REACTION OF PENTACHLOROPYRIDINE N-OXIDE WITH POTASSIUM HYDROGEN SULFIDE

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Depending on the conditions, the reaction of pentachloropyridine N-oxide with potassium hydrogen sulfide leads to the N-oxide of the potassium salt of 3,4,5,6-tetrachloropyridin-2-thiol or the dipotassium salt of 3,4,5-trichloropyridine-2,6-dithiol, which are converted by the action of dimethyl sulfate into the corresponding methylthio derivatives. Oxidation of the latter has given sulfones. It has been shown that for these sulfones, reactions with nucleophilic reagents take place at the methylsulfonyl group and not at the chlorine atoms.

Continuing a study of sulfur-containing derivatives of polychloropyridines [1], we have investigated the reaction of pentachloropyridine N-oxide (I) with potassium hydrogen sulfide. In contrast to pentachloropyridine itself, which reacts in ethanolic solution with potassium hydrogen sulfide at 50°C exclusively at position 4 of the pyridine nucleus with the formation of 2,3,5,6-tetrachloro-4-mercaptopyridine [2], compound (I) reacts with potassium hydrogen sulfide to give two products, depending on the temperature conditions: at 0°C the N-oxide of the potassium salt of 3,4,5,6-tetrachloropyridin-2-thiol (II) is obtained, and at 80°C the N-oxide of the dipotassium salt of 3,4,5-trichloropyridine-2,6-dithiol (III). On acidification, substances (II) and (III) give unstable products in which the N-oxide group is readily reduced on recrystallization, giving, in the case of (II) di(3,4,5,6-tetrachloropyridin-2-yl) disulfide mono-S-oxide (IV). The structure of (IV) was shown by a molecular weight determination and by IR spectroscopy. Its IR spectra lack an absorption band at 1150 cm^{-1} characteristic for a sulfoxide group [3]. By the action of dimethyl sulfate, (II) and (III) were converted into 3,4,5,6-tetrachloro-2-(methylthio)pyridine N-oxide (V) and 3,4,5-trichloro-2,6-di(methylthio)pyridine N-oxide (VI). The oxidation of (V) with nitric acid or hydrogen peroxide in acetic acid gave the N-oxide of methyl 3,4,5,6-tetrachloropyridin-2-yl sulfoxide (VII). Under the action of PCl_3, the latter lost the two oxygen atoms attached to the nitrogen and sulfur atoms and gave 3,4,5,6-tetrachloro-2-methylthiopyridine (VIII); the reaction of (V) with PCl_3 took place similarly. The action of phosphorus trichloride on (VI) yielded 3,4,5-trichloro-2,6-di(methylthio)pyridine (IX). The oxidation of (V) and (VI) with hydrogen peroxide in trifluoroacetic acid gave the corresponding sulfones (X and XI), which lost the N-oxide group under the action of PCl_3 with considerably greater difficulty than (V) and (VI). The prolonged heating of (X) with phosphorus trichloride gave 3,4,5,6-tetrachloro-2-methylsulfonylpyridine (XII). Attempts to remove the oxygen atom of the N-oxide group in (XI) under the same conditions were unsuccessful. [See structure on top of next page.]

The presence of strong electron-accepting substituents and the N-oxide group in the pyridine nucleus must strongly activate the 3-Cl and 5-Cl atoms with respect to nucleophilic reagents, as occurs in the case of the N-oxides of 3-halo-4-nitropyridines, in which the halogen atoms are activated considerably more strongly than in the analogous compounds having no N-oxide group [4, 5]. However, we have established that the action of nucleophilic reagents on (X) and (XI) leads to the replacement of the methylsulfonyl groups and not of the chlorine atoms of the pyridine nucleus. Thus, the action of methylamine or of an aqueous solution of caustic soda on (X) gave the corresponding N-oxides of 3,4,5,6-tetrachloro-2-(methylamino)-pyridine and of 3,4,5,6-tetrachloro-2-hydroxypyridine (XIII, XIV), and (XI) gave the N-oxides of 3,4,5-trichloro-2,6-di(methylamino)pyridine and of 3,4,5-trichloro-2,6-dihydroxypyridine (XV, XVI). When (XIV) and (XVI) were heated with phosphorus trichloride, the corresponding known 3,4,5,6-tetrachloro-2-hydroxy-

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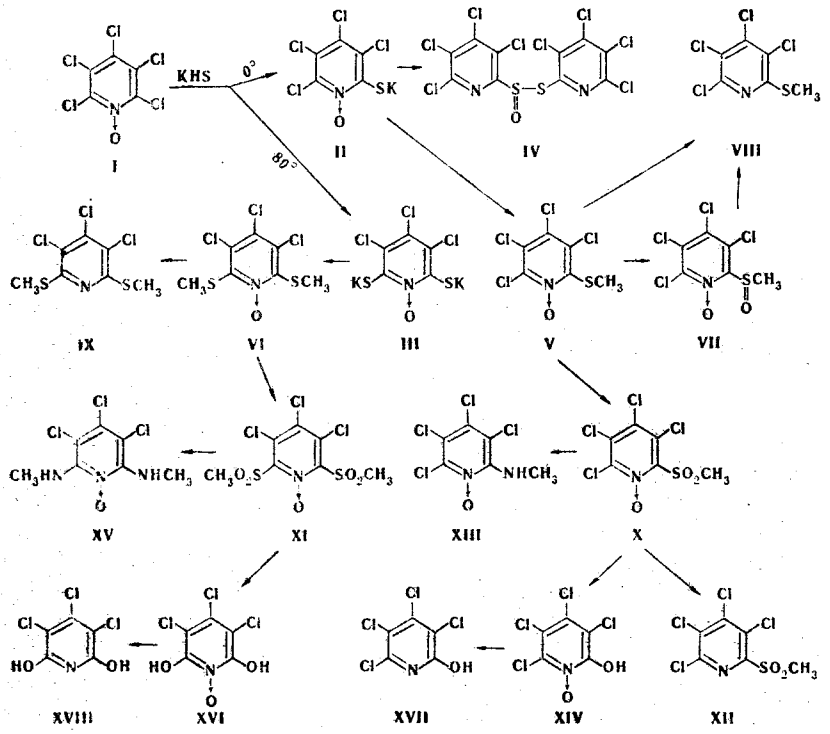

pyridine (XVII) [6] and 3,4,5-trichloro-2,6-dihydroxypyridine (XVIII) [7] were obtained; their formation shows the position of the substitution of the chlorine atoms in the pyridine ring by mercapto groups in the reaction of (I) with potassium hydrogen sulfide.

EXPERIMENTAL

N-Oxide of the Potassium Salt of 3,4,5,6-Tetrachloropyridin-2-thiol (II). A solution of 6.2 g (0.11 mole) of caustic potash in 500 ml of ethanol was saturated with hydrogen sulfide at 0°C for 2 h, and then, with stirring, 13.25 g (0.05 mole) of pentachloropyridine N-oxide was added and the mixture was again saturated with hydrogen sulfide at 0°C for 2 h. The temperature of the mixture was raised to 20°C, and the precipitate was filtered off and dissolved in 750 ml of water at 60°C; the filtrate was evaporated to dryness in vacuum. Yield 10.5 g (70%). Found %: S 10.2. C_5Cl_4NOSK. Calculated %: S 10.5.

N-Oxide of the Dipotassium Salt of 3,4,5-Trichloropyridine-2,6-dithiol (III). A solution of 5.6 g (0.1 mole) of caustic potash in 250 ml of ethanol was saturated with hydrogen sulfide at 0°C for 2 h and then, with stirring, 2.7 g (0.01 mole) of pentachloropyridine N-oxide was added. The reaction mixture was boiled for 1 h with the simultaneous passage of hydrogen sulfide through the mixture. The isolation of compound (III) was similar to that of (II). Yield 2.9 g (85%). Found %: S 18.7. $C_5Cl_3NOS_2K_2$. Calculated %: S 18.9.

Di(3,4,5,6-tetrachloropyridin-2-yl) Disulfide Mono-S-oxide (IV). A solution of 2.6 g (0.01 mole) of 3,4,5,6-tetrachloropyridine-2-thiol N-oxide in dioxane (or ethanol or acetone) was boiled for 5 min. The precipitate that had deposited was filtered off, giving 2.3 g (92%) of (IV) with mp 225-227°C (from dioxane). IR spectrum: 1080 cm^{-1} (SO). Found %: Cl 55.5; S 12.7; mol. wt. 475. $C_{10}Cl_8N_2OS_2$. Calculated %: Cl 55.5; S 12.5; mol. wt. 512.

3,4,5,6-Tetrachloro-2-(methylthio)pyridine N-Oxide (V). With stirring at 20°C, 7.6 g (0.06 mole) of dimethyl sulfate was added dropwise to a solution of 9 g (0.03 mole) of (II) in 500 ml of water, the mixture being kept alkaline by the addition of 50% aqueous caustic soda. Then the reaction mixture was stirred at 20°C for 2 h, and the product that had precipitated was filtered off. Yield 8 g (95%), mp 138-139°C (from ethanol). IR spectrum: 1165 cm^{-1} (N–O). Found %: Cl 50.9; S 11.8. $C_6H_3Cl_4NOS$. Calculated %: Cl 50.9; S 11.5.

3,4,5-Trichloro-2,6-di(methylthio)pyridine N-Oxide (VI). To a solution of 3.4 g (0.01 mole) of (III) in 50 ml of water, 5 g (0.04 mole) of dimethyl sulfate was added dropwise. Isolation of the product in the same way as in the case of compound (V) gave 2.8 g (96%) of (VI), mp 212-214°C (from dioxane). IR spectrum: 1050 cm^{-1} (N–O). Found %: Cl 36.5; S 22.2. $C_7H_6Cl_3NOS_2$. Calculated %: Cl 36.7; S 22.0.

3,4,5,6-Tetrachloro-2-(methylsulfinyl)pyridine N-Oxide (VII). A. A solution of 1.4 g (5 mmoles) of (V) in 25 ml of nitric acid (d_4^{20} 1.42) was kept at 20°C for 2 h, and was then heated at 60°C for 15 min. The nitric acid was eliminated by evaporation to dryness in vacuum, and the residue was treated with water. Yield 1.3 g (90%), mp 188-189°C (from aqueous dioxane). IR spectrum: 1150 (N–O), 1080 cm^{-1} (SO). Found %: Cl 48.1; S 10.7. $C_6H_3Cl_4NO_2S$. Calculated %: Cl 48.1; S 10.9.

B. In drops, 5 ml of a 30% aqueous solution of hydrogen peroxide was added to a solution of 1.4 g (5 mmoles) of (V) in 50 ml of glacial acetic acid and the mixture was kept at 20°C for 16 h. Then it was diluted with water and the product was filtered off. Yield 1.3 g (90%).

3,4,5,6-Tetrachloro-2-(methylthio)pyridine (VIII). A. A solution of 0.6 g (2 mmoles) of (VII) in 50 ml of absolute benzene was treated with 1 ml of PCl_3, and the mixture was boiled for 30 min. Then it was evaporated in vacuum to dryness, and the residue was treated with water. Yield 0.5 g (96%), mp 100-101°C (from ethanol). Found %: Cl 54.2; S 12.4. $C_6H_3Cl_4NS$. Calculated %: Cl 54.0; S 12.2.

B. Compound (VIII) was obtained from (V) in a similar manner to method A. Yield 87%.

3,4,5-Trichloro-2,6-di(methylthio)pyridine (IX). This was obtained in a similar manner to (VIII) by method A. Yield 73%, mp 148-149°C (from heptane). Found %: Cl 38.7; S 23.6. $C_7H_6Cl_3NS_2$. Calculated %: Cl 38.8; S 23.4.

3,4,5,6-Tetrachloro-2-(methylsulfonyl)pyridine N-Oxide (X). With cooling, 5 ml (0.045 mole) of a 30% aqueous solution of hydrogen peroxide was added to a solution of 2.8 g (0.01 mole) of (V) in 50 ml of trifluoroacetic acid, and the mixture was kept at 20°C for 72 h. Then the bulk of the solvent was distilled off in vacuum, and the residue was diluted with water. Yield 2.9 g (93%), mp 182-183°C (from ethanol). IR spectrum, cm^{-1}: 1330 and 1145 (SO_2), 1160 (N–O). Found %: Cl 45.8; S 10.2. $C_6H_3Cl_4NO_3S$. Calculated %: Cl 45.7; S 10.3.

3,4,5-Trichloro-2,6-di(methylsulfonyl)pyridine N-Oxide (XI). With cooling, 10 ml (0.09 mole) of 30% aqueous hydrogen peroxide was added to a solution of 2.9 g (0.01 mole) of (VI) in 25 ml of trifluoroacetic acid, and the mixture was kept at 20°C for 48 h. Then the product was isolated in the same way as (X). Yield 3.4 g (96%), mp 212-213°C (from ethanol). IR spectrum, cm^{-1}: 1330, 1150 (SO_2). Found %: Cl 29.7; S 18.2. $C_7H_6Cl_3NO_5S_2$. Calculated %: Cl 30.0; S 18.1.

3,4,5,6-Tetrachloro-2-(methylsulfonyl)pyridine (XII). A solution of 0.62 g (2 mmoles) of (X) in 25 ml of absolute benzene was treated in 1 ml of PCl_3 and the mixture was boiled for 3 h. Then the solution was evaporated in vacuum, and the residue was treated with water. Yield 0.5 g (85%), mp 165-167°C (from heptane). Found %: Cl 47.8; S 10.7. $C_6H_3Cl_4NO_2S$. Calculated %: Cl 48.1; S 10.8.

3,4,5,6-Tetrachloro-2-(methylamino)pyridine N-Oxide (XIII). A solution of 0.3 g (1 mmole) of (X) in 25 ml of absolute dioxane was saturated with methylamine at 20°C for 15 min. Then the solvent was distilled off in vacuum and the residue was treated with water. Yield 0.25 g (95%), mp 166-167°C (from aqueous ethanol). Found %: Cl 54.1; N 11.0. $C_6H_4Cl_4N_2O$. Calculated %: Cl 54.2; N 10.7.

3,4,5,6-Tetrachloro-2-hydroxypyridine N-Oxide (XIV). A mixture of 0.3 g (1 mmole) of (X) and 25 ml of a 2% aqueous solution of caustic soda was boiled for 15 min and was then partially evaporated under reduced pressure and acidified, and the precipitate that deposited was filtered off. Yield 0.2 g (80%), mp 176-178° (from heptane). According to the literature [8], mp 180°C.

3,4,5-Trichloro-2,6-di(methylamino)pyridine N-Oxide (XV). This was obtained from (XI) in a similar manner to the preparation of (XIII). Yield 75%, mp 156-157°C (from aqueous ethanol). Found %: Cl 41.2; N 16.1. $C_7H_8Cl_3N_3O$. Calculated %: Cl 41.5; N 16.4.

3,4,5-Trichloro-2,6-dihydroxypyridine N-Oxide (XVI). This was obtained from (XI) in a similar manner to the preparation of (XIV). Yield 75%, mp 177-178°C (from heptane). Found %: Cl 46.1; N 6.0. $C_5H_2Cl_3NO_3$. Calculated %: Cl 46.2; N 6.1.

3,4,5,6-Tetrachloro-2-hydroxypyridine (XVII). This was obtained from (XIV) in the same way as (VIII) by method A. Yield 75%, mp 220-222°C (from ethanol). According to the literature [6], mp 224-225°C.

3,4,5-Trichloro-2,6-dihydroxypyridine (XVIII). This was obtained from (XVI) in the same way as (VIII) by method A. Yield 78%, mp 190-191°C (from aqueous ethanol). According to literature [7], mp 193-195°C.

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