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DIRECT MODIFICATION OF BENZOANNELATED CROWN ETHERS WITH 1,2,4-TRIAZIN-5(2*H*)-ONE MOIETIES

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Abstract - A convenient method for one-step coupling of benzoannelated crown ethers with 1,2,4-triazinones based on the reaction of nucleophilic addition to unsubstituted carbon atom of the triazine ring has been worked out. It has been shown that the reaction of 3-substituted 1,2,4-triazin-5(2*H*)-ones (**1**) with benzocrown ethers (benzo-12-crown-4, benzo-15-crown-5, benzo-18-crown-6) in the presence of acetic or trifluoroacetic anhydride is accompanied by acylation of triazine ring and results in formation of 3-(1-acyl-5-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)benzocrown ethers (**7-12**). The latters were converted to 3-(5-oxo-2,5-dihydro-1,2,4-triazin-6-yl)benzocrown ethers (**18-20**) using two alternative routes: the elimination of acetic or trifluoroacetaldehyde or the deacylation followed by the oxidation of the 1,4,5,6-tetrahydro derivatives (**13-15**).

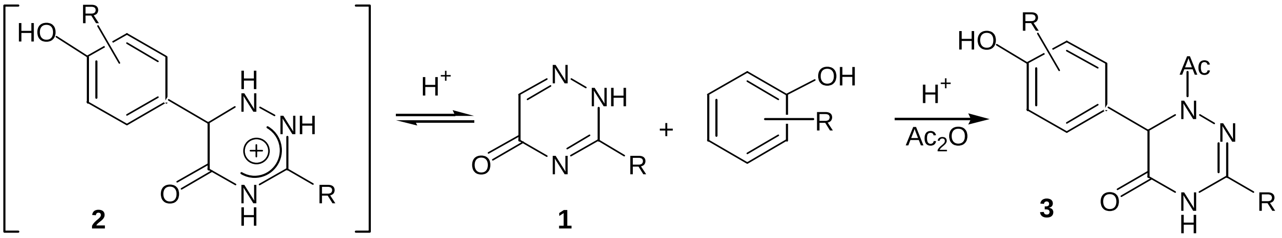
INTRODUCTION

Modification of benzoannelated crown ethers by heterocyclic moieties is of an interest. The coupling of two different centers of complexation can result in the changes of complexation ability. On the other hand, increasing the length of polyether moieties in the pharmacophore heterocycles can affect their biological activity.[1] However, most of the syntheses of heterocycle-substituted crown ethers cited in literature are multistep conversions.[2] It should be mentioned that the tendency of an azinium ring towards addition of electron-excess aromatic compounds[3] opens up new routes for direct modification of heterocyclic compounds with benzoannelated crown ethers.

RESULTS AND DISCUSSION

We have elaborated a new method for functionalization of aromatic ring of benzocrowns by 1,2,4-triazines, based on the reaction of nucleophilic addition to unsubstituted carbon atom of triazine ring. Recently, when studying the reactivity of 1,2,4-triazines towards electron-rich arenes (phenols and their ethers) we have found that despite electron-deficient character of 1,2,4-triazines they react with phenols only after activation of the triazine ring.[4] On dissolving 3-aryl-1,2,4-triazin-5(2*H*)-ones (**1**) in trifluoroacetic acid (TFA), the *N*-protonation product is formed. The interaction of the latter with phenols is an equilibrium process, and the addition product (**2**) can be characterized only by ^{1}H-NMR spectroscopy (Scheme 1).

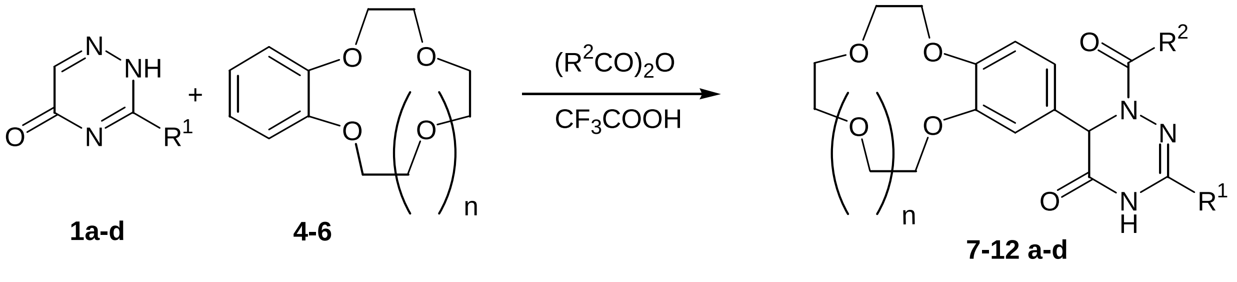
Scheme 1



The stable addition products (**3**) were isolated by the reaction of **1** with phenols in the presence of acetic anhydride.

Attempts to detect by ^{1}H-NMR spectroscopy the adducts of type (**2**), obtainable by the reaction of benzocrown ether with triazinones (**1**) failed in TFA solution without acid anhydride. The reaction with benzocrowns as well with phenols is possible in the presence of acylating agents.[5] Thus, the interaction of 3-aryl- or 3-ethylthio-1,2,4-triazin-5(2*H*)-one with benzoannelated crown ether in the mixture of TFA and trifluoroacetic anhydride (TFAA) at 20^{0}C results in forming of stable products of the addition of benzocrown to unsubstituted C6-atom of the triazinium ring in 47-94% yields (Scheme 2, Table 2).

Scheme 2



R^1 = Ph (**a**), *p*-Tol (**b**), 4-Cl-Ph (**c**), SC_2H_5 (**d**): (**1, 7-12**);
R^2 = CF_3: (**7-9**), CH_3:(**10-12**);
n = 1: (**4**; **7a-d**; **10a**); 2: (**5**; **8a,b,d**; **11a,c**); 3: (**6**; **9a,c; 12a**)

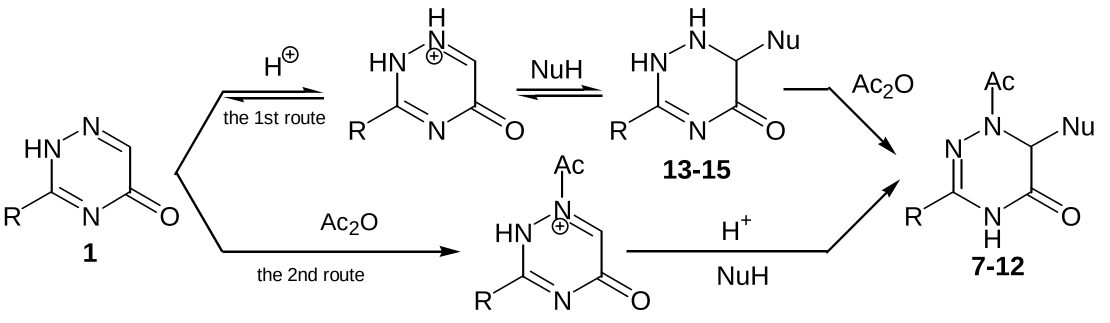
This reaction is accompanied by acylation of the nitrogen atom adjacent to the reaction center. The interaction of crown ether with triazinones in the presence of TFA and acetic anhydride proceeds in a similar way. It should be noted that this reaction does not take place in the presence of an acetic acid. Thus, attempts to isolate product by keeping the mixture of **1b** and benzo-12-crown-4 in acetic anhydride and acetic acid for 24 hours at 25^{0}C failed. After adding TFA to the reaction mixture the reagents are completely converted into compound (**10b**) during 4 h. So, the presence of TFA is necessary for interaction of 1,2,4-triazin-5(2*H*)-ones with benzoannelated crown ethers.

Three possible routes of the reaction of **1** with crown ethers can be discussed.

The first route, i.e., protonation of triazines (**1**), reversible nucleophilic addition of benzocrown ethers and acylation of the adducts, and the *second* one consisting of acylation of N1 atom of the triazine ring and nucleophilic addition, are not feasible (Scheme 3). Some facts lead to this conclusion. Based on the NMR spectral experiments it has been found that the reaction of **1b** with crown ether (**4**) in a TFA solution does not occur and the addition products are not formed. Moreover compounds (**13-15**) can not dissociate when being kept in a TFA solution. So, the first route can be excluded since there is no any equilibrium between starting compounds, triazin-5(2*H*)-ones (**1**) and benzocrown ethers, and compounds (**13-15**).

The second route is improbable because the acylation of N2 and N4 atoms is most likely than that of N1 atom, which has been confirmed by the NMR spectral experiment. In the NMR spectra the C6-H signal of **1** was not shifted on adding Ac_2O.

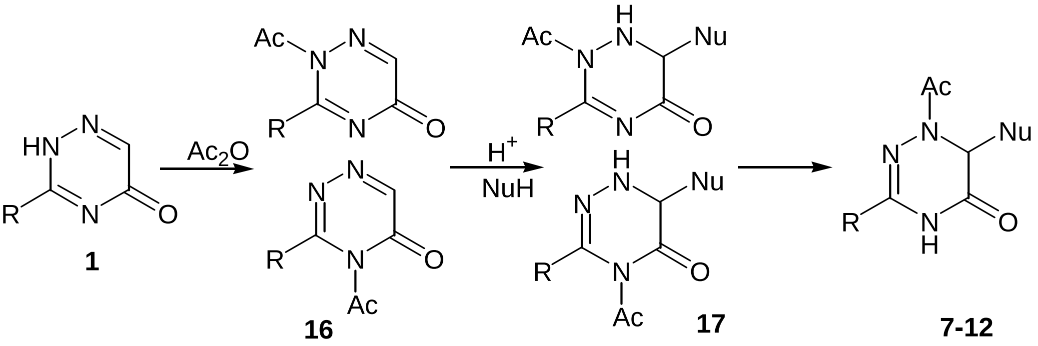
Scheme 3



The third path consists of acylation of N2 and N4 atoms, protonation of acyl derivatives (**16)**, addition of benzocrown ethers and rearrangement of compounds (**17**) into more stable N1-acyl derivatives (**7-12**) (Scheme 4).

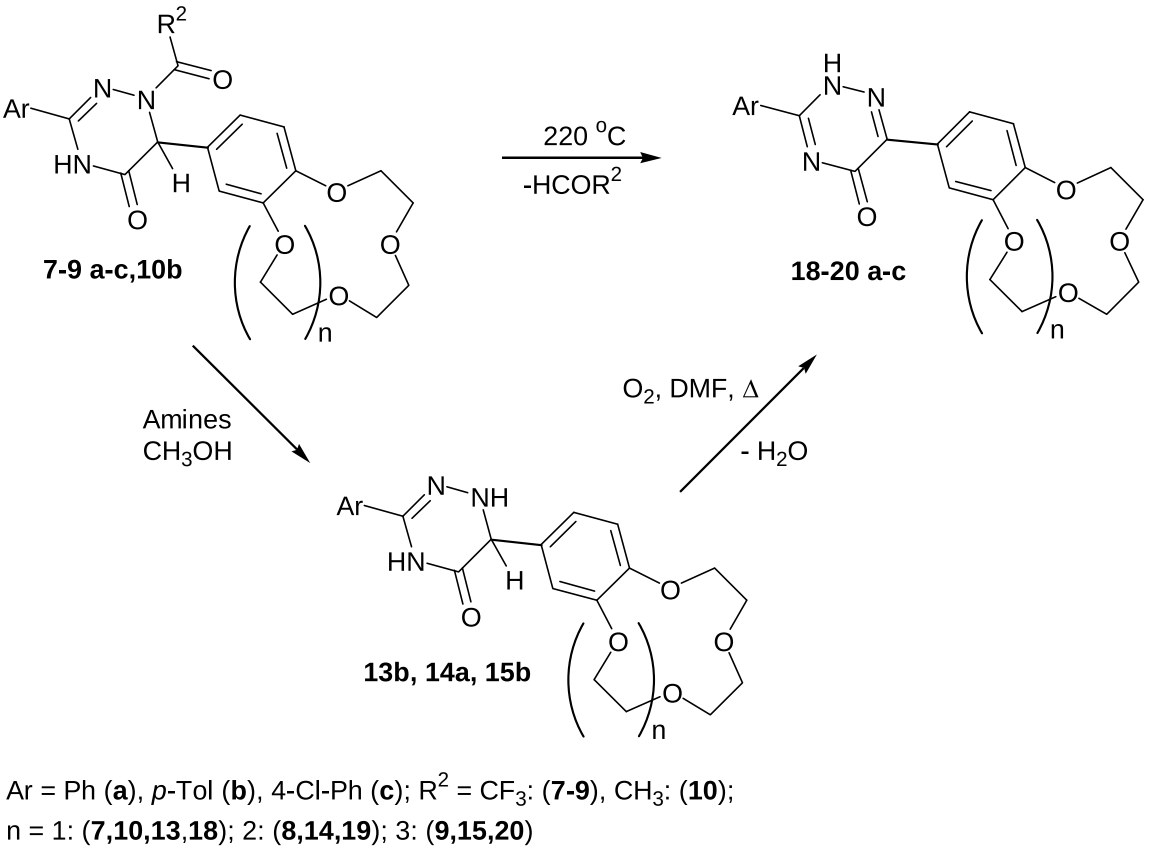
The following facts prove this reaction route. The mixture of stable acyl derivatives (**16a**) was isolated on the acylation of **1a** by Ac_2O. This product reacted with benzo-12-crown-4 in the presence of TFA to form **7a**. The rearrangement of **17a** into **7a** was predominantly an intramolecular process, since only the traces of trifluoroacetyl derivative corresponding to **7a** were detected by TLC in the reaction of **16a** with benzo-12-crown-4 in the presence of TFAA. Product (**7a**) was more likely to be formed from 4-acetyl-1,2,4-triazin-5(4*H*)-one.

Scheme 4



N-Acyl substituted tetrahydrotriazines (**7-12**) are analogues of the Reissert adducts and undergo transformation characteristic of the above ones - the elimination of aldehyde yielding S_N^H-products.[3]

Scheme 5



Ar = Ph (**a**), *p*-Tol (**b**), 4-Cl-Ph (**c**); R^2 = CF_3: (**7-9**), CH_3: (**10**);
n = 1: (**7,10,13,18**); 2: (**8,14,19**); 3: (**9,15,20**)

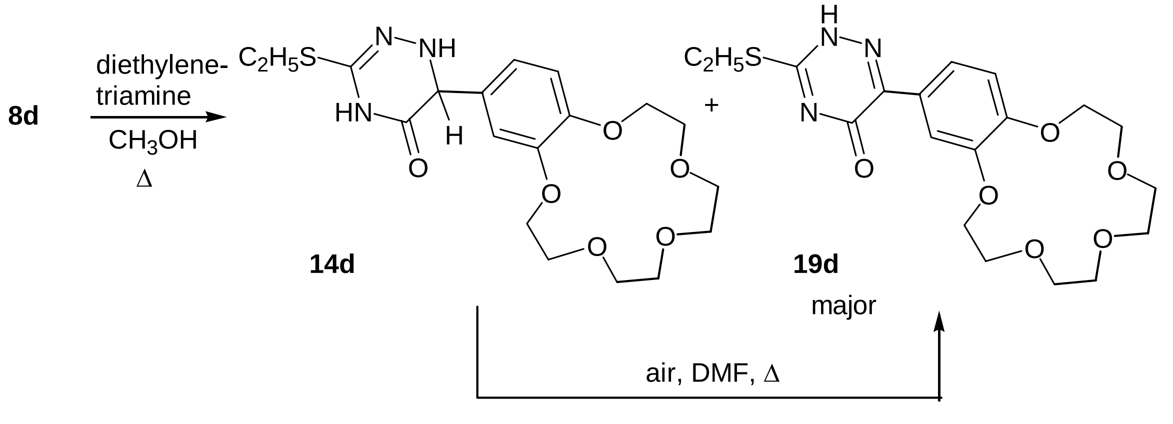
Heating compounds (**7b**), (**8a**), (**9c**), (**10b**) at 220^{0}C for 24-30 hours affords **18b**, **19a**, **20c** in 15-29% yields (Scheme 5). Yields of S_N^H-products can be increased up to 32% by use of an argon atmosphere. Therefore oxidative aromatization can be excluded from the discussion. We suggest that the dehydrogenation step can be realized according to the *auto*-aromatization mechanism by concerted elimination of the acyl residue and hydrogen at sp^3- carbon atom of triazine ring forming acetaldehydes. The reaction time and yields of the products depend on the nature of acyl substitutent. Thermolysis of 1-trifluoroacetyl-1,2,4-triazinylbenzocrown ethers proceeds more readily than that of the corresponding acetyl analogs. While the thermolysis of **7b** takes 30 h (yield of **18b** – 30%), the conversion of **10b** after 34 h is not complete (yield of **18b** < 16%).

Evidently the elimination rate increases in the presence of base facilitating H6 elimination. An attempt was made to carry out the reaction under mild conditions in the presence of amines. However, when compounds (**7b**), (**8a**) and (**9b**) were refluxed in methanol solution in the presence of amines (aniline, hydrazine, morpholine, polyethylenediamines, polyethylenepolyamines, etc.) the competitive reaction resulting in tetrahydrotriazines (**13b**), (**14a**), (**15b**) proceeded faster (Scheme 5).

Treatment of 3-ethylthio-substituted 1,2,4-triazin-5(2*H*)-one (**8d**) with diethylenetriamine results in both dihydrotriazine (**19d**) as the major products and tetrahydrotriazine (**14d**) (Scheme 6). For example, treatment of **8d** with diethylenetriamine gives crown ether (**19d**) in 53% yield, while **14d** can be prepared in 35% yield only.

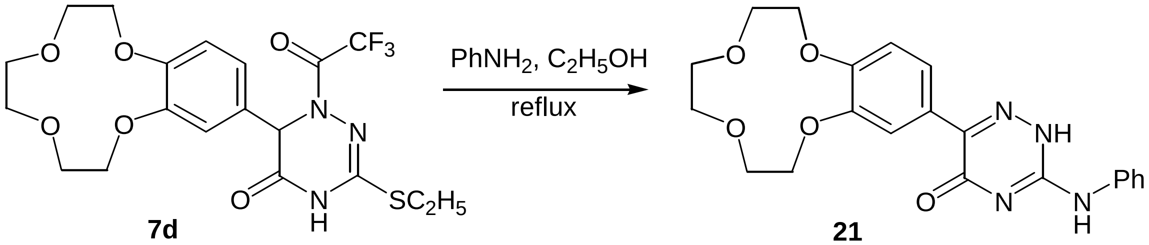
The formation of compounds (**14**) and (**19**) as result of acetaldehyde elimination is possible although two-step oxidation mechanism can not be excluded, since tetrahydrotriazines (**13-15**) are sensitive to oxidation. Heating of **13-15** in DMF by bubbling of air in the reaction mixture gives dihydrotriazines in 50-70% yields.

Scheme 6



Using the two-step synthesis of **18-20** makes it possible to increase yields compared with those obtained through thermal elimination of aldehyde. Another advantage of this approach is that readily leaving ethylthio group in the 3-position of the ring retains under the applied conditions. This property may be used for subsequent modifications of the molecule. For example, refluxing of **7d** and aniline in ethanol solution results in substitution of ethylthio group by aminophenyl group (Scheme 7). Two processes – nucleophilic substitution of hydrogen - S_N^H-process (according to Scheme 5) and *ipso*-substitution of good leaving group -S_N^{ipso} - take place in this reaction. Then the use of S_N^H-methodology to modification of structure of nitrogen containing heterocycles permits to increase the functionalization index of azine substrates.

Scheme 7



STRUCTURE ASSIGNMENT

The spectral data for the obtained compounds (Table 1) are in full agreement with the proposed structures. In ^{1}H-NMR spectra of products of the nucleophilic addition of crown ether to unsubstituted C6-atom of the triazine ring, the H6 signal is observed as a singlet at 5.75-5.95 ppm, while the signal of N4-H proton is shifted to higher field by 2-3 ppm. In ^{1}H-NMR spectra of the tetrahydrotriazines (**13-15**) the H6 signal is observed as a doublet at 4.5 ppm due to spin-spin coupling with the proton at N1 which gives the signal at 7.6 ppm. In ^{1}H-NMR spectra of the dihydrotriazines the H6 signal is absent and N2-H proton is observed in the region of 14 ppm.

Table 1. ^{1}H-NMR spectral data of products (δ, ppm; J, Hz)

No	C6-H (1H)	N1-R	N2-H, b.s.	3-R	6-R
1	2	3	4	5	6
7a	5.90 s	-	11.87	7.50-7.66 m (3H); 7.84-7.96 m (2H)	6.75-7.11 m (3H); 4.00-4.18 m (4H); 3.59-3.72 m (8H)
7b	5.96 s	-	11.44	7.72-7.83 d (2H), J = 8.1; 7.28-7.45 d (2H), J = 8.1; 2.37s (3H)	6.63-6.88 m (3H); 4.01-4.05 m (4H); 3.62-3.77 m (8H)
7c	5.89 s	-	11.98	7.62d (2H) J = 8.7; 7.91d (2H) J = 8.7	6.87-7.07 m (3H); 4.01-4.13 m (4H); 3.59-3.70 m (8H)
7d	5.78 s	-	11.81	3.09 q (2H), J = 7.3; 1.35 t (3H), J = 7.3	6.72-7.04 m (3H); 4.04-4.09 m (4H); 3.64-3.76 m (8H)
8a	5.89 s	-	11.89	7.52-7.62 m (3H); 7.85-7.97 m (2H)	6.80-7.01 m (3H); 3.90-4.05 m (6H); 3.59-3.75 m (10H)
8b	5.85 s		11.72	7.77 d (2H), J = 8.0; 7.32 d (2H), J = 8.0; 2.36 s (3H)	6.95 d (1H), J = 8.4; 6.88 d (1H), J = 2.3; 6.73 dd (1H), J = 2.3, 8.4; 3.74-3.81 m (4H); 3.53-3.58 m (12H)

1	2	3	4	5	6
8d	5.77 s		11.81	2.99 q (2H), J = 7.3; 1.35 t (3H), J = 7.3	6.63-6.91 m (3H); 3.97-4.04 m (6H); 3.77-3.82 m (10H)
9a	5.87 s		11.81	7.43-7.78 m (3H); 7.84-7.96 m (2H)	6.73-6.91 m (3H); 3.70-4.60 m (4H); 3.53-3.75 m (16H)
9c	5.89 s		11.89	7.52 d (2H), J = 7.8; 7.93 d (2H), J = 7.8	6.73-6.88 m (3H); 3.79-4.07 m (4H); 3.62-3.69 m (4H); 3.55-3.64 m (12 H)
10a	5.96 s	2.39 s (3H)	11.52	7.41-7.49 m (3H), 7.88-7.90 m (2H)	6.74 dd (1H), J = 2.0 Hz, J = 8.4; 6.87 d (1H), J = 2.0; 6.89 d (1H), J = 8.4; 3.62-3.71 m (8H); 4.03-4.06 m (4H)
10b	5.86 s	2.39 s (3H)	11.74	7.79 d (2H), J = 8.1; 7.27 d (2H), J = 8.1; 2.47 s (3H)	6.85-7.03 m (3H), 4.07-4.12 m (4H); 3.63-3.75 m (8H)
11a	5.96 s	2.38 s (3H)	11.49	7.87-7.89 m (2H); 7.41-7.47 m (3H)	6.67 d (1H), J = 8.5; 6.80 d (1H), J = 8.5; 6.82 b.s (1..H); 3.59 b.s (8H); 3.74-3.75 m (4H); 3.99 b.s (4H)
11c	5.95 s	2.37 s (3H)	11.56	7.89 d (2H), J = 8.8; 7.45 d (2H), J = 8.8	6.65 dd (1H), J = 1.74, 8.23; 6.79-6.82 m (2H); 3.59-3.62 m (8H); 3.73-3.77 m (4H); 3.98-4.00 m (4H)
12a	5.97 s	2.37 s (3H)	11.48	7.88 d (2H), J = 6.6; 7.40-7.48 m (3H)	3.52-3.61 m (12H); 3.73-3.77 m (4H); 4.01-4.04 m (4H); 6.67 dd (1H), J = 1.9, 8.3; 6.80 d (1H), J = 8.3; 6.87 d (1H), J=1.9
13b	4.48 d, J = 1.6	7.37 d, J = 1.7	10.76	7.61 d (2H), J = 8.3; 7.08 d (2H), J = 8.2; 2.34 c (3H)	6.91 m (3H); 4.03-4.13m (4H); 3.64-3.75m (8H)
14d	4.41 b.s	6.45 b.s.		3.04 q (2H), J = 7.1 1.35 t (3H), J = 7.1	6.76-6.95 m (3H); 3.95-4.04 m (4H), 3.75-3.78 m (4H), 3.62 s (8H)
14a	4.56 d, J = 1.6	7.64 d, J = 1.6	10.72	7.71- 7.73 m (2H); 7.36-7.39 m (3H)	6.95 d (1H), J = 1.91 Hz; 6.90 d (1H), J = 8.29 Hz; 6.84 dd (1H), J = 1.95, 8.24; 3.98-4.03 m (4H); 3.73-3.75m (4H); 3.57-3.61m (8H)

1	2	3	4	5	6
15b	4.54 d, J = 1.4 Hz	7.55 d, J = 1.5	10.70	7.61 d (2H), J = 8.3; 7.18 d (2H), J = 8.3; 2.30 s (3H)	6.95 d (1H), J = 1.89; 6.89 d (1H), J = 8.34; 6.82 dd (1H), J = 1.85, J = 8.33; 4.01-4.54 m (4H); 3.71-3.74 m (4H); 3.51-3.59m (12H)
18a	-	-	14.0	8.15-8.20 m (2H); 7.52-7.89 m (3H)	6.97-7.08 m (3H); 4.59-4.78 m (4H); 3.57-3.75 m (8H)
18b	-	-	13.99	8.02 d (2H), J = 8.2; 7.36 d (2H) J = 8.2; 2.44 s (3H)	7.05 d (1H), J = 9.06; 7.91-7.93 m (2H) 4.17-4.21 m (4H) 3.67-3.79 m (8H)
19a	-	-	13.86	8.08-8.20 m (2H); 7.54-7.63 m (3H)	7.81-8.02 m (1H); 6.93-7.04 m (2H); 3.87-4.12 m (4H); 3.81-3.85 m (4H); 3.65 s (8H)
19d	-	-	14.0	3.14 q (2H), J = 7.1; 1.32 t (3H), J = 7.1	7.00 d (1H), J = 8.5; 7.66 – 7.86 m (2H); 4.10 – 4.13 m (4H); 3.83-3.91 m (4H); 3.62 b.s. (8H)
20b	-	-	14.0	7.99 d (2H), J = 8.4; 7.35 d (2H), J = 8.4; 2.44 s (3H)	7.83-7.91 m (1H); 6.90-6.98 m (2H); 3.87-4.16 m (4H); 3.68-3.82 m (4H); 3.63 s (12H)
20c	-	-	14.0	8.28 d (2H), J = 8.6; 7.42 d (2H), J = 8.6	6.93 d (1H), J = 8.37; 8.10-8.13 m (2H); 4.15-4.19 m (4H); 3.83-3.88 m (4H); 3.52-3.67 m (12H)
21	-	-	12.09	7.04t (1H), J = 7.3; 7.29-7.34 m (2H); 7.59d (2H), J = 7.6; 9.12 b.s (1H)	3.64-3.69 m (4H); 3.73-3.80 m (4H); 4.13-4.17 m (4H); 6.98 d (1H), J = 8.2; 7.23-7.79 m (2H)

EXPERIMENTAL

Flash chromatography was performed on Kieselgel Woelm DC silica gel using CH_2Cl_2-CH_3OH (20:1 and 10:1) as an eluent. All melting points are uncorrected and were measured on a Boetius melting point apparatus. Elemental analyses were performed on Carlo Erba 1108 CHNO Analyzer. The ^{1}H-NMR spectra were recorded on a Bruker DRX 400 (400 MHz) spectrometer with TMS as an internal standard.

3-[5-Oxo-1-trifluoroacetyl(or acetyl)-3-*R*-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl]benzocrown ether (7-12) (General procedure).

A suspension of 3-*R*-1,2,4-triazin-5(2*H*)-one (0.3 mmol) and benzocrown ether (0.3 mmol) in the mixture of TFA (0.2 mL) and trifluoroacetic (acetic) anhydride (2.0 mL) was stirred for 4-6 h at 20^{0}C until reagents were completely dissolved. The solvent was removed *in vacuo*. The oil residue was washed with diethyl ether. The precipitate was recrystallized from methanol and dried over P_2O_5. Yields, melting points and elemental analysis data are given in Table 2.

3-(1-Acetyl-5-oxo-3-phenyl-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl)benzo-12-crown-4 (10a).

A suspension of 3-phenyl-1,2,4-triazine-5(2*H*)-one (100 mg, 0.57 mmol) in acetic anhydride (1 mL) was refluxed until complete dissolution of the crystals of parent compound. The mixture was kept over night at 20^{0}C. Then the solvent was removed *in vacuo*. The precipitate was dissolved in trifluoracetic acid (2 mL) and benzo-12-crown-4 (127.7 mg, 0.57 mmol) was added to the solution. The reaction mixture was kept for 30 h at 20^{0}C. The solvent was removed *in vacuo*. The residue was recrystallized from methanol to give **10a** in 38% yield. mp 166-168^{0}C.

3-[5-Oxo-3-*R*-1,4,5,6-tetrahydro-1,2,4-triazin-6-yl]benzocrown ether (13-15) (General procedure).

Diethylenetriamine (0.15 mmol) was added to a solution of **7-12** (0.1 mmol) in methanol (2 mL). The reaction mixture was refluxed for 4-5 h. The solvent was removed *in vacuo* and the oil residue was dissolved in CH_2Cl_2 and separated by flash chromatography. Compounds (**13-15 a-c**) were obtained from **7-12 a-c**, while **7-11 d** yielded **13-14 d** and **18-19 d.** Yields, melting points and elemental analysis data are given in Table 2.

3-[5-Oxo-3-*R*-2,5-dihydro-1,2,4-triazin-6-yl]benzocrown ether (18-20) (General procedure).

Method A and B: The solid of **7-9** (0.1 mmol) (Method A) or **10-12** (0.1 mmol) (Method B) was heated at 220^{0}C under argon for ~ 30 h. The reaction mixture was cooled to 20^{0}C. The residue was dissolved in methanol and separated by flash chromatography on silica gel.

Method C: A solution of benzocrown ether (**13-15**) (0.1 mmol) in DMF (2mL) was refluxed for 1 h with bubbling air through the solution. The solvent was evaporated *in vacuo*. The residue was recrystallized from methanol.

Method D: Diethylenetriamine (0.15 mmol) was added to a solution of **8d** (0.1 mmol) in methanol (2 mL). The reaction mixture was refluxed for 6 h. The solvent was evaporated to 1 mL. Residue was absorbed on silica gel and separated by flash chromatography to yield two products: tetrahydrotriazine (**14d**) and dihydrotriazine (**19d**). Yields, melting points and elemental analysis data are given in Table 3.

3-(5-Oxo-3-phenylamino-2,5-dihydro-1,2,4-triazin-6-yl)benzo-12-crown-4 (21).

Aniline (0.08 mL) was added to a solution of **7d** (70 mg, 0.17 mmol) in ethanol (2 mL). The reaction mixture was refluxed for 32 h. The precipitate was filtered off and recrystallized from methanol to give 42 mg (61 %) of **21**. mp 272-274°C. Anal. Calcd for $C_{21}H_{22}N_4O_5$: C, 61.51; H, 5.40; N, 13.67. Found: C, 61.16; H, 5.60; N, 13.34.

Table 2. Yields, melting points and elemental analysis data of obtained compounds (**7-15**).

№	Reaction time, h	Yield %	mp °C	Formula	Calculated /Found, %		
					C	H	N
1	2	3	4	5	6	7	8
7a	3	77	156-158	$C_{23}H_{22}N_3O_6F_3$	55.98	4.50	8.52
					55.96	4.53	8.54
7b	3	94	179-180	$C_{24}H_{24}N_3O_6F_3$	56.80	4.77	8.28
					56.82	4.80	8.03
7c	6	64	174-176	$C_{23}H_{21}N_3O_6ClF_3$	52.33	4.01	7.96
					52.52	4.14	7.82
7d	6	65	106-108	$C_{19}H_{22}N_3O_6F_3S$	47.79	4.65	8.80
					47.79	4.78	8.85
8a	4	64	174-177	$C_{25}H_{26}N_3O_7F_3$	55.86	4.88	7.82
					55.76	4.85	7.88
8d	6	50	132-134	$C_{21}H_{26}N_3O_7F_3S$	48.36	5.03	8.06
					48.32	5.02	8.08
9a	6	64	158-159	$C_{27}H_{30}N_3O_8F_3$	55.76	5.24	7.23
					55.47	5.23	7.18
9b	6	47	182-184	$C_{28}H_{32}N_3O_8F_3$	56.46	5.42	7.05
					56.32	5.56	7.03
9c	6	64	159-160	$C_{27}H_{29}N_3O_8ClF_3$	52.65	4.74	6.82
					52.60	4.59	6.91
10a	8	47	166-168	$C_{23}H_{25}N_3O_6$	62.86	5.73	9.56
					63.17	5.74	9.83
10b	3	69	179-180	$C_{24}H_{27}N_3O_6$	63.56	6.00	9.27
					63.52	5.85	9.20
11a	8	72	173-174	$C_{25}H_{29}N_3O_7$	62.10	6.05	8.69
					61.96	5.87	8.56
11c	6	49	160-162	$C_{25}H_{28}N_3O_7Cl$	57.97	5.45	8.11
					57.95	5.35	7.81
12a	8	56	159-160	$C_{27}H_{33}N_3O_8$	61.47	6.30	7.96
					61.20	6.58	7.85
13b	3	70	198-199	$C_{22}H_{25}N_3O_5$	64.22	6.12	10.21
					63.97	6.40	9.97
14a	4	83	138-139	$C_{23}H_{27}N_3O_6$	62.57	6.16	9.52
					62.39	6.26	9.48
3914d	6	35	139-140	$C_{19}H_{27}N_3O_6S$	53.69	6.40	9.89
					53.50	6.58	9.74
15b	3	78	178-179	$C_{26}H_{33}N_3O_7$	62.51	6.66	8.41
					62.50	6.68	8.47

Table 3. Yields, melting points and elemental analysis data of compounds (**18-20**)

№	Method	Reaction time, h	Yield %	mp °C	Formula	Calculated/Found, %		
						C	H	N
18b	A	30	30	123-124	$C_{22}H_{23}N_3O_5$	64.54	5.66	10.26
	B	34	16			64.29	5.75	10.14
	C	1	70					
19a	A	30	29	104-105	$C_{23}H_{25}N_3O_6$	62.86	5.73	9.51
	C	1	50			62.69	6.07	9.75
19d	D	6	35	138-140	$C_{19}H_{25}N_3O_6S$	53.89	5.95	9.92
						53.62	6.01	9.87
20a	A	30	29	105-106	$C_{25}H_{29}N_3O_7$	62.10	6.05	8.69
						61.96	6.23	8.52
20b	C	2		174-175	$C_{26}H_{31}N_3O_7$	62.76	6.28	8.45
						62.43	6.36	8.32
20c	A	30	31	138-140	$C_{25}H_{28}N_3O_7Cl$	57.97	5.45	8.11
						57.68	5.51	7.90

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