ISSN 1070-3632, Russian Journal of General Chemistry, 2014, Vol. 84, No. 2, pp. 272–276. © Pleiades Publishing, Ltd., 2014.
Original Russian Text © A.V. Rybakova, D.G. Kim, V.V. Sharutin, 2014, published in Zhurnal Obshchei Khimii, 2014, Vol. 84, No. 2, pp. 280–284.

Protonation Direction of 3-Allylthio[1,2,4]triazino[5,6-*b*]indole and 3-Methyl[1,3]thiazolo[3',2':2,3][1,2,4]triazino[5,6-*b*]indole

A. V. Rybakova, D. G. Kim, and V. V. Sharutin

Southern Ural State University, pr. V.I. Lenina 76, Chelyabinsk, 454080 Russia
e-mail: zhurav666@rambler.ru

Received April 10, 2013

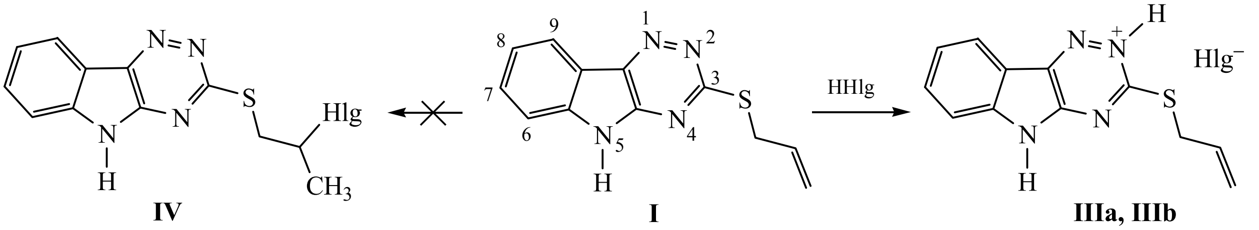
Abstract—X-ray diffraction studies have demonstrated that the protonation of 3-allylthio-5*H*-[1,2,4]triazino-[5,6-*b*]indole with hydrogen halides occurs at N^2 and that of 3-methyl[1,3]thiazolo[3',2':2,3][1,2,4]triazino-[5,6-*b*]indole, at N^{10}.

DOI: 10.1134/S1070363214020194

Elucidation of primary protonation sites of heterocyclic compounds containing several nitrogen atoms is a complicated problem. According to *ab initio* simulation of 1,2,4-triazines, usually N^1 and N^2 are the most favorable protonation sites [1]. The formation of N^1–H- and N^2–H-[1,2,4]triazinium cations can be thermodynamically favorable as protonation of one of the two adjacent nitrogen atoms reduces the electron pairs repulsion. According to ^{13}C NMR data, protonation of 7*H*-imidazo[4,5-*e*][1,2,4]triazines occurs at N^1 [2], whereas imidazo[1,2-*b*]-[1,2,4]triazines are protonated at N^5 [3].

In this work we for the first time studied the protonation of 3-allylthio-5*H*-[1,2,4]triazino[5,6-*b*]indole (**I**) and 3-methyl[1,3]thiazolo[3',2':2,3][1,2,4]triazino-[5,6-*b*]indole (**II**) by X-ray diffraction. Compound **I** was prepared by alkylation of 3-thio-5*H*-[1,2,4]triazino-[5,6-*b*]indole with allylbromide in the NaOH–DMSO–H_2O medium [4]. Compound **II** was obtained by iodocyclization of **I** followed by dehydrohalogenation of 3-iodomethyl-3,10-dihydro-2*H*-[1,3]thiazolo[3',2':2,3]-[1,2,4]triazino[5,6-*b*]indole with sodium carbonate [4] as well as by heterocyclization of 3-propargylthio-5*H*-[1,2,4]triazino[5,6-*b*]indole with alkali [5].

Theoretically, interaction of **I** with hydrogen halides can yield halides of 3-allylthio-2*H*,5*H*-[1,2,4]triazino-[5,6-*b*]indolium (**IIIa**, **IIIb**) or 3-(2-halopropylthio)-5*H*-[1,2,4]triazino[5,6-*b*]indole (**IV**), the latter being a product of hydrogen halide addition to the double bond of the allyl group. The products study is further complicated by prototropic tautomerism of **I** and possible protonation at different nitrogen atoms.



IV **I** **IIIa, IIIb**

Hlg = Br (**a**), Cl (**b**).

It was found that **I** reacted with hydrogen halides to form the hydrohalides **IIIa** and **IIIb**. In the case of hydrogen bromide, we could obtain a single crystal of the product and study it by X-ray diffraction (Tables 1, 2).

X-ray diffraction data revealed that the protonation occurred at the N^2 atom, compound **I** existing in the tautomeric form with proton at N^5. The general view of **IIIa** molecule showing the atoms numbering is given in Fig. 1.

Bromide atom was disordered by two positions (Br^1 and Br^2). The $H^5\cdots Br^2$ and $H^2\cdots Br^1$ distances were 2.498 and 2.289 Å, respectively. The $S^{1A}\cdots H^{7B}$ close

Table 1. Crystallographic data, experimental and refinement parameters of **IIIa** and **Va** structures analysis

Parameter	Value	
	IIIa	**Va**
M	323.22	276.74
T, K	293(2)	293(2)
Crystal system	Monoclinic	Monoclinic
Space group	$C2/c$	$P2_1/n$
a, Å	12.6418(4)	8.9740(3)
b, Å	6.7023(2)	12.8141(3)
c, Å	30.9379(9)	10.2075(3)
α, deg	90.00	90.00
β, deg	92.594(2)	96.481(2)
γ, deg	90.00	90.00
V, Å^3	2618.66(14)	1166.30(6)
Z	8	4
d_{calc}, g/cm^3	1.640	1.576
μ, mm^{-1}	3.286	0.491
$F(000)$	1296.0	568.0
Crystal size, mm	0.3×0.2×0.1	0.33×0.19×0.12
θ range, deg	5.28–70.12	5.56–64.68
Reflection indexes range	$-19 \le h \le 20$, $-10 \le k \le 10$, $-31 \le l \le 47$	$-9 \le h \le 13$, $-19 \le k \le 18$, $-15 \le l \le 15$
Reflections collected	18761	14948
Number of independent reflections	5440 (R_{int} 0.0507)	4138 (R_{int} 0.0373)
Parameters refined	173	164
GOOF	1.008	1.036
R-Factors along $F^2 > 2\sigma(F^2)$	R_1 0.0565, wR_2 0.1097	R_1 0.0537, wR_2 0.1178
R-Factors along all reflections	R_1 0.1347, wR_2 0.1305	R_1 0.0865, wR_2 0.1314
Residual electronic density (min/max), e/Å^3	1.08/–0.92	0.40/–0.44

intermolecular contacts were also observed with the distance of 2.819 Å (shorter than the sum of the atoms Van der Waals radii, 3.00 Å) [6]. The indolo[1,2,4]-triazine ring, the S^1, C^2, C^1, and C^{12} allylthio group atoms as well as [Br^1]$^-$ anion were located in the same plane. Crystal packing of **IIIa** molecules along c axis and the short intermolecular contacts are illustrated in Fig. 2.

Table 2. Bond lengths and bond angles in **IIIa** and **Va**

Bond	d, Å	Angle	ω, deg
IIIa			
S^1–C^3	1.733(3)	$C^3S^1C^2$	101.80(14)
S^1–C^2	1.819(3)	$N^5C^5C^{10}$	110.1(2)
C^5–N^5	1.402(4)	$C^6C^5N^5$	128.2(2)
C^5–C^{10}	1.402(3)	$C^6C^5C^{10}$	121.7(3)
C^5–C^6	1.382(4)	$N^5C^4C^{11}$	108.3(2)
C^4–N^5	1.332(3)	$N^4C^4N^5$	128.0(2)
C^4–C^{11}	1.448(3)	$N^4C^4C^{11}$	123.7(2)
C^4–N^4	1.320(3)	$C^4N^5C^5$	109.2(2)
C^{11}–N^1	1.309(3)	$N^1C^{11}C^4$	120.5(2)
C^{11}–C^{10}	1.433(4)	$N^1C^{11}C^{10}$	132.0(2)
N^4–C^3	1.332(3)	$C^{10}C^{11}C^4$	107.5(2)
C^3–N^2	1.341(3)	$C^4N^4C^3$	113.3(2)
N^1–N^2	1.341(3)	$N^4C^3S^1$	121.3(2)
C^{10}–C^9	1.389(4)	$N^4C^3N^2$	123.1(3)
C^6–C^7	1.379(4)	$N^2C^3S^1$	115.6(2)
C^9–C^8	1.373(4)	$C^{11}N^1N^2$	113.9(2)
C^7–C^8	1.392(5)	$N^1N^2C^3$	125.4(2)
C^2–C^1	1.484(5)	$C^5C^{10}C^{11}$	104.9(2)
C^1–C^{12}	1.008(8)	$C^1C^2S^1$	107.2(2)
Va			
S^1–C^2	1.7256(17)	$C^{12}S^1C^2$	90.18(8)
S^1–C^{12}	1.7072(17)	$C^{11}N^{11}C^{12}$	112.38(14)
N^{11}–C^{12}	1.337(2)	$C^{11}N^{10}C^{10}$	108.74(14)
N^{11}–C^{11}	1.318(2)	$C^4N^5N^4$	112.44(13)
N^{10}–C^{11}	1.338(2)	$N^5N^4C^{12}$	124.74(13)
N^{10}–C^{10}	1.405(2)	$N^5N^4C^3$	120.65(13)
N^5–N^4	1.3474(19)	$C^{12}N^4C^3$	114.61(13)
N^5–C^4	1.300(2)	$C^3C^2S^1$	114.21(13)
N^4–C^{12}	1.370(2)	$N^{11}C^{12}S^1$	124.85(12)
N^4–C^3	1.402(2)	$N^{11}C^{12}N^4$	124.05(15)
C^2–C^3	1.347(3)	$N^4C^{12}S^1$	111.08(11)
C^{11}–C^4	1.453(2)	$N^{11}C^{11}N^{10}$	127.73(15)
C^{10}–C^9	1.380(2)	$N^{11}C^{11}C^4$	123.35(15)
C^{10}–C^5	1.406(2)	$N^{10}C^{11}C^4$	108.92(14)
C^9–C^8	1.391(3)	$N^{10}C^{10}C^5$	110.36(15)
C^8–C^7	1.391(3)	$C^9C^{10}N^{10}$	128.01(16)
C^5–C^6	1.388(2)	$C^{10}C^5C^4$	105.14(14)
C^5–C^4	1.442(2)	$N^5C^4C^{11}$	123.04(15)
C^6–C^7	1.379(3)	$N^5C^4C^5$	130.11(15)
C^3–C^1	1.479(2)	$N^4C^3C^1$	118.91(15)
		$C^2C^3N^4$	109.90(14)

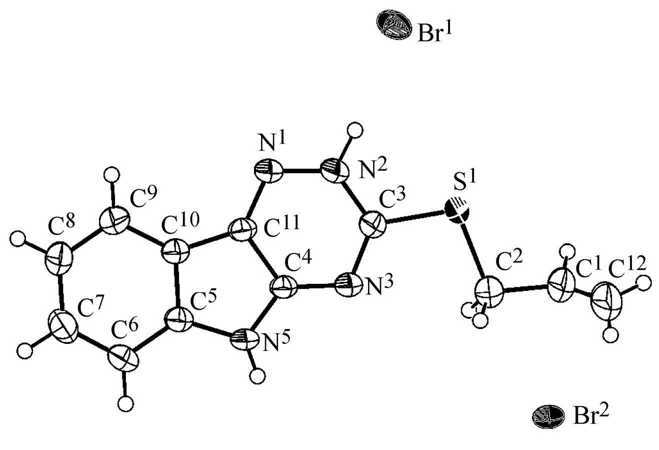


Fig. 1. General view of **IIIa** molecule.

^{1}H NMR features of **IIIa** and **IIIb** were equal to those of the initial compound **I** thus proving the dissociation of the hydrohalides in DMSO-d_6 solution. The IR spectra contained broadened band of N^+–H vibration [7] with maxima at 2541 and 2329 cm^{-1}.

Interaction of **II** with hydrogen halides yielded hydrohalides **Va** and **Vb**. Theoretically, the protonation of **II** could occur at nitrogen atoms nos. 4, 5, 10, and 11. Compound **Va** formed as a regular single crystal, its structure was studied by X-ray diffraction. According to the results, the protonation of **II** occurred at N^{10}, the nitrogen atom of the indole ring (Fig. 3), to form 3-methyl-10*H*-[1,3]thiazolo[3',2':2,3][1,2,4]triazino-[5,6-*b*]indolium chloride **Va**.

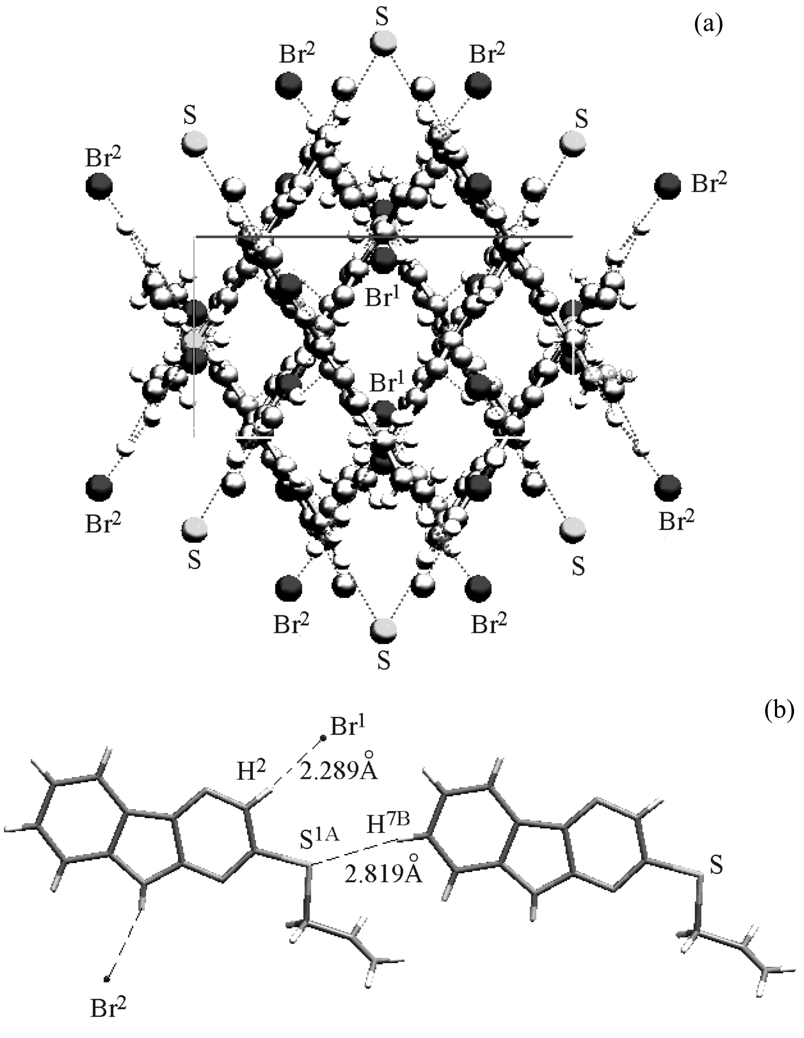
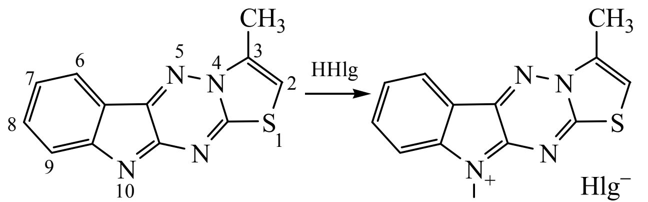


Fig. 2. Packing of **IIIa** molecules along *c* axis (a) and short intermolecular contacts in **IIIa** crystal (b).



II

Va, Vb

Hlg = Cl (**a**), Br (**b**).

According to X-ray diffraction data, the unit cell contained 4 molecules of protonated compound **II** and 4 chlorine atoms. Heterocyclic system was planar, Cl^1 was deviated from the plane by 0.27 Å. The found short contacts were as follows: $H^{10}\cdots Cl$ (2.250 Å), $N^{11A}\cdots S^{1B}$ (3.222 Å), and $S^{1B}\cdots Cl$ (3.219 Å) (Fig. 4).

^1H NMR spectrum of **Vb** was different from that of the initial compound **II**, thus demonstrating its stability in DMSO-d_6 solution. ^1H NMR spectrum of **Vb** contained a broadened N^+H proton signal at 13.99 ppm, the signals of aromatic protons and CH_3 group were shifted downfield as compared with the respective signals of **II**, due to positive charge on the heterocycle.

EXPERIMENTAL

IR spectra were recorded using Varian 800FT-IR Scimitar Serias spectrophotometer. ^1H NMR spectra

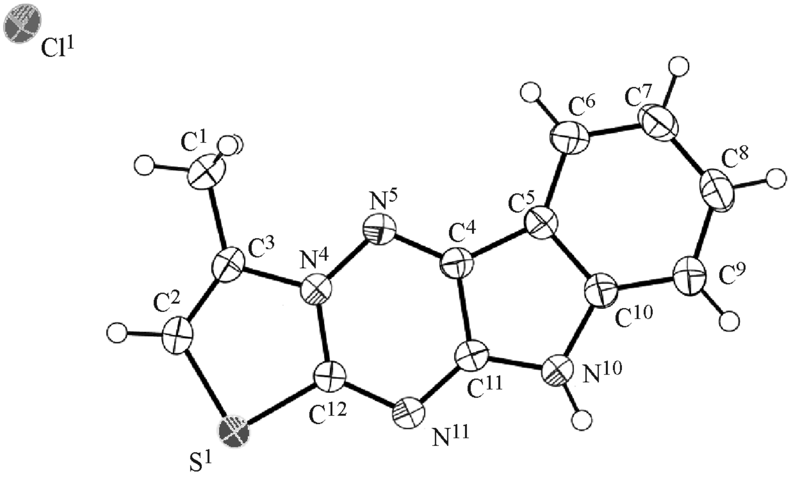


Fig. 3. General view of **Va** molecule.

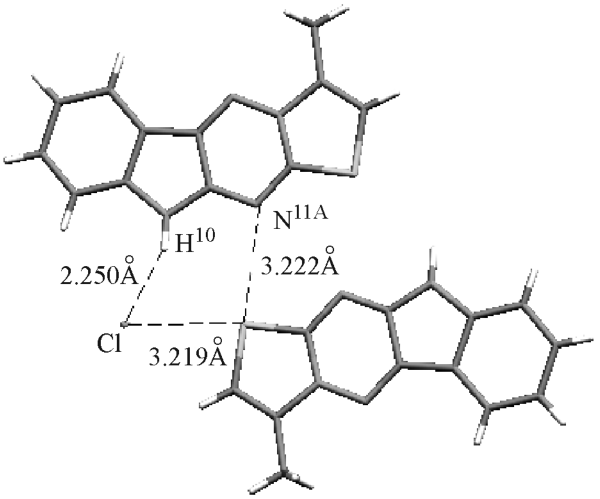


Fig. 4. Short intermolecular contacts in **Va** crystal.

were recorded on a Bruker DRX-400 spectrometer (400 MHz, TMS as internal reference) from solutions in DMSO-d_6.

Hydrohalides preparation *(general procedure)*. 1 mL of concentrated aqueous HCl or HBr was added to solution of 1 mmol of **I** or **II** in 2 mL of acetone. The reaction mixture was kept at 7°C during 2 h and then at room temperature during 24 h. The formed precipitate was filtered off.

3-Allylthio-2*H*,5*H*-[1,2,4]triazino[5, 6-*b*]indolium bromide (IIIa). Yield 36%, mp 202°C.

3-Allylthio-2*H*,5*H*-[1,2,4]triazino[5, 6-*b*]indolium chloride (IIIb). Yield 50%, mp 204°C.

3-Methyl-10*H*-[1,3]thiazolo[3',2':2,3][1,2,4]triazino-[5,6-*b*]indolium chloride (Va). Yield 38%, mp > 220°C (7 wt % HCl).

3-Methyl-10*H*-[1,3]thiazolo[3',2':2,3][1,2,4]triazino[5,6-*b*]indolium bromide (Vb). Yield 46%, mp > 220°C. ^{1}H NMR spectrum, δ, ppm: 2.79 s (3H, CH_3), 8.17 s (1H, SCH=), 7.35–8.49 (4H, Ar), 14.05 br.s (1H, NH).

X-ray diffraction study of **IIIa** and **Va** crystals was performed with automated four-circle Bruker D8 QUEST diffractometer (MoK_α, $\lambda = 0.71073$ Å, graphite monochromator) at $T = 293(3)$ K. Data collection, processing, and unit cells parameters refinement as well as correction for extinction were performed with SADABS [8], SMART, and SAINT-Plus [9] software. Structure was solved and refinement was performed with SHELXL/PC [10] software. Hydrogen atoms were placed in geometry-calculated positions. The basic crystallographic parameters and results of structure refinement are given in Table 1; selected bond lengths and bond angles are collected in Table 2. Complete data on atomic coordinates, bond lengths, and bond angles are deposited at Cambridge Crystallographic Data Center under CCDC 927963 and CCDC 927964.

REFERENCES

1. Mo, O., De Paz, J.L.G., and Yanez, M., *J. Mol. Struct.*, 1987, vol. 150, nos. 1–2, p. 135.
2. Barraclough, P., Firmin, D., Iyer, R., King, W.R., Lindon, J.C., Nobbs, M.S., Smith, S., Wharton, C.J., and Williams, J.M., *J. Chem. Soc. Perkin Trans. 2*, 1988, p. 1839.
3. Barraclough, P., Firmin, D., Lindon, J.S., Nobbs, M.S., Sanderson, P.N., Smith, S., and Gillam, J.M., *Magn. Res. Chem.*, 1991, vol. 29, no. 5, p. 468.
4. Kim, D.G., Zhuravlyova, A.V., *Chem. Heterocycl. Comp.*, 2010, vol. 46, no. 7, p. 896.
5. Zhuravlyova, A.V., *Chem. Heterocycl. Comp.*, 2009, vol. 45, no. 10, p. 1281.
6. Zefirov, Yu.V. and Zorkii, P.M., *Russ. Chem. Rev.*, 1989, vol. 58, no. 5, p. 721.
7. Nakanisi, K., *Infrared Spectra and the Structure of Organic Compounds*, Moscow: Mir, 1965, p. 45.
8. Sheldrick, G.M., *SADABS*, Program for Empirical X-Ray Absorption Correction, Bruker-Nonius, 1990–2004.
9. *SMART and SAINT-Plus*. Versions 5.0. Data Collection and Processing Software for the SMART System. Bruker AXS Inc., Madison, Wisconsin, USA, 1998.
10. Sheldrick, G.M., *SHELXTL/PC*. Versions 6.12. Structure Determination Software Suite. Bruker AXS Inc., Madison, Wisconsin, USA, 2000.