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Synthesis of 3-Pyridin-4-yl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepines

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Abstract—A method for the synthesis of the previously inaccessible 3-pyridin-4-yl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepines was developed. The X-Ray diffraction data for 8-*tert*-butyl-3-pyridin-4-yl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepine are presented.

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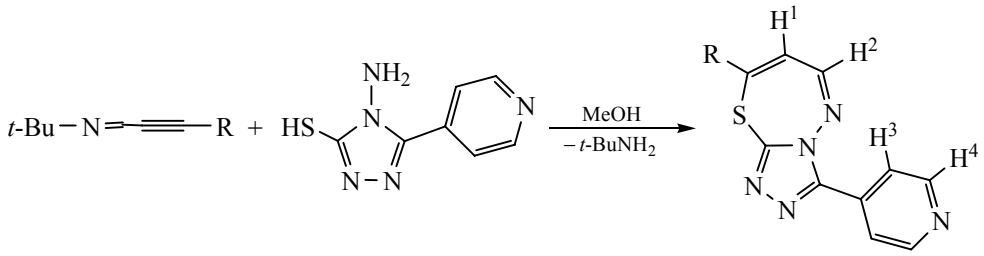
One of the methods of synthesis of 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepines is the condensation of 4-amino-4*H*-1,2,4-triazole-3-thiols with 3-substituted 2-propynals [1]. A disadvantage of this method is the formation of colored resinous substances as the reaction byproducts, which reduce the yield of the target compounds. Also, Heidel and Reid pointed out that this technique was not suitable for the synthesis of 3-pyridin-4-yl-8-phenyl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepine **IIIa**. An attempt to condense the 4-amino-5-pyridin-4-yl-4*H*-1,2,4-triazole-3-thiol **II** with 3-phenyl-2-propynal led to the formation of a black viscous multicomponent mixture.

Previously, we have reported that 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepines may also be obtained via the condensation of 4-amino-4*H*-1,2,4-triazole-3-thiols with *N*-*tert*-butylimine of 3-phenyl-2-propynal **Ia** [2]. Using this method, we succeeded in obtaining the previously inaccessible pyridine-containing thiadiazepines **IIIa**, **IIIb**.



Ia, Ib **II** **IIIa, IIIb**

R = Ph (a), *t*-Bu (**b**).

The structure of thiadiazepine **IIIb** was confirmed by the ^{1}H NMR spectroscopy and X-ray diffraction data (see the figure and the table). The bond lengths and bond angles of 8-*tert*-butyl-3-pyridin-4-yl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepine **IIIb** are listed in the table; within experimental error they coincide with the statistical average values [3]. The conformation of 7-membered cycle is a *boat* with the deviations of atoms S^1 and N^2, C^2 by 0.86 and 0.67 Å, respectively. The torsion angle $N^4C^5C^{10}C^{11}$ describing the rotation angle of the pyridine ring with respect to the five-membered ring, is 31.9 deg.

EXPERIMENTAL

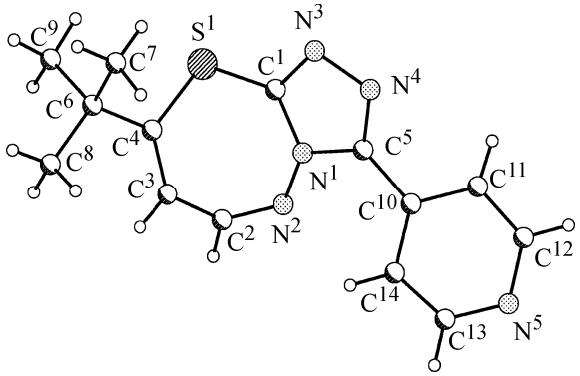
Solvents and reagents of analytical grade were used. The ^{1}H NMR spectra were recorded on a Varian XL-300 spectrometer operating at 300.13 MHz,

Bonds lengths *d* (Å) and bond angles ω (deg) in the molecule **IIIb**

Bond	*d*, Å	Bond	*d*, Å	Angle	ω, deg	Angle	ω, deg
S^1–C^1	1.7376(18)	C^3–C^4	1.339(3)	$C^1S^1C^4$	96.92(8)	$N^4C^5N^1$	109.21(16)
S^1–C^4	1.7903(19)	C^4–C^6	1.523(3)	$C^1N^1C^5$	104.91(14)	$N^4C^5C^{10}$	124.37(16)
N^1–C^1	1.375(2)	C^5–C^{10}	1.457(3)	$C^1N^1N^2$	129.76(15)	$N^1C^5C^{10}$	126.35(15)
N^1–C^5	1.377(2)	C^6–C^8	1.527(3)	$C^5N^1N^2$	124.03(15)	$C^4C^6C^8$	111.50(19)
N^1–N^2	1.398(2)	C^6–C^7	1.529(3)	$C^2N^2N^1$	116.62(15)	$C^4C^6C^7$	109.06(17)
N^2–C^2	1.283(2)	C^6–C^9	1.537(3)	$C^1N^3N^4$	107.07(15)	$C^8C^6C^7$	109.1(2)
N^3–C^1	1.309(2)	C^{10}–C^{14}	1.397(2)	$C^5N^4N^3$	108.18(15)	$C^4C^6C^9$	108.95(18)
N^3–N^4	1.386(2)	C^{10}–C^{11}	1.402(3)	$C^{13}N^5C^{12}$	116.20(17)	$C^8C^6C^9$	109.1(2)
N^4–C^5	1.321(2)	C^{11}–C^{12}	1.379(3)	$N^3C^1N^1$	110.58(16)	$C^7C^6C^9$	109.1(2)
N^5–C^{13}	1.332(3)	C^{13}–C^{14}	1.391(3)	$N^3C^1S^1$	126.28(14)	$C^{14}C^{10}C^{11}$	117.75(18)
N^5–C^{12}	1.337(3)	C^{13}–H^{13}	0.93(2)	$N^1C^1S^1$	122.86(13)	$C^{14}C^{10}C^5$	123.70(17)
C^2–C^3	1.464(3)			$N^2C^2C^3$	131.72(17)	$C^{11}C^{10}C^5$	118.42(15)
				$C^4C^3C^2$	127.01(16)	$C^{12}C^{11}C^{10}$	118.92(17)
				$C^3C^4C^6$	125.62(17)	$N^5C^{12}C^{11}$	124.24(18)
				$C^3C^4S^1$	118.80(14)	$N^5C^{13}C^{14}$	124.94(18)
				$C^6C^4S^1$	115.52(14)	$C^{13}C^{14}C^{10}$	117.92(18)

solvent DMSO-d_6, chemical shifts were measured relative to internal DMSO-d_6.

The X-ray diffraction analysis was performed on an automatic diffractometer SMART 1000 CCD (MoK_α-radiation, ω-scanning, θ ≤ 30°, graphite monochromator). The crystals of **IIIb** ($C_{14}H_{15}N_5S$) are rhombic, at 120 K: *a* 22.2612(11), *b* 6.7378(3), *c* 9.2686(5) Å, *V* 1390.21 (12) Å^3; space group *Pca*21, *Z* 4, d_{calc} 1.363 g cm^{-3}. After averaging the equivalent reflections 3634 independent reflections (R_{int} 0.0191) were obtained, which were used for solving and refining the structure. The structure was solved by the direct methods. All atoms were located in the difference electron density syntheses and refined anisotropically by F^2_{hkl}. The hydrogen atoms were refined in isotropic approximation. The final values of the reliability factors are as follows: R_1 0.0364 [calculated by F_{hkl} for 3300 reflections with $I > 2\sigma(I)$], wR_2 0.0837 (calculated by F_{hkl} for all 3634 independent reflections), *GOOF* 1.067. All calcula-tions were performed within SHELXTL PLUS 5 prog-rams (SHELXTL v. 5.10, Structure Determination Soft-ware Suite, Bruker AXS, Madison, Wisconsin, USA, 1998). Atomic coordinates, temperature factors, and full details of the geometric parameters are deposited in the Cambridge Structural Database (CCDC 725.041).



General view of the molecule of 8-*tert*-butyl-3-pyridin-4-yl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepine **IIIb**.

3-Pyridin-4-yl-8-phenyl-1,2,4-triazolo[3,4,-*b*]-1,3,4-thiadiazepine (IIIa). To a solution of 0.012 mol of aldimine **Ia** in 20 ml of methanol was added 0.01 mol of 4-amino-4*H*-1,2,4-triazole-3-thiol **II** in small portions over several minutes under stirring while a weak warm-up and a little darkening of the reaction mixture was observed. The reaction progress was monitored by TLC on Merck plates in the system ethyl acetate-petroleum ether (1:1 by volume). The reaction mixture was kept overnight at room temperature. Then the solvent was removed under a reduced pressure, and the residue was recrystallized from aqueous ethanol. Yield 58%, mp 225°C. ^{1}H NMR spectrum, δ, ppm: 6.89 d (1H, H^1, $^3J_{HH}$ 3.63 Hz), 7.46–7.53 m (3H, Ph), 7.84–7.91 m (2H, Ph), 7.96 d (2H, H^3, $^3J_{HH}$ 5.82 Hz), 8.28 d (1H, H^2, $^3J_{HH}$ 3.63 Hz), 8.70 d (2H, H^4, $^3J_{HH}$ 5.82 Hz). Found, %: C 62.61; H 4.01; N 22.82. $C_{16}H_{11}N_5S$. Calculated, %: C 62.93; H 3.63; N 22.93.

8-*tert*-Butyl-3-pyridin-4-yl-1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazepine (IIIb) was obtained similarly**.** Yield 62%, mp 190°C. ^{1}H NMR spectrum, δ, ppm: 1.30 s (9H, *t*-Bu), 6.34 d (1H, H^1, $^3J_{HH}$ 3.63 Hz), 7.95 d (2H, H^3, $^3J_{HH}$ 5.82 Hz), 8.18 (1H, H^2, $^3J_{HH}$ 3.63 Hz), 8.66 d (2H, H^4, $^3J_{HH}$ 5.82 Hz). Found, %: C 58.41; H 5.08; N 24.74. $C_{14}H_{15}N_5S$. Calculated, %: C 58.82; H 5.30; N 24.54.

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