Polyhalogeno-aromatic Compounds. Part XXII.[1] Some Reactions of Tetrachloro-4-methylsulphonylpyridine and Related Compounds [2]

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Tetrachloro-4-methylsulphonylpyridine (1a) reacted with small nucleophiles (*e.g.* NaCN, NaOH, NaOMe, and $MeNH_2$) by exclusive displacement of the methylsulphonyl group, with *NN*-dimethylamine by exclusive substitution in the 2-position, and with pyrrolidine by preferential substitution in the 2-position. With lithium aluminium hydride, compound (1a) gave a mixture of 2,3-dichloro-4-methylthiopyridine (major product), 2,3,6-trichloropyridine, and 2,3,6-trichloro-4-methylthiopyridine (trace). The mechanism of this reaction is discussed. Some reactions of tetrachloro-4-methylsulphinylpyridine and of the corresponding 4-methylthio-compound are also reported. Tetrachloro-2-dimethylamino- (and pyrrolidino-)pyridine reacted with potassium hydrogen sulphide in the 4-position. The resulting 4-mercapto-compounds were methylated, and 2,3,5-trichloro-6-dimethylamino-4-methylthiopyridine was oxidised with peroxyacetic acid to give 2,3,5-trichloro-6-dimethylamino-4-methylsulphinylpyridine.

BARLIN and BROWN [3,4] have studied the nucleophilic replacement reactions of a large number of methylsulphonyl-, methylsulphinyl-, and methylthio-substituted nitrogen heterocycles and have demonstrated the usefulness of the methylsulphonyl compounds as synthetic intermediates.[4] In continuation of our studies of the reactions of sulphur derivatives of polychloropyridines [5] we now report some nucleophilic substitution reactions of tetrachloro-4-methylsulphonylpyridine (1a) and the corresponding methylsulphinyl- (1b) and methylthio-compounds (1c). From a consideration of previous work,[1] small nucleophiles would be expected to displace preferentially the sulphur substituent in compounds (1a) and (1b), whilst larger nucleophiles would preferentially displace chlorine in the 2-position. The methylthio-compound (1c) would be expected to undergo exclusive substitution in the 2-position. However, the strong inductive electron-withdrawing effect of the sulphur substituent in (1a) and (1b) coupled in some cases with hydrogen bonding of the incoming nucleophile to the substituent can result in substitution in the 3-position. Tetrafluoro-4-nitropyridine, for example, reacts with ammonia to give 3-amino-2,5,6-trifluoro-4-nitropyridine as the major product,[6] 2,3,5,6-tetrafluoronitrobenzene with sodium methoxide gives exclusively 2,3,6-trifluoro-5-methoxy-4-nitrobenzene,[6] and the *N*-oxides (2) are substituted by amines exclusively in the *ortho*-positions.[7] Tetrachloro-4-nitropyridine is, however, found to react mainly by displacement of the nitro-group.[8]

Reactions of Tetrachloro-4-methylsulphonylpyridine.—The sulphone (1a) reacted with aqueous sodium hydroxide, methanolic sodium methoxide, and ethanolic methylamine under reflux in each case by exclusive displacement of the methylsulphonyl group to give excellent yields of compounds (1e—g). With sodium cyanide in boiling dimethylformamide [4] it gave a tar from which a low yield (35·5%) of pentachloropyridine

(1) a; R = SO_2Me
b; R = SOMe
c; R = SMe
d; R = SH
e; R = OH
f; R = OMe
g; R = NHMe
h; R = CN
i; R = C(:NH)·OEt
j; R = pyrrolidino

(2) X = $[CH_2]_{2-4}$ or $\cdot CH_2 \cdot O \cdot CH_2 \cdot$

(3) a; R = NMe_2
b; R = pyrrolidino

(4) a; R = Cl
b; R = NMe_2
c; R = pyrrolidino
d; R = $CH_2 \cdot COMe$

(5) a; R = NMe_2
b; R = pyrrolidino

[1] Part XXI, G. E. Chivers and H. Suschitzky, *J. Chem. Soc.* (*C*), 1971, 2867, and earlier papers in this Series.
[2] Presented at the International Symposium on Organic Polyhalogen Compounds, University of Salford, April 5th and 6th, 1971.
[3] G. B. Barlin and W. V. Brown, *J. Chem. Soc.* (*C*), 1969, 921; 1968, 1435.
[4] G. B. Barlin and W. V. Brown, *J. Chem. Soc.* (*C*), 1967, 2473.
[5] E. Ager, B. Iddon, and H. Suschitzky, *J. Chem. Soc.* (*C*), 1970, 1530.
[6] R. D. Chambers, J. Hutchinson, and W. K. R. Musgrave, *J. Chem. Soc.* (*C*), 1966, 220.
[7] M. Bellas, D. Price, and H. Suschitzky, *J. Chem. Soc.* (*C*), 1967, 1249.
[8] S. M. Roberts and H. Suschitzky, *J. Chem. Soc.* (*C*), 1968, 2844.

was isolated. However, when a solution of (1a) in the same solvent was kept for a week at room temperature, tetrachloro-4-cyanopyridine (1h) (23%) was obtained, and a similar reaction carried out in aqueous ethanol gave a mixture of the nitrile (1h) (22%) and the ethyl pyridine-4-carboximidate (1i) (65·5%). The formation of the latter can be attributed to addition of ethanol to the nitrile group of (1h).[9]

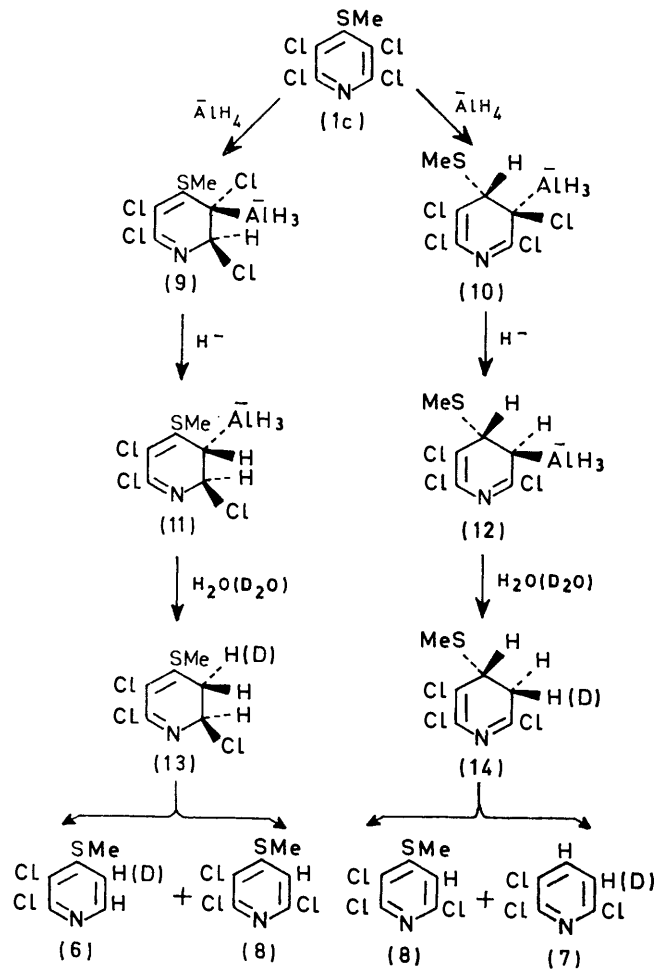
With *NN*-dimethylamine in ethanol, compound (1a) gave exclusively the 2-dimethylamino-derivative (3a), whilst with pyrrolidine in the same solvent a mixture of the 2-pyrrolidino-compound (3b) (38%) and tetrachloro-4-pyrrolidinopyridine (1j) (33·5%) was obtained. A higher proportion of (3b) was obtained from a similar reaction in benzene. A corresponding solvent dependence was observed during a study of the nucleophilic substitution reactions of pentachloropyridine.[10]

Thus, the sulphone (1a) reacted as expected; there was no evidence for reaction in the 3-position, which suggests that the ring nitrogen atom exerts the predominant orientating effect in these reactions.

The amino-sulphones (3a and b) were unambiguously synthesised in order to confirm their structures. Thus, the *N*-oxide (4a) of (1a) was prepared by oxidation of either (1a) or (1c) with a mixture of hydrogen peroxide, concentrated sulphuric acid, and acetic acid [1,11] and treated with *NN*-dimethylamine to give 2,3,5-trichloro-6-dimethylamino-4-methylsulphonylpyridine *N*-oxide (4b). This was deoxygenated with phosphorus trichloride to give a mixture of (3a) and tetrachloro-2-dimethylaminopyridine. 2,3,5-Trichloro-4-methylsulphonyl-6-pyrrolidinopyridine *N*-oxide (4c) was similarly prepared and its deoxygenation with phosphorus trichloride gave a mixture of (3b) and tetrachloro-2-pyrrolidinopyridine. The formation of the 2-aminotetrachloropyridines during the deoxygenation of (4b) and (4c) may be attributed to displacement of the methylsulphonyl group by chloride ion from the reagent.

In an alternative approach, 2,3,5-trichloro-6-dimethylamino-4-methylthiopyridine (5a) was prepared by the reaction of tetrachloro-2-dimethylaminopyridine with potassium hydrogen sulphide followed by methylation of the resulting 4-mercapto-compound with dimethyl sulphate. The corresponding pyrrolidino-compound (5b) was similarly prepared. Oxidation of (5a) with peroxyacetic acid readily gave the corresponding sulphoxide, but further oxidation required more vigorous conditions and resulted in the formation of a complex mixture of products. This was not unexpected since oxidation of 2-dialkylaminotetrachloropyridines is known [10] to take place under these conditions to give products which rearrange.

We also considered conversion of the sulphones (3a) and (3b) into the readily available sulphides (5a) and (5b). We were aware, however, that sulphones are normally resistant to reduction [12] and experiments with (1a) as a model compound were carried out first. This sulphone reacted readily with lithium aluminium hydride,[12] even at −20°, but surprisingly gave a mixture of 2,3-dichloro-4-methylthiopyridine (6) (the major product), 2,3,6-trichloropyridine (7), and 2,3,6-trichloro-4-methylthiopyridine (8) (trace) (Scheme). Reduction of tetrachloro-4-methylthiopyridine (1c) with lithium aluminium hydride gave a similar mixture of products. We suggest that these compounds may react *via trans*-addition of the AlH_4^- ion to the 2,3- and 3,4-bonds of (1c) to give the intermediates (9) and (10), respectively (Scheme). Addition across the 2,3-bond is apparently preferred, presumably because it is sterically favoured. The intermediates (9) and (10) are then considered to undergo reduction at the 3-position with inversion of configuration to give (11) and (12), and hydrolysis of these intermediates is followed by unusual *cis*-elimination reactions from the resulting intermediates (13)



SCHEME

[9] J. Bertrand, C. Dobritz, and H. Beerens, *Bull. Soc. pharm. Lille*, 1956, 39 (*Chem. Abs.*, 1957, **51**, 1168).

[10] S. M. Roberts and H. Suschitzky, *J. Chem. Soc.* (*C*), 1968, 1537; *Chem. Comm.*, 1967, 893.

[11] G. E. Chivers and H. Suschitzky, *Chem. Comm.*, 1971, 28.

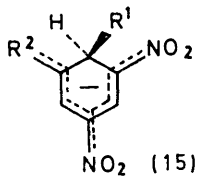
[12] F. G. Bordwell and W. H. McKellin, *J. Amer. Chem. Soc.*, 1951, **73**, 2251.

and (14) to give the observed products.* Since *cis*-elimination of hydrogen chloride from (13) is preferred to *cis*-elimination of hydrogen, compound (6) is the major product. Similarly, because *cis*-elimination of methanethiol from (14) predominates over *cis*-elimination of hydrogen, only a trace of (8) is formed. Support for the suggested mechanism was obtained by hydrolysis of a similar reaction mixture with deuterium oxide, which gave the products indicated in the Scheme (deuterium atoms in parentheses). We have already observed analogous mechanisms which account for the products from the interaction of pentachloropyridine and various other 4-substituted tetrachloropyridines and lithium aluminium hydride.[13] An attempt to trap the intermediates (11) and (12) by carboxylating the reaction mixture [13] failed.

Tetrachloro-4-methylsulphonylpyridine *N*-oxide (4a) reacted normally with *NN*-dimethylamine in acetone [(4a) was more soluble in this solvent than in ethanol] to give exclusively the amine (4b), but with pyrrolidine in acetone the solution turned red and on work-up gave a mixture of compound (4c) and 2-acetonyltrichloro-4-methylsulphonylpyridine *N*-oxide (4d). An attempt to separate these compounds by chromatography on silica afforded only the latter (4d); the former (4c) decomposed on the column.

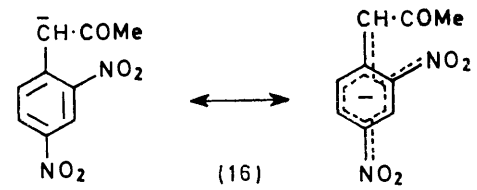
Our observation is reminiscent of the reactions of 1,3,5-trinitrobenzene with aliphatic amines in ionising solvents, which also produce intense red colours; for example, with diethylamine in acetone or ethanol the species (15a) is formed.[14,15] Under different conditions both 1,3,5-trinitrobenzene and 1,3-dinitrobenzene react with acetone in the presence of bases to give the coloured intermediate ions (15b) and (15c), respectively.[14,15] Where the base is hydroxide ion, the reaction is the well known Janovsky reaction.[14] Zimmerman has described an apparently similar reaction in which 1,3-dinitrobenzene is dissolved in ethanol to which the base and carbanion source (*e.g.*, acetone) are added.[14] It is now recognised that intermediates such as (15b) and (15c) are responsible for the blue colours which develop in the Janovsky reaction whilst intermediates such as (16) are responsible for the red colours which develop in the Zimmerman reaction.

The fact that the *N*-oxide (4a) reacts with pyrrolidine with the development of a red colour in acetone but not in ethanol suggests that acetone is essential and that the ion responsible for the colour is structurally akin to (15b) and (15c) or (16) and can be represented as (17) or (18). Attempts to isolate salts [14] of the ion (17) failed. In a Janovsky-type reaction, tetrachloro-4-methylsulphonylpyridine *N*-oxide (4a) gave a red colour, and acidification of the resulting reaction mixture gave tetrachloropyridin-4-ol. This result may by attributed to formation of the ion (19) followed by loss of the methylsulphonyl group as methanesulphinic acid, which reduces the resulting *N*-oxide. It is possible, therefore, that the species responsible for the development of the red colour during the reaction of (4a) with

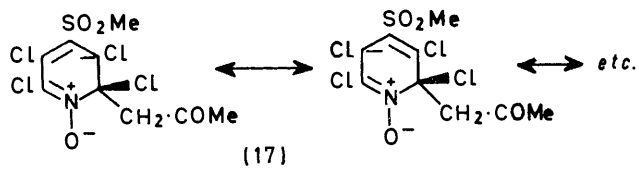


(15)

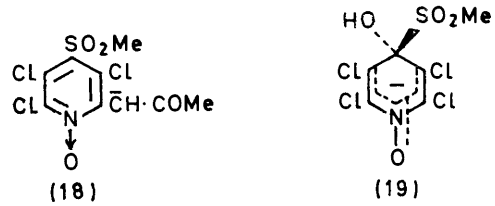
a; $R^1 = NEt_2$, $R^2 = NO_2$
b; $R^1 = CH_2{\cdot}COMe$, $R^2 = NO_2$
c; $R^1 = CH_2{\cdot}COMe$, $R^2 = H$



(16)



(17)



(18) (19)

pyrrolidine in acetone is (18), although other possibilities cannot be excluded.[14,15] In support of this suggestion, a red colour developed when (4d) was treated with pyrrolidine in acetone but not when (4c) was similarly treated. Further work is necessary to establish the structures of the intermediates involved in these reactions.

Reactions of Tetrachloro-4-methylsulphinylpyridine and Tetrachloro-4-methylthiopyridine.—The reactivities of methylsulphinyl- and methylsulphonyl-substituted nitrogen heterocycles with nucleophiles are comparable and a methylthio-group has been shown to be a poor leaving group, being less labile than a chlorine atom in the same environment.[3] The reactivity of tetrachloro-4-methylsulphinylpyridine (1b) was found to be qualitatively comparable to that of the methylsulphonyl compound (1a). It reacted readily with hot aqueous sodium hydroxide and hot ethanolic methylamine to give high yields of (1e) and (1g), respectively. In

* Initial *cis*-addition of the AlH_4^- ion followed by *trans*-eliminations would also give the observed products (see ref. 13 for a more detailed discussion of similar mechanisms).

[13] F. Binns, S. M. Roberts, and H. Suschitzky, *J. Chem. Soc.* (*C*), 1970, 1375; *Chem. Comm.*, 1969, 1211.

[14] R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, 1966, **16**, 61.

[15] E. Buncel, A. R. Norris, and K. E. Russell, *Quart. Rev.*, 1968, **22**, 123.

contrast, the reaction of tetrachloro-4-methylthiopyridine (1c) with hot aqueous sodium hydroxide required 4 days and gave (1e) in only 46% yield, together with starting material. The reaction of (1c) with hot methanolic sodium methoxide required 16 h and gave a mixture of products which was not investigated further. As expected, tetrachloro-4-mercaptopyridine (1d) could be recovered from its solution in aqueous sodium hydroxide or methanolic sodium methoxide even after being heated for a week under reflux.

EXPERIMENTAL

N.m.r. spectra were recorded with a Varian A60 spectrometer; tetramethylsilane was used as internal standard and the recorded signals were singlets unless otherwise stated. I.r. spectra were recorded with a Perkin-Elmer 257 spectrometer and molecular weights were determined with an A.E.I. MS12 spectrometer.

Reactions of Tetrachloro-4-methylsulphonylpyridine.[16]—(a) *With aqueous sodium hydroxide.* A mixture of the sulphone (1·0 g, 3·39 mmol), sodium hydroxide (0·27 g, 6·8 mmol), and water (20 ml) was heated under reflux for 8 h. Acidification of the resulting solution with concentrated hydrochloric acid gave a precipitate (0·74 g, 94%) of tetrachloropyridin-4-ol, m.p. 232—234° (from chloroform–dimethyl sulphoxide), identical with an authentic sample.

(b) *With methanolic sodium methoxide.* A solution of the sulphone (1·0 g, 3·39 mmol) and sodium methoxide (0·19 g, 3·5 mmol) in dry methanol (20 ml) was heated under reflux for 20 min. Evaporation of the solvent followed by addition of water (30 ml) to the residue gave tetrachloro-4-methoxypyridine (0·8 g, 96%), m.p. 114—115° (from methanol), identical with an authentic sample.

(c) *With ethanolic methylamine.* A solution of the sulphone (1·0 g, 3·39 mmol) and methylamine (1·0 ml of a 33% w/w solution in ethanol) in ethanol (30 ml) was heated under reflux for 3 min. Evaporation of the solvent followed by addition of water (30 ml) to the residue gave tetrachloro-4-methylaminopyridine (0·61 g, 73%), m.p. 130° (from ethanol), identical with an authentic sample.

(d) *With ethanolic dimethylamine.* A solution of the sulphone (1·0 g, 3·39 mmol) and dimethylamine (0·32 g, 6·8 mmol) in ethanol (30 ml) was heated under reflux for 24 h. Addition of water (30 ml) followed by evaporation of the ethanol gave *2,3,5-trichloro-6-dimethylamino-4-methylsulphonylpyridine* (0·78 g, 76%), m.p. 117—118° (from methanol), τ [CCl_4–$(CD_3)_2CO$] 6·69 (SO_2Me) and 6·91 (NMe_2) (1 : 2) (Found: C, 31·9; H, 2·9; N, 9·3%; *M*, 302. $C_8H_9Cl_3N_2O_2S$ requires C, 31·7; H, 3·0; N, 9·2%; *M*, 302).

(e) *With ethanolic pyrrolidine.* A solution of the sulphone (2·0 g, 6·77 mmol) and pyrrolidine (0·98 g, 14 mmol) in ethanol (30 ml) was heated under reflux for 24 h. The solvent was evaporated off, water (30 ml) was added to the residue, and the product (1·6 g) was extracted with benzene and chromatographed on silica. Benzene eluted tetrachloro-4-pyrrolidinopyridine (0·65 g, 33·5%), m.p. 108—109° (from ethanol) (identical with an authentic sample) and *2,3,5-trichloro-4-methylsulphonyl-6-pyrrolidinopyridine* (0·85 g, 38%), m.p. 130—131° (from ethanol) (Found: C, 36·4; H, 3·3; N, 8·3%; *M*, 328. $C_{10}H_{11}Cl_3N_2O_2S$ requires C, 36·45; H, 3·4; N, 8·5%; *M*, 328).

(f) *With pyrrolidine in benzene.* A similar reaction to that described in (e) carried out in benzene instead of ethanol gave tetrachloro-4-pyrrolidinopyridine (0·43 g, 22%), m.p. 108—109° (from ethanol) and 2,3,5-trichloro-4-methylsulphonyl-6-pyrrolidinopyridine (1·18 g, 53%), m.p. 130—131° (from ethanol).

(g) *With sodium cyanide in* NN*-dimethylformamide.* (i) Sodium cyanide (0·21 g, 3·5 mmol) was added in small amounts to a stirred solution of the sulphone (1·0 g, 3·39 mmol) in *NN*-dimethylformamide (30 ml) at room temperature. The mixture immediately turned black. It was then heated under reflux for 10 min, the solvent was distilled off under reduced pressure, and the residue was extracted with boiling benzene (50 ml) to give a solid (0·8 g), which was chromatographed on silica. Carbon tetrachloride eluted only pentachloropyridine (0·3 g, 35%), m.p. 119—120°.

(ii) A mixture of the sulphone (1·0 g, 3·39 mmol), sodium cyanide (0·21 g, 3·5 mmol), and *NN*-dimethylformamide (30 ml) was stirred at room temperature for 1 week. The solvent was distilled off under reduced pressure, water (30 ml) was added to the residue, and the precipitate (0·49 g) was filtered off and chromatographed on silica. Carbon tetrachloride–chloroform (10 : 1) eluted starting material (0·05 g, 5%) and tetrachloro-4-cyanopyridine (0·19 g, 23%), m.p. 135—138° (from benzene), identical with an authentic sample.

(h) *With sodium cyanide in aqueous ethanol.* A solution of sodium cyanide (0·21 g, 3·5 mmol) in water (10 ml) was added dropwise to a stirred solution of the sulphone (1·0 g, 3·39 mmol) in ethanol (20 ml) at room temperature, and the resulting mixture was stirred for a further 2 h. The mixture was worked up as described in (g) and the product was chromatographed on silica. Carbon tetrachloride–chloroform (10 : 1) eluted tetrachloro-4-cyanopyridine (0·16 g, 19·5%), m.p. 135—138° (from benzene) and *ethyl tetrachloropyridine-4-carboximidate* (0·6 g, 61·5%), m.p. 75—77° (from methanol), $\nu_{max.}$ (Nujol) 3300 (NH) and 1640 cm^{-1} (C:N) (Found: C, 33·7; H, 2·2; N, 9·8%; *M*, 286. $C_8H_6Cl_4N_2O$ requires C, 33·4; H, 2·1; N, 9·7; *M*, 286).

(i) *With lithium aluminium hydride.* The reaction was carried out as described later for the reduction of tetrachloro-4-methylthiopyridine with lithium aluminium hydride, and work-up gave an identical mixture of products.

(j) *With a mixture of hydrogen peroxide, acetic acid, and concentrated sulphuric acid.* The reaction was carried out as described later for the similar oxidation of tetrachloro-4-methylthiopyridine and gave the same product in an identical yield.

Reactions of Tetrachloro-4-methylsulphinylpyridine.[16]—(a) *With aqueous sodium hydroxide.* A mixture of the sulphoxide (0·5 g, 1·8 mmol), sodium hydroxide (0·14 g, 3·6 mmol), and water (20 ml) was heated under reflux with stirring for 16 h. Acidification of the resulting solution with concentrated hydrochloric acid gave tetrachloropyridin-4-ol (0·34 g, 81%), m.p. 232—234° (from chloroform–dimethyl sulphoxide).

(b) *With ethanolic methylamine.* A solution of the sulphoxide (1·0 g, 3·6 mmol) and methylamine (0·11 g, 3·6 mmol) in ethanol (20 ml) was heated under reflux for 1 h. Evaporation of the solvent followed by addition of water (10 ml) to the residue gave tetrachloro-4-methylaminopyridine (0·82 g, 93%), m.p. 130° (from ethanol).

[16] E. Ager, B. Iddon, and H. Suschitzky, *J. Chem. Soc.* (*C*), 1970, 193.

Reactions of Tetrachloro-4-methythiopyridine.[16]—(a) *With aqueous sodium hydroxide.* A stirred mixture of the sulphide (1·0 g, 3·8 mmol), sodium hydroxide (0·3 g, 7·6 mmol), and water (20 ml) was heated under reflux for 4 days. The mixture was filtered to give starting material (0·08 g, 8%), and acidification of the filtrate gave tetrachloropyridin-4-ol (0·4 g, 45%), m.p. 230—232° (from chloroform–dimethyl sulphoxide).

(b) *With a mixture of hydrogen peroxide, acetic acid, and concentrated sulphuric acid.* Aqueous hydrogen peroxide (85%; 30 ml) was added dropwise to a stirred mixture of the sulphide (9·85 g, 37·4 mmol), acetic acid (50 ml) and concentrated sulphuric acid (100 ml) at 0°, and the resulting mixture was stirred at room temperature for a further 24 h. It was then poured on crushed ice (500 g) and the precipitate was filtered off, washed with water, and recrystallised from acetone to give *tetrachloro-4-methylsulphonylpyridine* N-*oxide* (9·35 g, 80%), m.p. 205—206°, τ [$(CD_3)_2CO$–$(CD_3)_2SO$] 6·44 (SO_2Me) (Found: C, 23·6; H, 1·0; N, 4·4%; *M*, 309. $C_6H_3Cl_4NO_3S$ requires C, 23·2; H, 1·0; N, 4·5%; *M*, 309).

(c) *With lithium aluminium hydride.* Finely divided tetrachloro-4-methylthiopyridine (2·0 g, 7·6 mmol) was added in portions to a stirred suspension of lithium aluminium hydride (0·87 g, 22·8 mmol) in dry ether (50 ml) at −25°, and the resulting mixture was stirred at this temperature for a further 1·5 h. Water (10 ml) was added dropwise, the mixture was acidified with 4N-hydrochloric acid, the ethereal layer was separated, and the aqueous layer was extracted with ether. The combined ethereal layer and extracts were dried ($MgSO_4$), and evaporation of the solvent gave an oil (1·2 g). Part (0·9 g) of this oil was chromatographed on silica. Carbon tetrachloride–light petroleum (b.p. 60—80°) (1 : 3) eluted 2,3,6-trichloropyridine (0·13 g, 9%), m.p. 66—67° [from light petroleum (b.p. 60—80°)] (lit.,[13] 66—67°), 2,3,6-trichloro-4-methylthiopyridine (0·04 g, 2%), m.p. 129—130° (from carbon tetrachloride) (lit.,[16] 129—130°), and 2,3-*dichloro-4-methylthiopyridine* (0·41 g, 28%), m.p. 57—59° [from light petroleum (b.p. 40—60°)], τ (CCl_4) 7·45 (SMe), 2·98 (d, *J* 8·0 Hz, β-H), and 2·49 (d, *J* 8·0 Hz, α-H) (Found: C, 37·3; H, 2·4%; *M*, 193. $C_6H_5Cl_2NS$ requires C, 37·1; H, 2·6%; *M*, 193).

(ii) The reaction described in (i) was repeated but the resulting mixture was hydrolysed with deuterium oxide instead of water. 2,3,6-Trichloro-5-deuteriopyridine, 2,3,6-trichloro-4-methylthiopyridine, and 2,3-*dichloro-5-deuterio-4-methylthiopyridine* were detected in the product by n.m.r. and t.l.c. analysis. Chromatography on silica as described in (i) gave 2,3,6-trichloro-5-deuteriopyridine (0·13 g, 9%), m.p. 65—66° [from light petroleum (b.p. 60—80°)] (lit.,[13] 66—67°) and 2,3-dichloro-5-deuterio-4-methylthiopyridine (0·41 g, 28%), m.p. 56—57° [from light petroleum (b.p. 60—80°)], τ (CCl_4) 7·44 (SMe) and 2·48 (6-H).

Reactions of Tetrachloropyridine-4-thiol.[16]—(a) *With aqueous sodium hydroxide.* A mixture of the thiol (1·0 g, 4·0 mmol), sodium hydroxide (0·48 g, 12·0 mmol), and water (20 ml) was heated under reflux with stirring for 1 week. Acidification of the resulting solution gave only starting material (89% recovery).

(b) *With methanolic sodium methoxide.* A solution of the thiol (1·0 g, 4·0 mmol) and sodium methoxide (0·43 g, 8·0 mmol) in methanol (30 ml) was heated under reflux for 1 week. Addition of 4N-hydrochloric acid (30 ml) to the resulting solution gave only starting material (89% recovery).

Reactions of Tetrachloro-4-methylsulphonylpyridine N-*Oxide.*—(a) *With dimethylamine.* (i) *In ethanol–*NN-*dimethylformamide.* A solution of dimethylamine (1·49 g, 33 mmol) in ethanol (20 ml) was added dropwise to a stirred mixture of tetrachloro-4-methylsulphonylpyridine *N*-oxide (5·0 g, 16·1 mmol), ethanol (100 ml) and *NN*-dimethylformamide (50 ml) at room temperature, and the resulting solution was stirred for a further 4 h. The solvents were distilled off under reduced pressure, water (20 ml) was added to the residue, and the precipitate (4·9 g) was filtered off, dried in a desiccator over phosphorus pentoxide, and chromatographed on silica. Benzene–ethyl acetate (8 : 1) eluted starting material (0·9 g, 18%), 2,3,5-trichloro-6-dimethylamino-4-methylsulphonylpyridine (0·21 g, 4%), m.p. 117—118° (from methanol), and 2,3,5-*trichloro-6-dimethylamino-4-methylsulphonylpyridine* N-*oxide* (3·17 g, 62%), m.p. 156—157° (decomp.) [from carbon tetrachloride–light petroleum (b.p. 60—80°)] (Found: C, 30·1; H, 2·8; N, 8·8%; *M*, 318. $C_8H_9Cl_3N_2O_3S$ requires C, 30·1; H, 2·8; N, 8·8%; *M*, 318).

(ii) *In acetone.* A similar reaction to that described in (i) carried out in acetone gave the same products in approximately the same amounts.

(b) *With pyrrolidine.* (i) *In ethanol–*NN-*dimethylformamide.* A reaction carried out as described in (a) (i) using pyrrolidine instead of dimethylamine gave 2,3,5-*trichloro-4-methylsulphonyl-6-pyrrolidinopyridine* N-*oxide* (76%), m.p. 157—158·5° (decomp.) (from ethanol–acetone), τ ($CDCl_3$) 7·98 (m, β-CH_2), 6·65 (SO_2Me), and 6·52 (m, α-CH_2) (4 : 3 : 4). This compound was unstable and it was not possible to carry out an elemental analysis. However, its structure was confirmed by mass spectrometry (M^+, 344) and by its deoxygenation with phosphorus trichloride (see later).

(ii) *In acetone.* A solution of pyrrolidine (0·46 g, 6·48 mmol) in acetone (10 ml) was added dropwise to a stirred solution of tetrachloro-4-methylsulphonylpyridine *N*-oxide (1·0 g, 3·21 mmol) in acetone (50 ml) at room temperature, and the resulting mixture was stirred overnight. On addition of the first drop of pyrrolidine a red colour developed; the final solution was intensely coloured. The solvent was distilled off under reduced pressure at room temperature, water was added to the residue, and extraction with ether gave a solid (0·62 g) which t.l.c. showed to be a mixture of 2,3,5-trichloro-4-methylsulphonyl-6-pyrrolidinopyridine *N*-oxide and another component. Chromatography of the solid on silica with chloroform as eluant gave only 2-*acetonyl-3,5,6-trichloro-4-methylsulphonylpyridine* N-*oxide* (0·3 g, 28%), m.p. 174—175·5° (from chloroform), τ [$(CD_3)_2CO$] 7·67 (Me), 6·50 (SO_2Me), and 5·58 (CH_2) (3 : 3 : 2) (Found: C, 32·5; H, 2·3; N, 4·1%; *M*, 331. $C_9H_8Cl_3NO_4S$ requires C, 32·5; H, 2·4; N, 4·2%; *M*, 331).

(c) *With sodium hydroxide in aqueous acetone* (*Janovsky-type reaction*). Aqueous sodium hydroxide (20 ml; 50% w/v) was added to a stirred solution of tetrachloro-4-methylsulphonylpyridine *N*-oxide (1·0 g, 3·21 mmol) in acetone (10 ml) at room temperature. Water was added until a red colour developed and the mixture was stirred for 1 h. After this time two layers were present. The upper, red, aqueous acetone layer was separated and acidified with 4N-hydrochloric acid. Extraction of the product with chloroform gave tetrachloropyridin-4-ol (0·3 g, 40%),

m.p. 232—233° (from chloroform–dimethyl sulphoxide). The concentrated sodium hydroxide layer was not investigated further but it presumably contained more of the tetrachloropyridin-4-ol.

Deoxygenation of 2,3,5-*Trichloro*-6-*dimethylamino*-(*and pyrrolidino*-)4-*methylsulphonylpyridine* N-*Oxide*.—A solution of phosphorus trichloride (2·0 ml) in chloroform (10 ml) was added dropwise to a stirred solution of 2,3,5-trichloro-6-dimethylamino-4-methylsulphonylpyridine *N*-oxide (3·20 g, 10 mmol) in chloroform (30 ml) at room temperature, and the resulting mixture was stirred for a further 30 min. Water (10 ml) was then added, and the organic and aqueous layers were separated. The aqueous layer was extracted with chloroform, and the organic layer and extracts were combined and dried ($MgSO_4$). The solvent was distilled off to leave an oil (2·78 g). This was chromatographed on silica; benzene eluted starting material (0·1 g, 3%), tetrachloro-2-dimethylaminopyridine (0·47 g, 18%), m.p. 42—43° (identical with an authentic sample), and 2,3,5-trichloro-6-dimethylamino-4-methylsulphonylpyridine (1·2 g, 40%), m.p. 117—118° (from methanol), identical with the sample prepared as described before.

2,3,5-Trichloro-4-methylsulphonyl-6-pyrrolidinopyridine *N*-oxide (10 mmol) (reaction time 5 min) similarly gave tetrachloro-2-pyrrolidinopyridine (1%), m.p. 88—89° (identical with an authentic sample), and 2,3,5-trichloro-4-methylsulphonyl-6-pyrrolidinopyridine (61%), m.p. 130—131° (from ethanol), identical with the sample prepared as described before.

2,3,5-*Trichloro*-6-*dimethylaminopyridine*-4-*thiol*.—A solution of sodium hydroxide (12·3 g, 308 mmol) in water (20 ml) was saturated with hydrogen sulphide and added during 30 min to a stirred suspension of tetrachloro-2-dimethylaminopyridine [10] (20 g, 76·9 mmol) in ethylene glycol (500 ml) at 100°. The resulting mixture was stirred at 100° for a further 16 h then diluted with water (1 l) and acidified with concentrated hydrochloric acid. The crude product (16·6 g) was extracted with chloroform and dissolved in aqueous sodium hydroxide (1 equiv.). The resulting solution was decanted from a small amount of tar and acidified with concentrated hydrochloric acid to give 2,3,5-*trichloro*-6-*dimethylamino-pyridine*-4-*thiol* (13·8 g, 70%), m.p. 40—42° (from ethanol), τ (CCl_4) 7·02 (NMe_2) and 5·15 (exchangeable, SH) (6 : 1) (Found: C, 33·1; H, 2·5%; *M*, 256. $C_7H_7Cl_3N_2S$ requires C, 32·65; H, 2·7%; *M*, 256).

2,3,5-*Trichloro*-6-*pyrrolidinopyridine*-4-*thiol* (57%), similarly prepared from tetrachloro-2-pyrrolidinopyridine,[10] had m.p. 75—76° (from ethanol), τ (CCl_4) 8·1 (m, β-CH_2), 6·33 (m, α-CH_2), and 5·15 (exchangeable, SH) (4 : 4 : 1) (Found: C, 37·9; H, 3·2; N, 9·8%; *M*, 282. $C_9H_9Cl_3N_2S$ requires C, 38·1; H, 3·2; N, 9·9%; *M*, 282).

2,3,5-*Trichloro*-6-*dimethylamino*-4-*methylthiopyridine*.—Dimethyl sulphate (6·0 g, 47·6 mmol) was added dropwise to a stirred solution of 2,3,5-trichloro-6-dimethylaminopyridine-4-thiol (10 g, 38·8 mmol) and sodium hydroxide (1·9 g, 47·5 mmol) in water (100 ml) at room temperature, and the resulting mixture was stirred for a further 2 h. The *product* (9·5 g, 90%), extracted with ether in the usual way, had b.p. 140° at 1 mmHg, τ (CCl_4) 7·47 (SMe) and 6·97 (NMe_2) (1 : 2) (Found: C, 34·8; H, 3·2%; *M*, 270. $C_8H_9Cl_3N_2S$ requires C, 35·3; H, 3·4%; *M*, 270).

2,3,5-*Trichloro*-4-*methylthio*-6-*pyrrolidinopyridine* (94%), similarly prepared, had m.p. 101—102° (from ethanol) (Found: C, 40·4; H, 3·8; N, 9·55%; *M*, 296. $C_{10}H_{11}Cl_3N_2S$ requires C, 40·4; H, 3·7; N, 9·4%; *M*, 296).

2,3,5-*Trichloro*-6-*dimethylamino*-4-*methylsulphinylpyridine*.—Aqueous hydrogen peroxide (30%; 0·82 g, 7·4 mmol) was added dropwise to a stirred solution of 2,3,5-trichloro-6-dimethylamino-4-methylthiopyridine (1·0 g, 3·68 mmol) in acetic acid (20 ml) at room temperature. The resulting mixture was stirred for a further 16 h at room temperature and then at 100° for 10 min. Evaporation to dryness and chromatography of the residue on silica with benzene–chloroform (1 : 1) as eluant gave the *sulphoxide* (0·8 g, 76%), b.p. 227° at 2 mmHg, τ (CCl_4–C_6D_6) 7·50 (SOMe) and 7·32 (NMe_2) (1 : 2) (Found: C, 33·9; H, 3·4%; *M*, 286. $C_8H_9Cl_3N_2OS$ requires C, 33·4; H, 3·1%; *M*, 286).

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