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REACTIONS OF POLYHALOGENOPYRIDINES. 11.* SYNTHESIS OF 3-HYDROXY-4,6,7-TRICHLORO-2-ETHOXYCARBONYLTHIENO[3,2-c]PYRIDINE

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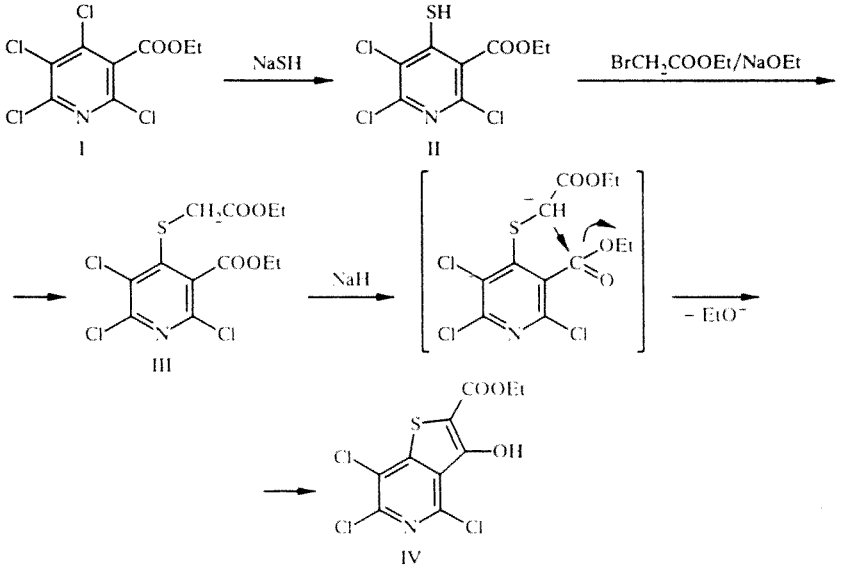
A derivative of thieno[3,2-c]pyridine was synthesized by intramolecular condensation of the substituents at positions 3 and 4 of the pyridine ring.

Polyhalogenopyridines are important intermediates in the synthesis of annellated heterocycles [2]. Earlier we studied the intramolecular transformations of N,N-dimethyldithiocarbamate derivatives of polychloropyridines into 1,3-dithiolo[4,5-c]pyridines and bis-1,3-dithiolo[4,5-b:4′,5′-e]pyridines [3-5]. In the present paper we describe the synthesis of a derivative of thieno[3,2-c]pyridine by intramolecular nucleophilic substitution at an unsubstituted carbon atom in the side substituents of the pyridine ring. A similar method was used earlier for the production of benzo[b]thiophenes [6].

During the investigation of the products from the reactions of derivatives of tetrachloronicotinic acid with a series of sulfur-containing nucleophilic agents we observed regioselective substitution at position 4 of the pyridine ring in ethyl tetrachloronicotinate (I) by the thiolate anion in the presence of sodium hydrosulfide. Here, ethyl 4-mercapto-2,5,6-trichloronicotinate (II) was obtained with a yield of more than 60%. Further alkylation of the thiol group with ethyl bromoacetate led to the diester (III), which was converted into the substituted thieno[3,2-c]pyridine (IV) as a result of subsequent intramolecular condensation under the influence of sodium hydride.



A fairly strong molecular ion is found in the mass spectrum. The main direction in its dissociation is the elimination of EtO and EtOH, which is characteristic of the ethyl esters of heterocyclic acids [7], and also the successive elimination of

*For Communication 10, see [1].

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two molecules of CO. The presence of a downfield singlet in the NMR spectrum at 10.55 ppm and also a strong absorption band in the IR spectrum indicates that compound (IV) exists predominantly in the enolic form [6].

EXPERIMENTAL

The IR spectra of the compounds were recorded in Vaseline oil on a Specord M-80 instrument. The NMR spectra were recorded in deuterochloroform solutions on a Bruker AC-200 instrument at 200 MHz (^{1}H) and 50 MHz (^{13}C) with TMS as internal standard. The mass-spectrometric measurements were made on a Finnigan 4021 instrument with direct injection at 70 eV.

4-Mercapto-2,5,6-trichloro-3-ethoxycarbonylpyridine (II) ($C_8H_6Cl_3NO_2S$). To a solution of 2 g (0.00692 mole) of compound (I) in 30 ml of ethanol with stirring at room temperature we added 0.8 g (0.0143 mole) of sodium hydrosulfide, dissolved in ethanol. The mixture was stirred for 0.5 h, and the solvent was removed under vacuum. The residue was dissolved in 50 ml of water, and the undissolved material was extracted with chloroform. The aqueous layer was acidified with hydrochloric acid, and the precipitate was separated by filtration, dried, and recrystallized from hexane. We obtained 1.27 g (64%) of compound (II) in the form of light-beige crystals; mp 71-72°C. Mass spectrum, m/z (I_{rel}, %): 285(31) M^+, 239(98) $[M\text{-EtOH}]^+$, 211(6) $[M\text{-EtOH}-CO]^+$, 177(6). IR spectrum, cm^{-1}: 1740 (C=O). ^{13}C NMR spectrum, ppm: 164.1 (C=O), 148.6 ($C_{(6)}$), 148.1 ($C_{(4)}$), 144.4 ($C_{(2)}$), 126.9 ($C_{(5)}$), 126.7 ($C_{(3)}$), 13.9 (Me), 61.1 (CH_2). NMR spectrum, ppm: 1.44 (3H, t, Me), 4.49 (2H, q, CH_2), 4.88 (2H, s, SH).

Ethyl (2,5,6-Trichloro-3-ethoxycarbonyl-4-pyridyl)thioacetate (III) ($C_{12}H_{12}Cl_3NO_4S$). A mixture of 1.85 g (0.0065 mole) of (II), 1.2 g (0.0072 mole) of ethyl bromoacetate, and an ethanol solution of sodium ethoxide, prepared from 0.165 g of sodium in 20 ml of absolute ethanol, was boiled with a reflux condenser for 3 h. The solvent was then removed under vacuum, and the residue was washed with water and extracted with ether. The extract was dried over sodium sulfate. After removal of the ether a red oil was obtained, and this was used without further purification or analysis.

3-Hydroxy-4,6,7-trichloro-2-ethoxycarbonylthieno[3,2-c]pyridine (IV) ($C_{10}H_6Cl_3NO_3S$). To a solution of 1.2 g of compound (III) in 10 ml of THF, while stirring, we added 0.12 g of an 80% dispersion of sodium hydride in mineral oil. When the release of gaseous hydrogen had stopped, the reaction mixture was heated for 5 min, cooled, and poured into water. The mixture was acidified and extracted with ether. The ether extract was dried over sodium sulfate, the solvent was removed, and the residue was recrystallized from heptane. We obtained 0.8 g [77% calculated on compound (II)] of pink needle crystals; mp 187-188°C. Mass spectrum, m/z, (I_{rel}, %): 325(11) M^+, 280(70) $[M\text{-EtO}]^+$, 279(71) $[M\text{-EtOH}]^+$, 251(3) $[M\text{-EtOH}-CO]^+$, 223(17) $[M\text{-EtOH}-2Co]^+$ IR spectrum, cm^{-1}: 3276(OH), 1682(C=O). PMR spectrum, ppm: 1.45 (3H, t, J = 7.5 Hz, Me), 4.50 (2H, q, J = 7.5 Hz, CH_2), 10.55 (1H, s, OH).

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