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# INVESTIGATION OF THE STEREOCHEMISTRY OF THE [3.3]-SIGMATROPIC REARRANGEMENT OF THE sp-ISOMER OF 2-ALLYLTHIO-5-ACETYL-6-METHYL-4-(2-NITROPHENYL)-3-CYANO-1,4-DIHYDROPYRIDINE

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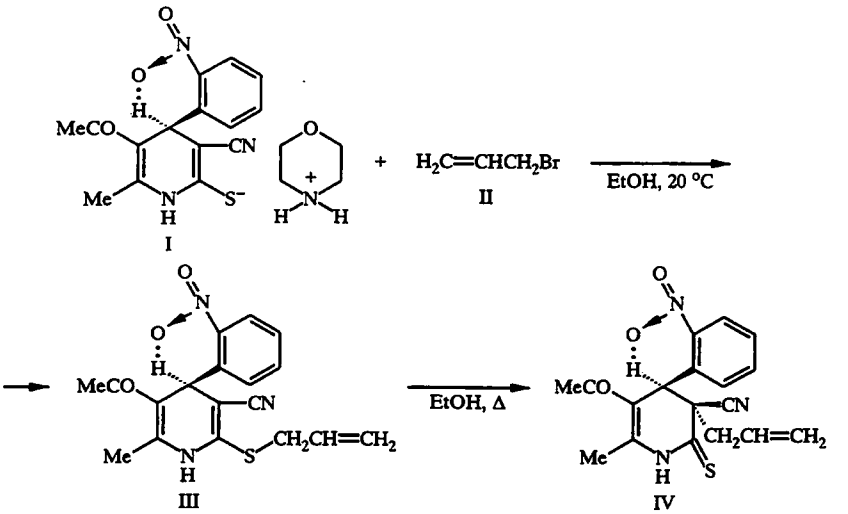
*The reaction of the syn-periplanar conformer (the sp-isomer) of morpholinium 5-acetyl-6-methyl-4-(2-nitrophenyl)-3-cyano-1,4-dihydropyridine-2-thiolate with allyl bromide proceeds regio- and stereoselectively with the formation of the sp-isomer of the substituted 2-allylthio-1,4-dihydropyridine. The [3.3]-sigmatropic rearrangement of the last leads to the sp-isomer of 3,4-trans-3-allyl-5-acetyl-6-methyl-4-(2-nitrophenyl)-3-cyano-1,2,3,4-tetrahydropyridine-2(1H)-thione.*

The regioselectivity of the [3.3]-sigmatropic rearrangement of substituted 2-allylthio(seleno)-4-aryl-3-cyano-1,4-dihydropyridines was established previously [1-4]. Substituted 2-allylthio(seleno)-4-aryl-3-cyano-1,4-dihydropyridines underwent rearrangement to 3-allyl-4-aryl-3-cyano-1,2,3,4-tetrahydropyridine-2(1H)-thiones on heating in ethanol or without a solvent [1, 2]. It was established by physicochemical methods that the [3.3]-sigmatropic rearrangement proceeds stereoselectively with the formation of trans-3-allyl-4-aryl-3-cyano-1,2,3,4-tetrahydropyridine-2(1H)-thiones [3, 4].

In the present communication, we investigated the atropoisomerism of the initial compounds and the final product of the [3.3]-sigmatropic rearrangement of 2-allylthio-5-acetyl-6-methyl-4-(2-nitrophenyl)-3-cyano-1,4-dihydropyridine.

The interaction of the morpholinium pyridine-2-thiolate (I) with allyl bromide (II) in ethanol at 20°C affords the 2-allylthiopyridine (III) with the yield of 87%. As was shown previously, the regioselectivity of alkylation reactions of 1,4-dihydropyridine-2-thiolate salts is determined by the formally negatively charged sulfur [5, 6], which favors the $S_{N2}$ reaction mechanism and the formation of alkylthiopyridines.




*Deceased.

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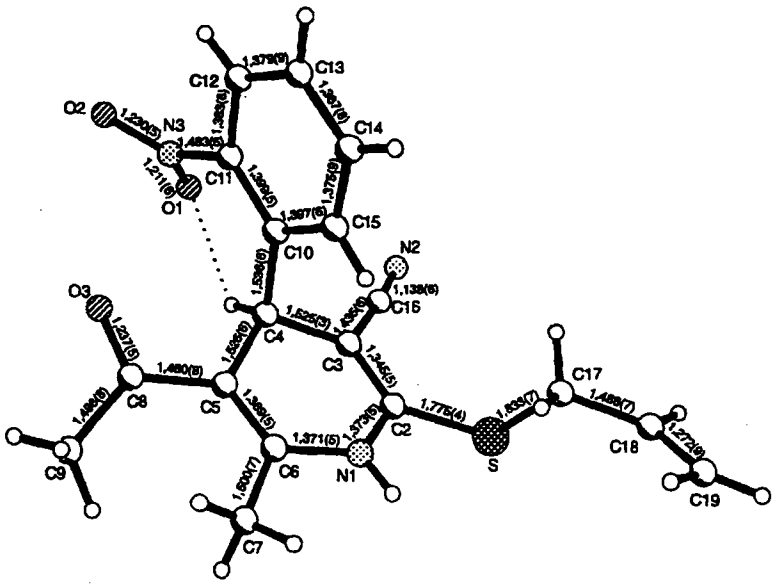



Fig. 1. General view of the molecule and the bond lengths of compound (III).

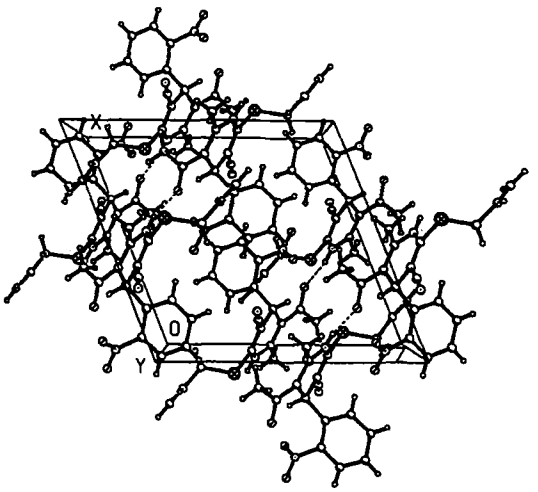



Fig. 2. AC projection of the crystal structure of compound (III). Intermolecular N–H...O hydrogen bonds are shown by dotted lines.

Compound (III) undergoes a [3.3]-sigmatropic rearrangement, when it is boiled briefly in ethanol, leading to the substituted 3-allyltetrahydropyridine-2(1H)-thiolate (IV).

Molecules of the initial salt (I) occur in the syn-periplanar conformation (the sp-isomer), the stability of which is determined by intramolecular steric interactions of the bulky substituents, as well as the intramolecular non-valence contact of $C_{(4)}-H_{(4)}...O(NO_2)$, which was found by the x-ray structural investigation of this compound [5] and was studied by other physicochemical methods [7]. The atropoisomerism is unchanged in the alkylation reaction: the substituted 2-allylthiopyridine (III) remains in the sp-isomeric form. The atropoisomerism is also unchanged as the result of the [3.3]-sigmatropic rearrangement, since compound (IV) is also the sp-isomer.

The data of physicochemical analysis confirm the structure of the products (III) and (IV) obtained. The IR spectra of these compounds contain absorption bands of the $NO_2$ group (1352-1358 and 1526-1530 $cm^{-1}$), as well as stretching and deformational vibrations of the NH group (see Experimental section). As a consequence of the decrease in the electronic conjugation, the absorption band of the CN group of the tetrahydropyridinethione (IV) has low intensity (2250 $cm^{-1}$) by comparison with the frequency of the CN group of the dihydropyridine (III) (2206 $cm^{-1}$). This comprises a characteristic fea-

TABLE 1. Bond Angles ω (deg) in the Molecule of (III)

| Angle | ω | Angle | ω |
|---|---|---|---|
| C(2)—S—C(17) | 100,3(2) | N(1)—C(6)—C(7) | 112,6(3) |
| C(2)—N(1)—C(6) | 122,6(3) | C(5)—C(6)—C(7) | 127,2(4) |
| O(1)—N(3)—O(2) | 124,2(4) | O(3)—C(8)—C(5) | 117,5(4) |
| O(1)—N(3)—C(11) | 118,7(3) | O(3)—C(8)—C(9) | 118,1(4) |
| O(2)—N(3)—C(11) | 117,1(4) | C(5)—C(8)—C(9) | 124,2(4) |
| S—C(2)—N(1) | 115,8(2) | C(4)—C(10)—C(11) | 126,2(4) |
| S—C(2)—C(3) | 124,0(3) | C(4)—C(10)—C(15) | 118,3(3) |
| N(1)—C(2)—C(3) | 120,1(3) | C(11)—C(10)—C(15) | 115,5(4) |
| C(2)—C(3)—C(4) | 121,5(3) | N(3)—C(11)—C(10) | 121,8(4) |
| C(2)—C(3)—C(16) | 121,9(3) | N(3)—C(11)—C(12) | 115,4(4) |
| C(4)—C(3)—C(16) | 116,4(3) | C(10)—C(11)—C(12) | 122,8(4) |
| C(3)—C(4)—C(5) | 109,8(3) | C(11)—C(12)—C(13) | 119,1(5) |
| C(3)—C(4)—C(10) | 109,6(3) | C(12)—C(13)—C(14) | 120,0(7) |
| C(5)—C(4)—C(10) | 111,3(3) | C(13)—C(14)—C(15) | 120,3(5) |
| C(4)—C(5)—C(6) | 120,1(3) | C(10)—C(15)—C(14) | 122,3(4) |
| C(4)—C(5)—C(8) | 113,8(3) | N(2)—C(16)—C(3) | 175,0(4) |
| C(6)—C(5)—C(8) | 126,0(4) | S—C(17)—C(18) | 109,4(5) |
| N(1)—C(6)—C(5) | 120,2(4) | C(17)—C(18)—C(19) | 126,4(7) |

TABLE 2. Bond Angles ω (deg) in the Molecule of (IV)

| Angle | ω | Angle | ω |
|---|---|---|---|
| C(2)—N(1)—C(6) | 127,1(5) | N(1)—C(6)—C(7) | 112,6(5) |
| O(1)—N(3)—O(2) | 124,1(6) | C(5)—C(6)—C(7) | 127,7(5) |
| O(1)—N(3)—C(11) | 118,5(7) | O(3)—C(8)—C(5) | 117,8(5) |
| O(2)—N(3)—C(11) | 117,4(5) | O(3)—C(8)—C(9) | 119,9(6) |
| S—C(2)—N(1) | 122,3(4) | C(5)—C(8)—C(9) | 122,2(6) |
| S—C(2)—C(3) | 122,9(3) | C(4)—C(10)—C(11) | 124,8(4) |
| N(1)—C(2)—C(3) | 114,6(4) | C(4)—C(10)—C(15) | 120,2(5) |
| C(2)—C(3)—C(4) | 112,7(3) | C(11)—C(10)—C(15) | 114,9(4) |
| C(2)—C(3)—C(16) | 110,4(4) | N(3)—C(11)—C(10) | 121,7(5) |
| C(4)—C(3)—C(16) | 108,9(4) | N(3)—C(11)—C(12) | 115,1(6) |
| C(2)—C(3)—C(17) | 105,8(4) | C(10)—C(11)—C(12) | 123,1(5) |
| C(4)—C(3)—C(17) | 109,4(4) | C(11)—C(12)—C(13) | 119,7(7) |
| C(16)—C(3)—C(17) | 109,6(4) | C(12)—C(13)—C(14) | 119,7(6) |
| C(3)—C(4)—C(5) | 110,2(4) | C(13)—C(14)—C(15) | 120,7(6) |
| C(3)—C(4)—C(10) | 113,9(4) | C(10)—C(15)—C(14) | 121,8(6) |
| C(5)—C(4)—C(10) | 111,8(3) | N(2)—C(16)—C(3) | 174,6(6) |
| C(4)—C(5)—C(6) | 119,3(4) | C(3)—C(17)—C(18) | 116,3(7) |
| C(4)—C(5)—C(8) | 114,0(5) | C(3)—C(17)—C(18a) | 121,6(8) |
| C(6)—C(5)—C(8) | 126,6(4) | C(17)—C(18)—C(19) | 133,3(14) |
| N(1)—C(6)—C(5) | 119,6(4) | C(17)—C(18a)—C(19a) | 125,7(23) |

ture of the IR spectra of the products of the [3.3]-sigmatropic rearrangement of substituted 3-cyanopyridines [1, 2,.7]. In the $^1H$ NMR spectra, the signal of the 4-H proton undergoes a paramagnetic shift of 0.4-1.0 ppm by comparison with tetrahydropyridines containing the $C_6H_5$, p-$ClC_6H_4$, or p-$NO_2C_6H_4$ substituent, not forming the intramolecular hydrogen bond, at the position 4 [8]. The protons of the 2-$NO_2C_6H_4$ substituent appear as a characteristic set of signals (see Experimental section). However, according to spectroscopic data of the compounds (III) and (IV), it is difficult to establish their atropoisomerism unambiguously and solve the problem of the stereoselectivity of the [3.3]-sigmatropic rearrangement. In this connection, the method of x-ray structure analysis was enlisted for a deeper study of the structure of the products (III) and (IV).

Figure 1 shows the general view of the molecule of compound (III) with the bond lengths. The bond angles are presented in Table 1. In this molecule, the 1,4-dihydropyridine heterocycle has the bath conformation; the $N_{(1)}$ and $C_{(4)}$ atoms

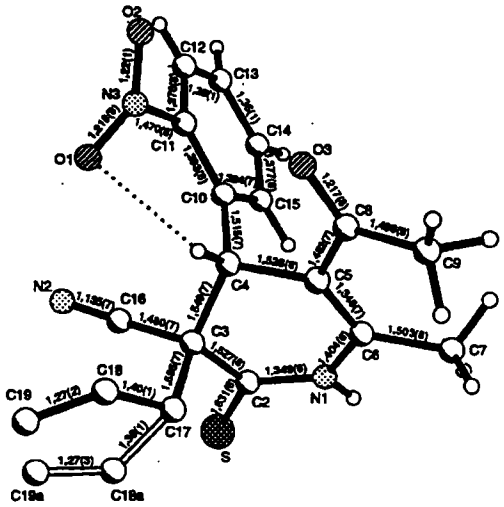


Fig. 3. General view of the molecule and the bond lengths of compound (IV).

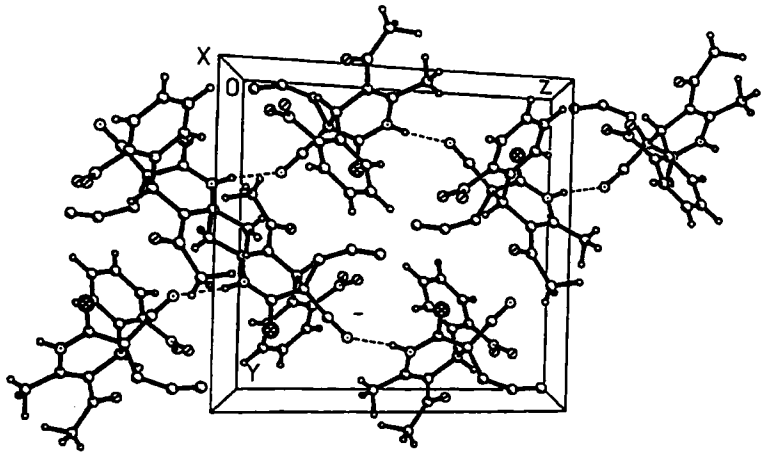



Fig. 4. BC projection of the crystal structure of compound (IV). Intermolecular N−H...N hydrogen bonds are indicated by dotted lines.

come out of the plane of the remaining atoms (the "bottom" of the bath, the plane being in the limits of ±0.012 Å) by 0.097 and 0.305 Å correspondingly. This corresponds with the bending of the ring at the line $C_{(2)}...C_{(6)}$ by 8.5°, at the line $C_{(3)}...C_{(5)}$ by 20.3°, and at the line $N_{(1)}...C_{(4)}$ by 18.3°, and the sum of the torsion angles in the ring (84.8°) somewhat exceeds the corresponding value in nifedipine [9]. We previously established [5] the analogous conformation of the heterocycle for the molecule of compound (I), as well as 2-allylthio-6-methyl-4-phenyl-3-cyano-5-ethoxycarbonyl-1,4-dihydropyridine (V) [3, 4].

The pseudoaxial o-nitrophenyl substituent is turned in relation to the "bottom of the bath" of the heterocycle by 91.1° [in compound (I), by 75.6°]. This was caused by forced shortened non-valence intramolecular contacts of $N_{(3)}...C_{(4)}$ 3.088(6) Å, $C_{(3)}...C_{(15)}$ 2.969(6) Å, $C_{(5)}...C_{(15)}$ 3.132(6) Å, $C_{(8)}...C_{(10)}$ 3.210(6) Å, and $C_{(10)}...C_{(16)}$ 3.163(6) Å (the sum of the van der Waals radii of N and C is 3.25 Å, and the doubled van der Waals radius of the C atom is 3.40 Å [10]), and the turning of the $NO_2$ group in relation to the benzene ring equals 40.7° [in compound (I), it is 31.6°]. As in the case of the molecule of (I), the o-nitrophenyl substituent in the molecule of (III) has the syn-periplanar orientation in relation to the $H_{(4)}$ atom (the torsion angles are $H_{(4)}C_{(4)}C_{(10)}C_{(11)}$ 9.3°, $C_{(4)}C_{(10)}C_{(11)}N_{(3)}$ −3.0°, and $C_{(10)}C_{(11)}N_{(3)}O_{(1)}$ −40.8°). This leads to the shortened non-valence contact $O_{(1)}...C_{(4)}$ 2.967(5) Å (the sum of the van der Waals radii is 3.22 Å [10]), and may indicate the C−H...O hydrogen bond [11, 12] with parameters [$C_{(4)}-H_{(4)}$ 0.97(6) Å, $H_{(4)}...O_{(1)}$ 2.27(3) Å, and the angle $C_{(4)}-H_{(4)}...O_{(1)}$ 128(2)°] agreeing with those established in the molecule of (I). The hydrogen bond prevents the rotation of

TABLE 3. Coordinates of Atoms ($\times 10^4$, and $\times 10^3$ for H) in the Molecule of (III)

| Atom | x | y | z |
|---|---|---|---|
| S | 5921(1) | 402(1) | 2483(1) |
| $O_{(1)}$ | 825(3) | -132(3) | -1653(3) |
| $O_{(2)}$ | -423(3) | -1486(4) | -2053(3) |
| $O_{(3)}$ | 2137(3) | -2452(3) | -1727(2) |
| $N_{(1)}$ | 5354(3) | -1568(3) | 1467(3) |
| $N_{(2)}$ | 3072(4) | 1800(3) | 580(4) |
| $N_{(3)}$ | 406(3) | -955(4) | -1407(3) |
| $C_{(2)}$ | 4960(3) | -497(3) | 1470(3) |
| $C_{(3)}$ | 3914(3) | -180(3) | 721(3) |
| $C_{(4)}$ | 3083(3) | -1015(3) | -69(3) |
| $C_{(5)}$ | 3779(3) | -2026(3) | -194(3) |
| $C_{(6)}$ | 4826(3) | -2297(3) | 623(3) |
| $C_{(7)}$ | 5508(5) | -3360(4) | 740(5) |
| $C_{(8)}$ | 3186(4) | -2663(3) | -1197(3) |
| $C_{(9)}$ | 3783(5) | -3503(5) | -1656(5) |
| $C_{(10)}$ | 2117(3) | -1353(3) | 353(3) |
| $C_{(11)}$ | 904(4) | -1351(4) | -254(3) |
| $C_{(12)}$ | 88(5) | -1718(5) | 171(5) |
| $C_{(13)}$ | 477(5) | -2084(5) | 1243(5) |
| $C_{(14)}$ | 1656(6) | -2096(5) | 1866(4) |
| $C_{(15)}$ | 2458(5) | -1750(4) | 1427(4) |
| $C_{(16)}$ | 3483(4) | 937(4) | 678(3) |
| $C_{(17)}$ | 5689(6) | -106(6) | 3705(4) |
| $C_{(18)}$ | 6590(5) | 392(6) | 4705(4) |
| $C_{(19)}$ | 7329(8) | -138(8) | 5506(6) |
| $H_{(1)}$ | 599(4) | -176(3) | 199(3) |
| $H_{(4)}$ | 273(3) | -68(3) | -79(3) |
| $H_{(7a)}$ | 600(5) | -350(5) | 148(5) |
| $H_{(7b)}$ | 505(5) | -401(5) | 51(4) |
| $H_{(7c)}$ | 599(5) | -337(5) | 35(5) |
| $H_{(9a)}$ | 331(5) | -357(5) | -242(5) |
| $H_{(9b)}$ | 463(5) | -334(4) | -149(4) |
| $H_{(9c)}$ | 376(4) | -416(4) | -129(4) |
| $H_{(12)}$ | -68(4) | -168(4) | -29(4) |
| $H_{(13)}$ | -9(5) | -231(5) | 151(4) |
| $H_{(14)}$ | 192(4) | -234(4) | 259(4) |
| $H_{(15)}$ | 324(4) | -183(3) | 184(3) |
| $H_{(17a)}$ | 573(5) | -91(5) | 374(4) |
| $H_{(17b)}$ | 491(5) | 8(4) | 363(4) |
| $H_{(18)}$ | 663(6) | 131(7) | 480(6) |
| $H_{(19a)}$ | 720(7) | -95(7) | 534(6) |
| $H_{(19b)}$ | 792(6) | 17(6) | 616(6) |

the aryl substituent about the $C_{(4)}-C_{(10)}$ bond, and generally favors the retention of the molecular conformation in chemical reactions, e.g., in the synthesis of compound (III) from (I).

Conjugation can be assumed in the approximately planar fragment $C_{(6)}=C_{(5)}-C_{(8)}=O_{(3)}$; this leads to some redistribution of the bond lengths (the lengthening of the double bonds and the shortening of the single bonds) by comparison with the standard values [13] and by comparison with those established in the structures (I) and (V).

It should be noted that the carbonyl group $C_{(8)}=O_{(3)}$ in the molecule of (III) has the trans orientation in relation to the double bond $C_{(5)}=C_{(6)}$ (the torsion angle $C_{(6)}C_{(5)}C_{(8)}O_{(3)}$ is 164.1°), whereas it has the cis orientation in the molecule of (I); this leads to contact with the neighboring $CH_3$ group with formation of the $C_{(7)}-H\ldots O_{(3)}$ hydrogen bond.

In compound (III), the conformation of the allyl substituent (the torsion angles $C_{(2)}SC_{(17)}C_{(18)}$ 169.2° and $SC_{(17)}C_{(18)}C_{(19)}$ −121.6°) excludes the possiblity of the occurrence of contacts (both intra- and intermolecular) in the crystal between the $C_{(19)}$ and $C_{(3)}$ atoms at the distance of 4.0 Å (the intramolecular distance $C_{(3)}\ldots C_{(19)}$ is 6.111(7) Å, and the intermolecular distance is 5.708(7) Å) and, consequently, also the possibility of the solid-phase allyl rearrangement, which we observed for compound (V).

TABLE 4. Coordinates of Atoms ($\times 10^4$, and $\times 10^3$ for H) in the Molecule of (IV)

| Atom | x | y | z |
|---|---|---|---|
| S | 3997(2) | 2146(2) | 8677(1) |
| $O_{(1)}$ | 7719(6) | 3658(5) | 6254(3) |
| $O_{(2)}$ | 9949(6) | 3716(4) | 6771(4) |
| $O_{(3)}$ | 9026(4) | 5204(3) | 8396(3) |
| $N_{(1)}$ | 5852(4) | 3541(3) | 9582(3) |
| $N_{(2)}$ | 5122(5) | 1906(4) | 6483(3) |
| $N_{(3)}$ | 8857(7) | 3431(4) | 6846(4) |
| $C_{(2)}$ | 5175(5) | 3015(4) | 8735(4) |
| $C_{(3)}$ | 5505(5) | 3369(4) | 7819(3) |
| $C_{(4)}$ | 7019(5) | 3750(4) | 8088(3) |
| $C_{(5)}$ | 7397(5) | 4482(4) | 8985(3) |
| $C_{(6)}$ | 6860(5) | 4313(4) | 9711(3) |
| $C_{(7)}$ | 7234(8) | 4849(6) | 10707(5) |
| $C_{(8)}$ | 8386(5) | 5310(4) | 8965(4) |
| $C_{(9)}$ | 8555(9) | 6279(5) | 9574(6) |
| $C_{(10)}$ | 8067(5) | 2883(3) | 8245(3) |
| $C_{(11)}$ | 8936(5) | 2749(4) | 7691(4) |
| $C_{(12)}$ | 9902(7) | 1967(5) | 7873(5) |
| $C_{(13)}$ | 10018(7) | 1274(5) | 8609(5) |
| $C_{(14)}$ | 9200(7) | 1370(5) | 9179(5) |
| $C_{(15)}$ | 8252(6) | 2164(4) | 9011(4) |
| $C_{(16)}$ | 5256(5) | 2516(4) | 7083(4) |
| $C_{(17)}$ | 4475(7) | 4297(5) | 7350(4) |
| $C_{(18)}$ | 4407(12) | 4631(8) | 6402(8) |
| $C_{(18a)}$ | 3128(12) | 4123(13) | 6707(15) |
| $C_{(19)}$ | 3509(20) | 4524(19) | 5535(11) |
| $C_{(19a)}$ | 2701(39) | 4211(29) | 5758(12) |
| $H_{(1)}$ | 567(4) | 334(3) | 1010(3) |
| $H_{(4)}$ | 703(4) | 415(3) | 756(3) |
| $H_{(7a)}$ | 827(7) | 509(5) | 1103(4) |
| $H_{(7b)}$ | 686(9) | 561(7) | 1064(6) |
| $H_{(7c)}$ | 697(5) | 452(4) | 1106(4) |
| $H_{(9a)}$ | 900(7) | 677(6) | 937(5) |
| $H_{(9b)}$ | 776(8) | 649(6) | 972(5) |
| $H_{(9c)}$ | 913(6) | 613(5) | 1041(5) |
| $H_{(12)}$ | 1038(5) | 196(4) | 750(4) |
| $H_{(13)}$ | 1059(5) | 74(4) | 869(4) |
| $H_{(14)}$ | 926(4) | 88(4) | 974(3) |
| $H_{(15)}$ | 768(5) | 223(4) | 943(3) |

In the crystal, the intermolecular hydrogen bonds $N_{(1)}-H_{(1)}\ldots O_{(3)}$ (0.5 + x, −0.5 − y, 0.5 + z), [$N_{(1)}\ldots O_{(3)}$ 2.813(5) Å, $N_{(1)}-H_{(1)}$ 0.85(4) Å, $H_{(1)}\ldots O_{(3)}$ 1.99(4) Å, and the angle $N_{(1)}-H_{(1)}\ldots O_{(3)}$ 163(2)°] join the molecules of (III) in chains along the direction (101) (Fig. 2).

The structure of compound (IV) was also studied by x-ray structure investigation. Figure 3 shows the general view of its molecule with the bond lengths, and the bond angles are presented in Table 2.

The tetrahydropyridine heterocycle in the molecule of (IV) has the conformation of the deformed half-chair: the atoms $C_{(3)}$ and $C_{(4)}$ come out at different sides, by 0.294 and −0.326 Å correspondingly, from the plane drawn through the remaining ring atoms $C_{(2)}$, $N_{(1)}$, $C_{(6)}$, and $C_{(5)}$ (the deviation of these atoms from the mean plane is ±0.030 Å). We previously [3, 4] established the analogous ring conformation in 3-allyl-6-methyl-4-phenyl-3-cyano-5-ethoxycarbonyl-1,2,3,4-tetrahydropyridine-2-thione (VI).

The o-nitrophenyl substituent in the molecule of (IV) is turned in relation to the planar part of the heterocycle by 95.2° (the torsion angle $C_{(5)}C_{(4)}C_{(10)}C_{(15)}$ equals 63.5°); this is associated with forced shortened non-valence intramolecular contacts of $N_{(3)}\ldots C_{(4)}$ 3.032(8) Å, $C_{(2)}\ldots C_{(10)}$ 3.287(8) Å, $C_{(2)}\ldots C_{(15)}$ 3.241(8) Å, $C_{(3)}\ldots C_{(15)}$ 3.155(8) Å, $C_{(5)}\ldots C_{(15)}$ 3.112(8) Å, $C_{(6)}\ldots C_{(10)}$ 3.332(8) Å, and $C_{(8)}\ldots C_{(10)}$ 3.274(8) Å (the sum of the van der Waals radii of the N and C is

3.25 Å, and the doubled van der Waals radius of the C atom is 3.40 Å [10]). The turning of the $NO_2$ group in relation to the benzene ring equals 44.1°. As in the case of the molecules considered above, (IV) shows preservation, on the one hand, of the syn-periplanar orientation of the o-nitrophenyl substituent in relation to the $H_{(4)}$ atom (the torsion angles $H_{(4)}C_{(4)}C_{(10)}C_{(11)}$ 1.9°, $C_{(4)}C_{(10)}C_{(11)}N_{(3)}$ −3.2°, and $C_{(10)}C_{(11)}N_{(3)}O_{(1)}$ −43.8°) and, on the other hand, of the hydrogen bond with the parameters $C_{(4)}...O_{(1)}$ 2.943(8) Å, $C_{(4)}-H_{(4)}$ 0.92(4) Å, $H_{(4)}...O_{(1)}$ 2.30(4) Å, and the angle $C_{(4)}-H_{(4)}...O_{(1)}$ 127(3)°.

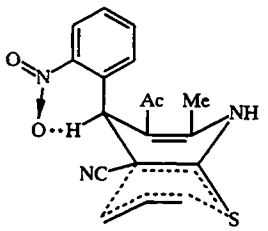
The allyl substituent occurs in the trans position in relation to the aryl substituent (the torsion angle $C_{(17)}C_{(3)}C_{(4)}C_{(10)}$ equals −162.5°). Therefore, in the rearrangement of compound (III), the attack of the $C_{(3)}$ atom by the terminal $C_{(19)}$ atom only proceeds from the opposite side with the formation of one isomer of the product (IV).

It should be noted that, as a result of the conversion (III)→(IV), the orientation of the fragment $C_{(6)}=C_{(5)}-C_{(8)}=O_{(3)}$ is also unchanged (the torsion angle $C_{(6)}C_{(5)}C_{(8)}O_{(3)}$ equals 162.1°).

In the molecule of (IV), the bond length of $C_{(2)}=S$ 1.636(6) Å is significantly less than the values of the conjugated multiple bond C=S 1.660(4) Å and 1.666(5) Å, established by us in substituted pyridine-2(1H)-thiones [14, 15], and agrees with the value established for the thione (VI) [1.626(3) Å].

In the crystal of compound (IV), the intermolecular hydrogen bonds $N_{(1)}-H_{(1)}...N_{(2)}$ (x, 0.5 − y, 0.5 + z) [$N_{(1)}...N_{(2)}$ 3.105(7) Å, $N_{(1)}-H_{(1)}$ 0.87(5) Å, $H_{(1)}...N_{(2)}$ 2.25(5) Å, and the angle $N_{(1)}-H_{(1)}...N_{(2)}$ 170.(3)°] join its molecules in chains parallel to the plane bc (Fig. 4).

On the basis of the results obtained, we will note that the [3.3]-sigmatropic rearrangement only proceeds from the side of the "bottom of the bath" of the 1,4-dihydropyridine ring, e.g., as the exo process via the intermediate (VII).




VII

It is probable that the syn-periplanar disposition of the pseudo-axial substituent 2-$NO_2C_6H_4$ is preserved in the transition state (VII), which favors the formation of the trans isomer. Therefore, the regio- and stereoselectivity of this reaction are determined by the conformation of the 1,4-dihydropyridine ring and steric effects of substituents associated with it.

## EXPERIMENTAL

**X-Ray Structure Investigation of the Compounds (III) and (IV).** Crystals of compound (III) (M 355.41) are monoclinic. At 20°C, a = 12.235(2) Å, b = 12.004(3) Å, c = 13.123(4) Å, $\beta$ = 111.86(2)°, V = 1789(2) Å$^3$, $d_{calc}$ = 1.320 g/cm$^3$, Z = 4, and the space group is P2(1)/n.

Crystals of compound (IV) (M 355.14) are monoclinic. At 20°C, a = 10.285(2) Å, b = 12.896(3) Å, c = 14.249(4) Å, $\beta$ = 110.27(2)°, V = 1773(2) Å$^3$, $d_{calc}$ = 1.332 g/cm$^3$, Z = 4, and the space group is P2(1)/c.

The cell parameters and intensities of 3652 [2955 in the case of compound (IV)] independent reflections were measured on the Siemens P3/PC four-circle automatic diffractometer ($\lambda$MoK$\alpha$, graphite monochromator, $\theta/2\theta$-scanning up to the $\theta_{max}$ = 28°). Structures were interpreted by the direct method, having shown all non-hydrogen atoms, and specified by the full-matrix MLS using the anisotropic approximation for non-hydrogen atoms from 2407 (2093) reflections with the $I > 3\sigma$ (I). In compound (IV), the atoms $C_{(18)}$ and $C_{(19)}$ are disordered in two positions; this is associated with rotation about the $C_{(3)}-C_{(17)}$ bond. The ratio of the occupancies for position $C_{(18)}$, $C_{(19)}$ and $C_{(18a)}$, $C_{(19a)}$ equals 0.60 and 0.40 correspondingly according to the specification of the MLS. All hydrogen atoms, except those connected to the atoms $C_{(18)}$, $C_{(18a)}$, $C_{(19)}$, and $C_{(19a)}$ in the molecule of (IV), were shown objectively by the difference Fourier synthesis and specified isotropically. The final values of the divergence factors are as follows: R = 0.058 and $R_W$ = 0.058 in compound (III), and R = 0.074 and $R_W$ =

0.074 in compound (IV). All calculations were performed using the SHELXTL PLUS program [16] (version PC). The atomic coordinates are given in the Tables 3 and 4 (the thermal parameters of the atoms can be obtained from the authors).

The IR spectra of the compounds synthesized were recorded on the Perkin-Elmer 457 instrument in tablets of KBr. The PMR spectra were obtained on the Bruker WM-250 spectrometer using DMSO-$D_6$ as the solvent. The initial morpholinium pyridinethiolate (I) was synthesized by the method of the work [5].

**2-Allylthio-5-acetyl-6-methyl-4-(o-nitrophenyl)-3-cyano-1,4-dihydropyridine (III).** The mixture of 4.02 g (10 mmole) of the salt (I) and 1.21 g (10 mmole) of allyl bromide (II) in 40 ml of ethanol is stirred at 20°C for 8 h. After the dilution of the reaction mixture with 10 ml of water, the residue is filtered off and washed with water, ethanol, and hexane. The yield of 2.56 g (72%) of compound (III) is obtained. The yellow crystals have the mp 170-173°C (from benzene). The IR spectrum is as follows: 1358 $cm^{-1}$, 1530 $cm^{-1}$ ($NO_2$), 1616 $cm^{-1}$ (C=O, NH), 2206 $cm^{-1}$ (C≡N), 3240 $cm^{-1}$, 3330 $cm^{-1}$, and 3448 $cm^{-1}$ (NH). The PMR spectrum is as follows: 2.12 ppm (1H, s, $CH_3$), 2.37 ppm (1H, s, $CH_3$), 3.65-3.72 ppm (2H, m, $CH_2S$), 5.25 ppm (1H, s, 4-$H_{Het}$), 5.06 ppm (1H, d, $^3J$ = 9.5 Hz, cis-H in $CH_2$), 5.09 ppm (1H, d, $^3J$ = 18.5 Hz, trans-H in $CH_2$), 5.3 ppm (1H, m, CH=$CH_2$), 7.41 ppm (1H, t, $^3J$ = 8.2 Hz, 4-$H_{Ar}$), 7.46 ppm (1H, d, $^3J$ = 8.0 Hz, 6-$H_{Ar}$), 7.66 ppm (1H, t, $^3J$ = 8.0 Hz, 5-$H_{Ar}$), 7.81 ppm (1H, d, $^3J$ = 8.0 Hz, 3-$H_{Ar}$), and 9.57 ppm (1H, s, NH). Found, %: C 60.83, H 4.82, N 11.83, and S 9.02. $C_{18}H_{17}N_3O_3S$. Calculated, %: C 60.72, H 4.70, N 11.71, and S 8.96.

**3-Allyl-5-acetyl-6-methyl-4-(o-nitrophenyl)-3-cyano-1,2,3,4-tetrahydropyridine-2(1H)-thione(IV).** Compound(III) (1.78 g, 5 mmole) is boiled for 4 h in 20 ml of ethanol. The reaction mixture is held further at 20°C for 24 h. The residue is filtered off and washed with ethanol and hexane. The yield of 1.51 g (85%) of the product (IV) is obtained; it has yellow crystals with the mp 210-213°C (from ethanol). The IR spectrum is as follows: 1352 $cm^{-1}$, 1526 $cm^{-1}$ ($NO_2$), 1636 $cm^{-1}$ (δNH), 2250 $cm^{-1}$ (C≡N), 3324 $cm^{-1}$, and 3340 $cm^{-1}$ (NH). The PMR spectrum is as follows: 2.19 ppm (3H, s, $CH_3$), 2.42 ppm (3H, s, $CH_3$), 2.68 ppm (2H, d, $CH_2$), 5.20 ppm (1H, s, 4-$H_{Het}$), 5.23 ppm (1H, d, $^3J$ = 17.0 Hz, trans-H in $CH_2$), 5.34 ppm (1H, d, $^3J$ = 9.5 Hz, cis-H in $CH_2$), 5.89 ppm (1H, m, CH=$CH_2$), 7.19 ppm (1H, d, $^3J$ = 7.5 Hz, 6-$H_{Ar}$), 7.56 ppm (1H, t, $^3J$ = 7.2 Hz, 4-$H_{Ar}$), 7.69 ppm (1H, t, $^3J$ = 8.5 Hz, 5-$H_{Ar}$), 8.03 ppm (1H, d, $^3J$ = 8.5 Hz, 3-$H_{Ar}$), and 12.5 ppm (1H, s, NH). Found, %: C 60.82, H 4.81, N 11.82, and S 9.01. $C_{18}H_{17}N_3O_3S$. Calculated, %: C 60.73, H 4.76, N 11.77, and S 8.98.

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