Polyfluoro-heterocyclic Compounds. Part XII.[1] Preparation and Nucleophilic Substitution of Tetrafluoropyridazine

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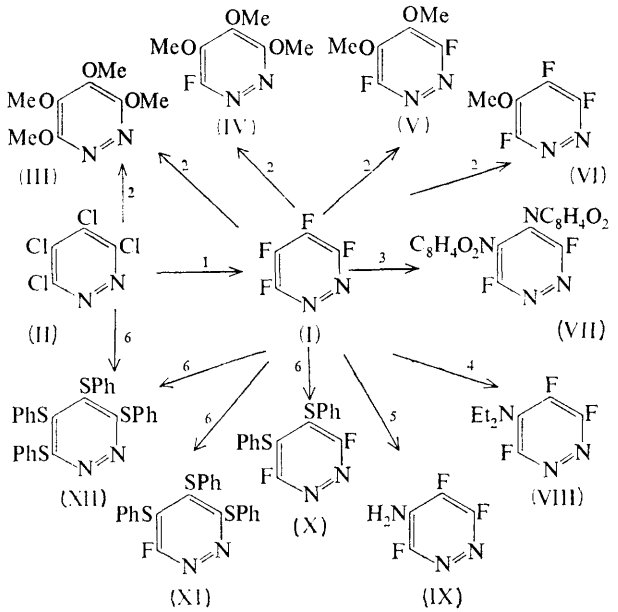
The known method of preparing perfluoro-aromatic nitrogen heterocyclic compounds from their perchloro-analogues by exchange with potassium fluoride in the absence of solvent has been extended to the pyridazine system. Tetrafluoropyridazine readily undergoes nucleophilic substitution of all the fluorine atoms, those at positions 4 and 5 being the most reactive. These reactions have been illustrated using various nucleophilic reagents in which the attacking atoms are nitrogen, oxygen, or sulphur. The factors affecting the orientation and reactivity of tetrafluoropyridazine, and of related perfluoro-aromatic nitrogen heterocyclic compounds, in nucleophilic substitution have been discussed.

PERFLUORO-DERIVATIVES of several monocyclic [2-4] and bicyclic [5] nitrogen heterocyclic compounds have been prepared by the action of potassium fluoride on the corresponding polychloro-compounds. These perfluoro-heterocyclic compounds are of particular interest in studies of nucleophilic aromatic substitution. We report [6] the extension of this preparative method to the pyridazine system, and some nucleophilic substitution reactions of tetrafluoropyridazine (I).



Reagents: 1, KF, 310°; 2, NaOMe–MeOH; 3, potassium phthalimide in *N*-methyl-2-pyrrolidone; 4, Et_2NH in *N*-methyl-2-pyrrolidone; 5, NH_3 aq.; 6, NaSPh in *N*-methyl-2-pyrrolidone

At the start of our work tetrachloropyridazine (II) had previously been prepared [7] from dichloromaleic anhydride but the high cost of this intermediate made this route unpractical. We therefore developed a cheaper synthesis, by chlorinating the readily available 3,6-dichloropyridazine [8] with phosphorus pentachloride at high temperature and pressure.

The reaction between tetrachloropyridazine (II) and anhydrous potassium fluoride, in a sealed tube at 310°, gives tetrafluoropyridazine (I) in 50—60% yield. This relatively low reaction temperature (the optimum temperature for the analogous preparation [2] of pentafluoropyridine is 470°) reflects the greatly increased ease of nucleophilic substitution of the 1,2-diazine system. The fast reactions between tetrafluoropyridazine and aqueous ammonia or methoxide ion at 0° also show that it is more reactive then pentafluoropyridine, while its ease of hydrolysis and high reactivity are again indicated by its pungent and lachrymatory nature. Like pentafluoropyridine [2,9] and tetrafluoropyrimidine,[3] the most easily substituted fluorine atoms of tetrafluoropyridazine are those at C-4 and C-5, *para* to nitrogen.

Each of the fluorine atoms of tetrafluoropyridazine can be consecutively replaced by nucleophilic reagents in the sequence 4-, 5-, (3-, 6-). Thus, each of the methoxy-derivatives (III)—(VI) is produced when the appropriate molecular proportion of sodium methoxide is added to tetrafluoropyridazine in methanol at 0°, although the fourth fluorine atom is replaced only slowly at this temperature. Initial substitution of the 4-fluorine is effected by ammonia,[6] and diethylamine, giving the amines (IX) and (VIII), and also by thiophenoxide and phthalimide anions, while Stone and his co-workers have shown [10] that this position is attacked by metal carbonyl anions.

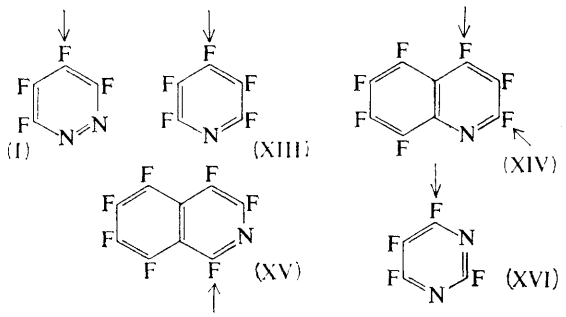
Reaction between tetrafluoropyridazine and one molecular proportion of sodium thiophenoxide in *N*-methyl-2-pyrrolidone at 0° gives only the 4,5-di-

[1] Part XI R. D. Chambers, D. Lomas, and W. K. R. Musgrave, *J. Chem. Soc.* (*C*), 1968, 625.
[2] (*a*) R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 1964, 3573; (*b*) R. E. Banks, R. N. Haszeldine, J. V. Latham, and I. M. Young, *ibid.*, 1965, 594.
[3] R. E. Banks, D. S. Field, and R. N. Haszeldine, *J. Chem. Soc.* (*C*), 1967, 1822.
[4] R. D. Chambers, J. A. H. MacBride, and W. K. R. Musgrave, *Chem. and Ind.*, 1966, 1721.
[5] R. D. Chambers, M. Hole, B. Iddon, W. K. R. Musgrave, and R. A. Storey, *J. Chem. Soc.* (*C*), 1966, 2328.
[6] R. D. Chambers, J. A. H. MacBride, and W. K. R. Musgrave, *Chem. and Ind.*, 1966, 904.
[7] P. Coad, R. A. Coad, S. Clough, J. Hyepock, R. Salisbury, and C. Wilkins, *J. Org. Chem.*, 1963, **28**, 218, and references there cited.
[8] R. H. Mizzoni and P. E. Spoerri, *J. Amer. Chem. Soc.*, 1951, **73**, 1873.
[9] (*a*) R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.*, 1964, 3736; (*b*) R. E. Banks, J. E. Burgess, W. M. Cheng, and R. N. Haszeldine, *ibid.*, 1965, 575.
[10] J. Cooke, M. Green, and F. G. A. Stone, *Inorg. Nuclear Chem. Letters*, 1967, **3**, 47.

substituted product (X) and unchanged diazine. Similarly, the addition of three molecular proportions of thiophenoxide under the same conditions gives a mixture of the di-, tri-, and tetra-substituted derivatives (X), (XI), and (XII); at −10° only the 4- and 5-fluorine atoms are replaced. These results are in accordance with the 'activating' effect of an initial phenylthio-substituent towards further substitution of fluorine from aromatic polyfluoro-compounds, which has been described recently [11] for *para*-substitution; the present work provides an example of '*ortho*-activation' by this group.

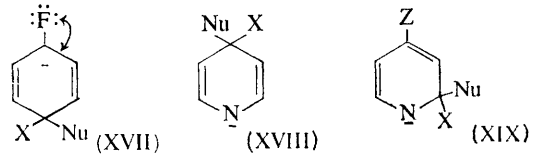
Our results, and those obtained recently in the re-examination of tetrafluoropyrimidine,[3] prompt us to make a new appraisal of the factors governing nucleophilic substitution in perfluoro-aromatic nitrogen heterocyclic compounds.

Each of the perfluoro-heterocyclic compounds (I) and (XIII)—(XVI) gives monosubstituted derivatives [2,3,9,12] by nucleophilic attack at the positions indicated by arrows, and these are also the positions where a single halogen [13–15] or methyl sulphonyl [16] group is most susceptible to nucleophilic displacement from the corresponding perhydro-compounds. We therefore conclude that the orientation of substitution in the perfluoro-heterocycles is controlled by the ring nitrogen atom(s) and is not primarily governed by the fluorine atoms in the molecule.



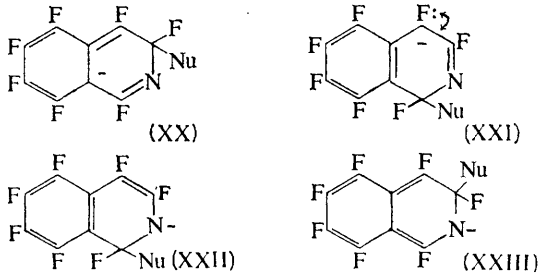
The orientation of nucleophilic substitution in polyfluorobenzene systems has been successfully explained in terms of the $I\pi$ effect of fluorine,[17,18] which depends on repulsion between non-bonding electron pairs on fluorine and the adjacent carbanionic carbon atom (XVII). It is assumed that the electron density at the position *para* to the entry of the nucleophile is greatest and that the transition state is similar to the intermediate (XVII). This type of argument has recently been extended,[3] however, to account for the orientation of substitution in some polyfluoro-aromatic nitrogen heterocyclic compounds.

While it is clear that this $I\pi$ effect should be considered in the nucleophilic substitution of these compounds, it appears that the localisation energies of the transition states are much more influenced by the *stabilising*



effect of ring nitrogen. This is indicated by forms like (XVIII) and (XIX). A high electron density on nitrogen in the transition state inevitably means a relatively lower electron density on the carbon atoms compared with substitution in a polyfluorobenzene, and hence a diminished importance of $I\pi$ destabilisation by fluorine in the heterocyclic system. This is quite consistent with the observed order of reactivity, hexafluorobenzene < pentafluoropyridine < heptafluoro-quinoline and -isoquinoline < tetrafluoropyridazine, and orientation of substitution in these systems.

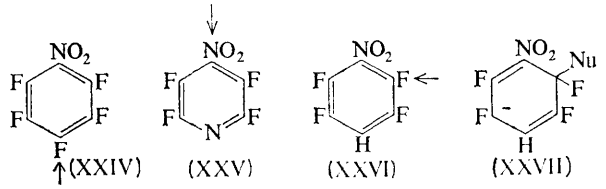
Assuming control by the $I\pi$ effect of fluorine, it may be predicted that the 4-positions of pentafluoropyridine, tetrafluoropyridazine, and tetrafluoropyrimidine will be the most reactive, and that positions 2 and 4 of perfluoroquinoline may be of similar reactivity. This approach appears, however, to predict that heptafluoroisoquinoline would be attacked at C-3, through a transition state represented by (XX). This is analogous to the observed [19] β-substitution of octafluoronaphthalene. Instead, 1-substitution occurs in spite of the apparently opposed $I\pi$ effect (XXI); this indicates control of orientation by nitrogen, with a high electron density as in (XXII). Substitution at C-1, through (XXII), in preference to C-3, through (XXIII), indicates a lower localisation energy for the transition state represented by (XXII), probably because it maintains the aromaticity of the carbocyclic ring.



Another result,[20] which indicates that the factors governing substitution in polyfluorobenzenes cannot be applied directly to perfluoro-aromatic nitrogen heterocyclic systems, is obtained when each of the nitro-compounds (XXIV)—(XXVI) is treated with sodium

[11] J. M. Birchall, M. Green, R. N. Haszeldine, and A. D. Pitts, *Chem. Comm.*, 1967, 338.
[12] R. D. Chambers, M. Hole, W. K. R. Musgrave, R. A. Storey, and B. Iddon, *J. Chem. Soc.* (*C*), 1966, 2331.
[13] N. B. Chapman and D. Q. Russell-Hill, *J. Chem. Soc.*, 1956, 1563.
[14] M. L. Belli, G. Illuminati, and G. Marino, *Tetrahedron*, 1963, **19**, 345.
[15] M. Bellas and H. Suschitzky, *J. Chem. Soc.*, 1964, 4561.
[16] G. B. Barlin and W. V. Brown, *J. Chem. Soc.* (*B*), 1967, 648.
[17] D. T. Clark, J. N. Murrell, and J. M. Tedder, *J. Chem. Soc.*, 1963, 1250.
[18] J. Burdon, *Tetrahedron*, 1965, **21**, 3373.
[19] B. Gething, C. R. Patrick, and J. C. Tatlow, *J. Chem. Soc.*, 1962, 186.
[20] R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.* (*C*), 1966, 220.

methoxide. Pentafluoronitrobenzene (XXIV) is substituted at C-4 (indicated by arrow) while 4-nitrotetra-



fluoropyridine (XXV) suffers, predominantly, replacement of the nitro-group. If both of these reactions were controlled by $I\pi$ interaction it would be expected that the nitro-group of 1,2,4,5-tetrafluoro-3-nitrobenzene (XXVI) would also be replaced. In fact, only substitution of fluorine *ortho* to the nitro-group is observed.

The different behaviour of the nitropyridine (XXV) and the hydro-compound (XXVI) shows that the position of substitution is due to extreme stabilisation of a transition state in which the high electron density can be placed on ring-nitrogen, or a nitro-group, rather than to avoidance of transition states destablished by '$I\pi$ interaction' of fluorine as in (XXVII).

EXPERIMENTAL

Infrared spectra were measured on either a Grubb Parsons spectromaster or GS2A spectrophotometer, ultraviolet spectra on a Unicam SP 800, mass spectra on an A.E.I. M.S.9 spectrometer, and n.m.r. spectra on a Perkin-Elmer R10 operating at 60 Mc./sec., using hexafluorobenzene as internal standard (downfield shifts are quoted as negative). Thin-layer chromatography was on Kieselgel-G (baked at 100° for 40 min.) using benzene as eluent and iodine vapour for detection. Solvents were evaporated using a rotary evaporator, and ether solutions were dried over sodium sulphate. *N*-Methyl-2-pyrrolidone was dried over barium oxide.

Tetrachloropyridazine.—3,6-Dichloropyridazine [8] (70 g.) and phosphorus pentachloride (420 g.) were closed *in vacuo* in a nickel-lined bomb (480 ml. capacity) and heated to 300—310° for 17 hr. The bomb was cooled, vented, and its contents added to ice. The mixture was extracted with ether, and the extract washed with water, dried, and evaporated. The residue was recrystallised from methylated spirits (150 ml.), to give tetrachloropyridazine (73·5 g., 70%), as light brown plates, m.p. 85—87°. Sublimation at 100°/0·05 mm. and a further recrystallisation from ethanol gave a colourless sample, m.p. 87—89° (lit.,[7] 85—86°) (Found: C, 22·2; Cl, 65·0. Calc. for $C_4Cl_4N_2$: C, 22·0; Cl, 65·1%).

Tetrafluoropyridazine.—Tetrachloropyridazine (15·0 g.) and freshly dried potassium fluoride (110 g.) were sealed in an evacuated thick-walled glass tube [33 × 2 cm. (internal diameter)], heated to 305—310° for 8 hr., cooled, and immersed in liquid air. The drawn-out stem of the tube was connected to two liquid-air traps, the system was evacuated, isolated, and the stem of the tube broken inside the rubber connection. The tube was warmed gently and the product (4·5—6·5 g.) which collected in the traps was distilled *in vacuo*. The fraction b.p. 58—60°/6·5 cm. (4·0—6·0 g., 40—60%) was shown by g.l.c. (dinonyl phthalate, 100°) to be pure *tetrafluoropyridazine* [Found: C, 31·1; F, 49·4%; *M* (mass spectrometer), 152. $C_4F_4N_2$ requires C, 31·6; F, 50·0%; *M*, 152], $\nu_{max.}$ (film), 2941w, 2632w, 1953w, 1779w, 1645, 1587, 1497, 1445vs, 1412, 1355, 1340, 1279, 1196, 1126, 1101vs, 1053, 1016vs, 990w, 971, 926, 855w, 763, 719w, 676, 662, 654, 538w, and 488 cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 248 and 283·5 mμ (log ε 4·15 and 3·49), $\lambda_{max.}$ (ethanol) 246·5 and *ca.* 270 (infl.) mμ (log ε 4·15 and 3·56). The ^{19}F n.m.r. spectrum of the pure liquid showed two absorptions of equal intensity at −18·1 and −71·7 p.p.m.

3,5,6-*Trifluoro*-4-*methoxypyridazine*.— Tetrafluoropyridazine (2·0 g.) in methanol (10 ml.) was treated dropwise with methanolic sodium methoxide (14·6 ml., 1·0 mol.; 0·9M) during 45 min. with vigorous stirring at 0°. The mixture was stirred for a further 10 min. at 0°, allowed to reach room temperature during 10 min., evaporated to *ca.* 3 ml., and extracted with ether. The extract was washed with water, dried, evaporated, and the residue was distilled *in vacuo*, to give the *monomethoxy-derivative* (1·70 g., 80%), b.p. 74—76°/3·0 mm. [Found: C, 36·9; H, 2·05; F, 35·4%; *M* (mass spec.), 164. $C_5H_3F_3N_2O$ requires C, 36·6; H, 1·85; F, 34·8%; *M*, 164], $\nu_{max.}$ (film) 3003, 2959, 2890, 1618, 1577, 1508—1425vs (multiplet), 1372, 1297, 1202, 1186, 1107, 1046, 1025, 990, 952, 840w, 757, 719w, 688, 667, 640, and 565w cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 251 and *ca.* 275 (infl.) mμ (log ε 3·34 and 2·74). The ^{19}F n.m.r. spectrum of the pure liquid showed absorption at −15·0, −65·5, and −73·7 p.p.m.

3,6-*Difluoro*-4,5-*dimethoxypyridazine*.—Tetrafluoropyridazine (1·5 g.) in methanol (7·5 ml.) was treated, during 1 hr., with methanolic sodium methoxide (2·0 mol.) as in the previous experiment, and the *dimethoxy-derivative* (1·24 g., 70%), similarly isolated, had b.p. 78—80°/0·52 mm. [Found: C, 40·8; H, 3·4; F, 21·8%; *M* (mass spec.), 176. $C_6H_6F_2N_2O_2$ requires C, 40·9; H, 3·4; F, 21·6%; *M*, 176], $\nu_{max.}$ (film) 3012, 2959, 2849, 1623, 1585, 1567sh, 1460, 1397vs, 1287, 1198, 1111vs, 1050vs, 985w, 954, 930w, 775w, 752, 680sh, 665, and 630w cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 230·5 and 253 (infl.) mμ (log ε 3·69 and 3·32). The ^{19}F n.m.r. spectrum of the pure liquid showed absorption at −70·6 p.p.m.

3-*Fluoro*-4,5,6-*trimethoxypyridazine*.— Tetrafluoropyridazine (697 mg.) in methanol (3·8 ml.) was treated, during 45 min., with methanolic sodium methoxide (3·0 mol.) as in the previous two preparations, and the *trimethoxy-derivative* (475 mg., 55%), similarly isolated, had b.p. 85—86°/0·4 mm. m.p. 29—31° [Found: C, 44·4; H, 4·8; F, 10·5%; *M* (mass spec.) 188. $C_7H_9FN_2O_3$ requires C, 44·65; H, 4·8; F, 10·1%; *M*, 188], $\nu_{max.}$ (film) 2985, 2941, 2833, 1600, 1555, 1481—1456 (multiplet), 1427, 1385vs, 1285, 1209, 1157, 1119, 1062, 1002, 957, 915, 778w, 750, and 683w cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 231·5 and 263 mμ (log ε 3·67 and 3·36). The ^{19}F n.m.r. spectrum (acetone) showed absorption at −65·6 p.p.m.

Tetramethoxypyridazine.—(a) *From tetrafluoropyridazine*. Tetrafluoropyridazine (152 mg.) in methanol (0·7 ml.) was treated dropwise with methanolic sodium methoxide (5·0 mol.) during 45 min. with stirring at *ca.* 20°. The mixture was stirred for a further 2 hr. and then at 60° for 1 hr. The methanol was evaporated and the residue was sublimed at 100°/0·005 mm., to give *tetramethoxypyridazine* (188 mg., 95%), m.p. 47—48·5° [Found: C, 47·7; H, 5·85%; *M* (mass spec.), 200. $C_8H_{12}N_2O_4$ requires C, 48·0; H, 6·0%; *M*, 200], $\nu_{max.}$ (KBr) 2985, 2950, 2849, 1901w, 1605, 1546w, 1460, 1372, 1274, 1206, 1189, 1139, 1106, 1076, 1026w, 997, 930, 905, 781w, 752, 691, and 500 cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 231 (infl.) and 273·5 mμ (log ε 3·72 and 3·39).

(b) *From tetrachloropyridazine.* Tetrachloropyridazine (1·09 g.) in methanol (10·0 ml.) was treated dropwise with methanolic sodium methoxide (5·0 mol.) during 30 min. with stirring at *ca.* 20°. The mixture was boiled under reflux for 3 hr., the methanol evaporated, and the residue sublimed at 100°/0·005 mm., to give tetramethoxypyridazine (810 mg., 80%), m.p. and mixed m.p. 47—48·5°.

Reactions with Sodium Thiophenoxide.—(a) *3,6-Difluoro-4,5-bisphenylthiopyridazine.* Tetrafluoropyridazine (2·02 g.) in *N*-methyl-2-pyrrolidone (20 ml.) was treated dropwise with sodium thiophenoxide (3·52 g., 2 mol.) in the same solvent during 45 min. with stirring at 0°. The mixture was stirred for a further 30 min., extracted with ether, and the extract washed with water, dried, and evaporated. The residue (3·65 g.) was recrystallised from a mixture of benzene and cyclohexane, to give the *bisphenylthio-derivative* (2·38 g., 55%), m.p. 97—99°, unchanged on recrystallisation from ethanol [Found: C, 57·3; H, 3·1; F, 12·0%; *M* (mass spec.), 332. $C_{16}H_{10}F_2N_2S_2$ requires C, 57·5; H, 3·0; F, 11·45%; *M*, 332], $\nu_{max.}$ (KBr) 3030, 1580w, 1531w, 1499, 1477, 1441, 1383vs, 1359sh, 1311, 1085w, 1071w, 1021, 1000, 952, 840, 746, 741, 700, 688, 667, 650, and 491 cm.$^{-1}$, $\lambda_{max.}$ (cyclohexane) 242·5 and 310 mμ (log ε 4·11 and 3·92). ^{19}F n.m.r. (acetone) showed absorption at −87·9 p.p.m.

(b) *Tetrakisphenylthiopyridazine.* (i) *From tetrafluoropyridazine.* Tetrafluoropyridazine (152 mg.) in *N*-methyl-2-pyrrolidone (1·0 ml.) was treated dropwise with sodium thiophenoxide (594 mg., 4·5 mol.) in the same solvent during 5 min. with stirring at *ca.* 20°. The mixture was stirred for a further 2 hr., poured into water, and the precipitate was washed with water, ether, and ethanol, and dried, to give *tetrakisphenylthiopyridazine* (435 mg., 85%), m.p. 204—207°. Recrystallisation from nitromethane gave pale yellow woolly needles, m.p. 208—210° [Found: C, 65·0; H, 3·6%; *M* (mass spec.), 512. $C_{28}H_{20}N_2S_4$ requires C, 65·6; H, 3·95%; *M*, 512], $\nu_{max.}$ (KBr) 3030, 1582, 1475, 1466, 1250vs, 1181w, 1156w, 1094w, 1073, 1024, 1002, 917w, 847, 781, 758, 740vs, 707, 688, 607, 582w, 559, 544, and 514 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 256·5 and 287 (infl.) mμ.

(ii) *From tetrachloropyridazine.* Tetrachloropyridazine (1·02 g.) in *N*-methyl-2-pyrrolidone (5·0 ml.) was treated dropwise with sodium thiophenoxide (2·78 g., 4·5 mol.) in the same solvent during 5 min. with stirring at *ca.* 20°. The mixture was stirred for a further 4 hr., and the tetrakisphenylthio-derivative, isolated and purified as in the previous experiment, had m.p. and mixed m.p. 208—210°.

(c) *3-Fluoro-4,5,6-trisphenylthiopyridazine.* Tetrafluoropyridazine (152 mg., 1·0 mmole) in *N*-methyl-2-pyrrolidone (1·0 ml.) was treated dropwise with sodium thiophenoxide n the same solvent (3·0 ml., 3·0 mmoles) during 30 min. with stirring at 0°. The mixture was stirred for a further 20 min. at 0°, diluted with ether, and poured into water. The precipitate of tetrakisphenylthiopyridazine (107 mg., 0·2 mmole) was washed with ether and water and dried, m.p. 203·5—206°. The filtrate was separated, and the ethereal layer was washed with water, dried, and evaporated. The residue (285 mg.) was extracted with warm ethanol (2 ml.; *ca.* 50°) and filtered; the solid which separated from the filtrate in the cold was re-extracted in the same way. The two less-soluble fractions (45 mg.) were combined and recrystallised from ethanol, to give pale yellow needles of *3-fluoro-4,5,6-trisphenylthiopyridazine*, m.p. 140·5—143° [Found: C, 62·7; H, 3·2%; *M* (mass spec.), 422. $C_{22}H_{15}FN_2S_3$ requires C, 62·5; H, 3·55%; *M*, 422], $\nu_{max.}$ (KBr) 3049w, 1572w, 1468, 1437, 1339, 1292, 1208, 1175w, 1149w, 1066, 1020, 995, 920, 840w, 780, 755, 743, 698, 685, 676sh, 619, and 543 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 253 and *ca.* 300 (infl.) mμ. ^{19}F n.m.r. ($CHCl_3$) showed absorption at −83·5 p.p.m. The filtrates from the extraction were combined and evaporated, and the residue was found (n.m.r.) to be mainly bisphenylthiopyridazine with a small amount (*ca.* 30 mg.) of the trisubstituted derivative.

(d) *With 1 mol. of reagent.* Tetrafluoropyridazine (157 mg.) in *N*-methyl-2-pyrrolidone was treated dropwise with sodium thiophenoxide in the same solvent (1·0 ml., 1 mol.) during 15 min. with stirring at 0°. The crude product (176 mg.), isolated as in (a), was washed with light petroleum (b.p. 40—60°) and twice recrystallised from ethanol, to give 3,6-difluoro-4,5-bisphenylthiopyridazine (110 mg., 67% on sodium thiophenoxide), m.p. and mixed m.p. 97—99°. No other involatile component was detected in the crude product by t.l.c. Tetrafluoropyridazine (17 mg.) was recovered from the light petroleum washings.

3,6-Difluoro-4,5-diphthalimidopyridazine.— Tetrafluoropyridazine (1·0 g.) in *N*-methyl-2-pyrrolidone (15 ml.) was treated with potassium phthalimide (2·44 g., 2 mol.) during 7 min. with stirring at *ca.* 20°. The mixture was stirred for *ca.* 48 hr., diluted with water, and the precipitate (1·34 g.) was recrystallised from nitromethane, to give the *diphthalimido-derivative* (838 mg., 30%), m.p. 326—328° (decomp.) [Found: C, 58·8; H, 1·75; F, 9·1%; *M* (mass spec.), 406. $C_{20}H_8F_2N_4O_4$ requires C, 59·2; H, 1·95; F, 9·35%; *M*, 406], $\nu_{max.}$ (KBr) 1799, 1745, 1587w, 1479, 1425, 1368, 1351, 1302, 1256, 1245, 1205w, 1171w, 1151, 1100, 1082, 953, 877, 794, 781, 763w, 714, 704w, 676, 662, 641, 606, 529, and 498w cm.$^{-1}$. ^{19}F n.m.r. (Me_2SO) showed absorption at −81·4 p.p.m.

4-Amino-3,5,6-trifluoropyridazine.—Tetrafluoropyridazine (2·0 g.) was treated dropwise with aqueous ammonia (*d* 0·880; 4·0 ml.) during 20 min. with stirring at 0°. The mixture was stirred for a further 10 min. at 0°, and the precipitate was recrystallised from water and sublimed at 100°/0·1 mm., to give the *amino-derivative* as needles (1·75 g., 90%), m.p. 89·5—91° [Found: C, 32·1; H, 1·45; F, 38·1%; *M* (mass spec.), 149. $C_4H_2F_3N_3$ requires C, 32·2; H, 1·35; F, 38·2%; *M*, 149], $\nu_{max.}$ (KBr) 3333, 3175, 2924w, 2857w, 1647, 1621, 1585, 1515w, 1453, 1385, 1319, 1264w, 1195, 1183sh, 1115, 953, 801w, 769, 697, and 660 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 251 (infl.) and 269 mμ (log ε 4·66 and 4·77). ^{19}F n.m.r. (CCl_4) showed absorption at −8·0, −60·1, and −70·8 p.p.m.

4-Diethylamino-3,5,6-trifluoropyridazine.— Tetrafluoropyridazine (312 mg.) in *N*-methyl-2-pyrrolidone (2·0 ml.) was treated dropwise with diethylamine (1·0 ml.) during 10 min. with stirring at *ca.* 18°. The mixture was stirred for a further 15 min., diluted with ether, washed with 2N-hydrochloric acid and water, and dried. The ether was evaporated and the residue was distilled *in vacuo*, to give the *diethylamino-derivative*, a pale yellow oil (380 mg., 90%), b.p. 64—66°/0·005 mm. [Found: C, 47·1; H, 4·75; F, 28·1%; *M* (mass spec.), 205. $C_8H_{10}F_3N_3$ requires C, 46·8; H, 4·9; F, 27·8%; *M*, 205], $\nu_{max.}$ (film) 2976, 2924, 1595, 1558, 1497, 1473, 1449, 1408, 1383, 1355, 1295, 1272, 1200, 1188, 1094, 1072sh, 1015, 980, 917w, 842, 825, 747, 660sh, 655, and 562w cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 263·5 and 293·5 mμ (log ε 3·82 and 3·92). ^{19}F n.m.r. (CCl_4) showed absorption at −14·9, −59·9, and −79·9 p.p.m.

[8/423 *Received, March 25th,* 1968]