# Heterocyclic Polyfluoro-compounds. Part XII.[1] Synthesis and Some Reactions of 2,3,5,6-Tetrafluoro-4-iodopyridine

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2,3,5,6-Tetrafluoro-4-iodopyridine, prepared by oxidation of 2,3,5,6-tetrafluoro-4-hydrazinopyridine in the presence of methyl iodide or, preferably, by reaction of pentafluoropyridine with sodium iodide in dimethylformamide, is readily converted into 2,3,5,6-tetrafluoropyridylmagnesium iodide or 2,3,5,6-tetrafluoropyridyllithium; some reactions of these organometallic compounds are described. Hydroxide ion, methoxide ion, and ammonia attack 2,3,5,6-tetrafluoro-4-iodopyridine at the 2-position, to give the corresponding 2-substituted trifluoro-4-iodopyridines, but iodide ion appears to attack the 4-iodo-substituent with the formation of the 2,3,5,6-tetrafluoropyridyl anion. Coupling of tetrafluoro-4-iodopyridine by the Ullmann technique affords perfluoro-4,4′-bipyridyl. Reaction of 3-chloro-2,4,5,6-tetrafluoropyridine with sodium iodide in dimethylformamide yields 3-chloro-2,5,6-trifluoro-4-iodopyridine.

2,3,5,6-TETRAFLUORO-4-IODOPYRIDINE, a low-melting solid, can be prepared by oxidation of 2,3,5,6-tetrafluoro-4-hydrazinopyridine[2] with silver oxide in the presence of an excess of methyl iodide (cf. the conversion of pentafluorophenylhydrazine into pentafluoroiodobenzene[3]) or, preferably, by direct nucleophilic displacement of the activated[2,4] 4-fluorine in pentafluoropyridine by iodide (anhydrous sodium iodide in dimethylformamide

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[1] Part XI, R. E. Banks, R. N. Haszeldine, and I. M. Young, preceding Paper.

[2] R. E. Banks, J. E. Burgess, W. M. Cheng, and R. N. Haszeldine, *J. Chem. Soc.*, 1965, 575.

[3] J. M. Birchall, R. N. Haszeldine, and A. R. Parkinson, *J. Chem. Soc.*, 1962, 4966.

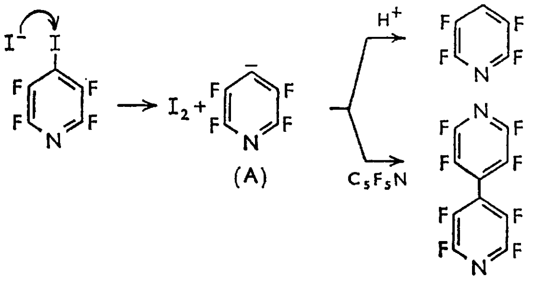
[4] Part X, R. E. Banks, D. S. Field, and R. N. Haszeldine, *J. Chem. Soc. (C)*, 1967, 1822.

at 150°). 3-Chloro-2,4,5,6-tetrafluoropyridine also reacts with sodium iodide in hot dimethylformamide to give the corresponding 4-iodo-derivative.

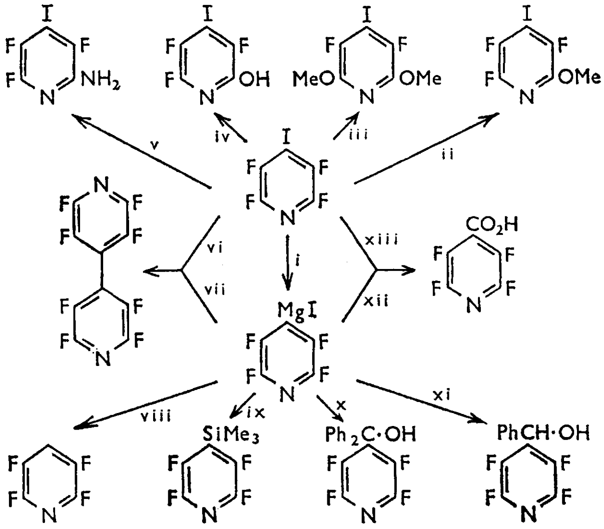
With a twenty-hour reaction period the second method provides tetrafluoro-4-iodopyridine in 84% based on 48% consumption of the pentafluoropyridine; perfluoro-4,4′-bipyridyl is also formed (9%). The conversion of pentafluoropyridine rises to 90% when the reaction period is doubled, but in addition to tetrafluoro-4-iodopyridine (57%) and the bipyridyl (13%), the product contains 2,3,5,6-tetrafluoropyridine (10%) and a brown solid which is probably polymeric material with a structure based on polyfluoropyridine units. No reaction occurs when pentafluoropyridine is heated with anhydrous sodium iodide in the absence of solvent at 165° for 22 hours, or when it is heated under reflux for 8 hours with a solution of lithium iodide in acetone.

Treatment of 2,3,5,6-tetrafluoro-4-iodopyridine with sodium iodide in dimethylformamide at 150° for 40 hours does not appear to yield either 2-*NN*-dimethylamino-3,5,6-trifluoro-4-iodopyridine or 3,5,6-trifluoro-2,4-di-iodopyridine, the expected products (see later) of nucleophilic attack on tetrafluoro-4-iodopyridine by dimethylamine (from thermal decomposition of dimethylformamide [5]) and iodide ion, respectively, but gives instead 2,3,5,6-tetrafluoropyridine (91% based on 45% conversion of the iodopyridine into product) and a yellow intractable solid with properties similar to those of the brown solid mentioned before. Although perfluoro-4,4′-bipyridyl is not formed in this reaction, nor during the slow formation of a black substance from tetrafluoro-4-iodopyridine at its boiling point (168°), it is obtained in good yield (64% based on pentafluoropyridine consumed) when an approximately equimolar mixture of pentafluoropyridine and tetrafluoro-4-iodopyridine is heated with sodium iodide in dimethylformamide at 150° for 20 hours. This suggests that iodide ion can attack the iodine in tetrafluoro-4-iodopyridine with formation of the pyridyl anion (A), which can abstract a proton from dimethylformamide or, preferentially, attack pentafluoropyridine to give perfluoro-4,4′-bipyridyl (see Scheme 1). Formation of 2,3,5,6-tetrafluoropyridine could also be explained by homolytic fission of the C–I bond in tetrafluoro-4-iodopyridine followed by attack by the 2,3,5,6-tetrafluoropyridyl radicals on dimethylformamide; such radicals, formed by oxidation of tetrafluoro-4-hydrazinopyridine [2,3] abstract hydrogen as well as iodine from methyl iodide. However, since attack of the trifluoromethyl free radical on pentafluoropyridine occurs predominantly at position 3,[6] the formation of perfluoro-4′,4′- rather than -3,4′-bipyridyl is a good argument against the incursion of free radicals in the tetrafluoro-4-iodopyridine–sodium iodide–pentafluoropyridine reaction.

Nucleophilic displacement by iodide on the iodine of picryl iodide has been proposed [7] to account for the formation of 1,3,5-trinitrobenzene, mesityl oxide, and iodine when picryl chloride is heated under reflux with sodium iodide in acetone. Similar treatment of tetrafluoro-4-iodopyridine gave iodine, 2,3,5,6-tetrafluoropyridine (78%), and a brown residue. Although no mesityl oxide could be detected the tetrafluoropyridyl anion (A) must be formed in this reaction.



Scheme 1



Scheme 2

Reagents: i, Mg in tetrahydrofuran; ii, NaOMe–MeOH, 0—20°; iii, NaOMe–MeOH, reflux; iv, KOH–$Bu^tOH$, reflux; v, $NH_3$ aq., 80—90°; vi, Cu, 200°; vii, $C_5F_5N$, —40°; viii, $H_2SO_4$ aq., —5°; ix, $Me_3SiCl$, —15°; x, $Ph_2CO$, —20°; xi, PhCHO, —15 to —5°; xii, $CO_2$, —15 to 20°; xiii, $Bu^nLi$ in ether–benzene at —35°, then $CO_2$ at —10°

Tetrafluoro-4-iodopyridine undergoes nucleophilic substitution at the 2-position by ammonia, hydroxide ion, or methoxide ion; it can be coupled with copper-bronze to provide perfluoro-4,4′-bipyridyl, and readily forms a Grignard reagent, which reacts in conventional fashion with water, carbon dioxide, benzaldehyde, benzophenone, or chlorotrimethylsilane (see Scheme 2) and attacks pentafluoropyridine to give perfluoro-4,4′-bipyridyl. Thus it resembles 4-bromotetrafluoropyridine, prepared less conveniently by diazotisation of 4-aminotetrafluoropyridine in hydrofluoric acid followed by treatment of the diazonium solution with cuprous

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[5] E. Felstead, H. C. Fielding, and B. J. Wakefield, *J. Chem. Soc.* (*C*), 1966, 708.

[6] R. E. Banks, R. N. Haszeldine, and G. Shaw, unpublished results.

[7] C. W. L. Bevan, J. Hirst, and E. C. Okafor, *J. Chem. Soc.*, 1964, 6248.

bromide.[8] Tetrafluoro-4-iodopyridine also undergoes halogen–metal interchange with n-butyl-lithium, to give 2,3,5,6-tetrafluoropyridyl-lithium which yields tetrafluoroisonicotinic acid with carbon dioxide. Tetrafluoro-4-iodopyridine is thus an important intermediate in polyfluoropyridine chemistry.

## EXPERIMENTAL

Products were identified by elemental analysis, measurement of physical constants, infrared spectroscopy (Perkin-Elmer spectrophotometer model 21 with rock salt optics), ultraviolet spectroscopy (Unicam SP 700 or Hilger-Watts Ultrascan spectrophotometer), $^{19}F$ nuclear magnetic resonance spectroscopy (Perkin-Elmer R10 instrument with trifluoroacetic acid as external reference), and gas–liquid chromatography (g.l.c.) (Perkin-Elmer Gas Chromatograph model 452). The n.m.r. spectra will be discussed in detail later.[9]

Pentafluoropyridine and 3-chloro-2,4,5,6-tetrafluoropyridine were prepared from pentachloropyridine and anhydrous potassium fluoride.[10] 2,3,5,6-Tetrafluoro-4-hydrazinopyridine was prepared from pentafluoropyridine and hydrazine hydrate.[2]

2,3,5,6-*Tetrafluoro-4-iodopyridine*.—(a) *From pentafluoropyridine*. A mixture of pentafluoropyridine (15·1 g., 89·4 mmoles), anhydrous sodium iodide (60·0 g., 0·4 mole), and dimethylformamide (15 ml.) was heated, with occasional agitation, at 150° for 20 hr. in a 200-ml. Pyrex ampoule. The solid violet product was extracted with 50 : 50 (v/v) ether–water (6 × 80 ml.) and the ether extract was shaken with a saturated aqueous solution of sodium thiosulphate (50 ml.) then with water, dried ($MgSO_4$), and distilled to give pentafluoropyridine (7·8 g., 46·2 mmoles, 52% recovery), b. p. 84°, 2,3,5,6-*tetrafluoro-4-iodopyridine* (10·1 g., 36·5 mmoles, 84% based on pentafluoropyridine consumed) (Found: C, 22·0; N, 5·0. $C_5F_4IN$ requires C, 21·7; N, 5·1%), m. p. 47—48°, b. p. 84°/40 mm., $\lambda_{max.}$ (hexane) 215, 237, and 272 m$\mu$ ($\varepsilon$ 4860, 9700, and 3820), $\lambda_{max.}$ (mull) 6·00w, 6·17s, 6·21m (sh), 6·36w, 6·80s, 6·87s, 6·93m (unsymmetrical triplet; polyfluoropyridine nucleus), 7·10w, 7·80w, 7·90w (doublet), 8·18s, 9·94w, 10·61s, 12·02s, 13·32w, 13·79w, 13·85w (doublet), 14·26w, and 14·42m $\mu$, $\delta$ (25% solution in ethanol) 11·1 (2- and 6-F) and 44·7 (3- and 5-F) p.p.m., $|J_{2,5}| = 28·3$, $|J_{2,3}| = 20·4$, $|J_{2,6}| = 13·3$, and $|J_{3,5}| = 3·0$ c./sec., and perfluoro-4,4′-bipyridyl (0·60 g., 2·0 mmoles, 9%) (Found: C, 40·2; N, 9·1. Calc. for $C_{10}F_8N_2$: C, 40·0; N, 9·3%), m. p. 82—83° (lit.,[8] 81—82°), $\lambda_{max.}$ (hexane) 218 and 280 m$\mu$ ($\varepsilon$ 8600 and 6900), $\lambda_{max.}$ (mull) 6·74, 6·83, and 6·90 $\mu$ (triplet; polyfluoropyridine nucleus), $\delta$ (30% solution in acetone) 13·0 (2- and 6-F) and 62·0 (3- and 5-F) p.p.m. (two band systems of equal intensity).

When pentafluoropyridine (8·7 g., 51·5 mmoles), sodium iodide (35·0 g., 0·233 mole), and dimethylformamide (8 ml.) were heated together at 150° for 40 hr., the product, worked up as above, consisted of pentafluoropyridine (0·89 g., 5·3 mmoles, 10% recovery), 2,3,5,6-tetrafluoropyridine (0·71 g., 4·6 mmoles, 10% based on pentafluoropyridine consumed), 2,3,5,6-tetrafluoro-4-iodopyridine (7·39 g., 26·4 mmoles, 58%), perfluoro-4,4′-bipyridyl (0·90 g., 3·0 mmoles, 13%), and a tacky brown intractable solid (*ca.* 1 g.) (Found: C, 35·4; H, 0·7; N, 8·3%), which contained fluorine and iodine (Lassaigne test) and as a mull showed a strong fairly broad absorption in the infrared at 6·8 $\mu$ (polyfluoropyridine nucleus).

(b) *From* 2,3,5,6-*tetrafluoro-4-hydrazinopyridine*. The hydrazino-compound (15·4 g., 85·1 mmoles) was added slowly to a cold (0°) stirred suspension of anhydrous silver oxide (60·0 g.) in freshly distilled methyl iodide (250 ml.). The reaction mixture was then heated under reflux (1 hr.), filtered, and the filtrate was distilled to provide 2,3,5,6-tetrafluoropyridine (5·1 g., 33·8 mmoles, 40%), b. p. 102°, and 2,3,5,6-tetrafluoro-4-iodopyridine (6·1 g., 22·0 mmoles, 26%), b. p. 84°/40 mm., 168° (decomp.)/758 mm., each with correct i.r. spectrum.

3-*Chloro*-2,5,6-*trifluoro-4-iodopyridine*.—A mixture of 3-chloro-2,4,5,6-tetrafluoropyridine (6·5 g., 35·0 mmoles), anhydrous sodium iodide (26·0 g., 0·17 mole), and dimethylformamide (10 ml.) was heated at 150° for 18 hr. in a 200-ml. ' Pyrex ' ampoule. Water (10 ml.) and ether (10 ml.) were then introduced into the reaction vessel to extract the solid violet product; this procedure was repeated five times. The ether extract was dried ($MgSO_4$) and distilled to give 3-chloro-2,4,5,6-tetrafluoropyridine (1·8 g., 9·7 mmoles, 28% recovery), b. p. 30°/4 mm., and 3-*chloro*-2,5,6-*trifluoro-4-iodopyridine* (2·6 g., 8·9 mmoles, 35% based on 3-chlorotetrafluoropyridine consumed) (Found: C, 20·1; I, 43·0; N, 4·6. $C_5ClF_3IN$ requires: C, 20·5; I, 43·3; N, 4·8%), m. p. 39—41°, b. p. 78—80°/10 mm., $\lambda_{max.}$ (ethanol) 246 and 276 m$\mu$ ($\varepsilon$ 6500 and 4820), $\lambda_{max.}$ (hexane) 221, 244, and 278 m$\mu$ ($\varepsilon$ 4750, 8120, and 4500), $\lambda_{max.}$ (melt) 6·05m, 6·26s, 6·77m, 6·94s, 7·04m (triplet; polyfluoropyridine nucleus), 7·43m, 7·99m, 8·35m, 9·30w, 9·54w, 10·31w, 10·60w, 10·83w, 11·24m, 11·45s, 12·17s, and 13·73m $\mu$. The $^{19}F$ n.m.r. spectrum of the iodo-compound showed three bands of equal intensity with $\delta$ −4·9 (2-F), 13·7 (6-F), and 44·0 (5-F) p.p.m.

*Reactions of* 2,3,5,6-*Tetrafluoro-4-iodopyridine*.—(a) *With sodium methoxide*. 2,3,5,6-Tetrafluoro-4-iodopyridine (1·2 g., 4·3 mmoles) in methanol (10 ml.) at 0° was treated with sodium methoxide (0·23 g., 4·3 mmoles) in methanol (3 ml.). The reaction mixture was warmed to 20°, kept at this temperature for 1 hr., then treated with water (50 ml.). The product was extracted with methylene chloride (5 × 20 ml.), and the extract was dried ($MgSO_4$) and distilled, to give 3,5,6-*trifluoro-4-iodo-2-methoxypyridine* (0·92 g., 3·2 mmoles, 74%) (Found: C, 24·9; H, 1·1; N, 5·2. $C_6H_3F_3INO$ requires C, 24·9; H, 1·0; N, 4·8%), b. p. 54—56°/*ca.* 0·3 mm., $\lambda_{max.}$ (hexane) 230 and 285 m$\mu$ ($\varepsilon$ 10,200 and 4800), $\lambda_{max.}$ (liquid film) 3·40 (C–H str.), 6·20, 6·40, 6·75, 6·95, 7·04 (doublet; polyfluoropyridine nucleus), 7·22, 7·80, 7·90, 8·20 (C·O·C asym. str.?), 8·40, 9·90, 10·63, 10·80, 12·02, 12·32, 13·69, 13·91, and 14·57 $\mu$, $\delta$ 14·1 (6-F), 43·8 (3-F), and 54·2 (5-F) p.p.m. (three band systems of equal intensity).

The product obtained by heating under reflux (1 hr.) a mixture of 2,3,5,6-tetrafluoro-4-iodopyridine (1·2 g., 4·3 mmoles), sodium methoxide (0·70 g., 13·0 mmoles), and methanol (15 ml.) was worked up as before to provide, after sublimation of the final product, 3,5-*difluoro-4-iodo*-2,6-*dimethoxypyridine* (1·1 g., 3·7 mmoles, 86%) (Found: C, 28·0; H, 2·3; N, 5·0. $C_7H_6F_2INO_2$ requires C, 27·9; H, 2·0; N, 4·7%), m. p. 141—142°, $\lambda_{max.}$ (mull) 3·31—3·48 (C–H str.), 6·19, 6·30, 6·79, 6·83, 6·86 (triplet; polyfluoropyridine nucleus), 7·12, 7·28, 7·88, 8·24, 8·36 (doublet;

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[8] R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 1965, 5040.

[9] M. G. Barlow and I. M. Young, in preparation.

[10] R. E. Banks, R. N. Haszeldine, J. V. Latham, and I. M. Young, *J. Chem. Soc.*, 1965, 594.

C·O·C str. ?), 9·88, 10·02 (doublet), 10·97, 12·59, 13·72, 13·81 (unsymmetrical doublet), and 14·74 μ, δ 57·0 p.p.m. (single band absorption system due to 3- and 5-F).

(b) *With potassium hydroxide.* A mixture of 2,3,5,6-tetrafluoro-4-iodopyridine (1·25 g., 4·51 mmoles), potassium hydroxide (0·60 g., 10·71 mmoles), and t-butyl alcohol (10 ml.) was heated under reflux for 2 hr., water (10 ml.) was added, and the t-butyl alcohol was distilled off. The aqueous product was acidified with 4N-sulphuric acid (10 ml.) and extracted with ether (3 × 75 ml.). The extract was dried ($MgSO_4$) and evaporated, to leave a solid which was sublimed *in vacuo* to provide 3,5,6-*trifluoro*-2-*hydroxy*-4-*iodopyridine* (1·03 g., 3·75 mmoles, 83%) (Found: C, 21·8; H, 0·4; I, 46·2; N, 5·1. $C_5HF_3INO$ requires C, 21·8; H, 0·4; I, 46·2; N, 5·1%), m. p. 149—150°, $\lambda_{max.}$ (mull) 3·25 (centre of broad band attributed to bonded OH), 6·09, 6·33, 6·70 (polyfluoropyridine nucleus), 7·17, 7·36 (doublet), 7·95, 8·04 (doublet), 8·31, 10·19, 10·53, 11·92 μ, δ 16·6 (6-F), 46·9 (3-F), and 58·3 (5-F) p.p.m. (three band systems of equal intensity).

(c) *With ammonia.* 2,3,5,6-Tetrafluoro-4-iodopyridine (1·20 g.) was heated at 80—90° for 27 hr. with aqueous ammonia (4 ml.; *d* 0·880) in a small 'Pyrex' ampoule. The product was extracted with ether (100 ml.), and the extract was washed with water, dried ($Na_2SO_4$), and evaporated; the residue was sublimed to provide 2,3,5,6-tetrafluoro-4-iodopyridine (0·43 g., 34% recovery) and 2-*amino*-3,5,6-*trifluoro*-4-*iodopyridine* (0·56 g., 73%) (Found: C, 22·0; H, 0·9; N, 10·1. $C_5H_2F_3IN_2$ requires C, 21·9; H, 0·7; N, 10·2%), m. p. 114—115°, $\lambda_{max.}$ (mull) 2·97, 3·03, 3·13 (triplet; N–H str.), and 6·68 μ (polyfluoropyridine nucleus), δ 15·6 (6-F), 44·4 (3-F), and 62·2 (5-F) (three band systems of equal intensity).

(d) *With copper.* The product obtained by heating 2,3,5,6-tetrafluoro-4-iodopyridine (1·5 g.) with copper-bronze (6·0 g.) in a 'Pyrex' ampoule at 200° for 27 hr. was extracted with ether (3 × 50 ml.). The ether extract was dried ($Na_2SO_4$) and evaporated. Sublimation of the residue afforded perfluoro-4,4′-bipyridyl (0·48 g., 59%), m. p. 82—83°, with correct i.r. spectrum.

(e) *With n-butyl-lithium.* A solution of n-butyl-lithium prepared from n-butyl bromide (4·0 g., 29·2 mmoles) and lithium (0·2 g.) in ether (75 ml.) was added dropwise during 30 min. to a cold (*ca.* −35°) solution of 2,3,5,6-tetrafluoro-4-iodopyridine (4·0 g., 14·4 mmoles) in a mixture of ether (100 ml.) and benzene (50 ml.). The reaction mixture was kept at −35° for 4 hr. then warmed to −10° and treated with an excess of powdered solid carbon dioxide. The product was washed with 2N-sodium hydroxide (2 × 10 ml.) and then water (2 × 15 ml.), and the combined aqueous washings were acidified with 2N-hydrochloric acid and extracted with ether. The ether extract was dried ($MgSO_4$) and evaporated, and the residue was sublimed (80°/< 1 mm.) to provide tetrafluoroisonicotinic acid (0·82 g., 4·2 mmoles, 65% based on 4-$IC_5F_4N$ consumed) with correct i.r. spectrum.[2] The organic phase from the preparation was distilled to give 2,3,5,6-tetrafluoro-4-iodopyridine (2·2 g., 55% recovery).

(f) *With sodium iodide.* A mixture of 2,3,5,6-tetrafluoro-4-iodopyridine (5·4 g., 19·5 mmoles), anhydrous sodium iodide (20·0 g., 133·3 mmoles), and dimethylformamide (10 ml.) was heated at 150° for 40 hr. in a 150-ml. 'Pyrex' ampoule. Water (20 ml.) and ether (15 ml.) were poured into the reaction vessel to extract the product; this was repeated four times. The ether extract was washed with saturated aqueous sodium thiosulphate (15 ml.) then with water (10 ml.), dried ($MgSO_4$), and distilled to provide 2,3,5,6-tetrafluoropyridine (1·2 g., 7·9 mmoles, 91% based on iodopyridine consumed), unchanged 2,3,5,6-tetrafluoro-4-iodopyridine (3·0 g., 10·8 mmoles, 55% recovery), and a sticky yellow solid (0·6 g.) (Found: C, 27·1; H, 0·3; N, 6·1%), which contained fluorine and iodine (Lassaigne test), infrared spectrum similar to that of the brown solid from the reaction between pentafluoropyridine, sodium iodide, and dimethylformamide at 150° for 40 hr.

2,3,5,6-Tetrafluoro-4-iodopyridine (3·4 g., 12·3 mmoles), anhydrous sodium iodide (12·0 g., 80·0 mmoles), and acetone (15 ml.), heated at 80° for 96 hr., gave, after working up as above, 2,3,5,6-tetrafluoropyridine (1·2 g., 7·9 mmoles, 78% based on iodopyridine consumed), 2,3,5,6-tetrafluoro-4-iodopyridine (0·6 g., 2·2 mmoles, 18% recovery), and a brown residue (0·2 g.) which was not examined. No mesityl oxide was detected (g.l.c.) in the products.

The product obtained by heating a mixture of pentafluoropyridine (3·3 g., 19·5 mmoles), 2,3,5,6-tetrafluoro-4-iodopyridine (5·4 g., 19·5 mmoles), sodium iodide (2·7 g.), and dimethylformamide (15 ml.) at 150° for 20 hr. was worked up as before, to give pentafluoropyridine (2·4 g., 14·2 mmoles, 73% recovery), 2,3,5,6-tetrafluoro-4-iodopyridine (5·2 g., 96% recovery), and perfluoro-4,4′-bipyridyl (0·49 g., 1·7 mmoles, 64% based on $C_5F_5N$ consumed), with correct i.r. and $^{19}F$ n.m.r. spectrum.

*Reactions of* 2,3,5,6-*Tetrafluoropyridylmagnesium Iodide.*—Reagents and apparatus must be dried carefully, and it is advisable to purify the 2,3,5,6-tetrafluoro-4-iodopyridine by sublimation just prior to use for optimum yields of product. All the experiments were carried out in an atmosphere of dry oxygen-free nitrogen.

(a) *With carbon dioxide.* A solution of 2,3,5,6-tetrafluoro-4-iodopyridine (2·0 g., 7·2 mmoles) in tetrahydrofuran (8 ml.) was added to magnesium (0·4 g., 16·5 mg.-atoms) in tetrahydrofuran (20 ml.) at room temperature. Reaction began 30 min. later, and the temperature of the mixture was lowered to *ca.* −15°; after 2 hr. at this temperature the mixture was treated with a fine stream of carbon dioxide for 3 hr. Without discontinuation of the passage of carbon dioxide, the mixture was then warmed to room temperature and set aside for 1 hr. The product was treated with 4N-sulphuric acid and the mixture was extracted with ether. The extract was dried ($MgSO_4$) and evaporated, to leave a residue which was sublimed under reduced pressure to provide 2,3,5,6-tetrafluoro-4-iodopyridine (1·1 g., 55% recovery), which sublimed at 20°/<1 mm., and tetrafluoroisonicotinic acid (0·3 g., 1·6 mmoles, 47% based on $C_5F_4NI$ consumed), which sublimed at 74°/<1 mm. (Found: C, 37·1; H, 0·5. Calc. for $C_6HF_4NO_2$: C, 36·9; H, 0·5%), with correct $^{19}F$ n.m.r. spectrum.

(b) *With water.* A few drops of a solution of 2,3,5,6-tetrafluoro-4-iodopyridine (2·75 g., 9·7 mmoles) in tetrahydrofuran (10 ml.) were added to magnesium (0·4 g., 16·5 mg.-atoms) in tetrahydrofuran (25 ml.) at room temperature. After 45 min. the reaction flask was warmed with the hand to start the reaction, and then the mixture was cooled to *ca.* −15° and the remainder of the 2,3,5,6-tetrafluoro-4-iodopyridine solution was added slowly. After 3·5 hr. at −15° and 1·5 hr. at −5°, the mixture was treated with 2N-sulphuric acid and worked up in standard fashion to provide spectroscopically pure (i.r.) 2,3,5,6-tetrafluoropyridine (0·67 g., 4·5 mmoles, 58% based on

$C_5F_4NI$ consumed) and 2,3,5,6-tetrafluoro-4-iodopyridine (0·61 g., 22% recovery).

(c) *With chlorotrimethylsilane.* The Grignard reagent was formed as in (b) from 2·0 g. (7·2 mmoles) of the iodopyridine, and 0·5 g. of magnesium in tetrahydrofuran (35 ml.). After 6 hr. at −15° under nitrogen, the Grignard reagent was treated with chlorotrimethylsilane (1·3 g., 12·2 mmoles) in tetrahydrofuran (5 ml.). The mixture was stirred at −15° for 2 hr., then at room temperature for 1 hr. It was hydrolysed and worked up by the usual methods to give *trimethyl-*(2,3,5,6-*tetrafluoropyridyl*)*silane* (0·77 g., 3·5 mmoles, 48%) (Found: C, 42·6; H, 4·2; N, 6·5. $C_8H_9F_4NSi$ requires C, 43·1; H, 4·0; N, 6·3%), b. p. 40°/*ca.* 0·5 mm., $\lambda_{max.}$ (liquid film) 3·36, 3·43 (C–H str.), 6·12, 6·84, 6·95, 7·04 (polyfluoropyridine nucleus), 7·26, 7·73, 7·95, 8·14, 10·69, 11·37, 11·79, 12·12, 12·98, 13·64, and 14·18 μ, δ 15·7 (2- and 6-F) and 53·4 (3- and 5-F) p.p.m., and a brown solid (0·2 g.) which was not examined.

(d) *With pentafluoropyridine.* Pentafluoropyridine (0·75 g., 4·4 mmoles) was added to a cold (−40°) solution of the Grignard reagent prepared by the addition of 2,3,5,6-tetrafluoro-4-iodopyridine (1·25 g., 4·5 mmoles) in tetrahydrofuran (1 ml.) to magnesium (0·22 g.) in tetrahydrofuran (9 ml.) at −20° followed by storage at −10 to −15° for 3 hr. The reaction mixture was stored at −40° for 3 hr. then hydrolysed with 2N-sulphuric acid and extracted with ether; the extract was washed with water, dried ($Na_2SO_4$), and evaporated, to leave a residue which was sublimed under reduced pressure to provide 2,3,5,6-tetrafluoro-4-iodopyridine (0·10 g., 8% recovery) and perfluoro-4,4′-bipyridyl (0·40 g., 1·3 mmoles; 32% based on $C_5F_4NI$ consumed), m. p. 82—83°, both of which were identified by i.r. spectroscopy.

(e) *With benzophenone.* A solution of 2,3,5,6-tetrafluoro-4-iodopyridine (2·0 g., 7·2 mmoles) in tetrahydrofuran (10 ml.) was added to magnesium (0·4 g.) in tetrahydrofuran (10 ml.) at −15°. Reaction occurred within 5 min., and the temperature of the reaction mixture was lowered to −20°. After 5 hr. at this temperature, the Grignard solution was treated with benzophenone (1·5 g., 8·7 mmoles) in tetrahydrofuran (5 ml.); the mixture was stirred at −20° for 3 hr., warmed to room temperature, hydrolysed with 2N-sulphuric acid (10 ml.), and extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and distilled to provide 2,3,5,6-tetrafluoro-4-iodopyridine (0·68 g., 34% recovery), benzophenone (0·81 g., 53% recovery), and a residue (0·96 g.), b. p. 150—152°/*ca.* 0·5 mm. The last, shown by $^1H$ and $^{19}F$ n.m.r. spectroscopy to be the required product contaminated with benzophenone, was dissolved in hot ethanol (20 ml.) and the solution was stirred with charcoal, filtered, treated with water (10 ml.), and extracted with ether. The extract was evaporated to give *diphenyl-*(2,3,5,6-*tetrafluoropyridyl*)*methanol* (0·47 g., 30% based on $C_5F_4NI$ consumed) (Found: C, 65·1; H, 3·5; N, 4·0. $C_{18}H_{11}F_4NO$ requires C, 64·9; H, 3·3; N, 4·2%), a yellow solid, m. p. 106—107°, δ (25% solution in benzene) 13·0 (2- and 6-F), 59·2 (3- and 5-F) p.p.m.

(f) *With benzaldehyde.* Tetrafluoro-4-iodopyridine (1·5 g., 5·4 mmoles) in tetrahydrofuran (20 ml.) was added to a stirred suspension of magnesium (0·40 g.) in cold (−15°) tetrahydrofuran (50 ml.). Ethylene dibromide (0·5 ml.) was added to the mixture and during the subsequent reaction the temperature was kept below −10°. After 1 hr. the mixture was cooled to −15°, stirred at this temperature for 1 hr., and then treated (dropwise) with a solution of benzaldehyde (0·40 g., 3·8 mmoles) in tetrahydrofuran (4·0 ml.). The mixture was stirred at −10 to −5° for 45 min., then hydrolysed with 3N-sulphuric acid (10·0 ml.) and extracted with ether (4 × 20 ml.); the extract (dried with $MgSO_4$) was evaporated to give a tarry residue, which was sublimed at 80°/*ca.* 1 mm. to provide *phenyl-*(2,3,5,6-*tetrafluoropyridyl*)*methanol* (0·40 g., 1·6 mmoles, 30% based on $C_5F_4NI$) (Found: C, 55·9; H, 2·5; N, 5·2. $C_{12}H_7F_4NO$ requires C, 56·0; H, 2·7; N, 5·5%), m. p. 100—101°, δ (20% solution in tetrahydrofuran) 14·9 (2- and 6-F) and 67·3 (3- and 5-F) p.p.m.

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