REACTION OF 2,3,5,6-TETRACHLOROPYRIDINE-4-SULFENYL CHLORIDE WITH OLEFINS

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The direction of the reaction of 2,3,5,6-tetrachloropyridine-4-sulfenyl chloride (I) with unsymmetrical 1-alkenes was established by means of the PMR spectra. The reaction gives primarily a mixture of two adducts. The oxidation of several adducts was studied.

Continuing our study [1] of the chemical properties of 2,3,5,6-tetrachloropyridine-4-sulfenyl chloride (I), we investigated the reaction of I with olefins containing a terminal double bond. In the case of ethylene, the reaction proceeds quantitatively to give 2,3,5,6-tetrachloro-4-pyridyl 2-chloroethyl sulfide (II). The reaction rate depends substantially on the nature of the solvent. In polar solvents, the reaction is complete in 20 min, while in nonpolar solvents the reaction goes to completion in 40 min. The reactivity of sulfide II differs somewhat from the analogous sulfide that does not contain a chlorine atom in the aliphatic chain. 2,3,5,6-Tetrachloro-4-pyridyl 2-chloroethyl sulfoxide (III) is obtained instead of the expected sulfone when II is oxidized with 30% hydrogen peroxide in acetic acid; III is also formed in the oxidation of II with nitric acid. We were able to oxidize sulfide II to 2,3,5,6-tetrachloro-4-pyridyl 2-chloroethyl sulfone (IV) by the action of chromic anhydride in sulfuric acid or 30% hydrogen peroxide in trifluoroacetic acid. In both cases, IV was obtained in quantitative yield. Splitting out of hydrogen chloride from sulfone IV by the action of triethylamine occurs rapidly in 15-20 min at 80°C. Splitting out of HCl from sulfoxide III of analogous structure under the same conditions is complete only after 2 h. This method was used to obtain 2,3,5,6-tetrachloro-4-pyridyl vinyl sulfone (V) and 2,3,5,6-tetrachloro-4-pyridyl vinyl sulfoxide (VI).

While the reaction with I proceeds unambiguously in the case of symmetrical olefins, the formation of two isomers is possible in the case of unsymmetrical olefins. The reaction of I with propylene was carried out in carbon tetrachloride, and the reaction products were analyzed from the PMR spectrum. Since I is an electrophilic reagent, one can expect that an increase in the nucleophilicity of the olefin double bond will increase the reaction rate. The reaction of I with propylene in carbon tetrachloride and in other solvents is completed more rapidly than with ethylene, and the nature of the solvent affects not only the reaction rate but also the isomer ratio (Table 1).

TABLE 1. Isomer Ratio in the Reaction of I with Propylene in Various Solvents

Solvent	Yield of add. prod. VII formed in accord. with Markovnikov rule, %	Yield of add. product VIII, formed counter to Markovnikov rule, %
Ethyl acetate	15	85
Chloroform	15	85
Methylene chloride	25	75
Carbon tetrachloride	35	65
Acetic acid	40	60

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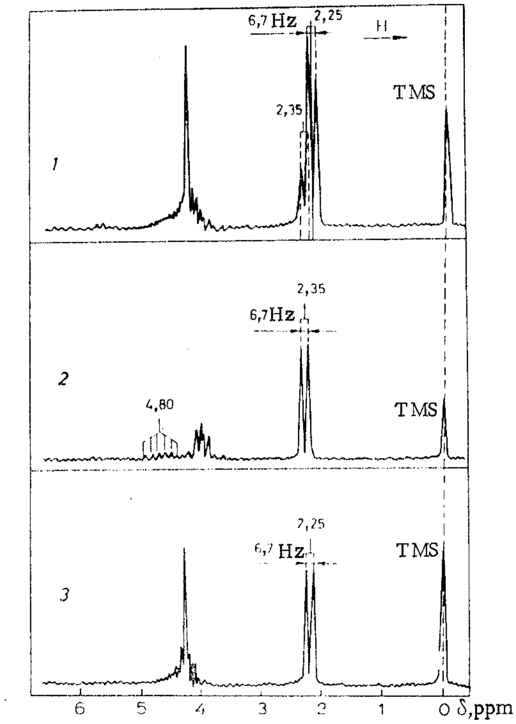


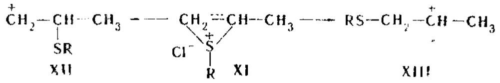
Fig. 1. PMR spectra: 1) mixture of 2,3,5,6-tetrachloro-4-pyridyl 2-chloropropyl sulfide (VII) and 2,3,5,6-tetrachloro-4-pyridyl 1-methyl-2-chloroethyl sulfide (VIII); 2) VII; 3) VIII.

The relative amounts of isomers were established by means of PMR spectroscopy by calculation of the integral intensity of the methyl signals. Mueller and Butler [2], in an investigation of the PMR spectra of a similar group of compounds, made several correlations with respect to the position of the absorption signals of different protons: the protons of the methyl group in the α position relative to the chlorine atom and in the β position with respect to sulfur are less shielded than the protons of the methyl group in the α position relative to the sulfur atom and in the β position relative to the chlorine atom. As a result of this, the signals of the protons of the more shielded methyl group will lie at stronger field.

The reaction mixture was analyzed without isolation of the individual reaction products. Three lines, of which the middle line is apparently the result of overlapping of the right-hand component of the doublet at δ 2.35 ppm and the left-hand component of the doublet at 2.25 ppm, are observed in the PMR spectrum in the region of methyl group resonance (Fig. 1). In both cases, the spin-spin coupling constant is identical (J = 6.7 Hz). Thus the doublet at 2.35 ppm corresponds to the structure in which the methyl group is separated from the sulfur atom by two carbon atoms – 2,3,5,6-tetrachloro-4-pyridyl 2-chloropropyl sulfide (VII); the doublet at 2.25 ppm corresponds to the structure in which the methyl group is separated from the sulfur atom by one carbon atom – 2,3,5,6-tetrachloro-4-pyridyl 1-methyl-2-chloroethyl sulfide (VIII). A comparison of the PMR spectra of the products of the reaction of I with propylene recorded immediately after the reaction and 5 days later indicates that the quantitative ratio of isomers VII and VIII remains virtually constant. Repeated crystallization of the reaction products led to the disappearance of signals corresponding to product VII, and a doublet at 2.25 ppm, which corresponds to product VIII, is observed in the spectrum in place of the three lines (Fig. 1).

Attempts were made to isolate individual isomers VII and VIII by carrying out a number of chemical transformations of 2,3,5,6-tetrachloro-4-mercaptopyridine [3]. The latter gives two sulfides with the two isomeric bromopropanols: 2,3,5,6-tetrachloro-4-pyridyl 2-hydroxypropyl sulfide (IX) and 2,3,5,6-tetrachloro-4-pyridyl 1-methyl-2-hydroxyethyl sulfide (X), which both give a single product (VII) on reaction with thionyl chloride. Three groups of lines with an intensity ratio of 1 : 2 : 3 are observed in the PMR spectrum of VII (Fig. 1). The weakest-field signal at 4.8 ppm is split into six components and apparently corresponds to a methylidyne proton. The minimal shielding of this methylidyne proton is evidence that the methyl group in this compound is separated from the sulfur atom by two carbon atoms. Thus it was established that, as a result of the action of thionyl chloride on sulfide X, which contains a terminal hydroxyl group, the hydroxyl group is replaced by chlorine with subsequent isomerization of VIII to the thermodynamically more stable VII. The isomerization of VIII to VII occurs only when VIII is heated in acetic acid. The isomerization does not occur when VIII is allowed to stand in acetic and trifluoroacetic acids at room temperature or when it is heated for a long time in nonpolar solvents.

Like the addition of sulfenyl chlorides to the double bond [4], the isomerization of some chloro sulfides [5] proceeds with the formation of an intermediate episulfonium ion (XI), the orientation of the opening of which depends on the nucleophilicity of the sulfur atom [6].



The comparative ease of the isomerization of VIII to VII in acetic acid can apparently be explained by the primary formation of the more stable carbonium ion XIII [7], which can be stabilized by capture of a chloride ion. The isomerization in acetic acid is explained by an increase in the solvation of the chloride ion, which has a substantial effect on the orientation of the opening of XI in the direction to favor formation of a Markovnikov addition product [8].

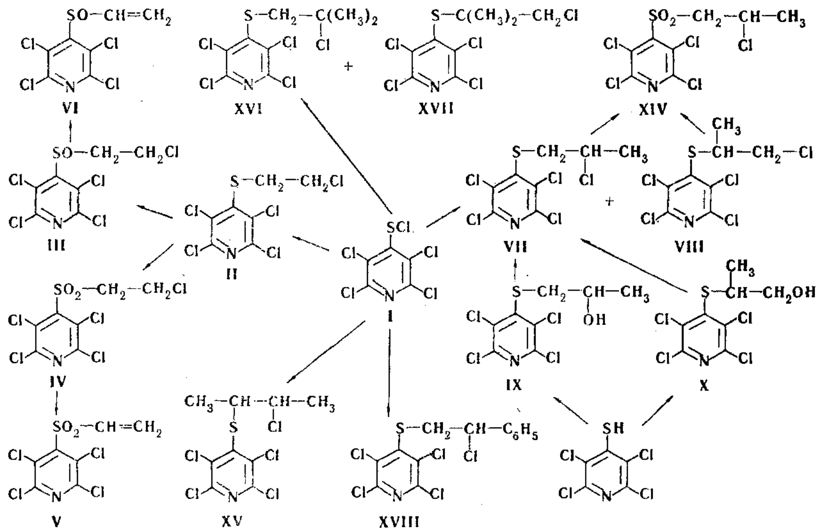
Attempts were made to obtain the two corresponding sulfones by oxidation of VII and VIII with hydrogen peroxide in acetic acid. However, only one product - 2,3,5,6-tetrachloro-4-pyridyl 2-chloropropyl sulfone (XIV) — was obtained under these conditions. The product of XIV from VIII is possible only when it undergoes preliminary isomerization to VII, which then gives XIV. Attempts to oxidize VIII to the corresponding sulfone at room temperature with subsequent heating also results in the formation of XIV.

The reaction of I with 2-butene gives a quantitative yield of 2,3,5,6-tetrachloro-4-pyridyl 1-methyl-2-chloropropyl sulfide (XV), in the PMR spectrum of which one observes two doublets of the methyl protons at 2.05 ppm (signal of the methyl protons in direct proximity to the sulfur atom) and 2.23 ppm (signal of the methyl protons in direct proximity to the chlorine atom) and, respectively, two quartets of methylidyne protons at 4.47 and 4.6 ppm, which confirms structure XV.

A mixture containing 60% 2,3,5,6-tetrachloro-4-pyridyl 2-methyl-2-chloropropyl sulfide (XVI) and 40% 2,3,5,6-tetrachloro-4-pyridyl 1,1-dimethyl-2-chloroethyl sulfide (XVII) is obtained in the reaction of I with isobutene. The structures and ratio of the isomers were established by means of the PMR spectra, which demonstrated the presence of four distinct signals. The chemical shifts of 2.37 and 4.15 ppm pertain, respectively, to the methyl and methylene protons in XVI, while the chemical shifts of 2.17 and 4.47 ppm correspond to the methyl and methylene protons in XVII. Repeated crystallization of the mixture of above products gave pure XVI, the PMR spectrum of which showed two singlets at 2.35 and 4.1 ppm, which correspond to the methyl and methylene protons.

The reaction of I with styrene gives exclusively 2,3,5,6-tetrachloro-4-pyridyl 2-chloro-2-phenylethyl sulfide (XVIII), the PMR spectrum of which is typical for an ABX system [9]. An analysis of the spectrum gives chemical shifts of 4.2 and 4.6 ppm for the H(A) and H(B) methylene protons and a chemical shift of 5.62 ppm for the H(X) methylidyne proton. The intensity ratio of the observed multiplets is 2 : 1, and the less intense group of lines lies at weaker field and consequently pertains to the methylidyne proton of the —CHCl group. Thus the product under consideration has the XVIII structure. Stabilization of the partially positive charge of the α-carbon atom due to overlapping of the p orbital of the depleted α-carbon atom of the episulfonium ion with the π electrons of the benzene ring will, in the case of styrene, lead to exclusively the Markovnikov addition product.

On the basis of the above investigation, it was established that the reaction of I with olefins containing a terminal double bond generally proceeds to give two adducts. The presence of an electron-acceptor tetrachloropyridyl substituent in the sulfenyl chloride stabilizes the reaction product considerably as compared with electron-donor substituents [10] and hinders isomerization of the products of addition formed counter to the Markovnikov rule to Markovnikov products. When olefins with linear structures are used,



products of addition counter to the Markovnikov rule are primarily obtained, and the use of bulky substituents in olefins, which create steric hindrance to the α-carbon atom of the carbon-carbon double bond, favors the primary formation of Markovnikov products.

EXPERIMENTAL

2,3,5,6-Tetrachloro-4-pyridyl 2-Chloroethyl Sulfide (II). A 2.8-g (10 mmole) sample of I was dissolved in 20 ml of CH_2Cl_2, and ethylene was bubbled into the mixture at 0° until the orange coloration disappeared (10-15 min). Slight warming of the reaction mixture took place. The solvent was removed by vacuum distillation to give 2.9 g (93%) of a product with mp 94-95° (from heptane). Found: Cl 56.9; S 10.8%. $C_7H_4Cl_5NS$. Calculated: Cl 57.0; S 10.3%.

2,3,5,6-Tetrachloro-4-pyridyl 2-Chloroethyl Sulfoxide (III). A 2.0-g (6.4 mmole) sample of II was dissolved in 15 ml of glacial acetic acid, and 3 ml of 30% H_2O_2 was added in small portions. The mixture was refluxed for 10-15 min and poured over ice to give 2 g (96%) of a product with mp 119-121° (from heptane). Found: Cl 54.1; S 10.0. $C_7H_4Cl_5NOS$. Calculated: Cl 54.2; S 9.8%.

2,3,5,6-Tetrachloro-4-pyridyl 2-Chloroethyl Sulfone (IV). A) A 2-g (6.4 mmole) sample of II was dissolved in 20 ml of trifluoroacetic acid, and 5 ml of 30% H_2O_2 was added. The mixture was heated to 60°, after which the reaction proceeded vigorously without additional heating. The mixture was cooled to precipitate 2 g (91%) of crystals with mp 183-184° (from aqueous ethanol). Found: Cl 51.6; S 9.4%. $C_7H_4Cl_5NO_2S$. Calculated: Cl 51.7; S 9.3%.

B) A mixture of 2 g (6.4 mmole) of II, 5 ml of H_2SO_4 (sp. gr. 1.84), 1 g of CrO_3, and 5 ml of water was heated with stirring at 140-150° for 1.5-2 h. The mixture was cooled and diluted with 10 ml of water, and the resulting precipitate was removed by filtration to give 2 g (90%) of a product with mp 184-185° (from heptane).

2,3,5,6-Tetrachloro-4-pyridyl Vinyl Sulfone (V). A 1-g (2.4 mmole) sample of IV was dissolved in 15 ml of anhydrous benzene, 0.3 ml of triethylamine was added, and the mixture was held at 80° for 20 min. The solvent was removed by vacuum distillation, and the residue was treated with acidified water and extracted with ether to give 0.8 g (90%) of a product with mp 111-113° (from heptane). Found: Cl 46.8; S 10.5%. $C_7H_3Cl_4NO_2S$. Calculated: Cl 46.2; S 10.4%.

2,3,5,6-Tetrachloro-4-pyridyl Vinyl Sulfoxide (VI). A 1.4-g (4 mmole) sample of III was dissolved in 15 ml of dry heptane, 0.45 g of triethylamine was added, and the mixture was refluxed for 2 h. The triethylamine hydrochloride was removed by filtration, and the solvent was removed by distillation to give 1 g (80%) of a product with mp 95-97° (from heptane). Found: Cl 49.0; S 10.8%. $C_7H_3Cl_4NOS$. Calculated: Cl 48.8; S 11.0%.

Reaction of I with Propylene. Propylene was bubbled for 10 min at 0° into a solution of 2.8 g (10 mmole) of I in 20 ml of CH_2Cl_2. According to the PMR spectrum, the mixture contained two isomers – 75% 2,3,5,6-tetrachloro-4-pyridyl 1-methyl-2-chloroethyl sulfide (VIII) and 25% 2,3,5,6-tetrachloro-4-pyridyl 2-chloropropyl sulfide (VII). Repeated crystallization gave VIII with mp 86-87° (from ethanol). Found: Cl 54.5; S 10.0%. $C_8H_6Cl_5NS$. Calculated: Cl 54.5; S 9.8%.

2,3,5,6-Tetrachloro-4-pyridyl 2-Hydroxypropyl Sulfide (IX). A 3.3-g (12 mmole) sample of the sodium salt of 2,3,5,6-tetrachloro-4-mercaptopyridine [3] was dissolved in 25 ml of ethanol, and 1.7 g (12 mmole) of 2-bromopropanol was added with stirring. The mixture was refluxed for 2.5 h, and the alcohol was removed by vacuum distillation. The residue was treated with water and extracted with ether to give 1.8 g (50%) of a product with mp 79-80° (from hexane). Found: Cl 46.2; S 10.6%. $C_8H_7Cl_4NOS$. Calculated: Cl 46.2; S 10.4%.

2,3,5,6-Tetrachloro-4-pyridyl 1-Methyl-2-hydroxyethyl Sulfide (X). A 6.5-g (24 mmole) sample of the sodium salt of 2,3,5,6-tetrachloro-4-mercaptopyridine was dissolved in 50 ml of ethanol, and 3.4 g (24 mmole) of 1-bromo-2-propanol was added with stirring. The mixture was refluxed for 1 h, the alcohol was vacuum-evaporated, and the residue was treated with water and extracted with ether to give 5.2 g (77%) of a product with mp 88-90° (from heptane). Found: Cl 46.0; S 10.3%. $C_8H_7Cl_4NOS$. Calculated: Cl 46.2; S 10.4%.

2,3,5,6-Tetrachloro-4-pyridyl 2-Chloropropyl Sulfide (VII). A) A mixture of 1.5 g (5 mmole) of X and 5 ml of thionyl chloride was refluxed 20-25 min, and the thionyl chloride was then removed by vacuum distillation to give 1.4 g (88%) of a product with mp 35-37° (from heptane). Found: Cl 54.5; S 9.9%. $C_8H_6Cl_5NS$. Calculated: Cl 54.5; S 9.8%.

B) The reaction of IX with thionyl chloride was carried out under similar conditions to give VII with mp 36-37° (from heptane).

C) A 1-g (3 mmole) sample of VIII was dissolved in 5 ml of glacial acetic acid, and the mixture was refluxed for 1 h. The acetic acid was removed by vacuum distillation to give 98% of a product with mp 35-36° (from heptane). Samples of VII obtained by methods A, B, and C did not depress one another's melting points. The PMR spectra of VII obtained by these methods were identical.

2,3,5,6-Tetrachloro-4-pyridyl 2-Chloropropyl Sulfone (XIV). A) A 2-g (6.2 mmole) sample of VII was dissolved in 20 ml of glacial acetic acid, and 5 ml of 30% H_2O_2 was added. The mixture was refluxed for 2 h, cooled, and poured over ice to give 1.5 g (68%) of a product with mp 109-111° (from heptane). Found: Cl 49.2; S 9.0%. $C_8H_6Cl_5NO_2S$. Calculated: Cl 49.6; S 9.0%.

B) Compound VIII was similarly oxidized to give a product with mp 110° (from heptane). This product did not depress the melting point of the product obtained by method A.

2,3,5,6-Tetrachloro-4-pyridyl 1-Methyl-2-chloropropyl Sulfide (XV). A 2.8-g (10 mmole) sample of I was dissolved in 20 ml of CH_2Cl_2, and 2-butene was bubbled through the solution at 0°. The product was isolated as in the case of the preparation of II to give 3 g (90%) of a product with mp 72-74° (from heptane). Found: Cl 52.6; S 9.3%. $C_9H_8Cl_5NS$. Calculated: Cl 52.3; S 9.4%.

Reaction of I with Isobutene. Isobutene was bubbled for 6 min at 0° into a solution of 2.8 g (10 mmole) of I in 20 ml of CH_2Cl_2. According to the PMR spectrum, the mixture contains two isomers – 60% 2,3,5,6-tetrachloro-4-pyridyl 2-methyl-2-chloropropyl sulfide (XVI) and 40% 2,3,5,6-tetrachloro-4-pyridyl 1,1-dimethyl-2-chloroethyl sulfide (XVII). Repeated crystallization gave XVI with mp 84-86° (from heptane). Found: Cl 52.2; S 9.3%. $C_9H_8Cl_5NS$. Calculated: Cl 52.3; S 9.4%.

2,3,5,6-Tetrachloro-4-pyridyl 2-Chloro-2-phenylethyl Sulfide (XVIII). A 1.4-g (5 mmole) sample of I was dissolved in 15 ml of CH_2Cl_2, and 0.52 g (5 mmole) of freshly distilled styrene was added dropwise at 0°. The solvent was removed by vacuum distillation to give 1.8 g (95%) of a product with mp 106-107° (from ethanol). Found: Cl 45.9; S 8.0%. $C_{13}H_8Cl_5NS$. Calculated: Cl 45.8; S 8.2%.

The PMR spectra of carbon tetrachloride and methylene chloride solutions (0.5 M) were recorded with a Jeol spectrometer at an operating frequency of 60 MHz with tetramethylsilane (TMS) as the internal standard.

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