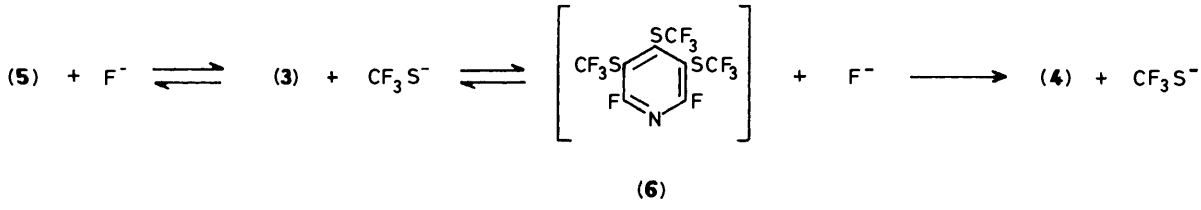
Scheme 2.

with the orientation rules which have been well established for nucleophilic aromatic substitution in pentafluoropyridine.[10] Position 4 and then 3 and 6 were found to be kinetically preferred for the attack by a nucleophile; therefore, the predominant formation of the disubstituted derivative (**3**) at 20 °C and the exclusive formation of compound (**4**) at an elevated temperature is exceptional. Compounds (**3**) and (**4**) are probably thermodynamic products derived from compound (**5**) in a sequence of addition-elimination processes involving the fluoride and the trifluoromethanethiolate ions (Scheme 3).



Scheme 5.

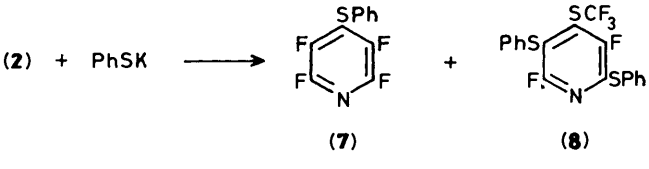
Compound (**2**) was converted into 2,3,5,6-tetrafluoro-4-trifluoromethylsulphonylpyridine (**12**) by oxidation with chromium(VI) oxide in concentrated sulphuric acid (Scheme 6).[11] The reaction was difficult to control and even small variations in temperature and the reaction time resulted in the decreased yield of compound (**12**). Prolonged reaction at 0 °C led to the total destruction of the organic material to give water-soluble products. Nevertheless, carefully controlled small-scale preparations resulted in a high yield of compound (**12**) (80%).



Scheme 3.

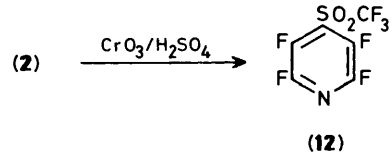
The intermediate (**6**) was not found, but it is quite obvious that, because of steric hindrance, it has to be the least stable compound in this reaction sequence. In contrast, the high stability of compound (**4**) is attributable to the low mobility of the CF_3S groups in the 3- and 5-positions.

The mobility of the CF_3S group in the 4-position is evident from the reaction of compound (**2**) with potassium thiophenolate in acetonitrile at 20 °C; 2,3,5,6-tetrafluoro-4-phenylthiopyridine (**7**) was isolated as the main product (39%). This reaction also gave a mixture of poly(phenylthio) substituted pyridines, in which only 2,5-difluoro-3,6-bis(phenylthio)-4-trifluoromethylthiopyridine (**8**) was identified by spectral methods (Scheme 4). However, a similar reaction of compound



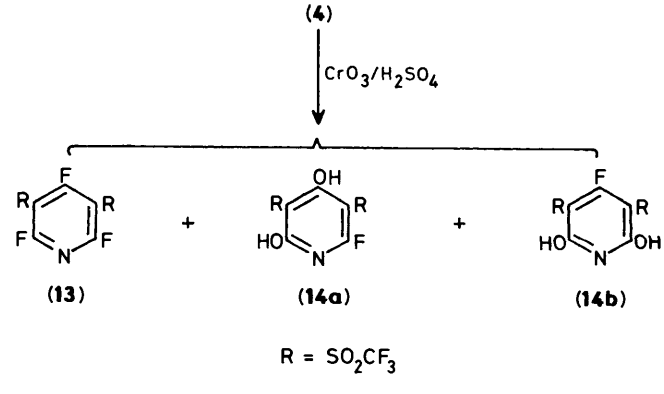
Scheme 4.

(**2**) with potassium phenolate gave 2,3,5-trifluoro-6-phenoxy-4-trifluoromethylthiopyridine (**9**), 2,3,6-trifluoro-5-phenoxy-4-trifluoromethylthiopyridine (**10**), and 2,3,5,6-tetrafluoro-4-phenoxypyridine (**11**) in the ratio of 90:5:5, respectively (Scheme 5). The predominant formation of compound (**9**) in this reaction and the formation of compound (**8**) in the reaction with thiophenolate confirms the applicability of the general orientation rules of nucleophilic aromatic substitution to the 4-trifluoromethylthio substituted pyridine (**2**) under kinetic conditions.



Scheme 6.

The oxidation of 2,4,6-trifluoro-3,5-bis(trifluoromethylthio)-pyridine (**4**) was even more difficult to control; in most cases mixtures of 2,4,6-trifluoro-3,5-bis(trifluoromethylsulphonyl)-pyridine (**13**) and its hydrolysis products, *viz.* 2-fluoro-3,5-bis(trifluoromethylsulphonyl)pyridine-4,6-diol (**14a**) and 4-fluoro-3,5-bis(trifluoromethylsulphonyl)pyridine-2,6-diol (**14b**) were obtained (Scheme 7). The ratio of (**13**) to (**14**) varied from



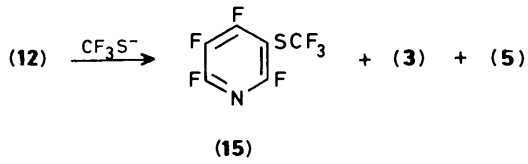
Scheme 7.

one experiment to another. The sulphone (**13**) was isolated by vacuum sublimation. Compounds (**2**) and (**4**) were found to be resistant to less powerful oxidizing agents such as 3-chloroperbenzoic acid and CrO_3–acetic acid.

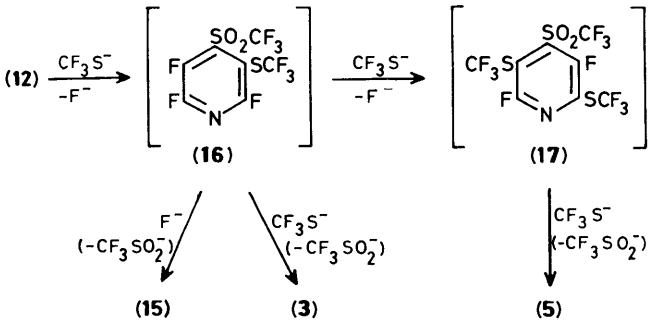
The hydroxy derivatives (**14a**) and (**14b**) are strong acids. They undergo metathesis with aqueous sodium chloride and barium chloride to form the appropriate metal salts. These salts precipitated out when solutions of the diols (**14**) and the chloride were intermixed.

The sulphone (**12**) showed higher reactivity compared with its precursor (**2**). It readily reacted in acetonitrile with monomeric thiocarbonyl difluoride–F^- at -5 °C or with its trimer at 20 °C. The reaction led to the substitution of the fluorine atoms as well as the CF_3SO_2 group for the CF_3S groups to give a mixture of mono-, bis-, and tris-(trifluoromethylthio)pyridines. The bis- and tris-substituted derivatives were identical with compounds (**3**) and (**5**) which were also formed in the reaction of $(CF_3S)_2C{=}S$ with compound (**2**) but, surprisingly enough, the monosubstituted derivative was identified by the ^{19}F n.m.r. spectrum as 2,3,4,6-tetrafluoro-5-trifluoromethylthiopyridine (**15**). In contrast, no higher trifluoromethylthio derivatives were obtained.

The formation of compounds (**3**), (**5**), and (**15**) from the sulphone (**12**) (Scheme 8) may be rationalised in terms of the irreversible reaction sequence, as shown in Scheme 9.

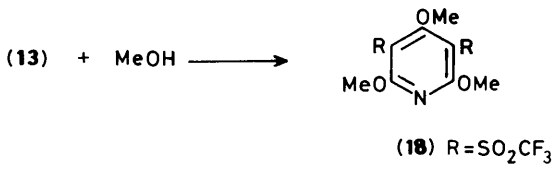


Scheme 8.



Scheme 9.

Although, intermediates (**16**) and (**17**) were not detected in the reaction mixture, there is no doubt that the directing effect of the strongly electron-withdrawing CF_3SO_2 group[12] overcomes that of the ring nitrogen atom, thus making the 3-position in the sulphone (**12**) the most susceptible to nucleophilic attack. The sulphone (**13**) is extremely susceptible to nucleophilic attack; it spontaneously reacts with methanol, even in the absence of a base, to give 2,4,6-trimethoxy-3,5-bis(trifluoromethylsulphonyl)pyridine (**18**) (Scheme 10). The *X*-ray molecular



Scheme 10.

Table 1. Atomic co-ordinates for structure (**18**)

Atom	*x*	*y*	*z*
S(1)	0.877 9(3)	0.061 7(3)	0.261 1(1)
S(2)	0.836 5(3)	−0.174 8(3)	0.015 7(1)
O(1)	0.687 7(8)	−0.104 5(8)	0.004 6(3)
O(2)	0.720 3(7)	0.113 4(8)	0.244 3(3)
O(3)	1.212 9(7)	−0.002 7(8)	0.255 2(3)
O(4)	0.936 6(7)	−0.189 1(8)	−0.033 7(2)
O(5)	0.714 8(7)	−0.027 4(8)	0.129 5(3)
O(6)	0.989 7(7)	0.145 7(7)	0.300 6(3)
O(7)	1.180 2(7)	−0.210 3(7)	0.058 6(3)
N(1)	1.196 6(9)	−0.095 4(9)	0.153 6(4)
C(2)	1.127 4(10)	−0.035 3(9)	0.199 6(4)
C(3)	0.966 2(11)	−0.007 6(10)	0.195 4(4)
C(4)	0.872 7(9)	−0.046 1(9)	0.135 3(4)
C(5)	0.945 2(9)	−0.114 8(9)	0.088 6(4)
C(6)	1.106 1(12)	−0.138 4(10)	0.099 6(5)
C(7)	0.782 7(15)	−0.350 2(14)	0.037 3(5)
C(8)	1.350 9(11)	−0.240 5(16)	0.072 9(6)
C(9)	0.663 1(18)	0.106 1(15)	0.101 6(7)
C(10)	0.842 6(17)	−0.090 6(15)	0.308 5(7)
C(11)	1.380 9(11)	−0.027 6(15)	0.259 6(6)

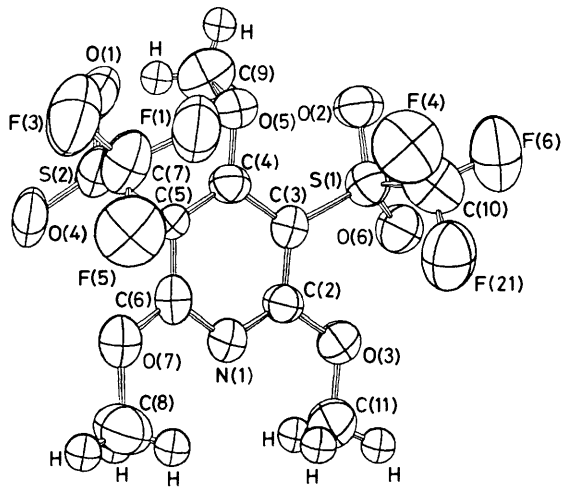


Figure. *X*-Ray molecular structure of 2,4,6-trimethoxy-3,5-bis(trifluoromethylsulphonyl)pyridine (**18**)

structure of compound (**18**) is shown in the Figure. This gives unequivocal proof for the CF_3SO_2 group positions in (**18**) and, therefore, in its precursor (**13**), and also for the CF_3S group positions in compound (**4**). The atomic co-ordinates for the skeleton atoms are given in Table 1, and selected bond lengths and bond angles in Table 2. The C(5)–S(2)–C(7) angle is 102.2 (5)° and the C(3)–S(1)–C(10) angle 103.4 (6)°.

The attempted reaction of the sulphone (**13**) with thiocarbonly difluoride resulted in the formation of a tar from which no particular compound could be isolated.

Experimental

All b.p.s and m.p.s are uncorrected. All n.m.r. spectra were recorded with a Bruker WM 250 FT spectrometer in $CDCl_3$ solution. Chemical shifts are upfield from internal CCl_3F (δ_F), or downfield from internal TMS (δ_C, δ_H). Mass spectra were obtained with a Varian MAT CH 7 spectrometer at 70 eV and 100 μA. G.l.c. analysis were performed with a Perkin-Elmer F20H instrument using a 2 mm × 3.5 m column packed with Chromosorb P AW coated with 10% OV-101 grease. Aceto-

Table 2. Selected parameters for structure (**18**)

Bond lengths (Å)			
S(1)–C(3)	1.763(10)	O(3)–C(2)	1.332(10)
S(1)–O(2)	1.442(7)	O(3)–C(11)	1.450(11)
S(1)–O(6)	1.434(6)	O(5)–C(4)	1.355(9)
S(1)–C(10)	1.799(15)	O(5)–C(9)	1.449(16)
S(2)–C(5)	1.779(8)	O(7)–C(6)	1.313(12)
S(2)–O(1)	1.436(7)	O(7)–C(8)	1.485(11)
S(2)–O(4)	1.415(6)		
S(2)–C(7)	1.808(13)		
Bond angles (°)			
C(3)–S(1)–C(10)	103.4(6)	C(5)–S(2)–C(7)	102.2(5)
C(3)–S(1)–O(2)	114.5(4)	C(5)–S(2)–O(1)	110.8(4)
C(3)–S(1)–O(6)	109.7(4)	C(5)–S(2)–O(4)	110.3(4)
O(2)–S(1)–O(6)	119.5(4)	O(1)–S(2)–O(4)	121.9(4)
O(2)–S(1)–C(10)	101.4(6)	O(1)–S(2)–C(7)	103.1(5)
O(6)–S(1)–C(10)	106.3(5)	O(4)–S(2)–C(7)	106.4(5)
C(2)–O(3)–C(11)	117.4(8)		
C(4)–O(5)–C(9)	114.1(9)		
C(6)–O(7)–C(8)	120.6(8)		

nitrile was purified by refluxing with P_2O_5, distillation, and redistillation from anhydrous K_2CO_3. Sulpholane was freshly distilled under reduced pressure. Caesium fluoride was dried at 200 °C for at least 72 h. All equipment was carefully dried before use.

Mass spectral results for compounds (**2**)—(**5**), (**7**)—(**15**), and (**18**) and ^{13}C n.m.r. spectral results for compounds (**2**), (**4**), (**5**), (**7**), (**9**), and (**12**)—(**14**) are available as a supplementary publication [Sup. No. 56680 (5 pp)]*.

2,3,5,6-*Tetrafluoro*-4-*trifluoromethylthiopyridine* (**2**).—(a) The reaction was carried out in a 100-ml 2-necked flask equipped with a thermometer, magnetic stirring bar, and connected *via* a flexible polypropylene tube to a vacuum line consisting of a storage container for gaseous thiocarbonyl difluoride, a differential manometer, and a MacLeod manometer. Caesium fluoride (4.3 g, 28 mmol) and a solution of pentafluoropyridine (13.5 g, 80 mmol) in acetonitrile (30 ml) were placed in the reaction flask and frozen in liquid nitrogen. The apparatus was evacuated to 0.05 Torr, then warmed up to *ca.* −20 °C and immersed in a cooling bath kept at −15 ± 5 °C.

Thiocarbonyl difluoride was introduced from the vacuum line (initial pressure 760 Torr) with vigorous stirring at a rate to keep the temperature between −15 and −10 °C and prohibit the appearance of the pink colour (a light yellow colour was correct). The reaction ceased after 2.5 h when 82 mmol of CF_2S had reacted (final pressure 280 Torr). The reaction mixture was diluted with water (*ca.* 200 ml) and the bottom organic layer was separated, washed with water (×3) and dried ($CaCl_2$). Distillation through a 10 cm long adiabatic column gave the *title compound* (**2**) (17.7 g, 88%) as a g.l.c.-pure colourless liquid, b.p. 136—137 °C (Found: C, 28.65; F, 53.15; N, 5.65; S, 12.75. C_6F_7NS requires C, 28.69; F, 52.96; N, 5.58; S, 12.77%).

(b) A solution of bis(trifluoromethyl)trithiocarbonate (2.0 g, 8 mmol) in acetonitrile (8 ml) was added dropwise during 2 h to a suspension of caesium fluoride (0.7 g, 4.6 mmol) in a vigorously stirred solution of pentafluoropyridine (2.0 g, 12 mmol) in acetonitrile (8 ml) at −5 °C. After an additional 1 h, the reaction mixture was worked up as in (a). Distillation gave the title compound (**2**) (2.2 g, 73% of a 98% purity, b.p. 134—136 °C).

Reaction of 2,3,5,6-*Tetrafluoro*-4-*trifluoromethylthiopyridine* (**2**) *with Bis(trifluoromethyl) Trithiocarbonate.*—(a) *At ambient temperature.* A mixture of the trifluoromethylthiopyridine (**2**) (3.0 g, 12 mmol), $(CF_3S)_2C{=}S$ (3.0 g, 12 mmol), and caesium fluoride (0.2 g, 2 mmol) in sulpholane (12 ml) were sealed in a glass pressure tube and stirred at ambient temperature for 300 h. The mixture was poured into water and extracted with CH_2Cl_2 (30 ml). The extract was washed with water (×4) and dried ($CaCl_2$). The residue obtained after removal of the solvent was vacuum distilled (*ca.* 10 Torr) to give a colourless liquid (1.2 g) which was shown by g.l.c. to consist of four compounds in the ratio 10:4.5:2:1. Combined g.l.c.–m.s. and ^{19}F n.m.r. (Table 3) analysis allowed these compounds to be identified, respectively, as unchanged (**2**), 2,3,6-trifluoro-4,5-bis(trifluoromethylthio)-pyridine (**3**), 2,4,6-trifluoro-3,5-bis(trifluoromethylthio)pyridine (**4**), and 2,5-difluoro-3,4,6-tris(trifluoromethylthio)pyridine (**5**).

(b) *At ambient temperature followed by heating at* 100 °C. The trifluoromethylthiopyridine (**2**) (1.0 g, 4 mmol), $(CF_3S)_2C{=}S$ (1.0 g, 4 mmol), and caesium fluoride (0.2 g, 1.3 mmol) in sulpholane (4 ml) were allowed to react at ambient temperature for 168 h. A small sample (0.5 ml) was worked up as in (a) and was shown by g.l.c. to contain compounds (**2**), (**3**), (**4**), and (**5**) in the same ratio as in (a). The reaction was then continued at 100 °C for 72 h. The g.l.c. and ^{19}F n.m.r. spectra showed the presence of the bis(trifluoromethylthio)pyridine (**4**) as the sole product.

2,4,6-*Trifluoro*-3,5-*bis(trifluoromethylthio)pyridine* (**4**).—The trifluoromethylthiopyridine (**2**) (5.0 g, 20 mmol), bis(trifluoromethyl)trithiocarbonate (5.0 g, 20 mmol), and caesium fluoride (1.7 g, 11 mmol) in sulpholane (20 ml) were sealed in a glass pressure tube, immersed in an oil bath, and stirred at 108 °C for 36 h. The mixture was poured into water and extracted with CH_2Cl_2 (2 × 30 ml). The extract was washed with water (4 × 50 ml) and dried ($CaCl_2$). After evaporation of the solvent, the residue was vacuum distilled to give the g.l.c.-pure *title compound* (**4**) (4.4 g, 66%) as a colourless liquid, b.p. 175 °C, 67—70 °C/12 Torr (Found: C, 25.5; F, 51.45; N, 4.25; S, 19.5. $C_7F_9NS_2$ requires C, 25.23; F, 51.32; N, 4.20; S, 19.25%).

Reaction of 2,3,5,6-*Tetrafluoro*-4-*trifluoromethylthiopyridine* (**2**) *with Potassium Thiophenolate.*—Dry potassium thiophenolate (0.77 g, 5.2 mmol) was added portionwise during 15 min to a stirred solution of compound (**2**) (1.24 g, 5 mmol) in acetonitrile (10 ml) at ambient temperature. The reaction was continued for an additional 15 min and then diluted with water (50 ml). Organic products were extracted with CH_2Cl_2 and the extract was washed with aqueous Na_2CO_3, followed by water, and dried ($CaCl_2$). Evaporation of the solvent gave a viscous yellow liquid (0.95 g) from which (150 °C, 0.05 Torr) 2,3,5,6-*tetrafluoro*-4-*phenylthiopyridine* (**7**) (0.5 g, 39%) was isolated as a yellow oil by a bulb-to-bulb distillation (Found: C, 50.7; H, 1.7; F, 29.3; N, 5.2; S, 12.3. $C_{11}H_5F_4NS$ requires C, 51.0; H, 1.9; F, 29.3; N, 5.3; S, 12.4%). Crystallisation of the residue from light petroleum (b.p. 80—90 °C) afforded bright yellow crystals (0.2 g) with no defined m.p. (90—200 °C). M.s. and the ^{19}F n.m.r. spectrum of this product revealed the presence of 2,5-difluoro-3,6-diphenylthio-4-trifluoromethylthiopyridine (**8**) as one of the components. Difluorotriphenylthiopyridine was also detected in the m.s. spectrum (M^+, 439).

Reaction of 2,3,5,6-*Tetrafluoro*-4-*trifluoromethylthiopyridine* (**2**) *with Potassium Phenolate.*—Compound (**2**) (1.24 g, 5 mmol) and dry potassium phenolate (0.7 g, 5.3 mmol) were allowed to

* For details of the Supplementary publications scheme see Instructions for Authors (1987), *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1.

Table 3. ^{19}F N.m.r. spectra of the pyridine derivatives (**2**)—(**5**), (**7**)—(**15**), and (**18**)

Compound	Chemical shift, $\delta(CDCl_3)$ p.p.m. 2-F	3-F	4-F	5-F	6-F	CF_3	Coupling constant $J_{F,F}$ (Hz)
(**2**)	87.8 m	131.8 m		131.8 m	87.8 m	40.7 t	$J_{CF_3,5} = J_{CF_3,5}$ = 5.8; AA′XX′P_3[a]
(**3**)	58.8 dm			127.6	76.8 dd	39.1 d 41.8 d	$J_{CF_3,5}$ 12.5, $J_{CF_3,2}$ 5.8, $J_{2,5}$ 27.5; $J_{5,6}$ 22.8, $J_{2,6}$ 10.3
(**4**)	51.6 dm		70.6 m		51.6 dm	42.3 br	$J_{2,6}$ 17.7
(**5**)		106.9 dqq			56.8 dq	38.6 d 39.1 dd 41.1 dd	$J_{CF_3,3}$ 11.6 and 2.6, $J_{CF_3,6}$ 6.8 and 1.3, $J_{3,6}$ 27.7
(**7**)	90.5 m	136.5 m		136.5 m	90.5 m		AA′XX′ system
(**8**)		112.2 dq			59.9 d	39.5 d	$J_{CF_3,3}$ 10.3, $J_{3,6}$ 27.7
(**9**)		129.3 dqn		138.0 dqn	88.5 dd	39.6 t	$J_{CF_3,3} = J_{CF_3,5}$ 5.6, $J_{5,6}$ 22.0; $J_{3,6}$ 30.8, $J_{3,5}$ 5.6
(**10**)	79.2 dd			131.4 ddq	87.9 dd	39.4 d	$J_{CF_3,5}$ 8.5, $J_{2,5}$ 30.0; $J_{5,6}$ 21.6, $J_{2,6}$ 13.3
(**11**)	89.2 v	54.8 m		154.8 m	89.2 m		AA′XX′ system
(**12**)	83.0 m	132.8 m		132.8 m	83.0 m	77.6 t	$J_{CF_3,3} = J_{CF_3,5}$ 5.0; AA′XX′ system
(**13**)	36.4 d		69.8 m		36.4 d	78.3 t	$J_{CF_3,2}$ 4.5, $J_{2,4}$ 17.1
(**14a**)[b]	48.9 s					77.1 s 76.5 s	
(**14b**)[b]			79.2 s			77.6 s	
(**15**)	61.9 m		102.5 m	163.1 dt	76.5 m	42.2 t	$J_{CF_3,4} = J_{CF_3,6}$ 4.5, $J_{2,5}$ 24.6; $J_{4,5} = J_{5,6}$ 21.0
(**18**)[c]						76.6 s	

[a] $J_{AA'}$ 13.9, $J_{XX'}$ 2.6, $J_{AX} - F_{AX}$ 10.3 Hz. [b] Measured in D_2O. [c] δ_{Me} = 4.18 p.p.m. (s).

react in acetonitrile (10 ml) and worked up as described for the reaction with potassium thiophenolate. Distillation gave a colourless oil (1.25 g, 77%) which by g.l.s.–m.s. and ^{19}F n.m.r. spectra was found to be a 90:5:5 mixture of 2,3,5-*trifluoro*-6-*phenoxy*-4-*trifluoromethylthiopyridine* (**9**), 2,3,6-trifluoro-5-phenoxy-4-trifluoromethylthiopyridine (**10**), and 2,3,5,6-tetrafluoro-4-phenoxypyridine (**11**), b.p. *ca.* 65 °C/0.01 Torr (Found: C, 44.6; H, 1.7; F, 35.0; N, 4.3; S, 9.7. $C_{12}H_5F_6NOS$ requires C, 44.30; H, 1.55; F, 35.05; N, 4.31; S, 9.86%).

2,3,5,6-*Tetrafluoro*-4-*trifluoromethylsulphonylpyridine* (**12**).—(a) The oxidizing agent was prepared by dissolving chromium(VI) oxide (3.2 g, 32 mmol) in hot concentrated sulphuric acid (96%) (40 ml) and then cooling the solution to *ca.* 30 °C. The trifluoromethylthiopyridine (**2**) (2 g, 8 mmol) was added to the resultant orange slush and vigorously shaken for 30 min. An exothermic reaction took place and the colour of the reaction mixture changed to green-brown; after *ca.* 10 min a white crystalline precipitate was formed. The mixture was poured onto crushed ice (800 ml) and the precipitate was filtered off, washed with ice-cold water (500 ml), and dried over P_2O_5 to give the *title compound* (**12**) (1.82 g, 80%) as white crystals, m.p. 56—58 °C. Vacuum sublimation (40 °C/ 0.05 Torr) gave m.p. 56.5—57.5 °C (Found: C, 25.4; F, 46.85; N, 5.0; S, 11.4. $C_7F_6NO_2S$ requires C, 25.45; F, 46.97; N, 4.95; S, 11.33%).

(b) Similar runs conducted for 20 and 15 min gave 1.7 (75%) and 1.5 g (66%) of compound (**12**), respectively.

(c) The larger scale preparation [compound (**2**) (5 g), CrO_3 (8 g), and H_2SO_4 (120 ml)] resulted in a stronger exothermic effect and substantially reduced yield of compound (**12**) (2 g, 35%).

(d) The reaction conducted at 0 °C for 16 h resulted in a mixture which was totally soluble in water. Neither compound (**12**) nor unchanged (**2**) were found.

Oxidation of 2,4,6-*Trifluoro*-3,5-*bis*(*trifluoromethylthio*)*pyridine* (**4**).—(a) The bis(trifluoromethylthio)pyridine (**4**) (2.8 g, 8.4 mmol) was added to a slush of CrO_3 (6.7 g, 67 mmol) in concentrated sulphuric acid (100 ml) and the mixture vigorously shaken for 30 min. It was then worked up as described for the preparation of compound (**12**) to give a white powder (2.7 g). Vacuum sublimation (60 °C/0.01 Torr) gave 2,4,6-*trifluoro*-3,5-*bis*(*trifluoromethylsulphonyl*)-*pyridine* (**13**) (1.35 g, 40%) as a white crystalline powder, m.p. 113—115 °C (Found: C, 21.1; F, 43.35; N, 3.7; S, 15.8. $C_7F_9NO_4S_2$ requires C, 21.16; F, 43.05; N, 3.53; S, 16.15%). The residue obtained after removal of compound (**13**) was found by spectral methods to be a 1:1 mixture of 2-*fluoro*-3,5-*bis*(*trifluoromethylsulphonyl*)*pyridine*-4,6-*diol* (**14a**) and 4-*fluoro*-3,5-*bis*(*trifluoromethylsulphonyl*)*pyridine*-2,6-*diol* (**14b**) (1.2 g, 36%), m.p. 185—195 °C (decomp.) (Found: C, 21.1; H, 0.7; F, 33.7; N, 3.5; S, 16.6. $C_7H_2F_7NO_6S_2$ requires C, 21.4; H, 0.5; F, 33.8; N, 3.6; S, 16.3%).

(b) The smaller scale preparation [compound (**4**) (0.8 g), CrO_3 (2 g), and H_2SO_4 (30 ml)] gave compound (**13**) practically as the only product (0.62 g, 65%).

Preparation of Metal Salts of the Dihydroxy Derivatives (**14**).—(a) *The sodium salt.* Saturated aqueous sodium chloride was added to a solution of a mixture of the diols (**14a**) and (**14b**) [0.8 g in H_2O (30 ml)]. After *ca.* 30 min a white voluminous precipitate was formed. The mixture was left overnight at 0 °C after which the precipitate was filtered off, washed with ice-cold water, and dried over P_2O_5 (0.5 g, 57%) (Found: C, 19.55; F, 33.55; N, 3.0; S, 14.85. $C_7F_7NO_6S_2Na_2$ requires C, 19.23; F, 30.42; N, 3.20; S, 14.64%).

(b) *The barium salt.* The barium salt was prepared similarly by addition of concentrated aqueous barium chloride to a

solution of a mixture of the diols (**14a**) and (**14b**) [0.6 g in H_2O (50 ml)]. A white precipitate was formed (0.4 g, 50%) (Found: C, 16.0; F, 25.2; N, 2.6; S, 12.1. $C_7F_7BaNO_6S_2$ requires C, 15.90; F, 25.16; N, 2.65; S, 12.13%).

Reaction of 2,3,5,6-*Tetrafluoro*-4-*trifluoromethylsulphonylpyridine* (**12**) *with Thiocarbonyl Difluoride*.—The reaction was, in general, conducted as described for the preparation of compound (**2**). Gaseous CF_2S was introduced with vigorous stirring to a solution of compound (**12**) (5 g, 17.6 mmol) in acetonitrile (25 ml) in the presence of caesium fluoride (1 g, 6.5 mmol) while the reaction temperature was kept between −5 and 0 °C. The reaction ceased when 55 mmol of CF_2S had reacted. The reaction mixture was poured into water and the organic layer was separated, washed with water, and dried ($CaCl_2$) to give a crude product (5 g) as a brown oil. The g.l.c. revealed the presence of four compounds in the ratio of 1.3:1:3.8:2.5 (in the order of the increasing retention time). The most abundant component was shown by g.l.c.–m.s. to be unchanged (**12**), and the three others to be mono-, bis-, and tris-(trifluoromethylthio) substituted fluoropyridines. Most of the unchanged (**12**) was filtered off as a crystalline precipitate (m.p. 56—58 °C) after dilution of the crude product with a small amount of light petroleum. The filtrate, after removal of the solvent, was vacuum distilled (*ca.* 15 Torr) to give three fractions. The lowest boiling fraction (55—70 °C) consisted mostly of the monosubstituted derivative which by the ^{19}F n.m.r. spectrum (Table 3) was identified as 2,3,6-tetrafluoro-5-trifluoromethylthiopyridine (**15**). The ^{19}F n.m.r. spectrum of the medium fraction allowed the bis(trifluoromethylthio) substituted compound to be identified as compound (**3**). Redistillation of the highest fraction gave 2,5-*difluoro*-3,4,6-*tris*(*trifluoromethylthio*)*pyridine* (**5**) (0.5 g, 7%) of *ca.* 98% purity (g.l.c. estimate), b.p. 200 °C (in a capillary) (Found: C, 23.1; F, 50.0; N, 3.4; S, 23.2. $C_8F_{11}NS_3$ requires C, 23.14; F, 50.33; N, 3.37; S, 23.16%).

Reaction of 2,3,5,6-*Tetrafluoro*-4-*trifluoromethylsulphonylpyridine* (**12**) *with Bis*(*trifluoromethyl*)*trithiocarbonate*.—$(CF_3S)_2C{=}S$ (0.3 g, 1.2 mmol) was added dropwise at 20 °C during 1 h to a vigorously stirred mixture of (**12**) (0.5 g, 1.8 mmol) and caesium fluoride (0.1 g, 0.6 mmol) in acetonitrile (2 ml). The reaction mixture was stirred at ambient temperature overnight and worked up analogously to the reaction with gaseous CF_2S. The crude product (0.5 g), in addition to tar, consisted of compounds (**15**), (**12**), (**3**), and (**5**) in the ratio of 1.2:2.2:1:2.8, respectively (g.l.c. estimate).

2,4,6-*Trimethoxy*-3,5-*bis*(*trifluoromethylsulphonyl*)*pyridine* (**18**).—2,4,6-Trifluoro-3,5-bis(trifluoromethylsulphonyl)pyridine (**13**) (0.5 g), was dissolved in methanol (*ca.* 2 ml) with slight heating. After a few minutes crystallisation occurred. The crystals were separated and dried *in vacuo* to give the *title compound* (**18**) (0.3 g, 73%), m.p. 131—133 °C (Found: C, 27.7; H, 2.0; F, 26.55; N, 3.2; S, 14.75. $C_{10}H_9F_6NO_7S_2$ requires C, 27.72; H, 2.09; F, 26.31; N, 3.23; S, 14.80%).

X-Ray Crystal Structure Analysis of Compound (**18**).—Crystal data: $C_{10}H_9F_6NO_7S_2$, M = 433.3, monoclinic, a_0 = 8.560 (9), b_0 = 9.553 (8), c_0 = 20.757 (20) Å, β = 96.49 (12°), Z = 4, V = 1 686.5 Å^3, space group $P2_1/c$ (Nr. 14), Mo-K_α radiation, single set of 2 434 reflections. The compound formed clear, colourless crystals and a specimen of dimensions (0.04 × 0.04 × 0.15) mm was used for data collection to a value of + 25°. No absorption correction was applied, μ = 1.98 cm^{-1}. The structure was solved by direct methods and refined using SHELXTL. The final R factor of 0.071 was calculated for 1 871 reflections with $F_{abs} > 2.5\ \sigma(F)$. The final difference Fourier shows highest maxima of 0.3 e/Å^3. The shift of the atoms in the last 'least-squares cycle' is <0.001 for the atomic and <0.007 for the thermal parameters. R_w = 0.059; weighting scheme: $W = 1/\sigma^2(F) + 0.000\,22F_0^2$). Atomic co-ordinates and selected bond lengths and bond angles are given in Tables 1 and 2. Thermal paramaters, tables of bond lengths and angles for the H atoms, and non-bonded distances are available on request from the Cambridge Crystallographic Data Centre.*

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* For details see Instructions for Authors (1987), *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1.

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