A convenient synthesis and spectral characterization of novel tetrazolo[1,5-*a*][1,5]benzodiazepine derivatives

Lidija Kosychova,[a,b]* Regina Vidziunaite,[a] Gema Mikulskiene,[a] Irina Bratkovskaja,[a] and Regina Janciene[a]

[a] *Vilnius University Institute of Biochemistry, Mokslininku 12, LT-08662 Vilnius, Lithuania*
[b] *Klaipeda University, H. Manto 84, LT-91001 Klaipeda, Lithuania*
E-mail: lidija.kosychova@bchi.vu.lt

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Abstract
Tetrazolo[1,5-*a*][1,5]benzodiazepine derivatives as products of the cyclization were synthesized and characterized by the methods of ^{1}H, ^{13}C NMR, IR, UV-Vis and elemental analysis. The NMR properties are described and compared with the known starting 4-hydrazino-1,5-benzodiazepines. The methods of molecular modeling were applied for examination of the structural features of the products. Fluorescent properties of the title compounds were studied and discussed.

Keywords: 1,5-Benzodiazepines, tetrazoles, cyclization, UV-Vis, fluorescence, molecular modeling

Introduction

The chemistry of heterocyclic compounds has been an interesting field of the research for a long time. Heterocycles containing nitrogen ring system undoubtedly belong to the most important natural compounds as latter take part in many biologically significant reactions. A great deal of attention owing to the high synthetic potential and the outstanding applications of this class of substances developed as pharmacologically active compounds or drugs.[1-5]

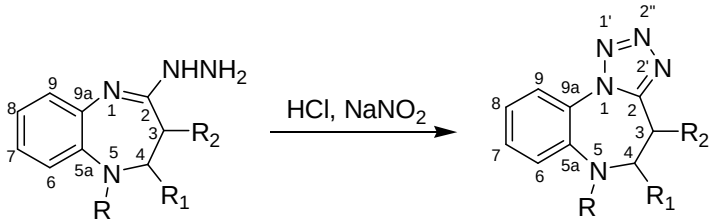
Tetrazoles are useful reagents in heterocyclic synthesis and are widely used in ring cleavage/ring closure reactions with electrophilic reagents to form new C–N and N–N bonds.[6] Main synthetic routes for these compounds are published in a wide range of scientific journals.[7-9] As a result, a variety of new improved compounds are being added to this field every year, the synthesis of tetrazoles has been carried out in the field of material sciences, explosives, and photography. The interest in the synthesis of molecules bearing tetrazole group and the application of tetrazoles as raw material for medicine, agrochemicals, foaming agents and in the

automobile inflator industry.[10] Some tetrazole and benzodiazepine derivatives are used as a fluorescent chemosensors.[11-13] This prompted us to incorporate the tetrazole moiety into the 1,5-benzodiazepines as continuation of our earlier work on the synthesis fused tricyclic molecules.[14-19] The present work was undertaken to prepare a series of tetrazolo derivatives based on the previously described 4-hydrazino-1,5-benzodiazepines. During this study, some new tetrazoles fused with molecule of 1,5-benzodiazepine, were synthesized, the peculiarities of structure and fluorescence properties were investigated.

Results and Discussion

During our research of 1,5-benzodiazepines, we have found that 1,5-benzodiazepin-2-thiones can be easily converted to 4-hydrazino-1,5-benzodiazepines.[18-20] This fact led us to carry out the synthesis of some tertazoles by making use of 4-hydrazino-1,5-benzodiazepines as starting materials.

The synthesis of tetrazolo[1,5-*a*][1,5]benzodiazepines **2a-j** was accomplished by the diazotization of 4-hydrazino-1,5-benzodiazepines **1a-j** with sodium nitrite and hydrochloric acid in water. Cyclization of the hydrazine group to a tetrazole was carried out with good yields.



1a-j **2a-j**

1a - R = H; R_1= H; R_2 = CH_3
2a - R = NO; R_1= H; R_2 = CH_3
1b - R = H; R_1= CH_3; R_2 = H
2b - R = NO; R_1= CH_3; R_2 = H
1,2 c - R = CH_3; R_1= H; R_2 = H
1,2 d – R = CH_3; R_1= H; R_2 = CH_3
1,2 e - R = $COCH_3$; R_1= H; R_2 = H
1,2 f - R = $COCH_3$; R_1= H; R_2 = CH_3
1,2 g - R = $COCH_3$; R_1= CH_3; R_2 = H
1,2 h - R = $CONHC_6H_5$; R_1= H; R_2 = H
1,2 i - R = $CONHC_6H_5$; R_1= H; R_2 = CH_3
1,2 j - R = $CONHC_6H_5$; R_1= CH_3; R_2 = H

Scheme 1. Synthesis of tetrazolo[1,5-*a*][1,5]benzodiazepines (**2a-j**).

The reaction yields depend on the nature of the substituent at the 1-N atom of 4-hydrazino-1,5-benzodiazepines **1a-j**. The synthesis pathway for tetrazolo[1,5-*a*][1,5]benzodiazepines **2a-j** is shown in Scheme 1. It was observed that under acidic conditions the nitrosonium cation reacts with an amine of compounds **2a, b** and to produces nitrosamine. The existence of nitroso group

in these molecules was confirmed by IR spectroscopy and elemental analysis. The purity of all synthesized compounds was controlled by thin layer chromatography and elemental analysis.

The structure of obtained products **2a-j** was proved by the methods of ^{1}H, ^{13}C NMR, IR spectroscopy. The numbering of atoms in compounds **2a-j** and their names expressed according IUPAC are presented in Experimental Section.

The main problem of present work was to ascertain the formation of tetrazole ring, therefore the NMR spectra of **2a-j** and **1a-j** were exhaustively studied. Additionally arbitrary numbering of atoms used for the NMR, molecular modeling, absorbance and fluorescence analysis due to plainly systematization and comparison of obtained data is presented in Scheme 1.

The synthesis and characterization of starting compounds **1a-j** were published previously[18-20] and not presented in Experimental, however these compounds were synthesized again, NMR spectra were recorded and examined for comparison purposes.

The substituents located at 5-N position made significant influence on NMR spectra due to donor/acceptor properties of later and alternation of the spatial structure of both type of molecules (**2a-j** and **1a-j)**. It should be noted that the starting compounds **1a-j** are flexible molecules possessing $NHNH_2$ and CHR_1-CHR_2 fragments causing broadening of spectral lines in ^{1}H NMR spectra. Consequently these spectra were less informative.

Table 1. ^{13}C NMR experimental and calculated (DFT) chemical shifts and Hückel charges of **1c** and **2c** carbon atoms

Atoms	δ_{exp}, ppm			δ_{calc}, ppm		$\delta_{exp} - \delta_{calc}$	$\delta_{exp} - \delta_{calc}$	Charges, a.u.	
	1c	**2c**	$\delta_{2c} - \delta_{1c}$	**1c**	**2c**	**1c**	**2c**	**1c**	**2c**
C-2	153.4	153.2	-0.2	147.4	156.8	6.0	-3.6	0.247	0.151
C-3	30.3	23.4	-6.9	42.9	29.5	-12.6	-6.1	-0.109	-0.093
C-4	58.3	56.1	-2.2	53.1	47.9	5.2	8.2	0.032	0.031
C-5a	141.2	141.8	0.6	145.9	147.0	-4.7	-5.2	0.061	0.085
C-6	119.4	119.7	0.3	121.8	120.3	-2.4	-0.6	-0.199	-0.168
C-7	124.6	130.1	5.5	123.2	130.3	1.4	-0.2	-0.097	-0.058
C-8	120.0	122.4	2.4	122.1	122.5	-2.1	-0.1	-0.160	-0.156
C-9	122.6	124.0	1.4	120.2	124.1	2.4	-0.1	-0.136	-0.081
C-9a	134.4	127.0	-7.4	139.3	131.5	-4.9	-4.5	0.057	0.000
5-NCH_3	41.4	41.5	0.1	47.3	37.2	-5.9	4.3	-0056	-0.054

The compounds **1c**,**d** and **2c**,**d** were selected for the detailed structural investigation as the most suitable one's owing to the simplest substituent at 5-N. The 2D $^{1}H/^{13}C$ HMBC NMR spectra allowed the complete assignment of the resonances of **1c**,**d** and **2c**,**d** compounds. ^{13}C NMR resonances (Table 1.) unambiguously ascribed to **1c** and **2c** suggested the most significant discrepancies in chemical shifts between C-3, C-9a, and C-7 atoms being -6.9 ppm, -7.4 ppm, and 5.5 ppm respectively. Taking into account the chemical shift theory, these values were stipulated by influence of formation of tetrazole ring on α (C-3) of aliphatic, and C_i (C-9a), C_p

(C-7) positions of aromatic moieties. Data of mentioned above studies of the particular spectral patterns evidenced the changes between the structures **1c,d** and **2c,d** confirming the formation of tetrazole ring. In addition the Hückel charges of carbon atoms obtained from models of **1c** and **2c** molecules (Table 1.) using MM2 method followed the same trend as ^{13}C chemical shift values. Following our interest in cyclization area, the $^{1}H/^{15}N$ HMBC NMR spectra for **1c** and **2c** compounds were recorded. The spectral data of **1c** demonstrated the presence of N-5, N-1, and N-2′ atoms, which have characteristic chemical shifts 44.82 ppm, 101.81 ppm and 248.08 ppm respectively, whereas **2c** indicate also N-5, N-1, and N-2′ atoms, but the chemical shifts of these atoms were changed – 47.24 ppm, 241.21 ppm, and 322.28 ppm respectively.

In addition, to verify the proposed structures of **1c** and **2c** a GIAO-DFT calculations of NMR spectra were carried out using Gaussian-03.[21] The geometry of models of molecules were optimized by MOPAC to obtain global energy minimum, and finally - by Gaussian-03. The ^{13}C chemical shifts were calculated by DFT method at level B3LYP/6-311+G(2d,p). The PCM solvation model was applied for calculation of spectra in $CDCl_3$ solutions. The pattern of calculated ^{13}C spectra depends on location methyl group at 5-N. The spectra calculated for models with equatorial location methyl group at 5-N showed better correlation with experimental ones for both of type of compounds.

Table 2. π-Bond order in extended conjugated system of **2a**-**j** compounds

Bonds	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**	**2j**
N(1)-C(2)	1.569	1.571	1.579	1.579	1.576	1.575	1.571	1.573	1.568	1.588
C(2)-N(2′)	1.704	1.702	1.695	1.695	1.698	1.699	1.703	1.701	1.705	1.704
N(2′)-N(2′′)	1.595	1.597	1.603	1.602	1.600	1.599	1.593	1.598	1.591	1.592
N(2′′)-N(1′)	1.749	1.747	1.741	1.742	1.744	1.745	1.751	1.746	1.752	1.751
N(1′)-N(1)	1.428	1.430	1.436	1.436	1.433	1.433	1.424	1.430	1.423	1.423
N(1)-C(9a)	1.257	1.257	1.250	1.250	1.253	1.252	1.258	1.254	1.261	1.262
C(9a)-C(5a)	1.612	1.612	1.608	1.608	1.609	1.607	1.628	1.610	1.639	1.636
C(5a)-C(6)	1.639	1.638	1.622	1.622	1.631	1.633	1.683	1.636	1.672	1.675
C(6)-C(7)	1.672	1.672	1.681	1.682	1.675	1.672	1.652	1.672	1.663	1.661
C(7)-C(8)	1.655	1.655	1.645	1.645	1.651	1.654	1.674	1.655	1.663	1.666
C(8)-C(9)	1.676	1.677	1.685	1.685	1.680	1.677	1.662	1.677	1.673	1.670
C(9)-C(9a)	1.634	1.633	1.624	1.624	1.629	1.632	1.649	1.632	1.637	1.640
C(5a)-N(5)	1.293	1.295	1.337	1.338	1.320	1.320	1.000	1.308	1.000	1.000
N(5)-N(5′)	1.369	1.327	-	-	-	-	-	-	-	-
N(5′)-O(1)	1.910	1.925	-	-	-	-	-	-	-	-
N(5)-C(5′)	-	-	1.000	1.000	1.062	1.049	1.000	1.231	1.000	1.000
C(5′)-O(1)	-	-	-	-	1.902	1.904	2.000	1.878	2.000	2.000
C(5′)-N(H)	-	-	-	-	-	-	-	1.000	1.000	1.000

Table 2 (continued)

Bonds	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**	**2g**	**2h**	**2i**	**2j**
N(H)-C(*i*)	-	-	-	-	-	-	-	1.000	1.000	1.000
C(*i*)-C(*o*)	-	-	-	-	-	-	-	1.667	1.667	1.667
								1.667	1.667	1.667
C(*o*)-C(*m*)	-	-	-	-	-	-	-	1.667	1.667	1.667
								1.667	1.667	1.667
C(*m*)-C(*p*)	-	-	-	-	-	-	-	1.667	1.667	1.667

The calculated correlation coefficient for ^{13}C spectra of model with equatorial methyl group at 5-N was 0.993 and 0.996 for **1c** and **2c** respectively. It is valuable to note, that calculated spectra represent shielding of atoms of motionally frozen structures as well as experimental – time averaged shielding of corresponding atoms from all available conformers involved into conformational-rotational movement. The comparison of calculated and experimental ^{13}C spectra of **1c** and **2c** are presented in Table 1. It should be concluded that experimental and theoretical NMR spectra of **1c** and **2c** correspond to the same structures.

It was observed that fluorescence is characteristic to all studied compounds. In most cases the fluorescent compounds possess aromatic systems.[22] Therefore **2a-j** compounds were also suitable for the examination in this point of view. The molecules containing benzene with coplanar heterocycles moieties show existence of extended system of conjugated bonds. To evaluate the existing conjugated bond system, the molecular models of all possible conformers of study compounds were created, optimized (MM2) and obtained data were analyzed. It was clarified, that the present of substituents at C-3, C-4 positions and their spatial location have no significant influence on the π-bond order values (less than ± 0.005).

Consequently the π-bond order values of molecular models with equatorial location of substituents were listed in Table 2. As shown in Table 2, some of substituents at 5-N are partially involved in extended π-bond system.

Changes in the extended π-bond system lead to a shift of the absorption and fluorescence spectra maximum and to the changes in the fluorescence quantum yield. The UV-visible spectra of compounds **2a-j** in ethanol, 1,4-dioxane and DMSO were recorded in the region 220-350 nm. Absorption spectra of **2a-j** in ethanol are presented in Fig. 1. Compounds containing electron donor group **2a-d** showed two bands in the 220-230 nm and 290 -340 nm regions and a shoulder near 250 nm region Fig. 1: a. Their adsorption spectra are similar, with the exception of compound **2b**, which absorption spectra is free of sharp absorption maximum and the increase of absorption was observed in the interval 300-220 nm. The maximums of absorption spectra for compounds **2e-j** containing electron acceptor groups are observed at the regions 220-225, 270-290 nm (Fig.1: b) or 230-235, 280-310 nm (Fig. 1: c), with shoulders near 240 or 250 nm, when R is acetyl or carbamoyl group, respectively.

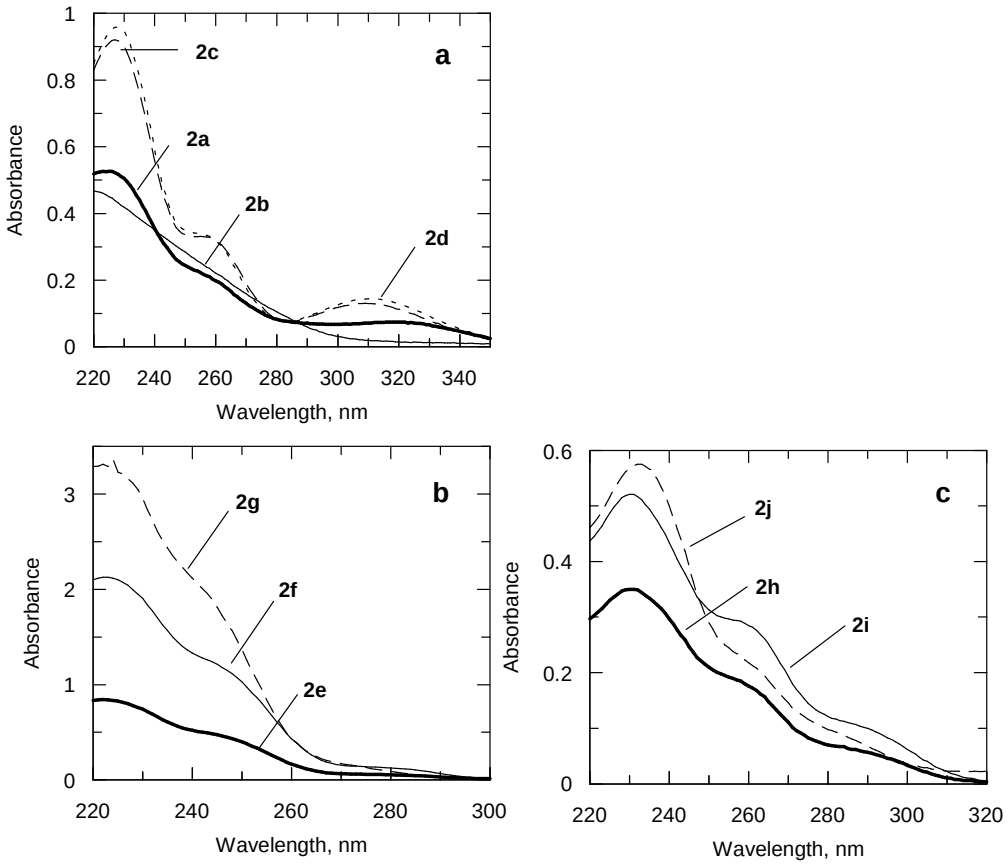


Figure 1. Absorption spectra of compounds containing: electron donor groups **2a-d** (a), electron acceptor group **2e-g** (b) and **2h-j** (c) in ethanol.

Absorption spectra maximums (λ_{abs}) of compounds **2h-j** are shifted about 10-15 nm to the longer wavelength band in comparison with compounds **2e-g**. Absorption spectra of **2a, d, i,** and **f** in ethanol, 1,4-dioxane and DMSO are presented in Fig. 2. The slight influence of solvents on absorption spectra of investigated compounds was observed. In 1,4-dioxane absorption spectra were observed at a longer wavelength (230-350 nm) in comparison with spectra in ethanol (220-350 nm). Whereas the absorption spectra in DMSO solution were observed in still narrow (250-350 nm) region. The calculated λ_{abs}, values of extinction coefficients (ε) in ethanol, 1,4-dioxane, and DMSO are presented in Table 3. Values of extinction coefficient (ε) were determined as the slope of the plot of absorbance *vs* concentration. The excitation wavelength at λ_{ex} = 280 nm and dry ethanol as solvent were used to study the fluorescence properties of new tricyclic 1,5-benzodiazepines, because all of synthesized compounds **2a-j** show absorption at this wavelength. Excitation and emission spectra of compounds in ethanol are presented in Fig. 3.

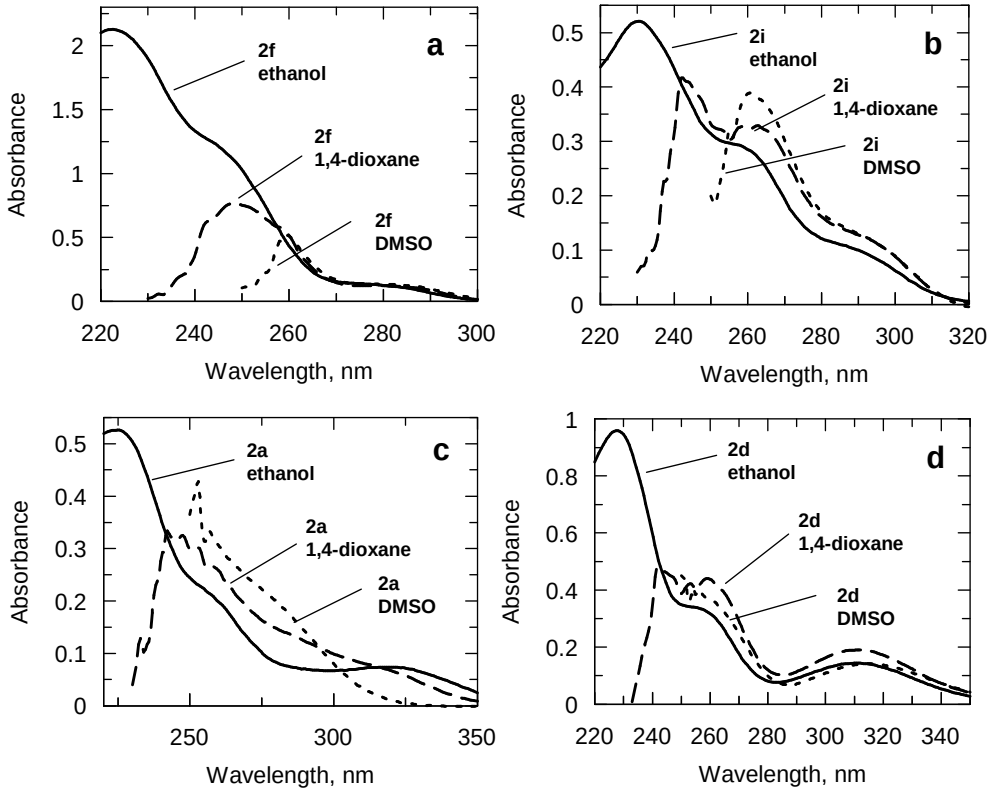


Figure 2. The absorption spectra of **2f** (a), **2i** (b), **2a** (c) and **2d** (d) in ethanol, 1,4-dioxane and DMSO.

Table 3. The absorption spectra maxima (λ_{abs}) and values of extinction coefficients (ε) of the tetrazolo[1,5-α][1,5]benzodiazepine derivatives **2a-j** in ethanol, 1,4-dioxane and DMSO

Com-pound	Substituents	Ethanol		1,4-dioxane		DMSO	
		λ_{abs}, nm	ε, $M^{-1}cm^{-1} \cdot 10^3$	λ_{abs}, nm	ε, $M^{-1}cm^{-1} \cdot 10^3$	λ_{abs}, nm	ε, $M^{-1}cm^{-1} \cdot 10^3$
2a	3-CH_3, 5-NO	230, 260, 280	11.2, 5.5, 2.9	260, 310	5.4, 2.7	260, 325	7.0, 3.0
2b	4-CH_3, 5-NO	260, 280	8.0, 4.0	260, 310	10.7, 10.9	260, 280	9.2, 4.9
2c	5-CH_3	230, 260, 310	17.3, 6.0, 2.6	260, 310	8.5, 3.3	260, 310	6.4, 2.6
2d	3-CH_3, 5-CH_3	230, 260, 310	20.1, 6.7, 3.1	260, 310	6.8, 2.6	260, 310	5.5, 2.3
2e	5-$COCH_3$	245, 280	22.1, 2.1	252, 257, 280	10.1, 7.6, 1.6	260, 280	5.9, 1.6

Table 3 (continued)

2f	3-CH_3, 5-$COCH_3$	245, 280	5.9, 0.8	252, 257, 280	7.7, 6.1, 1.3	260, 280	4.8, 1.3
2g	4-CH_3, 5-$COCH_3$	240, 280	10.9, 0.5	260, 280	4.0, 0.7	260, 280	3.2, 0.6
2h	5-CONHPh	230, 260, 280	24.4, 12.8, 5.1	260, 280	11.8, 5.4	260, 280	15.4, 7.7
2i	3-CH_3, 5-CONHPh	230, 260, 280	21.6, 11.8, 5.0	260, 280	13.7, 6.6	260, 280	12.3, 6.2
2j	4-CH_3, 5-CONHPh	233, 260, 280	22.5, 8.2, 3.8	260, 280	8.0, 4.8	260, 280	11.5, 6.0

The emission spectra of compounds containing electron-donor groups (Fig. 3: a) were similar and observed in the region 350-550 nm, whereas compounds containing electron- acceptor groups (Fig. 3: b, c) emission spectra were shifted to the shorter wavelength regions. Emission spectra of compounds containing in R position acetyl group (Fig. 3: b) were observed at 300-450 nm region, whereas compounds, which have carbamoyl group (Fig. 3: c) – at 320-500 nm. The emission spectra of **2i-h** and **2e-g** are very similar among themselves. The fluorescence emission spectra of tricyclic 1,5-benzodiazepines derivatives were measured in the 1,4-dioxane and DMSO (Fig. 4). The change of solvent had little influence on the absorption spectra, but strongly effected emission spectra. Excitation and emission spectra in the 1,4-dioxane (Fig. 4) as well as in the ethanol (Fig. 3) showed, that all of synthesized compounds show fluorescence. The emission spectra in DMSO gave only compounds containing electron donor groups **2a, c** and **d,** except compound **2b**. It is necessary to note, that fluorescence of tetrazoles in ethanol and DMSO is very weak or not observed when in R_1 position is a methyl group (**2b**, **g**, **j)**, but all synthesized compounds fluoresce in 1,4-dioxane.

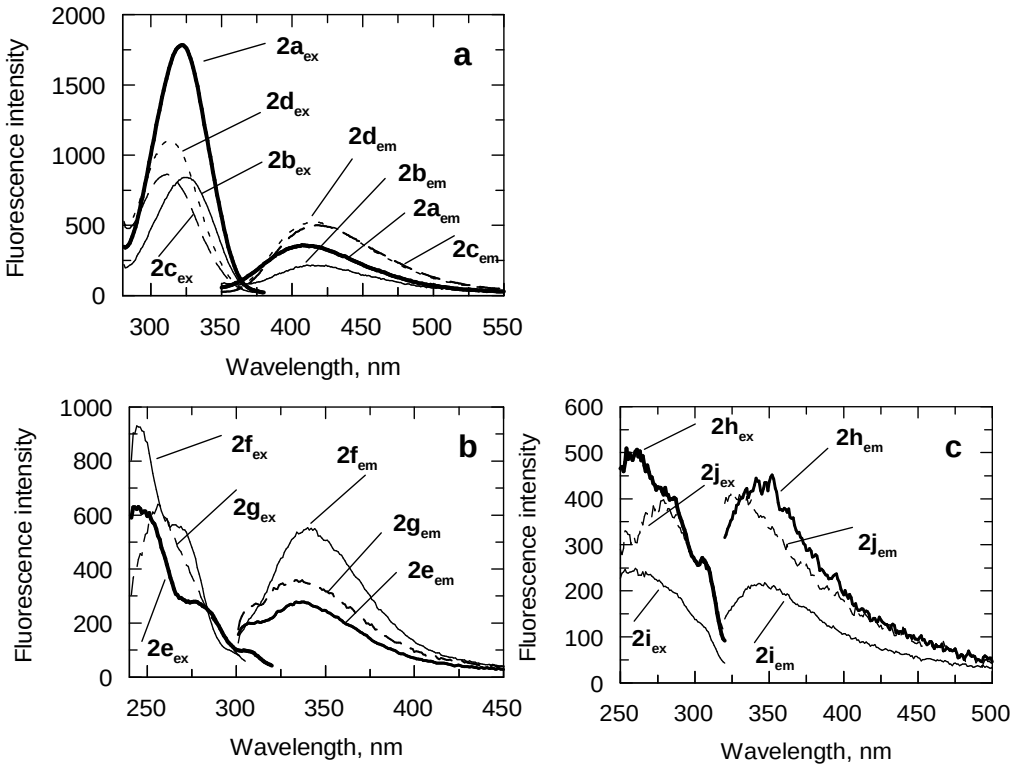


Figure 3. The excitation and emission spectra of **2a-j** in ethanol. Compounds in R position containing electron donor groups **2a–d** (a) and electron acceptor groups **2e-f** (b) and **2h-j** (c).

The emission spectra of compounds **2f, 2i, 2a** and **2d** (without methyl group in R_1 position) in different solvents (Fig. 4) showed, that compounds containing electron donor groups fluoresce in all used solvents, but compounds containing electron acceptor groups not fluoresce in DMSO. The fluorescence of all synthesized compounds depends on its structure, as well as on the nature of an appropriate solvent.

Fluorescence quantum yields (Φ_f) for all synthesized compounds in different solvents were calculated. The fluorescence quantum yields (Φ_f) of compounds **2a-j** were determined *via* comparison method, using tryptophan as a standard sample in 0.1 M potassium phosphate buffer solution, pH 7.0 [23] or quinine sulfate - in 0.1 M sulfuric acid solution.[24]

Absolute values are calculated using the standard samples which have a fixed and known fluorescence quantum yield value, according to the following equation:

$$\Phi_f = \Phi_{st} (F_f / F_{st})(\eta^2_f / \eta^2_{st})$$

Where the subscripts *st* and *f* denote standard and test respectively, Φ is the fluorescence quantum yield, F the gradient from the plot of integrated fluorescence intensity *vs* absorbance, and η the refractive index of the solvent. The maximal values of excitation (λ_{ex}) and emission

(λ_{em}) spectra in ethanol, 1,4-dioxane or DMSO and fluorescence quantum yield (Φ_f) data of synthesized compounds are presented in Table 4.

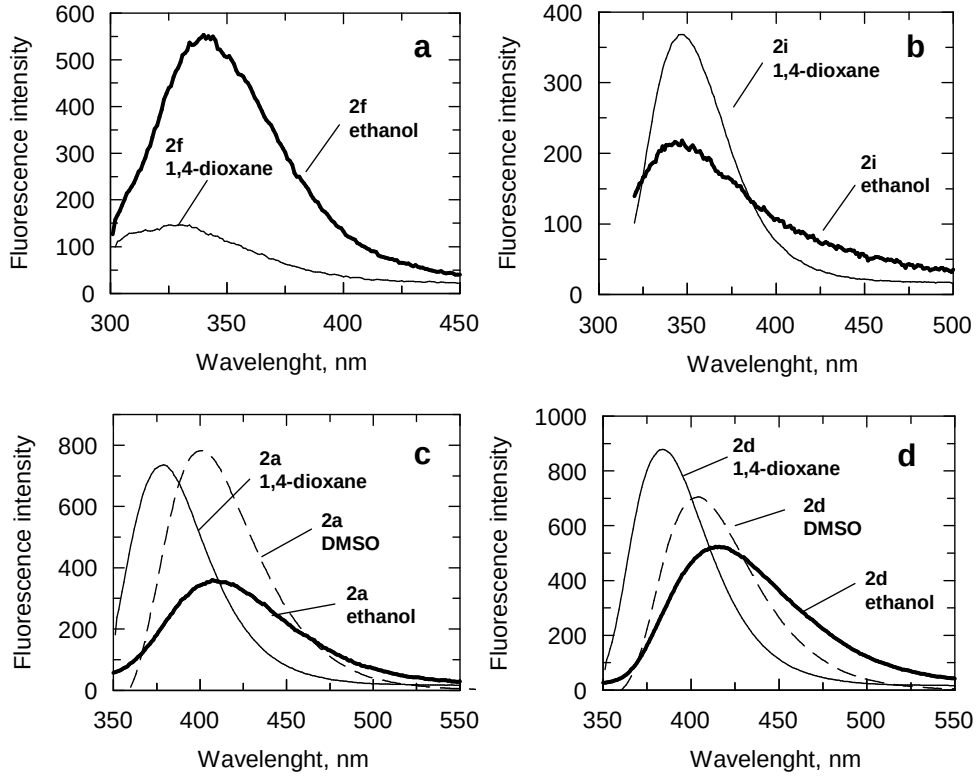


Figure 4. Emission spectra of **2f** (a), **2i** (b), **2a** (c), and **2d** (d) in ethanol, 1,4-dioxane, and DMSO. Compounds in R position containing electron donor groups **2a**,**d** or electron acceptor groups **2f**,**i**.

Table 4. The values of excitation (λ_{ex}) and emission (λ_{em}) spectra maximum, fluorescence quantum yields (Φ_f) of **2a-j** in ethanol, 1.4-dioxane, and DMSO

Com-pound	Substituent	Ethanol		1,4-dioxane		DMSO	
		λ_{ex} - λ_{em}, nm	$\Phi_f \cdot 10^3$	λ_{ex} - λ_{em}, nm	$\Phi_f \cdot 10^3$	λ_{ex} - λ_{em},nm	$\Phi_f \cdot 10^3$
2a	3-CH_3,	310 – 420	28*				
	5-NO	310 – 420	287**	310 – 380	155**	320 – 400	711**
2b	4-CH_3,	320 – 420	-				
	5-NO	320 – 420	93**	310 – 380	569**	320 – 420	-
2c	5-CH_3	310 – 420	120*				
		310 – 420	148**	310 – 380	235**	310 – 400	323**
2d	3-CH_3,	310 – 420	120*				
	5-CH_3	310 – 420	163**	310 – 420	242**	320 – 420	332**

Table 4 (continued)

Com-pound	Substituent	Ethanol		1,4-dioxane		DMSO	
		λ_{ex} - λ_{em}, nm	$\Phi_f \cdot 10^3$	λ_{ex} - λ_{em}, nm	$\Phi_f \cdot 10^3$	λ_{ex} - λ_{em},nm	$\Phi_f \cdot 10^3$
2e	5-$COCH_3$	280 – 340	5.8*	280 – 330	5.4*	280 – 340	-
2f	3-CH_3, 5-$COCH_3$	280 – 340	3*	280 – 330	4.3*	280 – 330	0.6*
2g	4-CH_3, 5-$COCH_3$	260 – 330	4*	280 – 330	0.6*	260 – 330	-
2h	5-CONHPh	280 – 340	1.9*	280 – 340	24*	280 – 330	-
2i	3-CH_3, 5-CONHPh	270 – 340	1.2*	280 – 340	26*	280 – 330	-
2j	4-CH_3, 5-CONHPh	270 – 340	-	280 – 340	10*	280 – 330	-

*reference tryptophan as a standard sample in 0.1 M potassium phosphate buffer solution, pH 7.0, ** reference quinine sulfate as a standard sample in 0.1 M sulfuric acid solution.

The compounds containing electron donor groups (**2a-d**) show respectable quantum yields (Φ_f) in used solvents, whereas quantum yields (Φ_f) of compounds containing electron acceptor groups (**2e-j**) are very low or its fluorescence is so insensible, that can not be calculated.

Conclusions

Tetrazolo[1,5-*a*][1,5]benzodiazepine derivatives were synthesized by the diazotization of 4-hydrazino-1,5-benzodiazepines with sodium nitrite and hydrochloric acid in water. The formation of tetrazole ring was proved by $^{1}H/^{13}C$, $^{1}H/^{15}N$ HMBC NMR spectra, and by calculated (DFT) ^{13}C NMR spectra. All synthesized compounds showed fluorescence in solutions. The fluorescence intensity and a quantum yield values of the new tetrazolo[1,5-*a*][1,5]benzodiazepine compounds depends on its structure, as well as on the nature of an appropriate solvent.

Experimental Section

General. Melting points were measured using a Barnstead International MEL-TEMP capillary melting point apparatus and are not corrected. Elemental analyses (C, H, N) were performed on Elemental Analyzer CE - 440. Absorption spectra were measured on a computer-controlled

"Nicolet evolution 300" spectrophotometer (Thermo electron corporation, USA), and fluorescence spectra on a Hitachi MPF-4 spectrofluorimeter (Japan). The optical path was 1 cm and spectra were collected at a resolution of one data points per nanometer. IR spectra (4000 – 400 cm^{-1}) were recorded on PERKIN Elmer Spectrum GX FT-IR spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Inova 300 and Bruker Ascend^{tm} 400 at 302 K. Chemical shifts (δ) are reported relative to tetramethylsilane (TMS) with the solvent reference: $CDCl_3$ (δ 7.26 ppm) for ^{1}H NMR and $CDCl_3$ (δ 77.0 ppm) for ^{13}C NMR. The values of chemical shifts are expressed in ppm and coupling constants (*J*) in Hz. The molecular modeling of the study compounds was carried out using Chem 3D Ultra 9.0 (Licence Cambridge Software Package, Serial number: 031 406391 4800). The reactions were monitored by TLC using TLC Silica gel 60 F_{254} (MERCK) plates in system: chloroform – ethyl acetate – methanol (v/v, 14:7:1.5). Visualization was made with UV light (254 nm) and with iodine vapor.

Procedures for preparation of tetrazolo[1,5-*a*][1,5]benzodiazepines (2a-j). 4-Hydrazino-1.5-benzodiazepines **1a-j** were synthesized from thiolactams by treatment with hydrazine hydrate in methanol.[18-20] To a mixture of **1a-j** (0.005 mol) in H_2O (20 mL) containing conc. HCl (6.6 mL) a solution of 0.75 g (0.0011mol) of $NaNO_2$ in H_2O (8 mL) was added drop wise at 0 ^{o}C with stirring. The mixture was stirred for 1 h at 0 ^{o}C and then neutralized with $NaHCO_3$. The fallen precipitate was collected, washed with H_2O and recrystallized from appropriate solvent to give the pure crystalline compound **2a-j**.

4-Methyl-6-nitroso-5,6-dihydro-tetrazolo[1,5-*a*][1,5]benzodiazepine (2a). Cream-colored crystals, yield 67.8%, 0.78 g, mp 155-157 ^{o}C (etanol); IR (ν_{max}, cm^{-1}): 1614.53 (C=N), 1507.59 (N=N), 1455.90 (NO), 1111.94 (NO). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.64 (3H, d (X part of $ABMX_3$), $^{3}J_{HH}$ 6.9 Hz, 4-CH_3), 3.52 (1H, m (M part of $ABMX_3$), 4-CH), 4.09, 4.20 (ABq of $ABMX_3$, $^{2}J_{HH}$ 14.3 Hz, $^{3}J_{HH}$ 4.8, 10.9 Hz, 5-CH_2), 7.61-7.78 (3H_{arom}, m, (7-9)CH), 8.22 (1H_{arom}, dd, $^{4}J_{HH}$ 1.7 Hz, $^{3}J_{HH}$ 7.8 Hz, 10-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C [11.2]15.6 (4-CH_3), 27.9[35.4] (C-3), 51.5 [57.1] (C-4), 123.7 (CH), 125.9 (CH), 127.0 (C-10a), 130.2 (CH), 130.4 (CH), 132.4 (C-6a), 155.6 (C-3a). Anal. Calcd for $C_{10}H_{10}N_6O$ (230.23): C, 52.17; H, 4.38; N, 36.50; O, 6.95%. Found: C, 52.18; H, 4.76; N, 36.65%.

5-Methyl-6-nitroso-5,6-dihydro-tetrazolo[1,5-*a*][1,5]benzodiazepine (2b). Cream-colored crystals, yield 72.3%, 0.83 g, mp 159-160 ^{o}C (isopropanol); IR (ν_{max}, cm^{-1}): 1594.03 (C=N), 1510.04 (N=N), 1455.53 (NO), 1126 (N-NO). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.24 ((0.9)3H, d (X part of $ABMX_3$), $^{3}J_{HH}$ 6.4 Hz, 5-CH_3), 1.67 ((0.1)3H, d (X part of $ABMX_3$), $^{3}J_{HH}$ 6.6 Hz, 5-CH_3), 2.91 ((0.1)1H, dd (A part of $ABMX_3$), $^{2}J_{HH}$ 15.5 Hz, $^{3}J_{HH}$ 11.3 Hz, 5-CH), 2.95 ((0.9)1H, dd (A part of $ABMX_3$), $^{2}J_{HH}$ 15.5 Hz, $^{3}J_{HH}$ 11.3 Hz, 4-CH), 3.63 ((0.9)1H, dd (B part of $ABMX_3$), $^{2}J_{HH}$ 15.5 Hz, $^{3}J_{HH}$ 5.4, 4-CH), 3.90 ((0.1)1H, dd (B part of $ABMX_3$), $^{2}J_{HH}$ 15.5 Hz, $^{3}J_{HH}$ 6.3, 4-CH), 5.47 ((0.9)1H, m (M part of $ABMX_3$), 5-CH), 5.87 ((0.1)1H, m (M part of $ABMX_3$), 5-CH), 7.23 ((0.1)1H_{arom}, dd, $^{4}J_{HH}$ 1.7 Hz, $^{3}J_{HH}$ 7.6 Hz, 7-CH), 7.60 ((0.9)1H_{arom}, dd, $^{4}J_{HH}$ 1.9 Hz, $^{3}J_{HH}$ 7.5 Hz, 7-CH), 7.60-7.78 (2H_{arom}, m, 8-CH and 9-CH), 7.92 ((0.1)1H_{arom}, dd, $^{4}J_{HH}$ 1.5 Hz, $^{3}J_{HH}$ 8.0 Hz, 10-CH), 8.03 ((0.9)1H_{arom}, dd, $^{4}J_{HH}$ 1.6 Hz, $^{3}J_{HH}$ 7.9 Hz, 10-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C

17.6[21.6] (5-CH_3), 27.0[28.6] (C-4), 53.6[61.0] (C-5), 123.6 (CH), 128.7 (CH), 130.3 (C-6a or C-10a), 130.9 (CH), 131.1 (CH), 131.6 (C-10a or C-6a), 151.63 (C-3a). Anal. Calcd for $C_{10}H_{10}N_6O$ (230.23): C, 52.17; H, 4.38; N, 36.50; O, 6.95%. Found: C, 52.73; H, 4.73; N, 36.61%.

6-Methyl-5,6-dihydro-tetrazolo[1,5-*a*][1,5]benzodiazepine (2c). Cream-colored crystals, yield 76.6%, 0.77 g, mp 61-63 °C (methanol); IR (ν_{max}, cm^{-1}): 1604.64 (C=N), 1504.15 (N=N). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.92 (3H, s, 6N-CH_3), 3.30 (2H, t, $^3J_{HH}$ 6.4 Hz, 4-CH_2), 3.52 (2H, t, $^3J_{HH}$ 6.4 Hz, 5-CH_2), 7.16 (1H_{arom}, t, $^3J_{HH}$ 7.7 Hz, 9-CH), 7.17 (1H_{arom}, d, $^3J_{HH}$ 8.4 Hz, 7-CH), 7.43 (1H_{arom}, td, $^4J_{HH}$ 1.2 Hz, $^3J_{HH}$ 7.2 Hz, 8-CH), 7.90 (1H_{arom}, dd, $^4J_{HH}$ 1.6 Hz, $^3J_{HH}$ 7.8 Hz, 10-CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 23.5 (C-4), 41.5 (6N-CH_3), 56.1 (C-4), 119.7 (7-CH), 122.4 (9-CH), 123.6 (10-CH), 127.1 (C-10a), 130.07 (8-CH), 142.8 (C-6a), 153.2 (C-3a). Anal. Calcd for $C_{10}H_{11}N_5$ (201.23): C, 59.69; H, 5.51; N, 34.80% Found: C, 59.46; H, 5.60; N, 34.96%.

4,6-Dimethyl-5,6-dihydro-tetrazolo[1,5-*a*][1,5]benzodiazepine (2d). Yellowish crystals, yield 62.0%, 0.67 g, mp 89-90 °C (ethanol); IR (ν_{max}, cm^{-1}): 1604.33 (C=N), 1505.56 (N=N). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.56 (3H, d, $^3J_{HH}$ 6.4 Hz, 4-CH_3), 2.93 (3H, s, 6N-CH_3), 3.15-3.46 (3H, m, 3-CH + 5-CH_2), 7.10-7.15 (2H_{arom}, m, 7-CH and 9-CH), 7.40 (1H_{arom}, td, $^4J_{HH}$ 1.5 Hz, $^3J_{HH}$ 7.5 Hz, 8-CH), 7.93 (1H_{arom}, dd, $^4J_{HH}$ 1.5 Hz, $^3J_{HH}$ 8.3 Hz, 10-CH), ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 16.1 (4-CH_3), 30.4 (C-4), 41.6 (6N-CH_3), 63.0 (C-5), 118.7 (7-CH), 122.1 (9-CH), 123.5 (10-CH), 126.9 (C-10a), 129.8 (8-CH), 143.4 (C-6a), 156.6 (C-3a). Anal. Calcd for $C_{11}H_{13}N_5$ (215.26): C, 61.38; H, 6.09; N, 32.54%. Found: C, 61.48; H, 6.09; N, 32.30%.

6-Acetyl-5,6-dihydro-tetrazolo[1,5-*a*][1,5]benzodiazepine (**2e**). White crystals, yield 52.5%, 0.60 g, mp 175-176 °C (ethanol); IR (ν_{max}, cm^{-1}): 1662.67 (C=O), 1601.54 (C=N), 1504.90 (N=N). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.99 (3H, s, 6-NCOCH_3), 3.22 (1H, ddd, $^2J_{HH}$ 13.9 Hz, $^3J_{HH}$ 4.6, 10.8 Hz, 5-CH), 3.38 (1H, td, $^2J_{HH}$ 17.8 Hz, $^3J_{HH}$ 4.2 Hz, 4-CH), 3.83 (1H, ddd, $^2J_{HH}$ 17.6 Hz, $^3J_{HH}$ 6.8, 10.6 Hz, 4-CH), 5.03 (1H, ddd, $^2J_{HH}$ 13.8 Hz, $^3J_{HH}$ 3.8, 6.7 Hz, 5-CH), 7.43 (1H_{arom}, dd, $^4J_{HH}$ 1.8 Hz, $^3J_{HH}$ 7.5 Hz, 7-CH), 7.53-7.63 (2H_{arom}, m, 8-CH and 9-CH), 8.26 (1H_{arom}, dd, $^4J_{HH}$ 1.8 Hz, $^3J_{HH}$ 7.8 Hz, 10-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 22.5 (6-CO*C*H_3), 24.1 (C-4), 43.6 (C-5), 124.1 (CH), 128.9 (CH), 129.5 (CH), 130.1 (CH), 131.0 (C-10a), 134.3 (C-6a), 152.4 (C-3a), 169.2 (6-*C*OCH$_3$). Anal. Calcd for $C_{11}H_{11}N_5O$ (229.24): C, 57.63; H, 4.84; N, 30.55, O, 6.98%. Found: C, 57.49; H, 4.91; N, 30.64%.

6-Acetyl-4-methyl-5,6-dihydro-tetrazolo[1,5-*a*][1,5]benzodiazepine (2f). White crystals, yield 57.6%, 0.70 g, mp 201-203 °C (ethanol); IR (ν_{max}, cm^{-1}): 1669.30 (C=O), 1600.69 (C=N), 1506.13 (N=N). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.54 ((0.7)3H, d, $^3J_{HH}$ 6.9 Hz, 4-CH_3), 1.66 ((0.3)3H, d, $^3J_{HH}$ 7.1 Hz, 4-CH_3), 1.79 ((0.3)3H, s, 6-NCO*C*H_3), 2.03 ((0.7)3H, s, 6-NCO*C*H_3), 2.85 ((0.7)1H, dd, $^2J_{HH}$ 13.9 Hz, $^3J_{HH}$ 12.2 Hz, 5-CH), 3.22-3.34 ((0.3)1H, m, 4-CH), 3.65 ((0.3)1H, dd, $^2J_{HH}$ 13.4 Hz, $^3J_{HH}$ 6.7 Hz, 5-CH), 3.96-4.09 ((0.7)1H, m, 4-CH), 4.83 ((0.3)1H, dd, $^2J_{HH}$ 13.4 Hz, $^3J_{HH}$ 10.5 Hz, 5-CH), 4.88 ((0.7)1H, dd, $^2J_{HH}$ 13.9 Hz, $^3J_{HH}$ 6.5 Hz, 5-CH), 7.39-7.69 (3H_{arom}, m, (7-9)CH), 7.94 ((0.3)1H_{arom}, dd, $^4J_{HH}$ 1.9 Hz, $^3J_{HH}$ 7.7 Hz, 10-CH), 8.33 ((0.7)1H_{arom}, dd, $^4J_{HH}$ 2.0 Hz, $^3J_{HH}$ 7.6 Hz, 10-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C [15.1]17.5 (4-CH_3),

22.4[22.7] (6-CO*C*H$_3$), [28.9]31.6 (C-4), 49.8[54.1] (C-5), 124.1[124.4] (CH), 128.1[129.9] (CH), 129.1[130.0] (CH), 129.5[130.6] (CH), 131.0[131.3] (C-10a), [134.1]134.6 (C-6a), [156.2]156.4 (C-3a), 168.8[170.3] (6-*C*OCH$_3$). Anal. Calcd for $C_{12}H_{13}N_5O$ (243.27): C, 59.25; H, 5.39; N, 28.79, O, 6.58%. Found: C, 59.36; H, 5.32; N, 28.84%.

6-Acetyl-5-methyl-5,6-dihydro-tetrazolo[1,5-*a*][1,5]benzodiazepine (2g). White crystals, yield 90.0%, 1.1 g, mp 209-210 ^{o}C (ethanol); IR (ν_{max}, cm^{-1}): 1661.95 (C=O), 1601.87 (C=N), 1505.82 (N=N). ^{1}H NMR (300 MHz, $CDCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.31 (3H, d, $^3J_{HH}$ 6.5 Hz, 5-CH$_3$), 1.68 (3H, s, 6-NCO*C*H$_3$), 2.57 (1H, dd, $^2J_{HH}$ 15.4 Hz, $^3J_{HH}$ 10.9 Hz, 4-CH), 3.64 (1H, dd, $^2J_{HH}$ 15.4 Hz, $^3J_{HH}$ 6.4 Hz, 4-CH), 5.46 (1H, pd, $^3J_{HH}$ 6.6, 10.9 Hz, 5-CH), 7.39 (1H$_{arom}$, dd, $^4J_{HH}$ 1.8 Hz, $^3J_{HH}$ 7.5 Hz, 7-CH), 7.60-7.71 (2H$_{arom}$, m, 8-CH and 9-CH), 7.93 (1H$_{arom}$, dd, $^4J_{HH}$ 1.7 Hz, $^3J_{HH}$ 7.8 Hz, 10-CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 19.4 (5-CH$_3$), 23.0 (6-CO*C*H$_3$), 28.6 (C-4), 53.6 (C-5), 124.3 (CH), 130.4 (CH), 130.7 (CH), 131.5 (C-10a), 131.8 (CH), 132.0 (C-6a), 152.9 (C-3a), 169.6 (6-*C*OCH$_3$). Anal. Calcd for $C_{12}H_{13}N_5O$ (243.27): C, 59.25; H, 5.39; N, 28.79, O, 6.58%. Found: C, 59.36; H, 5.43; N, 28.86%.

***N*-Phenyl-4,5-dihydro-6*H*-tetrazolo[1,5-*a*][1,5]benzodiazepine-6-carboxamide (2h)**. Cream-colored crystals, yield 68.6%, 1.05 g, mp 179-180 ^{o}C (ethanol); IR (ν_{max}, cm^{-1}): 3373.63 (NH), 1672.35 (C=O), 1596.40 (C=N), 1499.69 (N=N). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 3.59 (2H, t, $^3J_{HH}$ 5.9 Hz, 4-CH$_2$), 4.13 (2H, br.s, 5-CH$_2$), 6.68 (1H, s, N*H*CO), 7.00-8.28 (9H$_{arom}$, m, 9CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 25.2 (C-4), 43.5 (C-5), 119.6 (*o*-CH$_{Ph}$), 123.8 (CH), 124.6 (*p*-CH$_{Ph}$), 128.4 (CH), 128.9 (*m*-CH$_{Ph}$), 129.2 (CH), 130.3 (CH), 131.5 (C-10a), 133.3 (C-6a), 137.7 (*i*-C$_{Ph}$), 152.1 or 152.6 (C-3a), 152.6 or 152.1 (*C*ONHPh). Anal. Calcd for $C_{16}H_{14}N_6O$ (306.32): C, 62.73; H, 4.61; N, 27.44, O, 5.22%. Found: C, 62.63; H, 4.69; N, 27.51%.

4-Methyl-*N*-phenyl-4,5-dihydro-6*H*-tetrazolo[1,5-*a*][1,5]benzodiazepine-6-carboxamide (2i). White crystals, yield 78.7%, 1.26 g, mp 152-154 ^{o}C (ethanol); IR (ν_{max}, cm^{-1}): 3351.68 (NH), 1686.62. (C=O), 1598.16 (C=N), 1496.43 (N=N). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.56 (3H, d, $^3J_{HH}$ 6.9 Hz, 4-CH$_3$), 3.44, 3.76, 4.53 (3H, 3 br.s, 4-CH + 5-CH$_2$), 6.75 (1H, s, N*H*COPh), 7.00-8.20 (9H$_{arom}$, m, 9CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 17.2 (4-CH$_3$), 32.1 (C-4), 50.6 (C-5), 119.6 (*o*-CH$_{Ph}$), 123.7 (CH), 124.6 (*p*-CH$_{Ph}$), 127.9 (CH), 128.9 (*m*-CH$_{Ph}$), 128.9 (CH), 130.2 (CH), 131.5 (C-10a), 133.7 (C-6a), 137.9 (*i*-C$_{Ph}$), 152.4 (6-*C*ONHPh), 156.6 (C-3a). Anal. Calcd for $C_{17}H_{16}N_6O$ (320.35): C, 63.74; H, 5.03; N, 26.23, O, 4.99%. Found: C, 63.91; H, 4.96; N, 26.31%.

5-Methyl-*N*-phenyl-4,5-dihydro-6*H*-tetrazolo[1,5-*a*][1,5]benzodiazepine-6-carboxamide (2j). Cream-colored crystals, yield 74.3%, 1.19 g, mp 133-134 ^{o}C (ethanol); IR (ν_{max}, cm^{-1}): 3308.03 (NH), 1666.08 (C=O), 1595.31 (C=N), 1503.34 (N=N). ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.36 (3H, $^3J_{HH}$ 6.5 Hz, 5-CH$_3$), 2.68 (1H, dd, $^2J_{HH}$ 15.7, $^3J_{HH}$ 10.0 Hz, 4-CH), 3.69 (1H, dd, $^2J_{HH}$ 15.7, $^3J_{HH}$ 6.5 Hz, 4-CH), 5.37 (1H, pd, $^3J_{HH}$ 6.5, 10.0 Hz, 5-CH), 5.97 (1H, s, N*H*COPh), 6.98-8.04 (9H$_{arom}$, m, 9CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 19.7 (4-CH$_3$), 29.2 (C-4), 53.8 (C-5), 119.8 (*o*-CH$_{Ph}$), 123.8 (CH), 124.8 (*p*-CH$_{Ph}$), 128.8 (*m*-CH$_{Ph}$), 130.2 (C-10a), 130.4 (CH), 131.1 (CH), 131.8 (CH), 132.8 (C-6a), 137.7 (*i*-C$_{Ph}$), 152.8 or 153.0 (6-*C*ONHPh or C-3a), 152.8 or

153.0 (C-3a or 6-*C*ONHPh). Anal. Calcd for $C_{17}H_{16}N_6O$ (320.35): C, 63.74; H, 5.03; N, 26.23, O, 4.99%. Found: C, 63.84; H, 5.12; N, 26.36%.

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References

1. Wani, M. Y.; Bhat, A. R.; Azam, A.; Lee, D. H.; Choi, I.; Athar, F. *Eur. J. Med. Chem*. **2012**, *54*, 845. http://dx.doi.org/10.1016/j.ejmech.2012.03.049
2. Uttarwar, R. B.; Nawale, R. B.; Shamkuwa, P. B. *J. Chem. Pharm. Res.* **2013**, *5*, 41.
3. Upadhayaya, R. S.; Jain, S.; Sinha, N.; Kishore, N.; Chandra, R.; Arora S. K. *Eur. J. Med. Chem.* **2004**, *39*, 579. http://dx.doi.org/10.1016/j.ejmech.2004.03.004
4. Gundugola, A. S.; Chandra, K. L.; Perchellet, E. M.; Waters, A. M.; Perchellet, J.-P. H.; Rayat, S. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3920. http://dx.doi.org/10.1016/j.bmcl.2010.05.012
5. Dlugosz, A. *Pharmazie* **1995**, *50*, 180.
6. Chattopadhyay, B.; Vera, C. I. R.; Chuprakov, S.; Gevorgyan, V. *Org. Lett*. **2010**, *12*, 2166. http://dx.doi.org/10.1021/ol100745d
7. Eshghi, H.; Hassankhani, A. *Synthetic Commun*. **2005**, *35*, 1115. http://dx.doi.org/10.1081/SCC-200054219
8. Mphahlele, M. J.; Moekwa, T. B. *J. Heterocyclic Chem*. **2006**, *43*, 905. Doi: 10.1002/jhet.5570430414
9. Du, Z.; Si, Ch.; Li, Y.; Wang,Y.; Lu, J. *Int. J. Mol. Sci.* **2012**, *13*, 4696. http://dx.doi.org/10.3390/ijms13044696
10. Butler, R. N. in *Comprehensive Heterocyclic Chemistry* II, R. C. Storr, ed., Elsevier: Oxford, 1996, Vol. 4, p 621. http://dx.doi.org/10.1016/B978-008096518-5.00095-2
11. Wei-Hua Ding; Wei Cao; Xiang-Jun Zheng; Wan-Jian Ding; Jin-Ping Qiao; Lin-Pei Jin. *Dalton Trans*. **2014**, 43, 6429. http://dx.doi.org/10.1039/c4dt00009a

12. Li, J.; Zhou, X.; Zhou, Y.; Fang, Y.; Yao, C. *Spectrochim. Acta* A, *Mol. Biomol. Spectrosc*. **2013**.
http://dx.doi.org/10.1016/j.saa.2012.10.069
13. Rivero, I. A.; Peralta, M.; Heredia, S.; Madrigal, D.; Pina-Luis, G.; Chaves, D. *Arkivoc* **2003**, (*xi*), 27.
http://dx.doi.org/10.3998/ark.5550190.0004.b04
14. Kosychova, L.; Stumbreviciute, Z.; Janciene, R.; Staniulyte, Z.; Puodziunaite, B. D. *Arkivoc* **2011**, (*xi*), 82.
http://dx.doi.org/10.3998/ark.5550190.0012.b08
15. Jančienė, R.; Stumbrevičiūtė, Z.; Vektarienė, A.; Kosychova, L.; Sirutkaitis, R.; Palaima, A.; Staniulytė, Z.; Puodziunaitė, B. D. *Heteroatom Chem*. **2008**, *19*, 72.
http://dx.doi.org/10.1002/hc.20414
16. Kosychova, L.; Pleckaitiene, L.; Staniulyte, Z.; Janciene, R.; Palaima, A.; Puodziunaite, B. D. *Arkivoc* **2006**, (*xiii*), 158.
http://dx.doi.org/10.3998/ark.5550190.0007.d16
17. Jančienė, R.; Vektarienė, A.; Stumbrevičiūtė, Z.; Kosychova, L.; Klimavicius, A.; Puodžiūnaitė, B. D. Heteroatom Chem. **2004**, *15*. 363.
http://dx.doi.org/10.1002/hc.20026
18. Kosychova, L.; Stumbreviciute, Z.; Janciene, R.; Ragaleviciene, V.; Pleckaitiene, L.; Staniulyte, Z.; Puodziunaite, D.; Palaima, A. *Mater. Sci. Appl. Chem. Sci. J. Riga Techn. Univ.* **2010**, *22*, 94.
19. Kosychova, L.; Stumbrevičiūtė, Z.; Jančienė, R.; Klimavičius, A., Staniulytė, Z.; Palaima, A.; Puodžiūnaitė, B. D. *Chemija* **2011**, *22*, 60.
20. Puodžiūnaitė, B.; Kosychova, L.; Jančienė, R.; Stumbrevičiūtė, Z. *Monatsh. Chem*. **1997**, *128*, 1275.
http://dx.doi.org/10.1007/BF00807260
21. Gaussian 03, Revision B.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 2003.

22. Valeur, B. *Molecular Fluorescence Principles and Applications.* Wiley-VCH: Weinheim, New York, Chichester, Brisbane, Singapore, Toronto, 1997.
23. Lakowicz, J. R. *Principles of Fluorescence Spectroscopy*, 2nd Edn., Kluwer Academic/Plenum Publishers, New York, London, Moscow, Dordrecht, 1999. http://dx.doi.org/10.1007/978-1-4757-3061-6
24. Lui LiQin; Li Yuan Fang; Zhan Lei; Liu Yue; Huang Cheng Zhi. *Sci. China, ser B.* **2011**, *54*, 1.

