REACTION OF 2,3,5,6-TETRACHLORO-4-PYRIDYL VINYL SULFONE WITH NUCLEOPHILIC AGENTS

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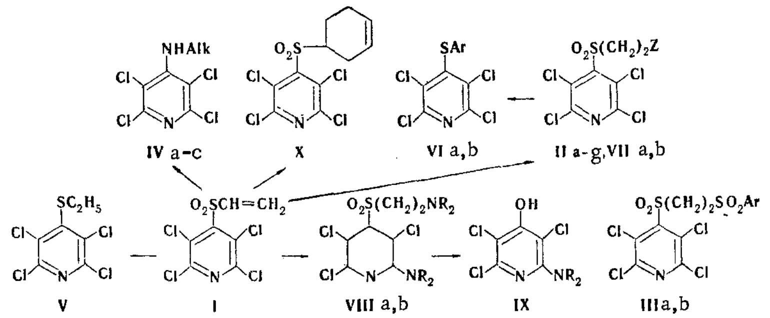
The reactions of 2,3,5,6-tetrachloro-4-pyridyl vinyl sulfone (I) with nucleophilic agents were studied. It was established that products of addition to the double bond of I are formed in the reaction of equivalent amounts of primary aliphatic amines and mercaptans, while the β-alkylamino and β-alkylthioethylsulfonyl groups are displaced to give 4-alkylamino- or 4-alkylthiotetrachloropyridines in the reaction with excess amines and mercaptans. Aromatic amines, phenols, thiophenols, and alcohols add to the double bond of I. Morpholine and piperidine add to the double bond of I when they are present in equivalent quantities, and the chlorine atom in the 2 position of the pyridine ring is also replaced when excess amine is present.

In a continuation of our previous investigation [1] of sulfur-containing derivatives of polyhalopyridines, we have studied the reaction of 2,3,5,6-tetrachloro-4-pyridyl vinyl sulfone (I) with various nucleophilic agents. The I molecule should have high reactivity with respect to nucleophilic agents in connection with the presence of chlorine atoms in the pyridine ring and a vinyl group in which the double bond has a clearly expressed electrophilic character under the influence of the strong electron-acceptor tetrachloropyridylsulfonyl group.

The direction and rate of the reaction of I with nucleophilic agents depend substantially on the nature of the nucleophile. The reaction of I with aniline, phenol, and ethanol requires brief heating and occurs with the formation of products of addition to the double bond (IIa-c). The use of ammonia, 4-mercaptotetrachloropyridine, and pentachlorothiophenol gives similar nucleophilic addition products, but, in this case, the reaction occurs at room temperature in 10 min. The resulting 2,3,5,6-tetrachloro-4-pyridyl β-(2,3,5,6-tetrachloro-4-pyridylthio)ethyl sulfone (IIe) and 2,3,5,6-tetrachloro-4-pyridylthio β-(pentachlorophenylthio)-ethyl sulfone (IIf) were oxidized with chromic anhydride in sulfuric acid to the corresponding disulfones (IIIa-b).



IV Alk = $CH_2C_6H_5$, C_3H_5, CH_3; III, VI Ar = C_5Cl_4N, C_6Cl_5; II a Z = NHC_6H_5, b OC_6H_5, c OC_2H_5, d NH_2, e SC_5Cl_4N, f SC_6Cl_5, g $NHCH_2C_6H_5$; VII Z = NR_2; VII a, VIII a, IX NR_2 = morpholino, VII b, VIII b NR_2 = piperidino

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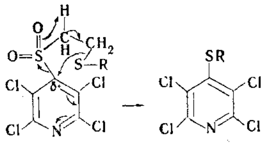
Depending on the reagent ratio, two types of compounds are formed in the reaction of I with strong nucleophilic agents – methyl-, allyl-, and benzylamines and ethyl mercaptan. Adducts II are obtained when equimolecular amounts are used; excess nucleophile results in an unusual reaction, which consists in the formation of 4-alkylaminotetrachloropyridines (IV), 4-ethylthiotetrachloropyridine (V), and the corresponding inner salts of β-alkylamino- or β-ethylthioethanesulfinic acid. The mechanism of this reaction includes initial addition of the nucleophile to the double bond of I to form adduct II. The latter is then attacked by excess nucleophile at the carbon atom in the 4 position of the pyridine ring, from which the electrons are withdrawn by the sulfonyl group, the chlorine atoms, and the nitrogen atom of the heterocyclic ring.

When IIe,f are heated in dimethylformamide (DMF), one observes decomposition of the molecule, which leads, via an internal nucleophilic substitution mechanism (S_Ni), to the formation of bis(2,3,5,6-tetrachloro-4-pyridyl) sulfide (VIa) in the case of IIe, and to (2,3,5,6-tetrachloro-4-pyridyl) pentachlorophenyl sulfide (VIb) in the case of IIf.



In the case of piperidine and morpholine, the reaction with I proceeds in two directions. The use of equimolecular amounts of morpholine gives 2,3,5,6-tetrachloro-4-pyridyl β-morpholinoethyl sulfone (VIIa). When excess morpholine is present, in addition to nucleophilic addition to the double bond, the chlorine atom in the pyridine ring is replaced to give 2-morpholino-3,5,6-trichloro-4-pyridyl β-morpholinoethyl sulfone (VIIIa). The position of the morpholine residue in the ring was proved by conversion of VIII to 2-morpholino-4-hydroxy-3,5,6-trichloropyridine (IX) by brief heating with 1 N alkali solution. No melting-point depression was observed for a mixture of IX with the substance that we previously obtained [2]. The stability of the products of the addition of morpholine and piperidine to I is apparently explained by steric hindrance to the approach of the cyclic nitrogen atom to the carbon atom in the 4 position.

Sulfone I undergoes the diene synthesis. It reacts with butadiene to give 4-(2,3,5,6-tetrachloro-4-pyridylsulfonyl)cyclohexene (X).

EXPERIMENTAL

2,3,5,6-Tetrachloro-4-pyridyl β-Phenylaminoethyl Sulfone (IIa). A 0.25-g (0.8 mmole) sample of I was dissolved in 10 ml of heptane, 0.2 g (2 mmole) of freshly distilled aniline was added, and the mixture was refluxed for 10 min. It was then treated with acidified water and extracted with benzene to give 0.26 g (80%) of a product with mp 139-141° (from heptane). Found,%: Cl 35.8; S 8.1. $C_{13}H_{10}Cl_4N_2O_2S$. Calculated,%: Cl 35.5; S 8.0.

2,3,5,6-Tetrachloro-4-pyridyl β-Phenoxyethyl Sulfone (IIb). Two drops of triethylamine were added to a mixture of 0.31 g (1 mmole) of I and 0.094 g (1 mmole) of phenol in 10 ml of anhydrous heptane, and the mixture was allowed to stand at 20° for 24 h. The heptane was removed by distillation to give 0.33 g (82%) of a product with mp 125-126° (from ethanol). Found,%: Cl 34.8; S 7.9. $C_{13}H_9Cl_4NO_3S$. Calculated,%: Cl 35.4; S 8.0.

2,3,5,6-Tetrachloro-4-pyridyl β-Ethoxyethyl Sulfone (IIc). Three drops of 2% aqueous KOH solution were added to a mixture of 0.31 g (1 mmole) of I in 10 ml of ethanol, and the mixture was refluxed for 5 h. The solvent was removed by distillation to give 0.37 g (80%) of a product with mp 108-110° (from heptane). Found,%: Cl 40.2; S 9.1. $C_9H_9Cl_4NO_3S$. Calculated,%: Cl 40.2; S 9.1.

2,3,5,6-Tetrachloro-4-pyridyl β-Aminoethyl Sulfone (IId). Ammonia was bubbled for 20 min into a solution of 0.8 g (2.6 mmole) of I in 20 ml of dry ether. The ether was removed by distillation to give 0.55 g (84%) of a product with mp 139-142° (from aqueous ethanol). Found,%: Cl 43.9; S 10.0. $C_7H_6Cl_4N_2O_2S$. Calculated,%: Cl 43.8; S 9.9.

2,3,5,6-Tetrachloro-4-pyridyl β-(2,3,5,6-Tetrachloro-4-pyridylthio)ethyl Sulfone (IIe). Three drops of triethylamine were added to a mixture of 0.31 g (1 mmole) of I and 0.25 g (1 mmole) of 4-mercapto-2,3,5,6-tetrachloropyridine in 20 ml of absolute ether, and the mixture was held at 20° for 20 min. The ether was removed by distillation to give 0.47 g (83%) of a product with mp 252-253° (from acetic acid). Found,%: Cl 51.0; N 5.0. $C_{12}H_4Cl_8N_2O_2S_2$. Calculated,%: Cl 51.1; N 5.0.

2,3,5,6-Tetrachloro-4-pyridyl β-(Pentachlorophenylthio)ethyl Sulfone (IIf). This compound was obtained in 86% yield by the method used to prepare IIe and had mp 222-223° (from nitromethane). Found,%: Cl 53.7; N 2.6. $C_{13}H_4Cl_9NO_2S_2$. Calculated,%: Cl 54.2; N 2.4.

2,3,5,6-Tetrachloro-4-pyridyl β-Benzylaminoethyl Sulfone (IIg). A 0.34-g (3.1 mmole) sample of benzylamine was added to a mixture of 0.98 g (3.1 mmole) of I in 20 ml of absolute ether, and the mixture was held at room temperature for 2 h. The ether was removed by distillation to give 0.93 g (68%) of a product with mp 103-105° (from benzene and heptane). Found,%: Cl 34.2; S 7.8. $C_{14}H_{12}Cl_4N_2O_2S$. Calculated,%: Cl 34.3; S 7.7.

Bis(α,β-2,3,5,6-tetrachloro-4-pyridylsulfonyl)ethane (IIIa). A mixture of 0.2 g (0.36 mmole) of IIe, 0.2 g (2 mmole) of chromic anhydride, 3 ml of H_2SO_4, and 1 ml of H_2O was heated at 130° for 20-25 min with stirring. It was then poured over ice, and the aqueous mixture was filtered to give 0.2 g (95%) of a product with mp 268-270° (from aqueous dioxane). Found,%: Cl 48.3; N 4.8. $C_{12}H_4Cl_8N_2O_4S_2$. Calculated,%: Cl 48.3; N 4.8.

A similar method was used to obtain IIIb in 72% yield with mp 272-274° (from acetic acid). Found,%: Cl 50.8; S 10.1. $C_{13}H_4Cl_9NO_4S_2$. Calculated,%: Cl 51.4; S 10.3.

4-Benzylamino-2,3,5,6-tetrachloropyridine (IVa). A 0.43-g (4 mmole) sample of benzylamine was added to a mixture of 0.62 g (2 mmole) of I in 15 ml of absolute ether, and the mixture was held at 20° for 30 min. The inner salt of β-benzylaminoethanesulfinic acid with mp 167-169° was then removed by filtration. Found,%: N 7.1; S 15.9. $C_9H_{13}NO_2S$. Calculated,%: N 7.0; S 16.1. The mother liquor was evaporated to dryness to give 0.57 g (89%) of IVa with mp 124-125° (from hexane) [3].

4-Allylamino-2,3,5,6-tetrachloropyridine (IVb). This compound was obtained in 68% yield by the procedure used to obtain IVa and had mp 46-48° (from heptane). Found,%: Cl 52.1; N 10.2. $C_8H_6Cl_4N_2$. Calculated,%: Cl 52.2; N 10.3.

4-Methylamino-2,3,5,6-tetrachloropyridine (IVc). This compound was similarly obtained in 71% yield and had mp 124-125° (from heptane). Found,%: Cl 57.6; N 11.5. $C_6H_4Cl_4N_2$. Calculated,%: Cl 57.7; N 11.4.

4-Ethylthio-2,3,5,6-tetrachloropyridine (V). Two drops of triethylamine and 2 ml of ethyl mercaptan were added to 0.31 g (1 mmole) of I in 15 ml of absolute ether, and the resulting flocculent precipitate of the inner salt of ethylthioethanesulfinic acid was removed by filtration. The ether was evaporated to give 0.2 g (72%) of V with mp 46-47° (from methanol). Found,%: Cl 51.5; N 11.3. $C_7H_5Cl_4NS$. Calculated,%: Cl 51.3; N 11.5.

Bis(2,3,5,6-tetrachloro-4-pyridyl) Sulfide (VIa). A. A mixture of 0.2 g (0.36 mmole) of IIe and 3 ml of dimethylformamide was heated at 155° for 10 min, after which it was cooled and treated with water to give 0.13 g (81%) of a product with mp 254-256° (from DMF). Found,%: Cl 60.9; N 6.1; S 6.9. $C_{10}Cl_8N_2S$. Calculated,%: Cl 61.2; N 6.0; S 6.9.

B. A mixture of 0.27 g (0.01 mole) of the sodium salt of 4-mercapto-2,3,5,6-tetrachloropyridine and 0.25 g (0.01 mole) of pentachloropyridine in 10 ml of DMF was refluxed for 2 h. The precipitated NaCl was removed by filtration, and the filtrate was diluted with water to give 0.4 g (90%) of VIa with mp 250-252° (from DMF).

A similar procedure was used to obtain 2,3,5,6-tetrachloro-4-pyridyl pentachlorophenyl sulfide (VIb) with mp 232° (from DMF). Found,%: Cl 63.9. $C_{11}Cl_9NS$. Calculated,%: Cl 64.0.

2,3,5,6-Tetrachloro-4-pyridyl β-Morpholinoethyl Sulfone (VIIa). A 0.31-g (1 mmole) sample of I was dissolved in 10 ml of absolute ether, 0.09 g (1 mmole) of morpholine was added, and the mixture was held at 20° for 2 h. The ether was removed to give 0.32 g (82%) of a product with mp 135-136° (from ethanol). Found,%: Cl 36.1; N 7.2. $C_{11}H_{12}Cl_4N_2O_3S$. Calculated,%: Cl 36.0; N 7.1.

2,3,5,6-Tetrachloro-4-pyridyl β-Piperidinoethyl Sulfone (VIIb). This compound was similarly obtained in 76% yield and had mp 134-135° (from heptane). Found,%: Cl 35.8; N 7.3. $C_{12}H_{14}Cl_4N_2O_2S$. Calculated,%: Cl 36.2; N 7.1.

2-Morpholino-3,5,6-trichloro-4-pyridyl β-Morpholinoethyl Sulfone (VIIIa). A 0.31-g (1 mmole) sample of I was dissolved in 10 ml of anhydrous ether, 0.27 g (3 mmole) of morpholine was added, and the mixture was allowed to stand at 20° for 2 h. The solvent was removed by distillation to give 0.38 g (86%) of a product with mp 160-161° (from ethanol). Found,%: Cl 23.8; N 9.5. $C_{15}H_{20}Cl_3N_3O_4S$. Calculated,%: Cl 23.9; N 9.4.

2-Piperidino-3,5,6-trichloro-4-pyridyl β-Piperidinoethyl Sulfone (VIIIb). This compound was obtained in 61% yield by the method used to prepare VIIIa and had mp 70-71° (from aqueous methanol). Found,%: Cl 24.2; N 9.9. $C_{17}H_{24}Cl_3N_3O_2S$. Calculated,%: Cl 24.2; N 9.5.

2-Morpholino-4-hydroxy-3,5,6-trichloropyridine (IX). A 0.22-g (0.5 mmole) sample of VIIa was dissolved in 15 ml of ethanol, 3 ml of 1 N NaOH solution was added, and the mixture was refluxed for 2 h. It was then cooled and acidified to give 0.1 g (74%) of a product with mp 221-222° (from ethanol) (mp 224-225° [2]). Found,%: Cl 37.3; N 10.2. $C_9H_9Cl_3N_2O_2$. Calculated,%: Cl 37.6; N 9.9.

4-(2,3,5,6-Tetrachloro-4-pyridylsulfonyl)cyclohexene (X). A 0.62-g (2 mmole) sample of I and 0.5 g of 1,3-butadiene in 10 ml of acetone was heated in a sealed tube at 150° for 5 h to give 0.58 g (80%) of a product with mp 145-147° (from isopropyl alcohol). Found,%: Cl 39.3; N 4.0. $C_{11}H_9Cl_4NO_2S$. Calculated,%: Cl 39.3; N 3.9.

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