FORMATION OF CONDENSED SULFUR-NITROGEN-CONTAINING HETEROCYCLIC COMPOUNDS THROUGH TRANSFORMATIONS OF ALLYL-2-PYRIDYLSULFIDE AND -SULFOXIDE

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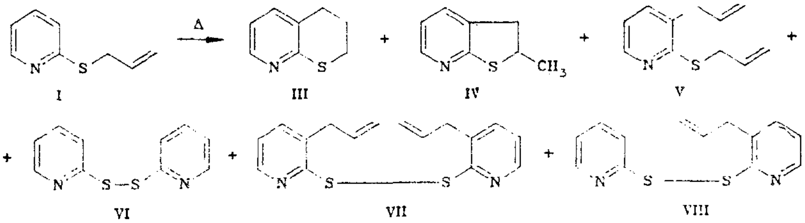
Allyl-2-pyridylsulfide gives upon heating in tetraline and DMF a mixture of 2-methyl-2,3-dihydrothieno[2,3-b]pyridine, dihydrothiopyrano[2,3-b]pyridine, and a mixture of sulfides and disulfides which are formed upon recombination of thiyl radicals. The S-oxide of this sulfide forms only 2-methyl-2,3-dihydrothieno[2,3-b]pyridine of cyclic compounds, which indicates a predominant 2,3- and not 3,3-sigmatropic rearrangement.

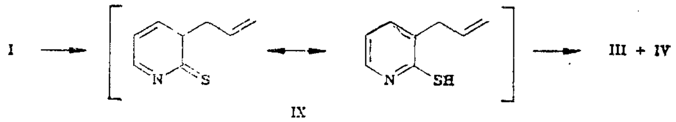
Among the various methods of synthesis of condensed sulfur-containing heterocyclic compounds, 3,3-sigmatropic rearrangements of allylaryl- and allylhetarylsulfides and -sulfoxides are distinguished as one of the most convenient approaches to systems containing thiophene and thiopyran fragments [1-4]. For example, the Claisen thiorearrangement of allyl-3- and -4-quinolylsulfides is known to lead to formation of dihydrothienoquinolines and dihydrothiopyranoquinolines isomeric with them (for example, see [5]). In this work, we made an attempt to use allyl-2-pyridylsulfide (I) and its S-oxide (II) for preparation of dihydrothienopyridine and dihydrothiopyranopyridine.

Heating of allyl-2-pyridylsulfide (I) either without solvent or in tetralin or DMF at 190°C leads to a mixture of compounds III-VIII:



The reaction mixture obtained was separated by preparative thin layer chromatography into two fractions, the first of which contained sulfides III and IV with a total yield of 64%, the second contained sulfide V and disulfides VI-VIII. Further separation of the individual compounds was done by separation of these fractions.

Formation of 2-methyl-2,3-dihydrothieno[2,3-b]pyridine (IV) and 2,3-dihydrothipyrano-[2,3-b]pyridine (III) apparently results from cyclization of 3-allyl-2-pyridinethiol (IX) which arises from a 3,3,-sigmatropic rearrangement of sulfide I:



The presence of sulfide V in the reaction mixture indicates the possibility of reversible reaction between sulfide I and thiol IX analogous to that which occurs with 3,3-sigmatropic rearrangement of allylphenyl- and allyl-2-thienylsulfides [6, 7]:

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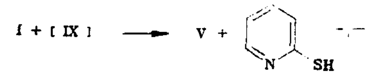
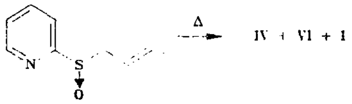


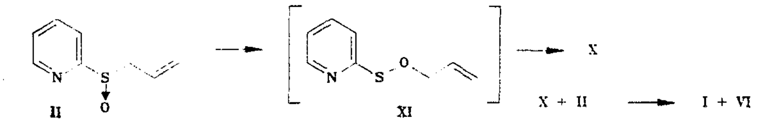
Evidence for the occurrence of such a reaction is the presence in the reaction mixture of disulfides VI and VIII which can be formed upon recombination of thiyl radicals corresponding to thiols IX and X.

An important feature of the conversion of sulfide I is the absence in the reaction products of compounds which correspond to migration of the allyl group to the nitrogen atom. Although this process is thermodynamically unfavorable [5], it was noticed earlier during study of the behavior of allyl-2-quinolylsulfide [5] and sulfide I in the presence of $PdCl_2$ [8].

Formation of 2-methyl-2,3-dihydrothieno[2,3-b]pyridine (IV), bis(2-pyridyl)disulfide (VI), and allyl-2-pyridylsulfide (I) occurs upon heating allyl-2-pyridylsulfoxide (II) in DMF at 150°C:



In contrast to allyl-1-naphthylsulfoxide, which gives 2,3-dihydronaphtho[1,2-b]-thiophene-1-oxide under similar conditions, only 2-methyl-2,3-dihydrothieno[2,3-b]pyridine of the cyclic compounds, and not its oxide, is formed upon rearrangement of sulfoxide II. Such a conversion path of sulfoxide II is apparently related to the significant difficulties of its 3,3-sigmatropic rearrangement by comparison with naphthylallylsulfoxides which arise as a result of lowered reactivity of pyridines in pericyclic reactions in which the pyridine π-system can participate in formation of a cyclic transition state. Formation of significant quantities of disulfide VI (34%) indicates that the main direction for conversion of sulfoxide II is 2,3-sigmatropic rearrangement into the isomeric sulphenate XI. Decomposition of this forms 2-pyridinethione (X) which gives disulfide VI and reduces sulfoxide II to sulfide I (yield 13%):



2-Methyl-2,3-dihydrothieno[2,3-b]pyridine (IV) is formed with further conversions of sulfide I, as described above.

EXPERIMENTAL

IR spectra were taken as film on a IKS-22 instrument. PMR spectra were taken on a Varian T-60 instrument in 5-10% CCl_4, $CDCl_3$, and $(CD_3)_2CO$ solutions with TMS and HMDS internal standards. Mass spectra were recorded on a MAT-112S chromato-mass-spectrometer with a Varian-3700 chromatograph (OV-101 capillary column) using electron impact at an ionization energy of 80 eV. Elemental analysis of compound II for C, H, and N corresponded to that calculated.

Allyl-2-pyridylsulfide (I) was synthesized by reaction of allyl bromide with 2-pyridinethiol according to [9]. Yield 88%. PMR spectrum (CCl_4, TMS): 3.8 (2H, d, $S-CH_2$), 5.0-5.5 (3H, m, $CH=CH_2$), 6.8-7.0 (2H, m, 3,5-H of pyridine), and 7.2 ppm (1H, m, 4-H of pyridine). Mass spectrum*: 151 (35), 136 (100), 124 (23), 118 (42), 117 (21), 79 (66), 78 (30), 73 (71), 52 (24), 51 (23), 44 (57), 42 (27), 41 (20), 39 (46).

Allyl-2-pyridylsulfoxide (II, C_8H_9NOS) was prepared by oxidation of sulfide I by 30% hydrogen peroxide in glacial acetic acid according to the improved method of [10]. A 30% solution of hydrogen peroxide calculated from sulfide: H_2O_2 = 1:1.5 was added slowly with constant

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*Here and further, mass spectra give values of m/z (% of maximal intensity).

stirring to a solution of 2 g (0.13 mole) allyl-2-pyridylsulfide in 15 ml glacial acetic acid. The progress of the reaction was monitored by TLC on-Silufol plates with hexane—CCl_4—ether, 47:43:10, and $CHCl_3$—hexane—acetone, 5:1:1, eluents. After completion of the reaction, the mixture was dissolved in 150 ml $CHCl_3$. The $CHCL_3$ extract was washed with water and 10% sodium bicarbonate and was dried with sodium sulfate. After removal of solvent, the residue was separated on a column with 40/100 silica gel using hexane-CCl_4—ether, 47:43:10, eluent. Yield of allyl-2-pyridylsulfoxide 98%, mp 46-48°C. PMR spectrum (($(CD_3)_2CO$, TMS): 3.9 (2H, m, SCH_2), 5.4 (3H, m, $CH{=}CH_2$), 7.8 (2H, m, 3-, 5-H of pyridine), 8.0 (1H, m, 4-H of pyridine), and 8.8 ppm (1H, d, 6-H of pyridine). IR spectrum: 1050-1030 cm^{-1} ($S{=}O$).

Conversion of sulfide I was done in an argon atmosphere. An ampul with the starting sulfide or its solution in tetralin (1:10) or DMF (1:10) was placed in a thermostat with a temperature regulated to an accuracy of ±1°C and held at this temperature. The progress of the reaction was monitored by TLC on Silufol plates visualized with iodine. Separation and purification of reaction products was done on plates with a recoverable Sealpearl silica gel layer in CCl_4—hexane—ether, 43:47:10, and $CHCl_3$—hexane—acetone, 5:1:1, systems.

Rearrangement of sulfoxide II was done by an analogous method using DMF (1:10) as solvent.

The following compounds were separated from the reaction mixtures:

2,3-Dihydrothiopyrano[2,3-b]pyridine (III). Yield 32%. PMR spectrum (CCl_4, TMS): 1.6-2.0 (2H, m, 2-H of thiopyran), 2.2-3.0 (4H, m, 3-, 4-H of thiopyran), 7.0 (1H, d, 5-H of pyridine), 7.6 (1H, t, 4-H of pyridine), 8.5 ppm (1H, d, 6-H of pyridine). Mass spectrum: 151 (64), 136 (100), 122 (48), 118 (70), 67 (54), 52 (68), 39 (94).

2-Methyl-2,3-dihydrothieno[2,3-b]pyridine (IV). Yield: from sulfide I, 32%; from sulfoxide II, 53%. PMR spectrum (CCl_4, TMS): 1.4 (3H, d, CH_3), 3.6-4.0 (3H, m, 2-, 3-H of dihydrothiophene), 7.0 (1H, t, 5-H of pyridine), 7.5 (1H, d, 4-H of pyridine), 8.5 ppm (1H, d, 6-H of pyridine). Mass spectrum: 151 (34), 136 (100), 118 (40), 79 (94), 67 (22), 51 (46), 39 (82).

Allyl(3-allyl-2-pyridyl)sulfide (V). Yield 8%. PMR spectrum (CCl_4, TMS): 3.8-4.0 (4H, m, CH_2, SCH_2), 5.0-6.0 (6H, m, $-CH{=}CH_2$), 6.8-7.0 (1H, d, 5-H of pyridine), 7.0-7.3 (1H, m, 4-H of pyridine), 8.4 ppm (1H, d, 6-H of pyridine). Mass spectrum: 191 (30), 176 (100), 150 (96), 136 (30), 118 (88), 41 (48), 39 (82).

Bis(2-pyridyl)disulfide (VI). Yield 34%. PMR spectrum (CCl_4, TMS): 7.0 (2H, m, 4-, 4'-H of pyridine), 7.8 (4H, m, 3-, 5-, 3'-, 5'-H of pyridine), 8.5 ppm (2H, m, 6-, 8-H of pyridine). Mass spectrum: 220 (100), 156 (64), 78 (73), 51 (30), 39 (22).

Mixture of bis(3-allyl-2-pyridine)disulfide (VII) and bis-2-pyridyl(3-allyl-2-pyridyl) disulfide (VIII). Total yield of VII and VIII, 11%. Mass spectrum: 300 (M^+) VII and 260 (M^+) VIII.

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