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Valence tautomerism of new pyrazolo[4,3-*e*]tetrazole[4,5-*b*][1,2,4]triazines

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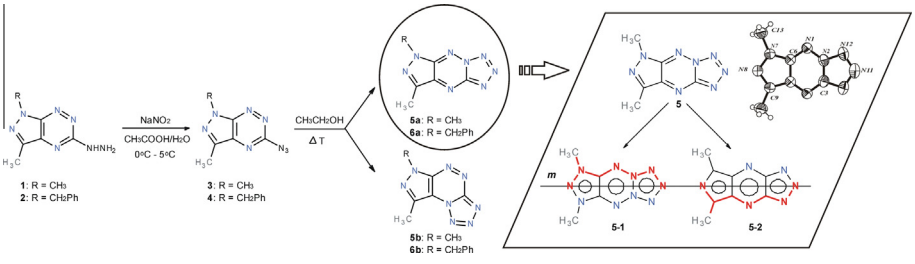
HIGHLIGHTS

- Five new pyrazolo[4,3-*e*]tetrazole[4,5-*b*][1,2,4]triazines were synthesized.
- Compounds were characterized by HRMS, NMR and X-ray.
- The structure and valence tautomeric equilibrium in gaseous phase and solutions were investigated theoretically by DFT.

GRAPHICAL ABSTRACT



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ABSTRACT

New pyrazolo[4,3-*e*]tetrazolo[4,5-*b*][1,2,4]triazines **5** and **6** were prepared as new biological active compounds with potential anticancer activity referring to our previous study. The ^{1}H NMR spectra reveal tautomeric equilibrium azido and tricyclic forms of these compounds in solution. The molecular and crystal structures of **5** and **6** were determined by the X-ray analysis. The X-ray investigations show that in the crystalline state the compounds **5** and **6** exist as the linear tricyclic pyrazolo[4,3-*e*]tetrazolo[4,5-*b*][1,2,4]triazine tautomeric form. The analysis of the intra- and intermolecular interactions indicates the weak C–H···N hydrogen bonds and $\pi\cdots\pi$ interactions in crystal of **6** and van der Waals forces only in crystal of **5** as the non-covalent interactions influencing the molecular packing. The theoretical calculations at the *ab initio* DFT/B3LYP/6-311++G(d,p) level showed the azido form (**3** and **4)** as one existing in the gaseous phase and the coexistence of the tricyclic linear (**5** and **6**) and azido tautomeric forms in solution, wherein the contribution of the linear form compared to the azido form changes with polarity of the solvent.

Introduction

The chemistry of 1,2,4-triazine and its derivatives has been studied due to their diverse biological activities [1]. More recently, some naturally occurring derivatives of condensed 1,2,4-triazines with pyrazole ring system e.g. pseudoiodinine and nostocine A were found to have anticancer and antifungal activity [2,3]. Keeping in mind the various biological activities of the pyrazolo[4,3-*e*][1,2,4]triazine ring system we have designed and synthesized a series of new derivatives of the system in our laboratory in the past decade [4–7]. Both pyrazolo[4,3-*e*][1,2,4]triazines and their annulated derivatives showed anticancer activity [8]. Recently, we have reported the formation of pyrazolo[4,3-*e*][1,2,4]triazines fused with tetrazole ring [9,10] and as a continuation of our ongoing investigation on preparation and searching of new potential anticancer tricyclic molecules as well structural study of that system we publish herein the synthesis of two new

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derivatives of pyrazolo[4,3-*e*] tetrazolo[4,5-*b*][1,2,4]triazine ring system **5** and **6** (Scheme 1), their ^{1}H NMR spectra, X-ray analysis and theoretical calculations in order to elucidate the exact structure of the obtained products in gaseous phase, polar and non-polar solutions and crystalline state due to possibility of existing valence tautomerism between azido and tricycle forms. It should be noted, that tricyclic fused system can exist in linear (**a**) and angular (**b**) fused isomers (Scheme 1). It is known from our previously study [9,10], that similar azido-pyrazolo-triazine compounds leads in solution to an equilibrium between azido and tricycle tautomeric forms with the latter crystallization to X-ray confirmed linearly fused solid products. However, we did not find direct experimental evidence that the angular fused form cannot be formed in solution, therefore, we investigated the tautomeric equilibrium of azido and both tricyclic linear and angular forms using theoretical calculation at *ab initio* DFT level.

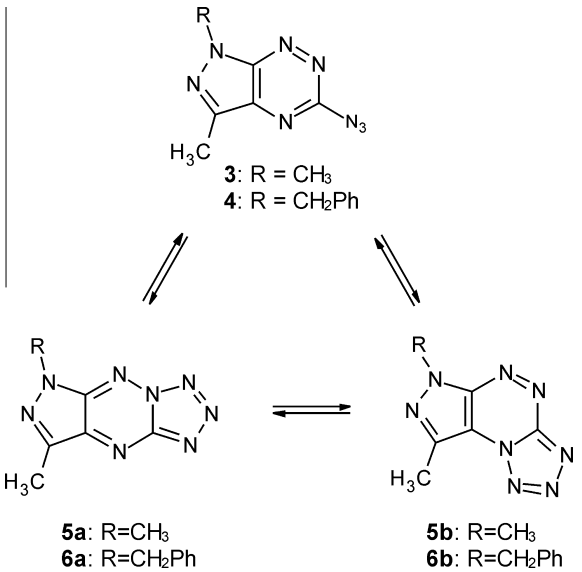
Experimental

General methods

Melting points were determined in open capillaries and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Gemini 200 MHz spectrometer using tetramethylsilane as the internal standard. The IR spectra were measured with a Magna IR-760 spectrophotometer in KBr pellets. Mass spectra were measured on AMD 604 spectrometer (electron impact, 70 eV). Elemental analyses were obtained on Perkin–Elmer 2400-CHN analyzer and the results for the indicated elements were within 0.3% of the calculated values. Starting compounds **1** and **2** were synthesized according to literature procedure [6,11]. Spectroscopic data for derivative **1** are described in literature [6]. Compounds **3** and **4** were used as crude products.

*1-Benzyl-5-hydrazine-3-methyl-1H-pyrazolo[4,3-e][1,2,4]triazine (**2**)*

Mp 98 °C. ^{1}H NMR (DMSO) δ: 2.43 (s, 3H); 5.68 (s, 2H); 7.25–7.34 (m, 5H). ^{13}C NMR (DMSO) δ: 10.74, 51.02, 127.60, 127.73, 128.61, 133.87, 136.80, 138.27, 145.95, 163.26. IR (KBr) cm^{-1}: 3278, 1526, 1467, 1110, 699. MS (EI 70 eV, *m*/*z*, %): 255 (100) [M$^+$], 226 (14), 210 (21), 196 (11), 91 (76), 65 (17). HRMS (EI, *m*/*z*) 255.12293, Calcd for $C_{12}H_{13}N_7$[M$^+$] 255.12324.



Scheme 1.

*Synthesis of 5-azido-1,3-dimethyl-1H-pyrazolo[4,3-e][1,2,4]triazine (**3**)*

The solution of **1** (108 mg, 0.6 mmol) in CH_3COOH/H_2O mixture (1:1, 4 mL) was cooled to 0–5 °C and aqueous $NaNO_2$ (81 mg in 2 mL of water) was added dropwise so that the temperature of reaction mixture was kept below 5 °C. After additional stirring for 15 min at 0–5 °C the yellow precipitate was filtered off, washed with water and dried at room temperature to give 108 mg (95%) of **3**. Mp 90 °C. ^{1}H NMR ($CDCl_3$) δ: 2.63 (s, 3H); 4.27 (s, 3H). IR (KBr) cm^{-1}: 2941, 2139 (N_3), 1596, 1535, 1262, 1179, 978. HRMS (EI, *m*/*z*) 190.07074, Calcd for $C_6H_6N_8$ [M$^+$] 190.07154.

*Synthesis of 5-azido-1-benzyl-3-methyl-1H-pyrazolo[4,3-e][1,2,4]triazine (**4**)*

The compound was prepared according to the procedure described for derivative **3** in a 95% yield. ^{1}H NMR ($CDCl_3$) δ: 2.60 (s, 3H); 5.74 (s, 2H); 7.29–7.44 (m, 5H). IR (KBr) cm^{-1}: 2961, 2923, 2853, 2225, 2140 (N_3), 1425, 1261, 1100; HRMS (EI, *m*/*z*) 266.10180, Calcd for $C_{12}H_{10}N_8$ [M$^+$] 266.10284.

*Synthesis of 5,7-dimethyl-5H-pyrazolo[4,3-e]tetrazolo[4,5-b][1,2,4]triazine (**5**)*

The azido compound **3** (105 mg, 0.55 mmol) was dissolved in boiling ethanol (4 mL) and the resulting mixture was left to slow crystallization at room temperature. The crystals and dry residue after evaporation of the alcohol were combined and purified on column chromatography using chloroform/ethanol mixture 30:1 as eluent to give **5** (97 mg, 0.51 mmol, 93%) as a red solid. Mp 193–195 °C. ^{1}H NMR ($CDCl_3$) δ: 2.79 (s, 3H), 4.18 (s, 3H). MS (EI 70 eV, *m*/*z*, %): 190 (44) [M$^+$], 185 (12), 115 (16), 93 (86), 78 (25), 67 (55), 41 (100). HRMS (EI, *m*/*z*) 190.07074, Calcd for $C_6H_6N_8$[M$^+$] 190.07154.

*Synthesis of 5-benzyl-7-methyl-1H-pyrazolo[4,3-e]tetrazolo[4,5-b][1,2,4]triazine (**6**)*

The compound was prepared according to the procedure described for derivative **5** in a 90% yield. Mp 135–136 °C. ^{1}H NMR ($CDCl_3$) δ: 2.76 (s, 3H); 5.61 (s, 2H); 7.28–7.31 (m, 3H); 7.40–7.45 (m, 2H). MS (EI 70 eV, *m*/*z*, %): 266 (12) [M$^+$], 169 (6), 142 (8), 91 (100), 65 (14). HRMS (EI, *m*/*z*) 266.10180, Calcd for $C_{12}H_{10}N_8$ [M$^+$] 266.10284.

X-ray structure analysis

Yellow plate crystals of **5** and **6** suitable for X-ray diffraction analysis were grown by slow evaporation of an ethanol solution. X-ray data of **5** were collected on the Enraf–Nonius MACH3 diffractometer; crystal size 0.42 × 0.32 × 0.10 mm, ω-2θ scans, psi-scan absorption correction [12], room temperature. Data collection for **6** was performed on the Bruker SMART APEXII CCD diffractometer; crystal size 0.25 × 0.25 × 0.10 mm, φ and ω scans, room temperature. The structures were solved by direct methods using SIR92 [13] and refined by full-matrix least-squares with SHELXL97 [14]. The H atoms were positioned geometrically and treated as riding on their parent C atoms with C–H distances of 0.96 Å (CH_3), 0.97 Å (CH_2), and 0.93 Å (aromatic). All H atoms were refined with isotropic displacement parameters taken as 1.5 times those of the respective parent atoms. The structure solution of **5** in the space group *Pbnm* (=*Pnma*) reveals special position of the molecule on the crystallographic mirror plane dividing the molecule on two symmetrical parts and generating pseudosymmetry inconsistent to expected molecular structure of **5** (Fig. 1). This pseudosymmetry

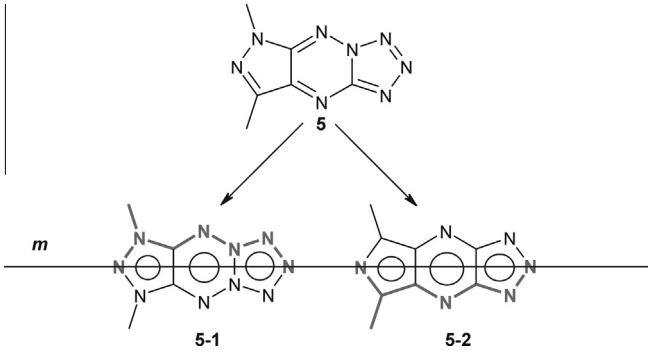


Fig. 1. Two possible pseudo-symmetric positions **5**–**1** and **5**–**2** of the molecule **5** relative to the mirror plane.

leads to two independent solutions with final *R* indices of 0.0621 (**5–1**) and 0.0776 (**5–2**) for 68 parameters and 886 reflections, resulting from necessity to consider two alternative positions for symmetrically positioned C and N atoms. The systematic absences allow the non-centrosymmetric space group $Pbn2_1$ without a mirror plane. Consequently, two further solutions in this space group are possible and attempts to refine the structure of **5** in space group $Pbn2_1$ lead to the *R* factors of 0.0498 and 0.0527 for 128 parameters and 886 reflections, and residual maps comparable with the centrosymmetric refinements. However, the large correlations, with largest correlation matrix elements more as 0.9, between parameters related by a pseudo-mirror plane of symmetry and the large values of shifts/esd for parameters (more as 0.7) are observed, rendering the refinements not conclusive. The best result is obtained on the assumption that the structure is centrosymmetric with the pseudo-mirror plane of symmetry and the atoms N7/C9 and N2/C3 sharing the same sites with the occupancy factors of 0.5, the same *x*, *y*, *z* coordinates and anisotropic displacement parameters. The refinement of this structure model of **5** by the use of EXYZ and EADP instructions in SHELXL97 give final R indices of 0.0572. All crystal and experimental data are listed in Table 1. Molecular graphics were prepared using ORTEP3 for Windows [15]. PARST [16] and PLATON [17] were used for geometrical calculations. All calculations were performed using WINGX ver. 1.64.05 package [15].

Theoretical calculations

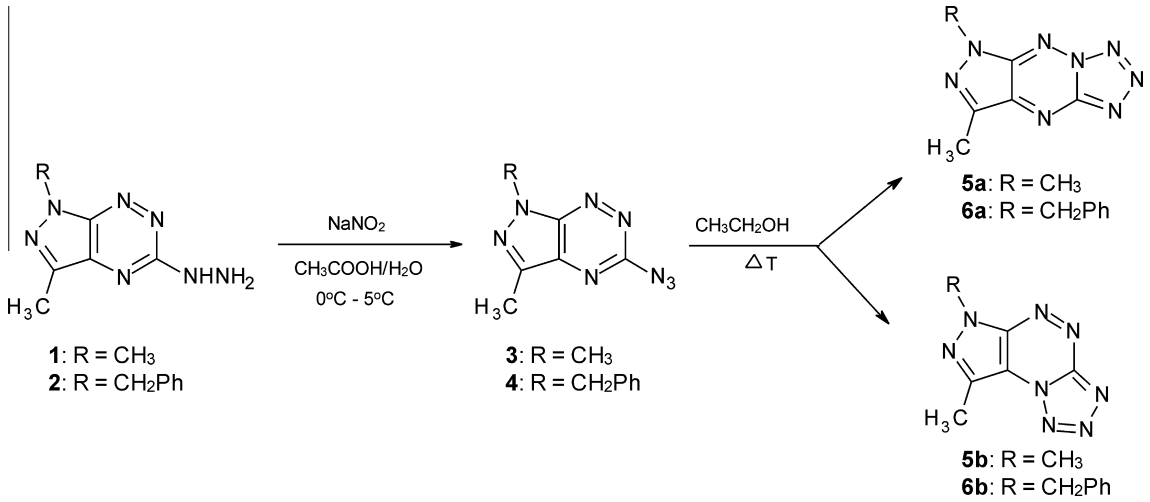
The energy and dipole moments for all structures **3**–**6** were calculated with GAUSSIAN 03 [18] at the *ab initio* DFT/B3LYP level with 6-311++G(d,p) basis set. The structures were fully optimized without any symmetry constraints and the initial geometries were built from the crystallographic data of **5** and **6**. The calculations were performed in gaseous phase and chloroform and ethanol solutions using Polarized Continuum Model CPCM [19]. The total energies and dipole moments are summarized in Supplementary Table 1S. The DFT/B3LYP/6-311++G(d,p) method was used because it reproduce geometrical parameters for **5** and **6** comparable to the experimental values obtained from X-ray analysis (Supplementary Table S2). Calculations were carried out at the Academic Computer Centre in Siedlce University.

Results and discussion

In general, both pyrazolo[4,3-*e*] tetrazolo[4,5-*b*][1,2,4]triazine derivative **5** and **6** were achieved starting from appropriate 5-hydrazine-1*H*-pyrazolo[4,3-*e*][1,2,4]triazine derivatives **1** and **2** obtained by convenient procedure published previously (Scheme 2) [9]. Hydrazine derivatives thus obtained were converted into the corresponding azido forms **3** and **4** upon treatment with an excess of $NaNO_2$ in CH_3COOH/H_2O mixture at 0 °C. Recrystallization of azido structures **3** and **4** from hot ethyl alcohol furnished the tetrazole derivatives **5** and **6** which appeared to be stable in crystal form. Furthermore, ^{1}H NMR investigation showed the equilibrium between azido form and tetrazole derivatives in the solution (Fig. 2). The ^{1}H NMR recorded spectrum immediately after dissolution of the compound **3** in deuterated chloroform exhibited two main singlets at δ = 2.63 ppm and δ = 4.27 ppm which can only correspond to the methyl groups present in the azido form **3** (Fig 2*a*) and two very small signals at δ = 2.79 ppm and δ = 4.18 ppm corresponding to the presence two methyl substituents in the examined molecule **5**. The integration of the related resonances in the ^{1}H NMR spectra indicated that the ratio of populations of tautomers present in the solution is 9:1 for the azido form **3** and tetrazole form **5**, respectively. The ^{1}H NMR measurement for the same sample repeated after 24 h showed the shift of the tautomeric equilibrium toward the slight dominance of the tetrazole form relative to azido form (Fig 2*b*). Much more effective increase of the tetrazole form was observed after 48 h and the ratio of the populations was 2:1 in favour of tetrazole form (Fig. 2c). After that time the equilibrium was constants and the ^{1}H NMR spectrum recorded after next 24 h did not show any changes in the integration of the present peaks to the previous spectra. The similar effect was observed for ^{1}H NMR spectrum recorded in different deuterated solvents (MeOH-d_4, acetone-d_6) (Supplementary Figs. S1 and S2, respectively). It should be noted that these experiments in analysed solvents showed that after 48 h in the measured samples the tetrazole form was predominant, however the trace quantities

Table 1
Crystal data and structure refinement for **5** and **6**.

	5	**6**
Empirical formula	$C_6H_6N_8$	$C_{12}H_{10}N_8$
Formula weight	190.19	266.28
Crystal system	Orthorhombic	Monoclinic
Space group	*Pbnm*	$P2_1/c$
Unit cell parameters		
a (Å)	6.3290(4)	10.5299(5)
b (Å)	9.5469(5)	11.4464(5)
c (Å)	13.9350(7)	21.2944(10)
β (deg)		95.381(5)
V (Å^3)	841.99(8)	2555.3(2)
Z	4	8
D_{calc} (g cm^{-3})	1.500	1.384
F(000)	392	1104
λ (Cu Kα) (Å)	1.54178	1.54178
Cell parameters from	11	4097 reflections
θ range for lattice parameters (deg)	11.24–22.80	4.17–66.86
Absorption coefficient μ (mm^{-1})	0.916	0.773
T_{min}/T_{max}	0.700/0.939	
θ range for data collection (deg)	6.35–74.28	4.17–67.76
Index ranges *h*, *k*, *l*	0/7, 0/11, −17/0	−12/12, −9/13, −25/24
No. of measured reflections	886	19062
No. of independent reflections	886	4564 (R_{int} = 0.0502)
No. of observed reflections	430 with $I > 2\sigma(I)$	3419 with $I > 2\sigma(I)$
Refinement method	Full-matrix least-squares on F^2	
Final *R* indices	0.057	0.042
$wR(F^2)$	0.125	0.116
Goodness-of-fit on F^2, *S*	1.042	0.982
Data/parameters	886/68	4564/362
Extinction coefficient	0.0079(11)	0.0032(3)
Largest diff. peak and hole (e Å^{-3})	+0.218 and −0.274	+0.173 and −0.167
$(\Delta/\sigma)_{max}$	0.000	0.000



Scheme 2.

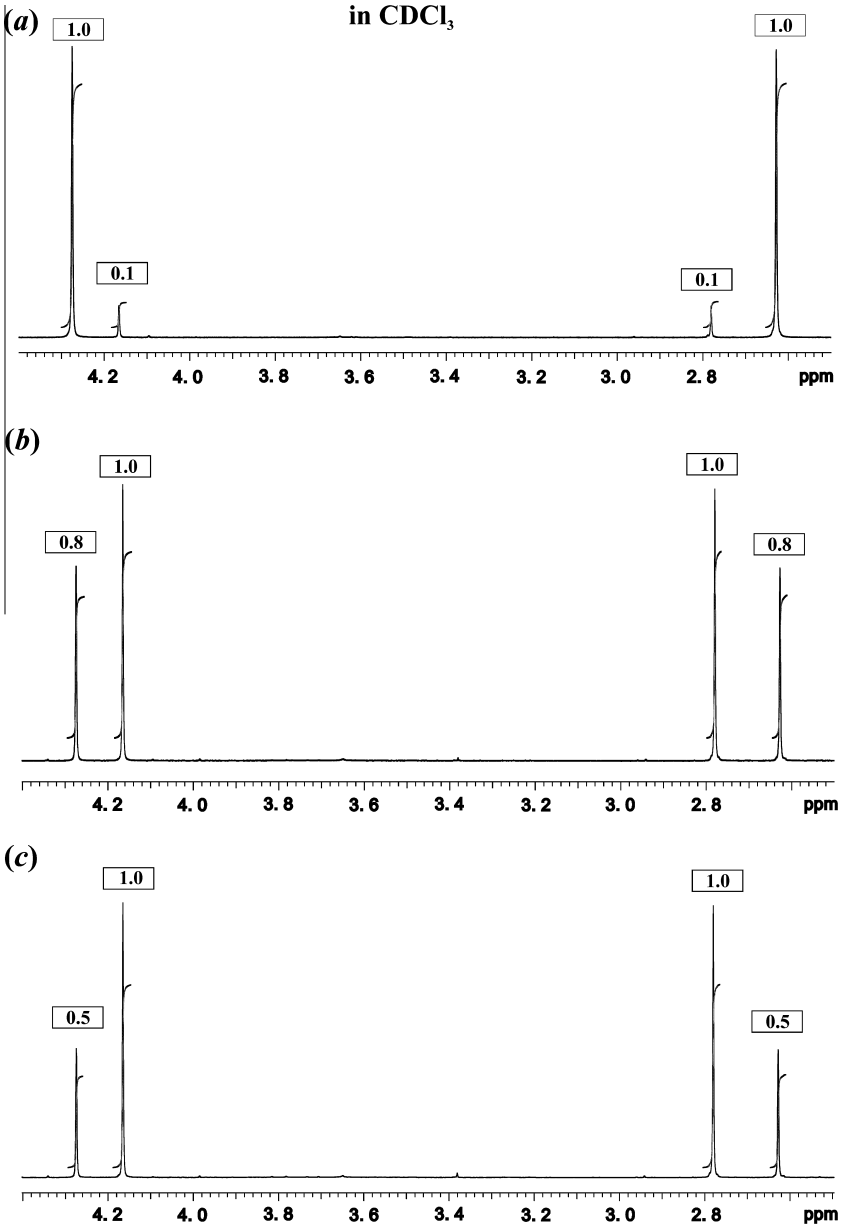


Fig. 2. The ^{1}H NMR spectrum (*a*) recorded immediately after solution of the compound **3** in deuterated chloroform and repeated (*b*) after 24 h and (*c*) after 48 h.

of azido form were also detected as reflected by very low intensity resonances at about 4.2 and 2.6 ppm characteristic for this form (Figs. S1c and S2c). Moreover, the experiments show different populations of tautomers in solution during measurements depending on the nature of the solvent. Thus, measurements in deuterated MeOH immediately after dissolution of the compound **3** show that the ratio of populations of azido to tetrazole forms in the solution is 9:1 and after 24 h this ratio was changed to 1:9, while after next 24 h the population of azido form was only a trace. In deuterated acetone the ratio of populations of azido to tetrazole forms at the beginning was 4:1, after 24 h – 1:9 and after next 24 h the contribution of the azido form decreased to value close to 0.

The same effect in ^{1}H NMR investigation was observed for the compound **4** and **6**. The results revealed that the tetrazole derivatives **4** and **6** can form tautomeric equilibrium in the solution but do not clarified the structure of the newly synthesized pyrazolo-tetrazolo-triazines. Thus, in order to establish the course of the intramolecular ring closure azido group, we decided structurally characterize the obtained final products **5** and **6** by X-ray analysis.

In the crystalline state, the compounds **5** and **6** exist as the linear tricyclic pyrazolo[4,3-*e*]tetrazolo[4,5-*b*][1,2,4]triazine tautomer form (**a**). View of the molecules **5** and **6** with numbering of atoms is shown in Fig. 3. The geometry (bond lengths, angles and planarity) of the tricyclic pyrazolo-tetrazolo-triazine skeleton is very similar in **5** and **6** and previously reported structures of 7-methyl-5-phenyl-1*H*-pyrazolo[4,3-*e*]tetrazolo[4,5-*b*][1,24]triazine [9] and 6,7-dimethyl-2*H*-pyrazolo[4,3-*e*]tetrazolo[4,5-*b*][1,2,4]triazine [10]. The molecule of **5** has a planar coformation as a whole with the methyl substituents lying almost in the plane of pyrazolo[4,3-*e*]tetrazolo[4,5-*b*][1,2,4]triazine ring. The X-ray structure analysis of **6** revealed, that the asymmetric part of the unit cell contains two independent molecules **A** and **B**, as shown in Fig. 3. The torsion angles φ_1 = N8–N7–C71–C21 and φ_2 = N7–C71–C21–C22 of 97.0(2) and −98.0(2)° in molecule **A** and 89.2(2)° and −14.4(3)° in molecule **B**, respectively, show that these molecules differ in the conformation of the benzyl group. The single point energy calculations on DFT/B3LYP/6-311++G(d,p) level showed that in the crystal the energy of molecule **6** in conformation **A** is lower by ΔE = 1.874 kcal/mol (1 kcal/mol = 4.184 kJ mol^{-1}) than its energy in conformation **B**. However, after energy minimization and geometry optimization with the experimental geometries taken as starting points, the conformation **B** converged to conformation **A** and both final (optimal) energetically equivalent conformations (ΔE is about 0.007 kcal/mol) do not differ significantly from that observed in crystalline state for molecule **A** with the torsion angles φ_1 = 80.68°, φ_2 = −85.47° for molecule **A** and φ_1 = 80.83°, φ_2 = −85.06° for molecule **B**.

The molecular packing in the crystal of **5** (Supplementary Fig. S3) is determined by van der Waals forces alone. The molecules form molecular layers parallel to (0 0 1) crystallographic plane. The distance between the centers of adjacent layers is c/2. The molecules are arranged at an angle of 59.39° relative to each other and perpendicular to the plane of the molecular layer retaining its *m* symmetry. Interesting seems to be the lack of the $\pi\cdots\pi$ interactions in the crystal structure of **5**. The shortest Cg···Cg distances between central triazine rings centroids for molecules related by 2_1 axis parallel to [0 1 0] direction are 4.775(2) Å and the mean planes of these rings are not parallel to each other forming the dihedral angle of 59.39°. Moreover, the short non-hydrogen intermolecular contacts between N11 and C6 atoms of analyzed molecules are also observed.

In the crystal structure of **6** (Supplementary Fig. S4), the inversion-related molecules **B** form molecular dimers by a pair of weak intermolecular hydrogen bonds C71B–H71F···N12B^i [C71B–H71F = 0.97, H71F···N12B = 2.51, C71B···N12B = 3.388(2) Å, C71B–H71F···N12B = 151° and (*i*) = −*x*, 1 − *y*, −*z*]. The π-electron

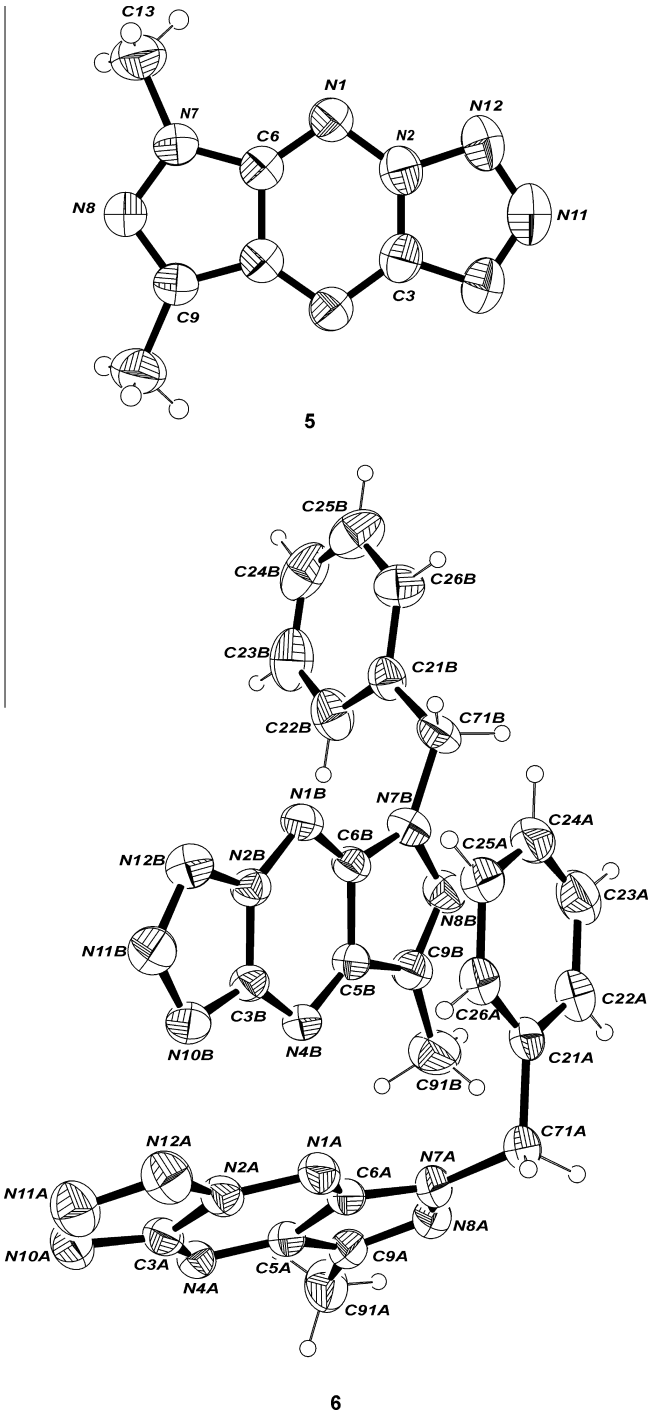


Fig. 3. A view of the molecules **5** and **6** with the atomic labelling. Non-H atoms are represented by displacement ellipsoids of 50% probability.

systems of the pairs of triazine and benzene rings in molecule **A** belonging to the molecules related by 2_1 axis overlap each other, with centroid-to-centroid separation of 3.7116(10) Å between the triazine ring at (*x*, *y*, *z*) and benzene ring at (−*x*, 1/2 + *y*, 1/2 − *z*) and benzene ring at (*x*, *y*, *z*) and triazine ring at (−*x*, −1/2 + *y*, −1/2 − *z*). The $\pi\cdots\pi$ distances are 3.412 and 3.465 Å, respectively, and the angle between overlapping planes is 3.10°. Similar interaction occurs between the π-electron systems of the pairs of benzene ring (molecule **A**) and triazine ring (molecule **B**) for molecules related by *c* glide plane. The centroid-to-centroid separation between the benzene ring at (*x*, *y*, *z*) and triazine ring at (*x*, 1/2 − *y*, 1/2 + *z*)

and triazine ring at (x, y, z) and benzene ring at $(x, 1/2 - y, -1/2 + z)$ is 3.6730(10), the $\pi\cdots\pi$ distances are 3.601 and 3.633 Å, respectively, and the angle between overlapping planes is 9.60°.

In conclusion, there are no classical hydrogen bonds in the crystals of compounds **5** and **6** due to the lack of classical hydrogen donor groups such as OH and NH. The analysis of the intra- and intermolecular interactions indicates the weak C–H···N hydrogen bonds and $\pi\cdots\pi$ interactions in crystal of **6** and van der Waals forces only in crystal of **5** as the non-covalent interactions influencing the molecular packing.

In order to find the relative stabilities in different environments of the azido (**3** and **4**), linear (isomer ***a***) and angular (isomer ***b***) possible tautomeric forms of compound **5** and compound **6** (Scheme 1) the energy calculations for each of them were performed in the gaseous phase and in ethanol and chloroform solution at the *ab initio* DFT/B3LYP/6-311++G(d,p) level. The azido chain in **3** and **4** can adopt *cis* (***a***) or *trans* (***b***) conformation with respect to N2–C3 bond (Supplementary Scheme S1) preferable in cyclization these compound to linear or angular form of **5** and **6**, respectively. The theoretical calculations in gaseous phase show that the *cis* and *trans* conformations of **3** and **4** correspond to the minimum of energy (affirmed by positive values of all calculated vibration frequencies) and they are practically equi-energetic with a small difference in energy between *trans* and *cis* conformations of ΔE = 0.604 kcal/mol for **3** and 0.563 kcal/mol for **4**. In the *gauche* conformation with perpendicular position of the azide chain with respect to the bicyclic pyrazolo-triazine system in **3** and **4** the energy is increased by 7.059 kcal/mol in **3** and 7.010 kcal/mol in **4** in relation to the energy of their *cis* conformation. It is clear that these energy values do not prevent molecules **3** and **4** against the possibility of changing from a *cis* to *trans* conformation and vice versa, so, we can assume that the *cis* conformation gives the possibility to form both linear and angular tricyclic systems of **5** and **6**.

The results of the energy calculations for all tautomeric forms of **3**–**6** are presented in Table 2. As can be seen from Table 2, the energetically most stable form existing in the gaseous phase is open azido form **3** and **4** for both investigated compounds **5** and **6**, respectively. The population of the remaining tricyclic tautomeric forms estimated using a non-degenerated Boltzmann distribution is close to zero. In the non-polar chloroform solution the linear tricyclic and azido forms co-exist with the ratio of populations of 0.7:0.3 for both **5a**, **3** and **6a**, **4** pairs of valency tautomers. In the polar ethanol solution the population of the linear tricyclic form increased to 95% and the population of the azido form decreased to 5%. In the two solvents considered the population of the tricyclic angular form **5b** and **6b** in tautomeric equilibrium does not exceed 0.02% and it is at the threshold of the detectability of conventional analytical methods. The shift of tautomeric equilibrium in the direction of significant domination of the linear tricyclic forms **5a** and **6a** in an ethanol solution in comparison with tautomeric equilibrium in a chloroform solution can be explained by the difference in polarity of tricyclic and azido forms, since the theoretical calculation showed that the dipole moments of 7.188 D for **5a** and 7.367 D for **6a** are significantly larger than the dipole moments of 3.389 D for **3** and 3.514 D for **4**. It should be noted that the tautomeric equilibrium in the gaseous phase and solutions do not depend on the type of the substituent in the pyrazole ring.

The annelation effect in azide-tetrazole equilibrium was intensively investigated *e.g.* for monoclinic azido-*as*-triazines and 3-azido-benzo-*as*-triazines. These studies showed that 3-azido-*as*-triazines cyclize on N-2 to give the tetrazolo-triazine linear form and their angular form is not detected [20]. The 3-azido-benzo-*as*-triazines cyclize predominantly on N-4 giving tetrazolo-benzo-triazine angular form and the other possible tetrazole linear form is only observed in dipolar aprotic solvents in small amounts [21]. The explanation of this annelation effect is connected with the heteroaromatic stability of the isomer linear and angular pairs. The estimation of the Clar's rule for heterocycles [21] shows that the isomer form with enhanced aromatic character is highly favored in linear and angular isomers equilibrium.

The interpretation of our experimental and theoretical findings based on the Clar's theorem does not seems to be appropriate, since both linear and angular isomers of pyrazolo-tetrazolo-triazine system in **5** and **6** do not differ significantly in aromaticity. However, significant differences are observed in the energy of these two isomers with a clear dominance of the linear isomer in the considered environments.

Table 2
The stabilization energy and population [ΔE (kcal/mol)/p_i (%)] for open azido (**3** and **4**) and cyclic tetrazole linear (**5a** and **6a**) and angular (**5b** and **6b**) forms in gaseous phase and chloroform and ethanol solution.

Compound	Gaseous phase	Chloroform	Ethanol
3	0/99.2	0.450/31.57	1.727/4.89
5a	2.832/0.8	0/68.42	0/95.09
5b	7.355/0.0	4.930/0.01	5.026/0.02
4	0/98.93	0.590/26.61	1.837/4.09
6a	2.635/1.07	0/73.37	0/95.90
6b	7.215/0.00	4.902/0.02	5.050/0.02

Conclusion

In conclusion, we described the synthesis of new pyrazolo[4,3-*e*]-tetrazolo[4,5-*b*][1,2,4]triazines. The theoretical calculations at the *ab initio* DFT/B3LYP/6-311++G(d,p) level and ^{1}H NMR spectra recorded in $CDCl_3$, CD_3OD and $(CD_3)_2CO$ showed the azido form (**3** and **4**) as one existing in the gaseous phase and the coexistence of the tricyclic linear (**5** and **6**) and azido tautomeric forms in solution, wherein the contribution of the linear form compared to the azido form increases with increasing polarity of the solvent. The X-ray analysis of **5** and **6** showed that both compounds exist in tricyclic linear tautomeric form in the crystalline state.

Appendix A. Supplementary material

Total energy and dipole moment calculated using DFT/B3LYP/6-311++G(d,p) method for **3**–**6** (Table S1). The experimental X-ray and optimized at DFT/B3LYP/6-311++G(d,p) method geometric parameters for **5** and **6** (Table S2). The ^{1}H NMR spectrum of the compound **3** in deuterated methanol (Fig. S1) and deuterated acetone (Fig. S2). Unit-cell packing in crystal of **5** (Fig. S3) and **6** (Fig. S4). CCDC-971836 for **5** and CCDC-971952 for **6** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 (0) 1223 336 033; email: deposit@ccdc.cam.ac.uk]. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molstruc.2014.03.025.

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