# \* New 1,2,4-triazine-containing podands: synthesis and properties

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A method of one-step C—C coupling of 1,5-bis(2,6-dimethylphenoxy)-3-oxapentane (1a) and 1,8-bis(2,6-dimethylphenoxy)-3,6-dioxaoctane (1b) with 3-methylthio- (2) and 3-amino-1,2,4-triazine (3) and 3-aryl-1,2,4-triazin-5-one (6–8) has been described. The reaction of compounds 1a,b with compounds 2 and 3 in the presence of trifluoroacetic acid results in the addition of the dimethylphenoxy group to the unsubstituted C(5) carbon atom of the triazine ring. The reactions of triazinones 6–8 with compounds 1a,b in a mixture of trifluoroacetic acid and organic anhydrides are accompanied by the acylation of the nitrogen atom adjacent to the reaction center and affords bis[(3-R-1-acyl-5-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3-oxapentane or -3,6-dioxaoctane. The obtained adducts can smoothly be oxidized under mild conditions to form more stable products of nucleophilic hydrogen substitution in the triazine ring. The extraction and transport of Ca<sup>2+</sup> and Mg<sup>2+</sup> cations through an organic membrane by the compounds synthesized are discussed.

**Key words:** 1,2,4-triazines, 2,6-dimethylphenyl-containing podands,  $A_{\rm N}$ -reaction,  $S_{\rm N}^{\rm H}$  methodology, receptor ability.

A combination of heterocyclic moieties with a flexible spacer is of great interest in modern organic chemistry. These compounds can be used as sensors for cations and small organic molecules. Moreover, it is known that heterocycle-containing receptors with donor groups are widely used for molecular recognition.<sup>1-4</sup> In this work, the synthesis of new podands based on di- and triethylene glycol fragments and containing terminal 1.2.4-triazine moieties by the direct C-C coupling of hetarenes with podands is discussed. As a rule, Friedel–Crafts reactions,<sup>5</sup> cross-coupling,<sup>6</sup> and nucleophilic substitution of good leaving groups  $(S_N^{ipso}Ar)^7$  are used to create a C–C bond in (hetero)arenes. Recently, to construct a carbon-carbon bond in  $\pi$ -deficient aromatic or heteroaromatic compounds, a methodology of nucleophilic aromatic substitution of hydrogen  $(S_N^H Ar)^8$  has been used successfully. This method is also appropriate for the direct coupling of 1,2,4-triazines with  $\pi$ -excessive carbon- and heterocyclic compounds. For example, the reactions of derivatives of aromatic amines, phenols, and heterocycles with 1,2,4-triazines afford products of nucleophilic addition to the unsubstituted carbon atom of the azine ring.<sup>9-11</sup> Using the elaborated method, we have succeeded in synthesizing 1,2,4-triazine-containing podands.

#### Synthesis of 1,2,4-triazine-containing podands

We applied a well known method for alkylation of 2,6-dimethylphenol with Chlorex or polyether ditosylates

for the synthesis of podands **1a,b** containing a nucleophilic aromatic moiety.

It should be mentioned that podands **1a,b** possess an insufficient nucleophilicity to interact with 1,2,4-triazines. To enhance the electrophilicity of the triazine system, we used a general method based on the protonation of nitrogen atoms. The resulting NH-triazinium salts are more reactive than the starting 1,2,4-triazines and react readily with podand **1**. For instance, the reaction of 3-substituted 1,2,4-triazines **2** and **3** with **1a** in the presence of trifluoroacetic acid affords a product of nucleophilic addition to a more electrophilic C(5) atom of the triazine ring (Scheme 1).

The structures of products **4** and **5** were established by NMR spectroscopy (Table 1). The <sup>1</sup>H NMR spectrum of

Table 1. Data of <sup>1</sup>H NMR spectra of compounds 4 and 5

Com- pound	δ ( <i>J</i> /Hz)						
	C(5)—H (d, 1 H)	C(6)—H (d, 1 H)	R	Fragment of podand			
4	4.44 ( <i>J</i> = 1.8)	6.54 ( <i>J</i> = 1.8)	2.37 (s, 3 H,	6.93 (s, 2 H, Ar); 2.97 (m, 4 H,			
			SMe)	CH <sub>2</sub> -CH <sub>2</sub> -O); 2.27 (s, 6 H, Me)			
5	4.49 ( <i>J</i> = 2.4)	6.65 ( <i>J</i> = 2.4)	_	6.92 (s, 2 H, Ar); 3.60-3.86 (m, 4 H, CH <sub>2</sub> -CH <sub>2</sub> -O); 2.24 (s, 6 H, Me)			

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 $R = SMe(2, 4), NH_2(3, 5)$ 

the products contains a characteristic signal of a proton at the C(5) atom of the triazine ring at 4.50–4.80 ppm as doublets with the constant  $J_{C(5)H,C(6)H} = 1.8$  Hz.<sup>11</sup> The signals of aromatic protons of the 2,6-dimethylphenol fragment are present as a singlet at 6.90–7.00 ppm, indicating the exhaustive heterylation of podand **1a**.

Thus, the introduction of a heterocycle into a polyether substrate is a one-step reaction of nucleophilic addition to the unsubstituted atom of the triazine ring. This method differs substantially from those published previously for syntheses of podands of this type, which represented a ring closure of open-chain structures and nucleophilic substitution of good leaving groups in a heterocycle.<sup>12–14</sup>

As should be expected, 1,2,4-triazin-5-ones exhibited a lower reactivity in the reactions with podands than 1,2,4-triazines 2 and 3, and no products of the reaction of triazines 6-8 with compound 1a in the presence of trifluoroacetic acid were found in a detector of the NMR spectrometer.

Similarly to the reaction with phenols and benzoannelated crown ethers,<sup>9,10</sup> more reactive 2-acyl-1,2,4triazin-5-ones, obtained *in situ* when triazinones **6–8** are dissolved in a mixture of trifluoroacetic acid and organic anhydrides, react with podands **1a,b** under mild conditions to produce stable adducts **9–13** in high yields (Scheme 2). In our opinion, the process is similar to the mechanism of the reaction of triazinones **6–8** with benzoannelated crown ethers<sup>9</sup> and includes nucleophilic addition of NH salts to the unsubstituted carbon atom of 2-acyl-1,2,4-triazin-5-ones followed by acylotropic rearrangement to form a more stable N(1)-acyl-substituted isomer of compounds **9–13**.

In the <sup>1</sup>H NMR spectrum of the compounds synthesized, the characteristic signal of a proton at the sp<sup>3</sup>-hybri-



 $R^1$  = Ph (6, 9, 11), 4-Tol (7, 12), SEt (8, 10, 13)  $R^2$  = Me (9, 10), CF<sub>3</sub> (11–13) n = 1 (a), 2 (b)

dized C(6) carbon atom is observed as a singlet at 5.90 ppm. The absence of signals from the terminal phenol groups indicates the 1 : 2 stoichiometry of the reaction. The N(4)—H tautomers are usually characterized<sup>15</sup> by the chemical shifts of NH protons at 11.50-11.74 ppm (Table 2).

Using compounds 9-13, we studied the ability of the triazine ring to undergo aromatization and showed that 6-substituted tetrahydrotriazin-5-ones are readily oxidized to the corresponding 1,2,4-triazin-5-(2H)-ones. When a methanolic solution of compound **11b** is refluxed in the presence of diethylenetriamine, both the triazine ring is deacylated and tetrahydro-substituted derivative **14** spontaneously oxidizes to form podand **15b**. Tetrahydro-substituted derivatives can be isolated only when the reaction occurs in an inert atmosphere. For instance, refluxing a methanolic solution of **11a** in the presence of diethylenetriamine under argon affords compound **14a**, which was isolated by flash chromatography in 26% yield (Scheme 3).

The <sup>1</sup>H NMR spectrum of **14a** contains the characteristic signals of the C(6)—H and N(1)—H protons in 1,4,5,6-tetrahydro-1,2,4-triazin-5-one which are present as doublets with the constant J = 1.2 Hz at 4.43 and 7.75 ppm, respectively. The shift of the signal of the NH proton in compound **15b** toward 13.80 ppm indicates, in our opinion, the formation of the N(2)H tautomer, being the most stable<sup>16</sup> for 1,2,4-triazin-5-ones.

Thus, 1,2,4-triazine-containing podands were synthesized for the first time using the methodology of nucleophilic addition and nucleophilic hydrogen substitution in azines.

Com-		δ (J/Hz)								
pound	n	NH (1 H)	R <sup>2</sup> (3 H)	R <sup>1</sup>	C(6)—H (s, 1 H)	Podand				
9a	1	11.55 br.s	2.37	7.88–7.90 (m, 2 H); 7.46–7.56 (m, 3 H)	5.94	6.86 (s, 2 H, Ar); 3.71–3.74, 3.83–3.85 (both m, 4 H); 2.19 (s, 6 H, Me)				
9b	2	11.84 br.s	2.38 (s)	7.85–7.91 (m, 2 H); 7.40–7.49 (m, 3 H)	5.91	6.82 (s, 2 H, Ar); 3.61 (br.s), 3.67–3.80, 3.81–3.83 (both m, 6 H); 2.21 (s, 6 H, Me)				
12a	1	11.78 br.s	_	7.78, 7.33 (both d, 2 H each, $J = 8$ ); 2.36 (s, 3 H)	5.82	6.91 (s, 2 H, Ar); 3.77–3.83 (m, 4 H, CH <sub>2</sub> –CH <sub>2</sub> –O); 2.16 (s, 6 H, Me)				
11b	2	11.79 br.s	_	8.10—8.25 (m, 2 H); 7.91 (m, 3 H)	5.81	6.88 (br.s, 2 H, Ar); 3.60–3.84 (m, 8 H, CH <sub>2</sub> –CH <sub>2</sub> –O); 2.13 (br.s, 6 H, Me)				
11a	1	11.81 s	_	7.89–7.91 (m, 2 H); 7.44–7.54 (m, 3 H)	5.81	6.87 (s, 2 H, Ar); 3.76 (t, 2 H, CH <sub>2</sub> , <i>J</i> = 4.4); 3.87 (t, 2 H, CH <sub>2</sub> OAr, <i>J</i> = 4.4); 2.21 (s, 6 H, Me)				
10a	1	11.50 br.s	2.24 (s)	3.09 (q, 2 H, <i>J</i> = 7.2); 1.31 (t, 3 H, <i>J</i> = 7.2)	5.86	6.83 (s, 2 H, Ar); 3.76 (t, 2 H, CH <sub>2</sub> , J = 3.8); 3.88 (t, 2 H, CH <sub>2</sub> OAr, J = 3.8); 2.19 (s, 6 H, Me)				
13a	1	11.70 br.s	_	3.00 (q, 2 H); 1.32 (t, 3 H)	5.68	6.82 (s, 2 H, Ar); 3.75 (t, 2 H, CH <sub>2</sub> , <i>J</i> = 4.4); 3.87 (t, 2 H, CH <sub>2</sub> OAr, <i>J</i> = 4.4); 2.20 (s, 6 H, Me)				

Table 2. Data of the <sup>1</sup>H NMR spectra of compounds 9–13

## Liquid extraction of Ca<sup>2+</sup> and Mg<sup>2+</sup> picrates

The liquid extraction of Ca<sup>2+</sup> and Mg<sup>2+</sup> picrates from an aqueous phase to dichloromethane at 25 °C was studied to compare the complexation ability of triazine-containing podands with **1a,b**. The distribution constant of picrate between the aqueous and organic phases (*D*) is a quantitative characteristic of the extraction ability of molecules **9**, **11**, and **13** (Table 3). Since a complex with the same composition is formed due to the reaction, a stoichiometric coefficient *m* and an extraction constant  $K_{ex}$ depend linearly on *D* (Fig. 1) and can be calculated by the known equation<sup>17</sup>

$$\log D = \log K_{\rm ex} + m \log[L], \tag{1}$$

L is ligand.

To determine D, a decrease in the absorbance of the aqueous phase was measured by spectrophotometry.

It is found that podands **1a,b** do not extract Ca<sup>2+</sup> and Mg<sup>2+</sup> picrates from the aqueous to organic phases. The introduction of triazine moieties induces receptor properties toward the metal cations. The extraction constants ( $K_{ex}$ ) of the Ca<sup>2+</sup> and Mg<sup>2+</sup> cations by the triazine-containing podands are presented in Table 3.

**Table 3.** Extraction constants  $(K_{ex})$  of Mg<sup>2+</sup> and Ca<sup>2+</sup> cations by triazine-containing podands and the stoichiometry of the complexes

Com-	$\mathbb{R}^1$	$R^2$ <i>n</i> $Mg^{2+}$		g <sup>2+</sup>	Ca <sup>2+</sup>		
pound			/mc	$K_{\rm ex}$	M : L	$K_{\rm ex}$ /mol <sup>-1</sup>	M : L
9a	Ph	Me	1	185	1:1	213	1:2
9b	Ph	Me	2	0	_	0	_
11a	Ph	$CF_3$	1	0	_	0	_
11b	Ph	$CF_3$	2	372	1:2	274	1:1
13a	SEt	$CF_3$	1	132	1:1	326	1:2

It is established that the stoichiometry of a complex depends on the polyether chain length. For instance, when compounds **11a** and **13a** bind  $Mg^{2+}$  cations, a 1 : 1 complex is formed. However, two ligand molecules are involved in the formation of a complex with a more bulky  $Ca^{2+}$  cation. An increase in the polyether chain length (for example, in compound **11b**) results in binding of the  $Ca^{2+}$  cation with one "host" molecule. It is of interest that two podand molecules are involved in the formation of complex **11b** with the  $Mg^{2+}$  cation.

The extraction constant depends on both the length of a polyether chain and the nature of substituent  $R^2$ . Com-



pounds with n = 1 bind Ca<sup>2+</sup> cations better than Mg<sup>2+</sup> cations. The study of the extraction ability of triazinecontaining podands with n = 2 shows a higher  $K_{ex}$  value for binding Mg<sup>2+</sup> cations. The substituent effect can be considered by a comparison of the receptor properties of compounds 9 and 11. In the case of R<sup>2</sup> = CF<sub>3</sub>, extraction is carried out only by podands with a long polyether chain (compound 11b). The inverse dependence is observed for R<sup>2</sup> = Me. It is found that more flexible and longer podand 9b does not extract Ca<sup>2+</sup> and Mg<sup>2+</sup> cations. The highest difference in extraction ability for the Ca<sup>2+</sup> and Mg<sup>2+</sup> cations is observed for compound 13a (see Table 3).

## Transport of Ca<sup>2+</sup> and Mg<sup>2+</sup> cations through a liquid organic membrane

The synthesized compounds are highly lipophilic and, hence, can be used as carriers through a liquid membrane. The transfer rate of  $Ca^{2+}$  and  $Mg^{2+}$  cations, as well as



Fig. 1. Dependences of the logarithms of the distribution constants between the aqueous and organic phases (*D*) on the logarithm of the ligand concentration for the formation of a complex with  $Mg^{2+}(a)$  and  $Ca^{2+}(b)$  cations of compounds 9a (*I*), 11b (2), and 13a (3).

selectivity, are presented in Table 4. These data show that an increase in the length of the polyether moiety de-

 Table 4. Membranotropic properties of the triazine-containing podands

Com- pound	п	$v^* \cdot 10^{-7}$ /mol h <sup>-1</sup>		
		Ca <sup>II</sup>	Mg <sup>II</sup>	
1a	1	15.9	42.9	
9a	1	27.7	23.0	
9b	2	0.0	6.8	
11a	1	1.9	5.5	
11b	2	0.0	5.8	
13a	1	28.6	28.6	

\* *v* is the transfer rate through the liquid membrane.

creases the membranotropic ability. For instance, compounds **9b** and **11b** with longer polyether chains (n = 2) do not transfer Ca<sup>2+</sup> cations. Compound **1a** is the most efficient carrier of Mg<sup>2+</sup> cations. However, this podand cannot be used as a selective cation carrier. The introduction of triazine substituents decreases the transfer rate but increases the selectivity with respect to a certain type of cations. For instance, compound **11b** can be used for selective transport of Mg<sup>2+</sup> cations through an organic membrane.

## Experimental

The reaction course and purity of the synthesized products were monitored by TLC on Sorbfil PTSKh-UF plates using a methanol—methylene dichloride (1 : 20) mixture as eluent. <sup>1</sup>H NMR spectra were recorded on a Bruker DRX 400 spectrometer in DMSO-d<sub>6</sub> or CDCl<sub>3</sub> using Me<sub>4</sub>Si as internal standard. Elemental analysis was carried out on a Carlo Erba EA 1108 automated analyzer. Preparative flash chromatography was performed on Kieselgel Woelm DC silica gel using a methylene dichloride—methanol (20 : 1) mixture as eluent.

The membranotropic studies were carried out according to a procedure described previously.<sup>18</sup> Cations of Ca<sup>2+</sup> and Mg<sup>2+</sup> were transferred through a liquid organic membrane using a  $10^{-4}$  M solution of triazine-containing podand in dichloromethane at 20±0.5 °C for 6 h with magnetic stirring at a velocity of 100 rotation min<sup>-1</sup>.

Metal picrates were synthesized *in situ* by the dissolution of metal chlorides in picric acid. Extraction was carried out at concentrations of a "host" molecule of  $1.0 \cdot 10^{-4}$ ,  $2.5 \cdot 10^{-4}$ ,  $5.0 \cdot 10^{-4}$ , and  $10 \cdot 10^{-4}$  mol L<sup>-1</sup>. A  $10^{-4}$  *M* aqueous solution of picrate (2 mL) and a solution (2 mL) of podand in CH<sub>2</sub>Cl<sub>2</sub> were mixed in a cell, and the mixture was stored in a thermostat for 30 min at 20 °C. After this, the mixture was shaken for 2 min. Measurements were performed in three parallel experiments. The extraction ability was determined spectrophotometrically by a decrease in the absorbance of the aqueous phase.

**1,5-Bis(2,6-dimethylphenoxy)-3-oxapentane (1a).** Sodium hydroxide (4.0 g, 0.1 mol) was added to a stirred solution of 2,6-dimethylphenol (12.2 g, 0.1 mol) in DMF (150 mL). The reaction mixture was stirred in an inert atmosphere until NaOH dissolved completely. Then  $\beta$ , $\beta'$ -dichlorodiethyl ether (7.15 g, 0.05 mol) dissolved in DMF (20 mL) was added dropwise to the reaction mixture for 30 min. The reaction mixture was heated to 110–115 °C and stirred for 20 h at this temperature. The precipitate that formed was filtered off and washed with water. The product was purified by column chromatography using CH<sub>2</sub>Cl<sub>2</sub> as eluent. The yield was 60%, m.p. 31–32 °C. Found (%): C, 76.19; H, 8.45. C<sub>20</sub>H<sub>26</sub>O<sub>3</sub>. Calculated (%): C, 76.43; H, 8.28. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>), & 6.99 (m, 4 H, Ar); 6.89 (dd, 2 H, Ar, J = 6.9 Hz, J' = 8.0 Hz); 3.88–3.90 (m, 4 H, ArOCH<sub>2</sub>CH<sub>2</sub>); 3.75–3.90 (m, 4 H, ArOCH<sub>2</sub>CH<sub>2</sub>); 2.24 (s, 12 H, Me).

**1,8-Bis(2,6-dimethylphenoxy)-3,6-dioxaoctane (1b)** was synthesized similarly to **1a** from 2,6-dimethylphenol (12.2 g, 0.1 mol) and triethylene glycol ditosylate (24.25 g, 0.05 mol). The product was isolated by column chromatography on  $Al_2O_3$  using chloroform as eluent. The yield was 76%, oil. Found (%):

C, 73.92; H, 8.43.  $C_{22}H_{30}O_4$ . Calculated (%): C, 73.74; H, 8.38. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>), & 6.98-7.00 (m, 4 H, Ar); 6.87-6.90 (m, 2 H, Ar); 3.57-3.86 (m, 12 H, ArOCH<sub>2</sub>CH<sub>2</sub>); 2.22-2.24 (m, 12 H, Me).

Synthesis of 1,5-bis[2,6-dimethyl-4-(3-R-1,2,4-triazine-5-yl)phenoxy]-3-oxapentanes (4, 5) (general procedure). 3-R-1,2,4-Triazine (1.04 mmol) and podand (0.52 mmol) were dissolved in a mixture (4.5 mL) of dichloromethane and trifluoroacetic acid (2 : 1). The reaction mixture was refluxed with a reflux condenser for 20 h, and then the solvent was evaporated *in vacuo*. An oily residue was washed with water and neutralized with an aqueous solution of NaHCO<sub>3</sub> to pH 8. The precipitate that formed was filtered off.

**1,5-Bis[2,6-dimethyl-4-(3-methylthio-1,2,4-triazin-5-yl)phenoxy]-3-oxapentane (4).** The yield was 40%, m.p. 96-98 °C. Found (%): C, 59.00; H, 6.47; N, 14.54.  $C_{28}H_{36}N_6O_3S_2$ . Calculated (%): C, 59.13; H, 6.38; N,14.78.

**1,5-Bis[4-(3-amino-1,2,4-triazin-5-yl)-2,6-dimethylphenoxy]-3-oxapentane (5).** The yield was 62%, m.p. 110-112 °C. Found (%): C, 62.02; H, 6.98; N, 21.89. C<sub>26</sub>H<sub>34</sub>N<sub>8</sub>O<sub>3</sub>. Calculated (%): C, 61.64; H, 6.76; N, 22.12.

Synthesis of 1,5-bis[4-(3-R-1-acyl-5-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3-oxapentanes and 1,8-bis[4-(3-R-1-acyl-5-oxo-1,4,5,6-tetrahydro-1,2,4triazin-6-yl)-2,6-dimethylphenoxy]-3,6-dioxaoctanes (9–13a,b) (general procedure). 3-R-1,2,4-Triazin-5(2H)-one (1.16 mmol) and podand (0.58 mmol) were dissolved in a mixture (2 mL) of trifluoroacetic acid and organic anhydride (1 : 1). The reaction mixture was stirred for 24 h at room temperature, and the solvent was removed *in vacuo*. The product was purified by flash chromatography.

**1,5-Bis[4-(1-acetyl-5-oxo-3-phenyl-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3-oxapentane (9a).** The yield was 70%, m.p. 198–200 °C. Found (%): C, 67.93; H, 6.25; N, 10.89.  $C_{42}H_{44}N_6O_7$ . Calculated (%): C, 67.73; H, 5.95; N, 11.28.

**1,8-Bis[4-(1-acetyl-5-oxo-3-phenyl-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3,6-dioxaoctane (9b).** The yield was 47%, m.p. 87–88 °C. Found (%): C, 67.00; H, 5.99; N, 10.73.  $C_{44}H_{48}N_6O_8$ . Calculated (%): C, 66.99; H, 6.13; N, 10.65.

**1,5-Bis[4-(1-acetyl-5-oxo-3-ethylthio-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3-oxapentane (10a).** The yield was 43%, m.p. 178–180 °C. Found (%): C, 57.45; H, 5.89; N, 11.73.  $C_{34}H_{44}N_6O_7S_2$ . Calculated (%): C, 57.28; H, 6.22; N, 11.79.

**1,5-Bis[4-(5-oxo-3-phenyl-1-trifluoroacetyl-1,4,5,6-tetra-hydro-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3-oxapentane** (11a). The yield was 63%, m.p. 223–226 °C. Found (%): C, 58.86; H, 4.14; N, 9.92.  $C_{42}H_{38}F_6N_6O_7$ . Calculated (%): C, 59.15; H, 4.49; N, 9.85.

1,5-Bis{4-[5-oxo-3-(4-tolyl)-1-trifluoroacetyl-1,4,5,6-tetrahydro-1,2,4-triazin-5-on-6-yl]-2,6-dimethylphenoxy}-3-oxapentane (12a). The yield was 52%. Found (%): C, 59.78; H, 4.56; N, 9.83.  $C_{44}H_{42}F_6N_6O_7$ . Calculated (%): C, 60.00; H, 4.81; N, 9.54.

**1,5-Bis**[**4-(3-ethylthio-5-oxo-1-trifluoroacetyl-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3-oxapentane (13a).** The yield was 75%, m.p. 85-86 °C. Found (%): C, 50.01; H, 4.29; N, 9.89.  $C_{34}H_{38}F_6N_6O_7S_2$ . Calculated (%): C, 49.75; H, 4.67; N, 10.24.

**1,5-Bis[4-(5-oxo-3-phenyl-1,4,5,6-tetrahydro-1,2,4-tri-azin-6-yl)-2,6-dimethylphenoxy]-3-oxapentane (14a).** Compound **11a** (30 mg, 0.045 mmol) was dissolved in methanol (2 mL), and diethylenetriamine (12.9 mg, 1.36 mmol) was added to the resulting solution. The reaction mixture was refluxed with a reflux condenser in an inert atmosphere for 5 h. The solvent was removed *in vacuo*. The product was purified by flash chromatography. The yield was 26%. Found (%): C, 69.07; H, 6.10; N, 12.72.  $C_{38}H_{40}N_6O_5$ . Calculated (%): C, 68.98; H, 6.24; N, 12.57. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>),  $\delta$ : 10.77 (br. s, 1 H, NH); 7.75 (d, 1 H, N(1)–H, J = 1.2 Hz); 7.72–7.74 (m, 2 H, Ph); 7.34–7.37 (m, 3 H, Ph); 6.98 (s, 2 H, Ar); 4.43 (d, 1 H, C(6)–H, J = 1.2 Hz); 3.89, 3.79 (both t, 2 H each, CH<sub>2</sub>, J = 5.2 Hz); 2.25 (s, 6 H, Me).

**1,8-Bis[4-(5-oxo-3-phenyl-1,2,4-triazin-6-yl)-2,6-dimethylphenoxy]-3,6-dioxaoctane (15b).** Compound **9b** (30 mg, 0.033 mmol) was dissolved in methanol (2 mL), and diethylenetriamine (7.58 mg, 0.86 mmol) was added to the resulting solution. The reaction mixture was refluxed with a reflux condenser in an inert atmosphere for 3 h. The solvent was purified by flash chromatography. The yield was 65%, m.p. 176–178 °C. Found (%): C, 68.87; H, 6.11; N, 11.98. C<sub>40</sub>H<sub>40</sub>N<sub>6</sub>O<sub>6</sub>. Calculated (%): C, 68.56; H, 5.75; N, 11.99. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>),  $\delta$ : 13.8 (br.s, 1 H, NH); 8.48 (m, 2 H, Ph); 7.55 (m, 3 H, Ph); 8.13 (s, 2 H, Ar); 3.60–3.79 (m, 4 H, ArOC<u>H</u><sub>2</sub>CH<sub>2</sub>); 3.54 (br.s, 2 H, ArOCH<sub>2</sub>C<u>H</u><sub>2</sub>), 2.24 (s, 6 H, Me).

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