

## 2, 3, 5, 6-TETRACHLOROPYRIDINE-4-SULFENYL CHLORIDE

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UDC 822.5'425.07:543.422.4

2,3,5,6-Tetrachloropyridine-4-sulfenyl chloride has been prepared, and its reactions with nucleophilic reagents have been examined.

Among the sulfur-containing polychloropyridine derivatives so far described are 2,3,5,6-tetrachloropyridine-4-thiol (I) [1], and 4-polychloropyridyl alkyl and aryl sulfides, sulfoxides, and sulfones [2, 3].

By chlorination of I in carbon tetrachloride, we have obtained 2,3,5,6-tetrachloropyridine-4-sulfenyl chloride (II). The chlorinating agents used were sulfonyl chloride and gaseous chlorine. Vacuum distillation of II afforded the product as an orange crystalline solid which was readily hydrolyzed by solutions of acids and bases. Hydrolysis of II in 1 N hydrochloric acid led to the formation of di-(2, 3, 5, 6-tetrachloro-4-pyridyl) disulfide (III) and di-(2, 3, 5, 6-tetrachloro-4-pyridyl)sulfonyl sulfide (IV). The structure of these compounds was proved by conversion of III into the starting material II by gaseous chlorine and by the presence in the IR spectrum of IV of absorptions at 1150 and 1325  $\text{cm}^{-1}$  characteristic of symmetrical and asymmetrical stretching of the  $\text{SO}_2$  group [4]. A 1 N solution of NaOH hydrolyzed II to the sodium salt of I, 4-hydroxy-2, 3, 5, 6-tetrachloropyridine (V), and sulfuric acid. This reaction proceeds via III, which was isolated on brief treatment of II with alkali. Further hydrolysis of III resulted in a mixture of the compounds mentioned above.

Reaction of II with phenylmagnesium bromide gave 2, 3, 4, 6-tetrachloropyridyl phenyl sulfide (VI). The reaction with ethylmagnesium bromide proceeded similarly to afford 2, 3, 5, 6-tetrachloro-4-pyridyl ethyl sulfide (VII). The latter was also obtained by alkylation of the potassium salt of I with ethyl bromide in alcohol. Alkaline hydrolysis of VII yielded the sodium salt of V. The location of the thiol group in the 4-position of the pyridine ring in V is confirmed by the hydrolysis of II and VII to V (no proof of the orientation of the thiol group in the pyridine nucleus is given in the patent [1]).

Oxidation of VII and VI with hydrogen peroxide in acetic acid gives 2, 3, 5, 6-tetrachloro-4-pyridyl ethyl sulfone (VIII) and 2, 3, 5, 6-tetrachloro-4-pyridyl phenyl sulfone (IX), whereas oxidation of VII with nitric acid affords 2, 3, 5, 6-tetrachloro-4-pyridyl ethyl sulfoxide (X). Reaction of II with triethyl phosphite does not give the Arbuzov rearrangement product (cf. [5]), but VII. This anomalous behavior is apparently due to the specific influence of the nitrogen atom of the pyridine ring [6].

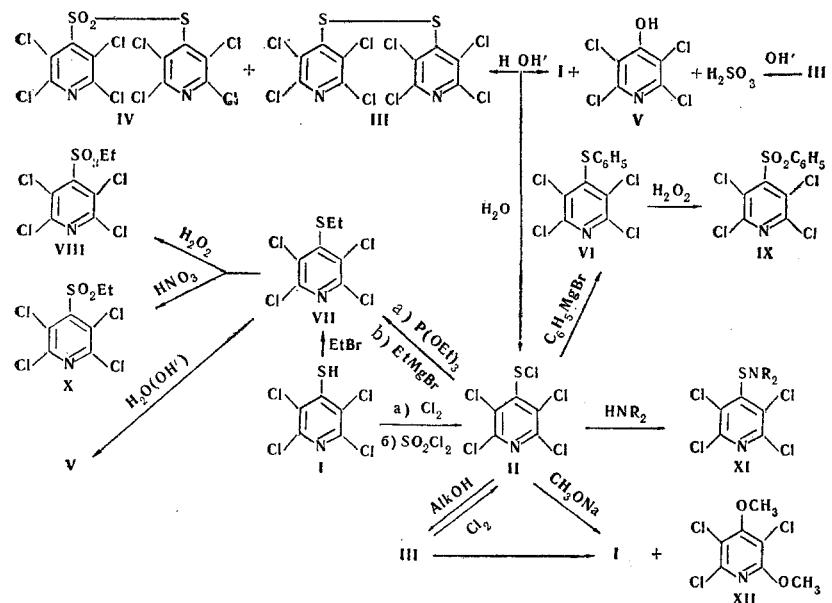
Compound II reacts readily with ammonia and amines to yield the corresponding 2,3,5,6-tetrachloropyridine-4-sulfenamides (XI). The reaction with ammonia and arylamines proceeds only in anhydrous media, while 2, 3, 5, 6-tetrachloropyridine-4-dialkylsulfenamides may be obtained either in anhydrous media, or by treatment of II with aqueous solutions of dialkylamines.

We did not succeed in obtaining aliphatic esters of 2,3,5,6-tetrachloropyridine-4-sulfenic acid. The principal product of the reaction of II with alcohols in presence or absence of triethylamine is III. Reaction of II with sodium methoxide gives the Na salt of I and 2,4-dimethoxy-3,5,6-trichloropyridine (XII). The latter reaction may proceed via III, since on treatment with methanolic sodium methoxide, III is converted into I and XII.

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Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev. Translated from *Khimiya Geterotsiklichesikh Soedinenii*, No. 9, pp 1232-1235, September, 1970. Original article submitted May 26, 1969.

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## EXPERIMENTAL

2, 3, 5, 6-Tetrachloropyridine-4-sulfenyl Chloride (II). A. A portion of I [10 g (0.04 mole)] in 150 ml of carbon tetrachloride was chlorinated for 3 h with gaseous chlorine, until hydrogen chloride was no longer evolved. The solvent was removed by distillation, and the residual orange oil was distilled in vacuo to give 9.3 g (82%), bp 109–112° (0.15 mm). After distillation, II crystallized as orange needles, mp 64–66° (from heptane). Found: Cl 62.59%.  $\text{C}_5\text{Cl}_5\text{NS}$ . Calculated: Cl 62.70%.

B. To a mixture of 10 g (0.04 mole) of I in 150 ml of carbon tetrachloride and 3 g of pyridine was added dropwise 10.8 g (0.08 mole) of sulfonyl chloride at 50° (exothermic reaction), and stirred for 1 h at the boil. The precipitate of pyridine hydrochloride was filtered off. Worked up as in method A, yield 8.2 g (72%).

C. A portion of III [2.5 g (0.005 mole)] was chlorinated with an excess of chlorine in 20 ml of carbon tetrachloride at the boil for 3 h. Isolation of II was carried out as above, yield 100%.

Hydrolysis of II. A. A portion of II [5.1 g (0.018 mole)] was finely ground, mixed with 50 ml of 1 N HCl, and stirred vigorously for 6 h at 20°. During this time, the orange II was converted into a rose-pink mixture of hydrolysis products. The precipitate was filtered off, washed with water, dried in air, and treated with ether (3 × 20 ml). The ether extracts were evaporated in vacuo, and the residue consisted of di(2,3,5,6-tetrachloro-4-pyridyl)disulfide (III), yield 3.9 g, yellow prisms from hexane, mp 134–135°. Found: Cl 57.29%; S 12.87%; M 492.  $\text{C}_{10}\text{Cl}_8\text{N}_2\text{S}_2$ . Calculated: Cl 57.27%; S 12.90%; M 496. After removal of III, there remained di-(2,3,5,6-tetrachloro-4-pyridyl)sulfonyl sulfide (IV), 0.9 g, yellow prisms, mp 164–166° (from benzene). Found: Cl 54.10%.  $\text{C}_{10}\text{Cl}_8\text{N}_2\text{O}_2\text{S}_2$ . Calculated: Cl 53.78%.

B. 5.2 g (0.018 mole) of II was finely ground, mixed with 50 ml of 1 N NaOH, and stirred for 24 h at 20°. The solid dissolved during this time. The solution was acidified with dilute hydrochloric acid, and the precipitate was filtered off, air-dried, extracted with heptane, and the insoluble portion filtered off. The filtrate was evaporated to give a residue of I, mp 158°. The heptane-insoluble fraction was 4-hydroxy-2,3,5,6-tetrachloropyridine (V), mp 228° (from benzene) (literature mp [7] 232–233°). I and V were identified by mixed mp's.

2, 3, 5, 6-Tetrachloro-4-pyridyl Phenyl Sulfide (VI). To an ethereal solution of phenylmagnesium bromide from 0.5 g (0.02 mole) of magnesium turnings in 20 ml of dry ether was added dropwise 5 g (0.018 mole) of II in 20 ml of dry ether. The mixture was stirred for 30-40 min, treated with water, the ether layer separated, the aqueous layer extracted several times with ether, the ether extracts combined and dried over  $\text{Na}_2\text{SO}_4$ . Removal of the ether gave 5.1 g (90%), mp 95-96° (from isopropanol). Found: Cl 42.90%.  $\text{C}_{11}\text{H}_5\text{Cl}_4\text{NS}$ . Calculated: Cl 43.69%.

2, 3, 5, 6-Tetrachloro-4-pyridyl Ethyl Sulfide (VII). A. To a mixture of 5 g (0.02 mole) of NaOH in 80 ml of ethanol was added dropwise 3.3 g (0.03 mole) of ethyl bromide in 10 ml of ethanol at 60-70°. The mixture was stirred for 2 h at this temperature, then it was cooled, diluted with 150 ml of water, and the VII extracted with ether. The ether extracts were dried over sodium sulfate, and the ether was removed to give 4.9 g (87%) of colorless needles (from isopropanol), mp 49-51°. Found: Cl 51.17; S 11.30%.  $\text{C}_7\text{H}_5\text{Cl}_4\text{NS}$ . Calculated: Cl 51.26; S 11.55%.

2, 3, 5, 6-Tetrachloro-4-pyridyl methyl sulfide was obtained similarly in 72% yield, as needles, mp 62-64° (from isopropanol). Found: Cl 53.71; S 11.96%.  $\text{C}_6\text{H}_3\text{Cl}_4\text{NS}$ . Calculated: Cl 53.95; S 12.16%.

B. To a mixture of 5.7 g (0.02 mole) of II in 50 ml of benzene at 20° (exothermic reaction) was added 3.5 g (0.021 mole) of triethyl phosphite in 15 ml of benzene. The mixture was heated at 80-90° for 30 min, then the benzene was removed and the residue distilled in vacuo to give 3.4 g (63%), bp 108-110° (0.4 mm). Identified by mixed mp.

C. Similarly was obtained VI, in 82% yield.

2, 3, 5, 6-Tetrachloro-4-pyridyl Phenyl Sulfone (IX). A portion of VI [1 g (0.003 mole)] was dissolved in 15 ml of glacial acetic acid, 2 ml of 30% hydrogen peroxide was added, and the mixture was kept for 12 h at 20°. After boiling for 1 h, the mixture was cooled and poured into ice water, and the precipitate was filtered off to give 1 g (90%), mp 207-209° (from heptane). Found: Cl 39.88%.  $\text{C}_{11}\text{H}_5\text{Cl}_4\text{NO}_2\text{S}$ . Calculated: Cl 39.77%.

2, 3, 5, 6-Tetrachloro-4-pyridyl ethyl sulfone (VIII) was obtained similarly in 90% yield, mp 137-138° (from heptane). Found: Cl 45.58%.  $\text{C}_7\text{H}_5\text{Cl}_4\text{NO}_2\text{S}$ . Calculated: Cl 45.95%.

2, 3, 5, 6-Tetrachloro-4-pyridyl Ethyl Sulfoxide (X). A portion of VII [1 g (0.0035 mole)] was added in small portions to 10 ml of  $\text{HNO}_3$  (d 1.42), and the mixture was boiled for 20 min. After cooling, the mixture was diluted with water, and the crystals which separated were filtered off to give 0.7 g (66%) of material, mp 113-115° (from hexane). Found: Cl 48.50%.  $\text{C}_7\text{H}_5\text{Cl}_4\text{NOS}$ . Calculated: Cl 48.46%.

Di-(2, 3, 5, 6-tetrachloro-4-pyridyl) disulfide (III). A portion of II [2 g (0.007 mole)] was mixed with 15 ml of aliphatic alcohols ( $\text{C}_1$  to  $\text{C}_5$ ). As II dissolved, III separated as a yellow precipitate. Yield 1.5 g (70%), mp 134-135° (from heptane).

2, 3, 5, 6-Tetrachloropyridine-4-sulfenamide (XI). A portion of II [2.8 g (0.01 mole)] was dissolved in 20 ml of dry ether, and dry ammonia was passed in at -5° to 0° for 1 h. The mixture was then warmed slowly to 20°, and stirred for 30 min. The solvent was distilled off to dryness, and the residue was washed with water to give 1.7 g (66%), mp 174-176° (from heptane). Found: Cl 53.05%.  $\text{C}_5\text{H}_2\text{Cl}_4\text{N}_2\text{S}$ . Calculated: Cl 53.78%.

2, 3, 5, 6-Tetrachloropyridine-4-sulfenylanilide (XI). To 2.24 g (0.24 mole) of aniline in 20 ml of benzene was added dropwise with stirring 3.1 g (0.0107 mole) of II in 20 ml of benzene at 20°. The mixture was stirred for 2-2.5 h, the precipitate of aniline hydrochloride was filtered off, and the solvent was removed to give 96%, mp 116-118° (from heptane). Found: Cl 42.15; S 9.47%.  $\text{C}_{11}\text{H}_6\text{Cl}_4\text{N}_2\text{S}$ . Calculated: Cl 41.76; S 9.41%.

2, 3, 5, 6-Tetrachloropyridine-4-sulfenmorpholide was obtained similarly, in 90% yield, mp 108-110° (from isopropanol). Found: Cl 42.28%.  $\text{C}_9\text{H}_8\text{Cl}_4\text{N}_2\text{OS}$ . Calculated: Cl 42.21%; and also 2,3,5,6-tetrachloropyridine-4-sulfendiethylamide, 87% yield, yellow prisms, mp 33-34° (from isopropanol). Found: Cl 44.34%.  $\text{C}_{10}\text{H}_{10}\text{Cl}_4\text{N}_2\text{S}$ . Calculated: Cl 44.39%.

2, 3, 5, 6-Tetrachloropyridine-4-sulfendimethylamide (XI). A portion of II [2.8 g (0.01 mole)] was added gradually to 4.3 g of 33% aqueous dimethylamine (0.03 mole) and the mixture was triturated until the orange crystals had disappeared. The solid was filtered off, and washed with water to give 2.8 g (75%) of yellow needles (from methanol), mp 94-96°. Found: Cl 48.62; S 10.81%.  $C_7H_6Cl_4N_2S$ . Calculated: Cl 48.60; S 10.97%.

2, 4-Dimethoxy-3, 5, 6-trichloropyridine (XII). A. To a solution of 0.64 g (0.028 g-atom) of Na in 20 ml of absolute methanol was added dropwise a solution of 4 g (0.014 mole) of II in 15 ml of benzene at a temperature between -10 and -5°. The mixture was then slowly warmed to 20° and stirred for 1 h. The solvent was removed in vacuo, and the residue was treated with water. The solid was filtered off to give 2.2 g (64%) of XII, mp 120° (from ethanol) (literature [8] mp 124-125°). Found: Cl 43.24%.  $C_7H_6Cl_3NO_2$ . Calculated: Cl 43.91%. The aqueous filtrate was acidified to give 1.3 g (36%) of I, mp 163°.

B. To a solution of 0.6 g (0.026 g-atom) of Na in 50 ml of absolute methanol was added 1.5 (0.003 mole) of III, and the mixture was stirred at 20° for 11 h. XII and I were isolated as in method A.

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