SYNTHESIS OF 2-METHYL-3,5,6-TRICHLORO-4-PYRIDYL VINYL SULFONE AND ITS REACTIONS WITH NUCLEOPHILIC REAGENTS

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The reaction of excess primary aliphatic amines and mercaptans with 2-methyl-3,5,6-trichloro-4-pyridyl vinyl sulfone gives products of addition to the double bond.

In the reaction of 2,3,5,6-tetrachloro-4-pyridyl vinyl sulfone (I) with several nucleophilic reagents the sulfonyl group is replaced to give 4-substituted tetrachloropyridines [1]; this was explained by reduction of the electron density of the γ-carbon atom of the pyridine ring owing to the effect of electron-acceptor groups, which favor attack of a nucleophile at the 4 position. The behavior of a sulfonyl group in a molecule in which one of the ortho chlorine atoms is replaced by some electron-donor group, which weakens the electron-acceptor effect of N_1, has remained unclear. We therefore attempted to synthesize analogs of pyridine I containing methyl, morpholyl, and piperidyl groups in the 2 position from 2-methyl-, 2-morpholino-, and 2-piperidino-3,4,5,6-tetrachloropyridines (IIa-c), which were converted to 2-methyl-, 2-morpholino-, and 2-piperidino-4-mercapto-3,5,6-trichloropyridines (IIIa-c) by a modified method [2]. The corresponding 3,5,6-trichloro-4-pyridyl β-chloroethyl sulfides (IVa-c) were obtained by the action of dichloroethane on the sodium salts of sulfides IIIa-c. However, we were able to realize oxidation of pyridines IVa-c with hydrogen peroxide in trifluoroacetic acid to the corresponding sulfones only in the case of 2-methyl-substituted pyridine IVa. The resulting 2-methyl-3,5,6-trichloro-4-pyridyl β-chloroethyl sulfone (V) readily splits hydrogen chloride on heating with triethylamine to give 2-methyl-3,5,6-trichloro-4-pyridyl vinyl sulfone (VI), for which reactions with nucleophilic reagents were also studied.

In contrast to I, which gives several products with various nucleophiles [1], pyridine VI gives exclusively products of addition to the double bond (VIIa-d) with benzylamine, ethyl mercaptan, morpholine, and 4-mercaptotetrachloropyridine. Sulfide VIId was oxidized to sulfone VIII. The sulfonyl group is not replaced even by the action of excesses of the above-indicated nucleophiles; this is probably due to the electron-donor effect of the α-methyl group.

An interesting rearrangement to give bis(2,3,5,6-tetrachloro-4-pyridyl) sulfide was previously observed when 2,3,5,6-tetrachloro-4-pyridyl β-(2,3,5,6-tetrachloro-4-pyridylthio)ethyl sulfone (from I and 4-mercaptotetrachloropyridine) was heated in dimethylformamide (DMFA) [1]. This sort of rearrangement does not occur in the case of pyridine VIIc, and this is also explained by an increase in the electron density in the position in comparison with analogous substances obtained from I.

EXPERIMENTAL

2-Morpholino-3,5,6-trichloro-4-mercaptopyridine (IIIb). A heated solution of 1 g (18 mmole) of freshly prepared sodium hydrosulfide in 50 ml of absolute DMFA was added to a hot solution of 2.42 g (8 mmole) of 2-morpholino-3,4,5,6-tetrachloropyridine [3] in 50 ml of absolute DMFA, and the mixture was refluxed for 2 min, after which it was poured into water and acidified with concentrated HCl.

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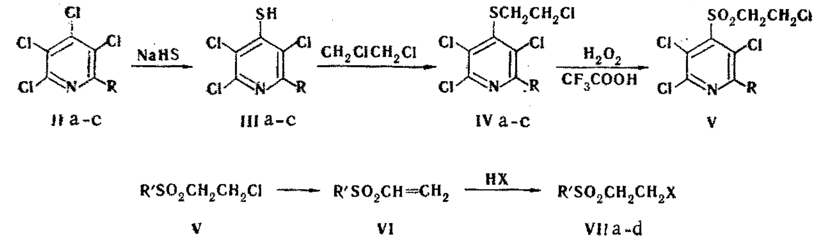

IIa R = CH_3, b R = morpholino, c R = piperidino; IIIa R = CH_3, b R = morpholino, c R = piperidino; IV a R = CH_3, b R = morpholino, c R = piperidino; V R = CH_3, R' = 2-methyl-3,5,6-trichloro-4-pyridyl; VI R' = 2-methyl-3,5,6-trichloro-4-pyridyl; VII R' = 2-methyl-3,5,6-trichloro-4-pyridyl, a X = $NHCH_2C_6H_5$, b X = morpholino, c X = SC_5Cl_4N, d X = SC_2H_5

The product solidified some time after its isolation to give 2.3 g (95%) of a product with mp 70-72° (from aqueous ethanol). Found: Cl 35.9; S 10.9%. $C_9H_9Cl_3N_2OS$. Calculated: Cl 35.5; S 10.7%. A similar procedure was used to obtain 2-piperidino-3,5,6-trichloro-4-mercapto pyridine (IIIc) [mp 83-84° (from propanol)] in 91% yield. Found: Cl 35.3; S 10.8%. $C_{10}H_{11}Cl_3N_2S$. Calculated: Cl 35.8; S 10.7% and 2-methyl-3,5,6-trichloro-4-mercaptopyridine (IIIa) [mp 105-107° (from propanol] in 89% yield. Found: Cl 46.4; S 14.2%. $C_6H_4Cl_3NS$. Calculated: Cl 46.6; S 14.0%.

2-Morpholino-3,5,6-trichloro-4-pyridyl β-Chloroethyl Sulfide (IVb). A 0.17-g (7.4 mg-atom) sample of sodium was dissolved in 50 ml of absolute methanol, and 2.2 g (7.3 mmole) of pyridine IIIb was added to the solution. After IIIb had dissolved completely, 30 ml of dichloroethane was added, and the mixture was refluxed for 2 h. The solvent was then removed by vacuum evaporation, and the residue was treated with water to give 2.3 g (87%) of a product with mp 125-127° (from aqueous ethanol). Found: Cl 39.2; S 8.8%. $C_{11}H_{12}Cl_4N_2OS$. Calculated: Cl 39.2; S 8.8%. A similar procedure was used to obtain 2-piperidino-3,5,6-trichloro-4-pyridyl β-chloroethyl sulfide (IVc) [mp 87-89° (from aqueous ethanol] in 82% yield. Found: Cl 39.6; S 9.0%. $C_{12}H_{14}Cl_4N_2S$. Calculated: Cl 39.4; S 8.9%] and 2-methyl-3,5,6-trichloro-4-pyridyl β-chloroethyl sulfide (IVa) [with mp 74-76° (from aqueous ethanol)] in 91% yield. Found: Cl 48.5; S 11.1%. $C_8H_7Cl_4NS$. Calculated: Cl 48.8; S 11.0%.

2-Methyl-3,5,6-trichloro-4-pyridyl β-Chloroethyl Sulfone (V). A 2.9-g (10 mmole) sample of IVa was dissolved in 20 ml of trifluoroacetic acid, 7 ml of 30% H_2O_2 was added, and the mixture was allowed to stand for 12 h. It was then refluxed for 10-15 min and poured over ice. Workup gave 3 g (93%) of a product with mp 182-184° (from heptane). Found: Cl 43.4; S 9.6%. $C_8H_7Cl_4NO_2S$. Calculated: Cl 43.9; S 9.9%.

2-Methyl-3,5,6-trichloro-4-pyridyl Vinyl Sulfone (VI). A 2.8-g (8.7 mmole) sample of V was dissolved in 20 ml of anhydrous benzene, 2 ml of triethylamine was added, and the mixture was held at 80° for 20 min. The triethylamine hydrochloride was removed by filtration, and the solvent was removed by vacuum distillation to give 2.2 g (87%) of a product with mp 115-116° (from ethanol). Found: Cl 37.2; S 10.9%. $C_8H_6Cl_3NO_2S$. Calculated: Cl 37.2; S 11.2%.

2-Methyl-3,5,6-trichloro-4-pyridyl β-Benzylaminoethyl Sulfone (VIIa). A 0.3-g (1.04 mmole) sample of pyridine VI was dissolved in 10 ml of absolute benzene, and 0.2 ml of freshly distilled benzylamine was added. The mixture was then held at 20° for 1 h, after which the benzene was removed in vacuo to give 0.36 g (88%) of a product with mp 131-132° (from heptane). Found: Cl 26.9; S 7.9%. $C_{15}H_{15}Cl_3N_2O_2S$. Calculated: Cl 27.1; S 8.1%.

2-Methyl-3,5,6-trichloro-4-pyridyl β-Morpholinoethyl Sulfone (VIIb). This compound was similarly obtained in 85% yield and had mp 137-138° (from alcohol–heptane). Found: Cl 28.5; S 8.2%. $C_{12}H_{15}Cl_3N_2O_3S$. Calculated: Cl 28.5; S 8.5%.

2-Methyl-3,5,6-trichloro-4-pyridyl β-(2,3,5,6-Tetrachloro-4-pyridylthio)ethyl Sulfone (VIIc). Three to four drops of triethylamine were added to a mixture of 0.77 g (2.68 mmole) of VI and 0.67 g (2.68 mmole) of 2,3,5,6-tetrachloro-4-pyridylsulfene hydrate in 20 ml of anhydrous benzene, and the mixture was allowed to stand at 20° for 24 h. Workup gave 1.3 g (91%) of a product with mp 244-245° (dec., from aqueous dioxane). Found: Cl 46.1; S 11.7%. $C_{13}H_7Cl_7N_2O_2S_2$. Calculated: Cl 46.4; S 11.9%. A similar procedure was used to obtain 2-methyl-3,5,6-trichloro-4-pyridyl β-ethylthioethyl sulfone (VIId) with mp 137-138° (from ethanol) in 83% yield. Found: Cl 30.4; S 17.9%. $C_{10}H_{12}Cl_3NO_2S_2$. Calculated: Cl 30.5; S 18.4%.

2-Methyl-3,5,6-trichloro-4-pyridyl β-Ethylsulfonylethyl Sulfone (VIII). A 0.35-g (1 mmole) sample of sulfide VIId was dissolved in 10 ml of trifluoroacetic acid, and 2 ml of 30% H_2O_2 was added. The mixture was held at 20° for 12 h, after which it was refluxed for 10 min and poured over ice. Workup gave 0.32 g (84%) of a product with mp 226-228° (dec., from ethanol). Found: Cl 27.8; S 16.8%. $C_{10}H_{12}Cl_3NO_4S_2$. Calculated: Cl 28.0; S 16.8%.

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