

A modified Biginelli reaction toward oxygen-bridged tetrahydropyrimidines fused with substituted 1,2,4-triazole ring

Mustafa K. Gümüş^{1,2,3*}, Nikolay Yu. Gorobets², Yuriy V. Sedash²,
Valentin A. Chebanov^{2,3}, Sergey M. Desenko^{2,3}

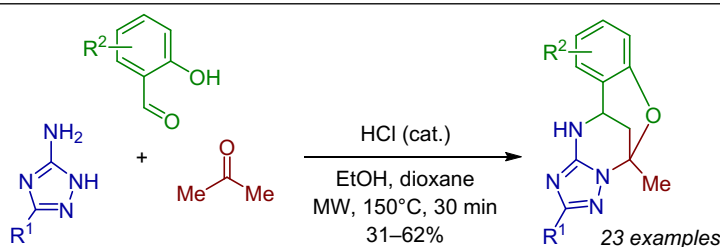
¹ Science-Technology Research and Application Center, Artvin Coruh University, Artvin 08000, Turkey; e-mail: mkgumus@artvin.edu.tr

² SSI "Institute for Single Crystals" of National Academy of Sciences of Ukraine, 60 Nauky Ave., Kharkiv 61072, Ukraine; e-mail: gorobets@isc.kharkov.com

³ V. N. Karazin Kharkiv National University, 4 Svobody Sq., Kharkiv 61077, Ukraine; e-mail: chebanov@karazin.ua

Published in Khimiya Geterotsiklicheskih Soedinenii, 2017, 53(11), 1261–1267

Submitted August 18, 2017
Accepted November 9, 2017



A microwave-assisted Biginelli-like three-component condensation using salicylic aldehyde derivatives, acetone, and 5-substituted 3-amino-1,2,4-triazoles instead of the urea component results in the formation of oxygen-bridged tetrahydrotriazolopyrimidine derivatives (11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocines) in good yields and high purity. A plausible reaction mechanism for this transformation is discussed in details using literature and experimental data.

Keywords: 3-amino-1,2,4-triazole, benzoxadiazocine, oxygen-bridged structure, Biginelli reaction, cascade reaction, microwave-assisted synthesis, multicomponent reaction, reaction mechanism.

The Biginelli multicomponent reaction discovered in 1891¹ has been intensively used as an efficient tool for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-one derivatives.² This approach is still topical, especially in the last decades its facile performance and wide scope have attracted a considerable attention of scientists working in the fields of process development³ and drug discovery.⁴ An intriguing and challenging task is also to broaden the horizons of classical multicomponent reactions (MCRs) by means of replacing the conventional building blocks with novel and

often more complex starting molecules,⁵ which can be considered as synthetic equivalents, but due to their different nature the resulting modified Biginelli reaction can lead even beyond the classical Biginelli products.

This happens, in particular, when salicylic aldehydes are applied in Biginelli-like MCRs leading to the formation of oxygen-bridged benzoxadiazocines **1**⁶ (Fig. 1). Also, the use of heterocyclic building blocks instead of urea in such MCRs makes these reactions to be even more complicated.^{7,8} A literature overview of three-component Biginelli-

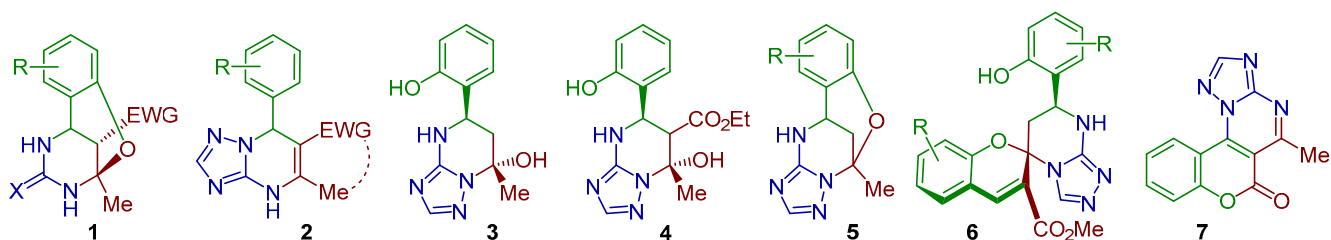


Figure 1. Different reaction products of modified Biginelli reactions using salicylic aldehydes and 3-amino-1,2,4-triazole as unconventional building blocks. Relative configuration of the stereogenic centers is shown.

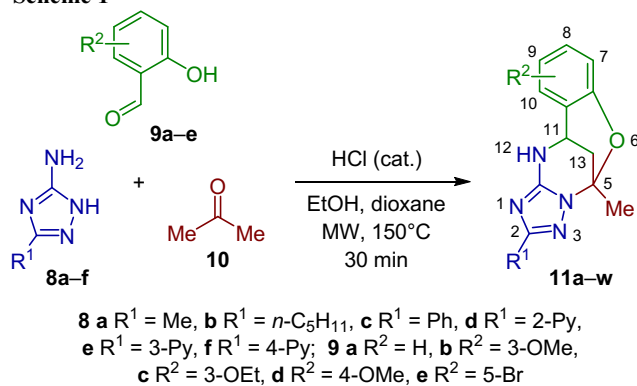
like condensations using 3-amino-1,2,4-triazole as a 1,3-binucleophile showed that 4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines (**2**) are the most common products obtained under harsh reaction conditions,⁹ however, variations of the conditions and specific substituents in the starting materials can switch these reactions to the formation of other product types, which are mainly formed as intermediates or side reaction products in the mainstream to compound **2**. A Biginelli-type condensation using both salicylic aldehydes and 3-amino-1,2,4-triazoles also has several reaction pathways depending on the third reaction component and the reaction conditions applied. In our preliminary communication, the formation of alternative structures has been described, e.g., compounds **3**¹⁰ and **4**^{10a} formed in very good yields at 40°C in MeOH in the presence of HCl. Interestingly, the formation of products of type **3**, but without the *o*-hydroxy group in the aromatic ring, proceeds in acetone taken as solvent, and it requires much higher reaction temperature (125°C for 45 min under microwave irradiation in the presence of TsOH), giving only moderate product yields.¹¹ The oxygen-bridged products **5** were obtained by microwave heating of the reaction mixture at 150°C for 30 min in the presence of HCl.^{10a} This work was followed by a report from Světlík and coworkers¹² describing a pseudo-four component MCR of methyl acetoacetate, 3-amino-1,2,4-triazole, and 2 equiv of salicylic aldehydes in refluxing EtOH–HCl (cat.) for 20 h that led to spiro compounds **6** as a major products and their diastereoisomers accompanied with 3-acetylcoumarin (derived from the reaction of salicylic aldehyde and methyl acetoacetate) as minor ones.

More recently, Magedov's group published one example of MCR starting practically with the same reagents in refluxing acetic acid in the presence of piperidine that resulted in the formation of heterocyclic system **7**.¹³ In all these cases, several substituted salicylic aldehydes, a few α -carbonyl CH acids, and single unsubstituted 3-amino-1,2,4-triazole were applied as initial compounds giving quite a narrow chemical diversity of the final products.

Taking into account the preliminary character of our previous publication^{10a} and the limited number of the described compounds **5**, here we aimed to explore the possibility of introducing 5-substituted 3-amino-1,2,4-triazoles into the three-component microwave-assisted reaction with salicylic aldehydes and acetone to elucidate the scope and limitations of this modified Biginelli reaction.

For the present study, several 5-substituted 3-amino-1,2,4-triazoles **8a–f** were used as 1,3-binucleophiles in three-component interaction with salicylic aldehyde or its derivatives **9a–e** and acetone (**10**) (Scheme 1). Application of the reaction conditions previously described for unsubstituted 3-amino-1,2,4-triazole^{10a} provided expectedly the novel derivatives of methano[1,2,4]triazolo[1,5-*c*][1,3,5]-benzoxadiazocine **11a–w** obtained in moderate to good yields (31–62%, Table 1). The products, whose purity was ascertained by NMR,¹⁴ precipitated from the reaction mixture at room temperature as colorless crystalline substances and were easily collected by filtration. The application of higher temperature or longer reaction times did not result in any significant increase of the reaction yields.

Scheme 1

Table 1. Yields of oxygen-bridged heterocycles **11a–w**

Compound	R ¹	R ²	Yield, %	Compound	R ¹	R ²	Yield, %
11a	Me	H	48	11m	Ph	7-OEt	55
11b	Me	7-OMe	51	11n	Ph	9-Br	57
11c	Me	7-OEt	55	11o	2-Py	H	52
11d	Me	8-OMe	35	11p	2-Py	7-OMe	54
11e	Me	9-Br	53	11q	2-Py	7-OEt	53
11f	<i>n</i> -C ₅ H ₁₁	H	55	11r	3-Py	H	60
11g	<i>n</i> -C ₅ H ₁₁	7-OMe	57	11s	3-Py	7-OMe	62
11h	<i>n</i> -C ₅ H ₁₁	7-OEt	62	11t	3-Py	7-OEt	60
11i	<i>n</i> -C ₅ H ₁₁	8-OMe	31	11u	4-Py	H	48
11j	<i>n</i> -C ₅ H ₁₁	9-Br	60	11v	4-Py	7-OMe	53
11k	Ph	H	52	11w	4-Py	7-OEt	58
11l	Ph	7-OMe	53				

Moderate product yields (compound **11d,i**) were obtained only when 4-methoxysalicylaldehyde (**9d**) was used as a starting material in reactions with 5-alkyl-substituted 3-amino-1,2,4-triazoles **8a,b** and acetone (**10**). The limitation of this reaction was also found in the case when the same aldehyde **9d** reacted with pyridyl-derived 3-amino-1,2,4-triazoles **8d–f**, where only in the case of compound **8e** (R¹ = 3-Py) formation of the expected oxygen-bridged product **11y** was observed. However this product was isolated in a mixture with the corresponding Schiff base **12b**, while in the cases of starting compounds **8d,f** only Schiff bases **12a,c** were obtained as the final products (Scheme 2). In all other cases such Schiff bases could be obtained under mild conditions and transformed into the desired oxygen-bridged products **11a–w** by the reaction with acetone. Contrary, in the cases of azomethines **12a,c** this reaction did not proceed even at elevated temperature (170°C) during 1 h.

Such influence of the substituents on the reactivity can be rationalized taking into account a set of different data about this type of heterocyclization collected from the literature to date and our assumptions about a possible reaction mechanism. In contrast to one of the previously suggested mechanisms for this reaction type,¹⁵ the formation of Schiff base **12** is the most probable first stage of the whole cascade. This Schiff base begins to form already after mixing all reagents at room temperature and can be readily isolated; it often accompanies the product's

stereochemical characteristic of this reaction. This feature may be reasonably explained on the basis of the suggested reaction mechanism.

The reaction **15** → **3** (Scheme 3) could proceed *via* two rotamers, *s-trans-14* and *s-cis-14* giving two corresponding diastereomers. The widely accepted theory holds that the preferred approach of a nucleophile is in the plane bisecting the carbonyl group and orthogonal to the molecular plane, and that the Nu···C=O angle (α) is maintained constant at the value of Bürgi–Dunitz angle ($107 \pm 5^\circ$).¹⁹ Obviously, in rotamer *s-trans-14* the approach of the triazole nitrogen atom at such angle would be associated with steric hindrances, while nothing prevents this attack at the favorable angle in rotamer *s-cis-14*, and simple rotation around C–CO σ -bond (*s-trans-14* → *s-cis-14*) provides more favorable disposition for ring closure and the product is formed only as diastereomer **3**.

The further closure of the oxygen bridge also should proceed according to Baldwin rules,²⁰ and the mechanism for this cyclization type was initially suggested by Světlík²¹ in his first report devoted to such heterocyclization. Following his logic, we can suggest here that direct transformation **3** → **11** *via* 6/8-*endo-tet* process is hardly possible. The reason is that the original favored trajectory for tetrahedral cyclization (attack on sp^3 -atom) with an attack angle α of 180° is unrealizable in structure **3**. Similarly, 6-*endo*/8-*exo-trig* nucleophilic addition (**16** → **11**) must be excluded due to unfavorable attack trajectory with a value of angle α much lower than Bürgi–Dunitz angle. Thus, to rationalize the final formation of benzoxadiazocine **11** we have to postulate the formation of protonated intermediate **17** (in fact, it is a carbocation) or terminal alkene **18**, in which the final nucleophilic attack can proceed following the original favored trajectory. Thus, both the substituent influence and the stereochemical control of the reaction are in line with the suggested reaction mechanism.

In conclusion, the reaction studied is suitable for a wide range of starting salicylic aldehyde derivatives and 5-substituted 3-amino-1,2,4-triazoles, which allows obtaining an increased diversity of methanobenzoxadiazocines fused with 1,2,4-triazole ring and enlarges the scope of the Biginelli reaction. A plausible reaction mechanism rationalizing all known experimental data about such transformation is first proposed, which includes the formation of the Schiff bases between 3-amino-1,2,4-triazoles and salicylic aldehydes followed by the further reaction with enol form of acetone to form the tetrahydropyrimidine intermediates that give the final oxygen-bridged heterocycles *via* the above-discussed cascade of transformations.

Experimental

IR spectra were recorded in KBr pellets on a Shimadzu IR Prestige-21 Fourier spectrometer fitted with an attenuated total reflectance sampling accessory. ¹H and ¹³C NMR spectra and APT were registered on a Varian Inova 400 NMR spectrometer (400 and 100 MHz, respectively) in DMSO-*d*₆, internal standard TMS. ¹³C NMR spectra of compounds **11a,g,j,m,r,v,w** were registered in the APT

mode. Mass spectra were recorded with a Varian 1200L Triple Quadrupole GC/MS spectrometer (EI, 70 eV). Elemental analyses were performed on a vario MACRO cube CHNS elemental analyzer. Melting points were determined on a WRS-1B Digital Melting-point apparatus and were not corrected. Microwave experiments were carried out using a monomode Anton Paar Monowave 300 microwave reactor (2.45 GHz) in G10 microwave process vials. Reaction temperatures were monitored by an IR sensor. Microwave experiments were carried out in sealed microwave process vials (10 ml). After completion of the reaction, the vial was cooled to 50°C by air jet cooling. All reagents and solvents were purchased from commercial suppliers and used without further purification.

Synthesis of compounds 11a–w (General method). 3-Amino-1,2,4-triazole **8a–f** (1.0 mmol), *o*-hydroxybenzaldehyde **9a–e** (1.0 mmol), acetone (**10**) (0.22 ml, 3.0 mmol), and abs. EtOH (2 ml) were mixed in a microwave process vial, and then 4 N solution of HCl in dioxane (0.07 ml, 0.3 mmol) was added. The mixture was irradiated at 150°C for 30 min. The reaction mixture was cooled by an air flow and stirred for 24 h at room temperature for complete precipitation of the product. The precipitate was filtered off, washed with EtOH (1 ml) and Et₂O (3×1 ml), and dried. Compounds **1a–w** were obtained in a form of white solids.

2,5-Dimethyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11a). Yield 48%, mp 310–311°C. IR spectrum, ν , cm⁻¹: 757, 1091, 1138, 1325, 1485, 1548, 1625, 2885, 2922, 3070, 3421. ¹H NMR spectrum, δ , ppm: 7.76 (1H, s, NH); 7.33–7.26 (1H, m, H Ar); 7.20–7.12 (1H, m, H Ar); 6.98–6.90 (1H, m, H Ar); 6.82–6.76 (1H, m, H Ar); 4.52 (1H, s, 11-CH); 2.30 (2H, s, 13-CH₂); 2.02 (3H, s, 2-CH₃); 1.91 (3H, s, 5-CH₃). ¹³C NMR spectrum, δ , ppm: 157.3 (C); 153.9 (C); 151.0 (C); 130.0 (CH); 129.4 (CH); 124.4 (C); 121.2 (CH); 116.7 (CH); 82.3 (C); 44.3 (CH); 32.3 (CH₂); 24.0 (CH₃); 14.2 (CH₃). Mass spectrum, m/z : 242 [M]⁺. Found, %: C 64.34; H 5.54; N 23.29. C₁₃H₁₄N₄O. Calculated, %: C 64.45; H 5.82; N 23.12.

7-Methoxy-2,5-dimethyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11b). Yield 51%, mp 279–280°C. IR spectrum, ν , cm⁻¹: 734, 922, 1055, 1078, 1183, 1265, 1328, 1452, 1482, 1582, 1626, 2838, 2923, 3076, 3420. ¹H NMR spectrum, δ , ppm: 7.80 (1H, s, NH); 6.95–6.79 (3H, m, H Ar); 4.50 (1H, s, 11-CH); 3.70 (3H, s, OCH₃); 2.32–2.22 (2H, m, 13-CH₂); 2.02 (3H, s, 2-CH₃); 1.95 (3H, s, 5-CH₃). ¹³C NMR spectrum, δ , ppm: 157.6; 154.3; 148.4; 140.8; 125.2; 121.5; 121.3; 111.9; 82.5; 55.7; 44.7; 32.6; 24.4; 14.6. Mass spectrum, m/z : 272 [M]⁺. Found, %: C 61.64; H 5.46; N 20.96. C₁₄H₁₆N₄O₂. Calculated, %: C 61.75; H 5.92; N 20.57.

7-Ethoxy-2,5-dimethyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11c). Yield 55%, mp 259–260°C. IR spectrum, ν , cm⁻¹: 628, 850, 1031, 1088, 1129, 1269, 1332, 1504, 1552, 1625, 2944, 3070, 3141, 3226. ¹H NMR spectrum, δ , ppm (J , Hz): 7.89 (1H, s, NH); 6.94–6.79 (3H, m, H Ar); 4.49 (1H, br. s, 11-CH); 3.95 (2H, q, $J = 6.7$, OCH₂CH₃); 2.31–2.21 (2H, m, 13-CH₂); 2.01 (3H, s, 2-CH₃); 1.94 (3H, s, 5-CH₃); 1.30

(3H, t, $J = 6.8$, OCH_2CH_3). ^{13}C NMR spectrum, δ , ppm: 157.6; 154.2; 147.6; 141.0; 125.3; 121.6; 121.3; 113.1; 82.5; 64.1; 44.7; 32.6; 24.4; 15.1; 14.6. Mass spectrum, m/z : 286 $[\text{M}]^+$. Found, %: C 62.91; H 5.98; N 19.36. $\text{C}_{15}\text{H}_{18}\text{N}_4\text{O}_2$. Calculated, %: C 62.92; H 6.34; N 19.57.

8-Methoxy-2,5-dimethyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11d). Yield 35%, mp 263–264°C. IR spectrum, ν , cm^{-1} : 734, 922, 1055, 1078, 1183, 1265, 1328, 1452, 1482, 1582, 1626, 2838, 2923, 3076, 3420. ^1H NMR spectrum, δ , ppm (J , Hz): 7.81 (1H, br. s, NH); 7.21–7.13 (1H, m, H Ar); 6.58–6.48 (1H, m, H Ar); 6.41–6.33 (1H, m, H Ar); 4.46 (1H, d, $J = 2.7$, 11-CH); 3.67 (3H, s, OCH_3); 2.32–2.22 (2H, m, 13- CH_2); 2.01 (3H, s, 2- CH_3); 1.92 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 160.1; 157.3; 154.0; 152.0; 130.4; 116.7; 108.2; 101.2; 82.3; 55.2; 43.9; 32.6; 23.9; 14.2. Mass spectrum, m/z : 272 $[\text{M}]^+$. Found, %: C 61.34; H 5.54; N 20.29. $\text{C}_{14}\text{H}_{16}\text{N}_4\text{O}_2$. Calculated, %: C 61.75; H 5.92; N 20.58.

9-Bromo-2,5-dimethyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11e). Yield 53%, mp 280–281°C. IR spectrum, ν , cm^{-1} : 641, 762, 827, 868, 1090, 1138, 1326, 1473, 1484, 1547, 1619, 2938, 2990, 3065, 3420. ^1H NMR spectrum, δ , ppm: 7.90–7.83 (1H, m, NH); 7.49–7.44 (1H, m, H Ar); 7.33–7.29 (1H, m, H Ar); 6.80–6.74 (1H, m, H Ar); 4.58–4.53 (1H, m, 11-CH); 2.35–2.25 (2H, m, 13- CH_2); 2.00 (3H, s, 2- CH_3); 1.91 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 157.8; 154.2; 150.7; 132.6; 132.3; 127.2; 119.5; 112.8; 83.0; 44.3; 32.2; 24.1; 14.5. Mass spectrum, m/z : 322 $[\text{M}^{81}\text{Br}]^+$, 320 $[\text{M}^{79}\text{Br}]^+$. Found, %: C 48.50; H 3.90; N 17.25. $\text{C}_{13}\text{H}_{13}\text{BrN}_4\text{O}$. Calculated, %: C 48.62; H 4.08; N 17.44.

5-Methyl-2-pentyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11f). Yield 55%, mp 209–210°C. IR spectrum, ν , cm^{-1} : 757, 1091, 1138, 1325, 1485, 1548, 1625, 2885, 2922, 3070, 3421. ^1H NMR spectrum, δ , ppm (J , Hz): 7.88 (1H, s, NH); 7.32–7.25 (1H, m, H Ar); 7.20–7.13 (1H, m, H Ar); 6.98–6.91 (1H, m, H Ar); 6.85–6.78 (1H, m, H Ar); 4.52 (1H, d, $J = 2.8$, 11-CH); 2.34 (2H, t, $J = 7.7$, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 2.30 (2H, s, 13- CH_2); 1.93 (3H, s, 5- CH_3); 1.58–1.47 (2H, m) and 1.32–1.19 (4H, m, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 0.83 (3H, t, $J = 7.7$, $(\text{CH}_2)_4\text{CH}_3$). ^{13}C NMR spectrum, δ , ppm: 161.1; 153.9; 151.0; 129.9; 129.3; 124.4; 121.2; 116.7; 82.4; 44.3; 32.3; 31.1; 28.2; 27.2; 23.9; 21.9; 13.9. Mass spectrum, m/z : 298 $[\text{M}]^+$. Found, %: C 67.92; H 6.90; N 18.53. $\text{C}_{17}\text{H}_{22}\text{N}_4\text{O}$. Calculated, %: C 68.43; H 7.43; N 18.78.

7-Methoxy-5-methyl-2-pentyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11g). Yield 57%, mp 227–228°C. IR spectrum, ν , cm^{-1} : 742, 918, 1071, 1266, 1486, 1546, 1611, 2858, 2945, 3063, 3208. ^1H NMR spectrum, δ , ppm (J , Hz): 7.88 (1H, s, NH); 6.96–6.80 (3H, m, H Ar); 4.50 (1H, br. s, 11-CH); 3.70 (3H, s, OCH_3); 2.33 (2H, t, $J = 7.4$, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 2.27 (2H, s, 13- CH_2); 1.94 (3H, s, 5- CH_3); 1.58–1.48 (2H, m) and 1.32–1.19 (4H, m, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 0.88–0.79 (3H, m, $(\text{CH}_2)_4\text{CH}_3$). ^{13}C NMR spectrum, δ , ppm: 161.0 (C); 153.8 (C); 148.0 (C); 140.4 (C); 124.9 (C); 121.2 (CH); 121.0 (CH); 111.6 (CH); 82.2 (C); 55.4 (CH₃); 44.3 (CH); 32.3 (CH₂); 31.2 (CH₂); 28.2 (CH₂); 27.2 (CH₂); 24.0 (CH₃); 21.9 (CH₂); 14.0 (CH₃). Mass spectrum, m/z : 328 $[\text{M}]^+$. Found, %:

C 66.19; H 7.65; N 17.20. $\text{C}_{18}\text{H}_{24}\text{N}_4\text{O}_2$. Calculated, %: C 65.83; H 7.37; N 17.06.

7-Ethoxy-5-methyl-2-pentyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11h). Yield 62%, mp 209–210°C. IR spectrum, ν , cm^{-1} : 742, 924, 1049, 1068, 1195, 1262, 1472, 1544, 1625, 2885, 2938, 3065, 3237, 3420. ^1H NMR spectrum, δ , ppm (J , Hz): 7.82 (1H, s, NH); 6.93–6.79 (3H, m, H Ar); 4.50 (1H, br. s, 11-CH); 4.05–3.90 (2H, m, OCH_2CH_3); 2.35 (2H, t, $J = 7.0$, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 2.27 (2H, s, 13- CH_2); 1.94 (3H, s, 5- CH_3); 1.58–1.49 (2H, m) and 1.34–1.21 (7H, m, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$, OCH_2CH_3); 0.88–0.79 (3H, m, $(\text{CH}_2)_4\text{CH}_3$). ^{13}C NMR spectrum, δ , ppm: 161.0; 153.7; 147.2; 140.7; 125.0; 121.3; 120.9; 112.9; 82.2; 63.8; 44.3; 32.2; 31.1; 28.2; 27.2; 24.1; 21.9; 14.7; 13.9. Mass spectrum, m/z : 342 $[\text{M}]^+$. Found, %: C 66.36; H 7.25; N 15.95. $\text{C}_{19}\text{H}_{26}\text{N}_4\text{O}_2$. Calculated, %: C 66.64; H 7.65; N 16.36.

8-Methoxy-5-methyl-2-pentyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11i). Yield 31%, mp 169–170°C. IR spectrum, ν , cm^{-1} : 850, 977, 1092, 1132, 1270, 1445, 1502, 1614, 1620, 2937, 3067, 3017. ^1H NMR spectrum, δ , ppm (J , Hz): 7.79 (1H, br. s, NH); 7.22–7.12 (1H, m, H Ar); 6.57–6.48 (1H, m, H Ar); 6.40–6.34 (1H, m, H Ar); 4.46 (1H, d, $J = 2.7$, 11-CH); 3.67 (3H, s, OCH_3); 2.33 (2H, t, $J = 7.4$, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 2.27 (2H, s, 13- CH_2); 1.92 (3H, s, 5- CH_3); 1.58–1.48 (2H, m) and 1.33–1.19 (4H, m, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 0.90–0.78 (3H, m, $(\text{CH}_2)_4\text{CH}_3$). ^{13}C NMR spectrum, δ , ppm: 162.0; 160.1; 153.9; 152.0; 130.5; 116.7; 108.2; 101.2; 82.4; 55.2; 43.9; 32.6; 31.1; 28.3; 27.2; 23.9; 21.9; 13.9. Mass spectrum, m/z : 328 $[\text{M}]^+$. Found, %: C 65.91; H 7.88; N 17.36. $\text{C}_{18}\text{H}_{24}\text{N}_4\text{O}_2$. Calculated, %: C 65.83; H 7.37; N 17.06.

9-Bromo-5-methyl-2-pentyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11j). Yield 60%, mp 236–238°C. ^1H NMR spectrum, δ , ppm: 7.83 (1H, s, NH); 7.49–7.43 (1H, m, H Ar); 7.34–7.26 (1H, m, H Ar); 6.82–6.74 (1H, m, H Ar); 4.55 (1H, br. s, 11-CH); 2.39–2.24 (4H, m, 13- CH_2 , $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 1.91 (3H, s, 5- CH_3); 1.57–1.42 (2H, m) and 1.29–1.14 (4H, m, $\text{CH}_2(\text{CH}_2)_3\text{CH}_3$); 0.86–0.75 (3H, m, $(\text{CH}_2)_4\text{CH}_3$). ^{13}C NMR spectrum, δ , ppm: 161.6 (C); 154.1 (C); 150.7 (C); 132.6 (CH); 132.3 (CH); 127.3 (C); 119.5 (CH); 112.8 (C); 83.1 (C); 44.4 (CH); 32.2 (CH₂); 31.5 (CH₂); 28.6 (CH₂); 27.6 (CH₂); 24.1 (CH₃); 22.3 (CH₂); 14.3 (CH₃). Found, %: C 54.32; H 5.26; N 14.50. $\text{C}_{17}\text{H}_{21}\text{BrN}_4\text{O}$. Calculated, %: C 54.12; H 5.61; N 14.85.

5-Methyl-2-phenyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11k). Yield 52%, mp 295–297°C. IR spectrum, ν , cm^{-1} : 686, 735, 1085, 1147, 1344, 1444, 1621, 2873, 2959, 3039, 3429. ^1H NMR spectrum, δ , ppm: 8.24–8.19 (1H, m, NH); 7.91–7.87 (2H, m, H Ar); 7.43–7.30 (4H, m, H Ar); 7.20–7.14 (1H, m, H Ar); 6.99–6.93 (1H, m, H Ar); 6.87–6.82 (1H, m, H Ar); 4.63–4.59 (1H, m, 11-CH); 2.39 (2H, s, 13- CH_2); 2.04 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 158.6; 154.9; 151.3; 131.8; 130.3; 129.8; 129.3; 128.9 (2C); 126.0 (2C); 124.6; 121.8; 117.1; 83.3; 44.7; 32.6; 24.3. Found, %: C 71.21; H 5.12; N 18.24. $\text{C}_{18}\text{H}_{16}\text{N}_4\text{O}$. Calculated, %: C 71.04; H 5.30; N 18.41.

7-Methoxy-5-methyl-2-phenyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11l).

Yield 53%, mp 320–321°C. IR spectrum, ν , cm^{-1} : 650, 691, 732, 1075, 1267, 1344, 1439, 1485, 1614, 2931, 2961, 3112, 3207. ^1H NMR spectrum, δ , ppm: 8.23–8.17 (1H, m, NH); 7.90–7.85 (2H, m, H Ar); 7.61–7.56 (3H, m, H Ar); 6.92–6.82 (3H, m, H Ar); 4.63–4.59 (1H, m, 11-CH); 3.70 (3H, s, OCH_3); 2.43–2.32 (2H, m, 13- CH_2); 2.04 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 158.5; 154.8; 148.4; 140.6; 131.8; 129.3; 128.9 (2C); 126.0 (2C); 125.1; 121.5; 121.4; 112.0; 83.3; 55.7; 44.7; 32.6; 24.3. Mass spectrum, m/z : 334 $[\text{M}]^+$. Found, %: C 68.21; H 5.18; N 16.54. $\text{C}_{19}\text{H}_{18}\text{N}_4\text{O}_2$. Calculated, %: C 68.25; H 5.43; N 16.76.

7-Ethoxy-5-methyl-2-phenyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11m). Yield 55%, mp 269–271°C. IR spectrum, ν , cm^{-1} : 691, 743, 1045, 1071, 1115, 1266, 1343, 1470, 1504, 1582, 1612, 2922, 2980, 3059, 3173, 3220, 3502. ^1H NMR spectrum, δ , ppm (J , Hz): 8.06 (1H, br. s, NH); 7.90–7.85 (2H, m, H Ar); 7.47–7.30 (3H, m, H Ar); 6.98–6.78 (3H, m, H Ar); 4.59 (1H, br. s, 11-CH); 4.04–3.91 (2H, m, OCH_2CH_3); 2.41–2.34 (2H, m, 13- CH_2); 2.14–2.04 (3H, m, 5- CH_3); 1.30 (3H, t, $J = 6.3$, OCH_2CH_3). ^{13}C NMR spectrum, δ , ppm: 158.1 (C); 154.4 (C); 147.3 (C); 140.4 (C); 131.4 (C); 129.0 (CH); 128.6 (2CH); 125.7 (2CH); 124.9 (C); 121.2 (CH); 121.1 (CH); 112.8 (CH); 82.7 (C); 63.7 (CH_2); 44.3 (CH); 32.1 (CH_2); 24.1 (CH_3); 14.7 (CH_3). Mass spectrum, m/z : 348 $[\text{M}]^+$. Found, %: C 68.66; H 5.61; N 15.86. $\text{C}_{20}\text{H}_{20}\text{N}_4\text{O}_2$. Calculated, %: C 68.95; H 5.79; N 16.08.

9-Bromo-5-methyl-2-phenyl-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11n). Yield 57%, mp 284–285°C. IR spectrum, ν , cm^{-1} : 699, 754, 1047, 1138, 1342, 1480, 1615, 2885, 2925, 3056, 3421. ^1H NMR spectrum, δ , ppm: 8.15 (1H, s, NH); 7.91–7.83 (2H, m, H Ar); 7.50 (1H, s, H Ar); 7.42–7.28 (4H, m, H Ar); 6.85–6.78 (1H, m, H Ar); 4.64 (1H, br. s, 11-CH); 2.46–2.33 (2H, m, 13- CH_2); 2.03 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 158.7; 154.8; 150.7; 132.7; 132.4; 131.7; 129.4; 128.9 (2C); 127.1; 126.0 (2C); 119.6; 113.0; 83.6; 44.3; 32.1; 24.1. Found, %: C 56.04; H 4.05; N 15.04. $\text{C}_{18}\text{H}_{15}\text{BrN}_4\text{O}$. Calculated, %: C 56.41; H 3.95; N 14.62.

5-Methyl-2-(pyridin-2-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11o). Yield 52%, mp 338–337°C. IR spectrum, ν , cm^{-1} : 647, 754, 1089, 1131, 1345, 1481, 1586, 2869, 2962, 3040, 3142, 3200. ^1H NMR spectrum, δ , ppm: 8.57 (1H, br. s, NH); 8.30–8.19 (1H, m, H Ar); 7.94–7.74 (2H, m, H Ar); 7.40–7.26 (2H, m, H Ar); 7.21–7.11 (1H, m, H Ar); 7.02–6.90 (1H, m, H Ar); 6.87–6.76 (1H, m, H Ar); 4.67–4.56 (1H, m, 11-CH); 2.40 (2H, br. s, 13- CH_2); 2.03 (3H, s, 5- CH_3). Mass spectrum, m/z : 305 $[\text{M}]^+$. Found, %: C 67.13; H 4.51; N 23.09. $\text{C}_{17}\text{H}_{15}\text{N}_5\text{O}$. Calculated, %: C 66.87; H 4.95; N 22.94.

7-Methoxy-5-methyl-2-(pyridin-2-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11p). Yield 54%, mp 333–334°C. IR spectrum, ν , cm^{-1} : 750, 1048, 1131, 1266, 1483, 1605, 2931, 2962, 3061, 3154, 3396. ^1H NMR spectrum, δ , ppm: 8.61–8.56 (1H, m, NH); 8.30–8.25 (1H, m, H Ar); 7.91–7.78 (2H, m, H Ar); 7.38–7.32 (1H, m, H Ar); 6.91–6.81 (3H, m, H Ar); 4.63–4.58 (1H, m, 11-CH); 3.69 (3H, s, OCH_3); 2.41–2.36 (2H, m, 13- CH_2); 2.04 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 155.1 (2C); 154.3; 147.6; 140.7; 130.0; 127.2;

124.9; 124.5; 124.1; 121.7; 121.5; 113.2; 83.4; 64.1; 44.4; 32.1; 24.3. Mass spectrum, m/z : 335 $[\text{M}]^+$. Found, %: C 64.17; H 4.81; N 20.83. $\text{C}_{18}\text{H}_{17}\text{N}_5\text{O}_2$. Calculated, %: C 64.47; H 5.11; N 20.88.

7-Ethoxy-5-methyl-2-(pyridin-2-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11q). Yield 53%, mp 333–334°C. IR spectrum, ν , cm^{-1} : 598, 744, 1049, 1198, 1266, 1271, 1346, 1474, 1504, 1582, 1621, 2971, 3095, 3421. ^1H NMR spectrum, δ , ppm (J , Hz): 8.65–8.56 (1H, m, NH); 8.50–8.41 (1H, m, H Ar); 7.96–7.86 (1H, m, H Ar); 7.85–7.77 (1H, m, H Ar); 7.41–7.31 (1H, m, H Ar); 6.94–6.77 (3H, m, H Ar); 4.67–4.58 (1H, m, 11-CH); 4.00–3.86 (2H, m, OCH_2CH_3); 2.45–2.32 (2H, m, 13- CH_2); 2.10–2.01 (3H, m, 5- CH_3); 1.29 (3H, t, $J = 6.8$, OCH_2CH_3). ^{13}C NMR spectrum, δ , ppm: 158.5; 154.9; 150.3; 149.8; 147.6; 140.8; 137.2; 125.2; 124.2; 121.8; 121.6; 121.5; 113.1; 83.2; 64.1; 44.7; 32.4; 24.4; 15.1. Mass spectrum, m/z : 349 $[\text{M}]^+$. Found, %: C 65.51; H 5.26; N 20.16. $\text{C}_{19}\text{H}_{19}\text{N}_5\text{O}_2$. Calculated, %: C 65.32; H 5.48; N 20.04.

5-Methyl-2-(pyridin-3-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11r). Yield 60%, mp 280–282°C. ^1H NMR spectrum, δ , ppm: 9.02 (1H, s, H Ar); 8.59–8.50 (1H, m, NH); 8.31 (1H, s, H Ar); 8.20–8.11 (1H, m, H Ar); 7.45–7.37 (1H, m, H Ar); 7.34–7.26 (1H, m, H Ar); 7.21–7.11 (1H, m, H Ar); 6.99–6.90 (1H, m, H Ar); 6.86–6.79 (1H, m, H Ar); 4.62 (1H, br. s, 11-CH); 2.40 (2H, br. s, 13- CH_2); 2.04 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 156.5 (C); 155.0 (C); 151.2 (C); 150.3 (CH); 147.2 (CH); 133.3 (CH); 130.3 (CH); 129.9 (CH); 127.5 (C); 124.5 (C); 124.2 (CH); 121.9 (CH); 117.1 (CH); 83.4 (C); 44.6 (CH); 32.5 (CH_2); 24.2 (CH_3). Mass spectrum, m/z : 305 $[\text{M}]^+$. Found, %: C 66.55; H 4.99; N 22.51. $\text{C}_{17}\text{H}_{15}\text{N}_5\text{O}$. Calculated, %: C 66.87; H 4.95; N 22.94.

7-Methoxy-5-methyl-2-(pyridin-3-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11s). Yield 62%, mp 280–281°C. IR spectrum, ν , cm^{-1} : 753, 1072, 1270, 1484, 1583, 2941, 2962, 3017, 3189, 3420. ^1H NMR spectrum, δ , ppm: 9.02 (1H, s, H Ar); 8.59–8.51 (1H, m, NH); 8.32 (1H, s, H Ar); 8.21–8.12 (1H, m, H Ar); 7.47–7.37 (1H, m, H Ar); 6.94–6.78 (3H, m, H Ar); 4.60 (1H, br. s, 11-CH); 3.69 (3H, s, OCH_3); 2.37 (2H, br. s, 13- CH_2); 2.04 (3H, s, 5- CH_3). ^{13}C NMR spectrum, δ , ppm: 156.5; 154.9; 150.3; 148.4; 147.1; 140.6; 133.3; 127.5; 125.0; 124.2; 121.6; 121.5; 112.0; 83.2; 55.7; 44.6; 32.4; 24.3. Mass spectrum, m/z : 335 $[\text{M}]^+$. Found, %: C 64.21; H 5.14; N 20.51. $\text{C}_{18}\text{H}_{17}\text{N}_5\text{O}_2$. Calculated, %: C 64.47; H 5.11; N 20.88.

7-Ethoxy-5-methyl-2-(pyridin-3-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-*c*][1,3,5]benzoxadiazocine (11t). Yield 60%, mp 248–249°C. IR spectrum, ν , cm^{-1} : 750, 1050, 1069, 1199, 1268, 1470, 1504, 1582, 2978, 3080, 3369. ^1H NMR spectrum, δ , ppm (J , Hz): 9.10 (1H, br. s, H Ar); 8.86–8.82 (1H, m, NH); 8.76–8.71 (1H, m, H Ar); 8.65–8.57 (1H, m, H Ar); 7.98–7.92 (1H, m, H Ar); 6.92–6.80 (3H, m, H Ar); 4.65 (1H, br. s, 11-CH); 3.93 (2H, q, $J = 6.9$, OCH_2CH_3); 2.44–2.34 (2H, m, 13- CH_2); 2.07 (3H, s, 5- CH_3); 1.29 (3H, t, $J = 6.9$, OCH_2CH_3). ^{13}C NMR spectrum, δ , ppm: 159.9 (2C); 154.3; 147.6 (2C); 140.6; 140.1; 130.0; 127.2; 125.0; 121.7; 121.6; 113.2; 83.4; 64.1; 44.4; 32.1; 24.3; 15.1. Mass spectrum, m/z : 349 $[\text{M}]^+$.

Found, %: C 65.00; H 5.14; N 19.96. C₁₉H₁₉N₅O₂. Calculated, %: C 65.32; H 5.48; N 20.04.

5-Methyl-2-(pyridin-4-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11u). Yield 48%, mp 255–257°C. ¹H NMR spectrum, δ, ppm: 8.62–8.54 (2H, m, H Ar); 8.39–8.28 (1H, m, NH); 7.80–7.72 (2H, m, H Ar); 7.05–6.90 (4H, m, H Ar); 4.62 (1H, br. s, 11-CH); 3.34 (2H, br. s); 2.40 (2H, br. s, 13-CH₂); 2.03 (3H, s, 5-CH₃). ¹³C NMR spectrum, δ, ppm: 158.7; 155.2; 151.1; 150.6 (2C); 138.8; 124.5; 121.9; 120.4 (2C); 120.2; 120.1; 117.1; 83.5; 44.6; 32.4; 24.2. Found, %: C 66.55; H 4.80; N 23.17. C₁₇H₁₅N₅O. Calculated, %: C 66.87; H 4.95; N 22.94.

7-Methoxy-5-methyl-2-(pyridin-4-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11v). Yield 53%, mp 302–304°C. ¹H NMR spectrum, δ, ppm: 8.64–8.55 (2H, m, H Ar); 8.40–8.30 (1H, m, NH); 7.82–7.71 (2H, m, H Ar); 6.93–6.80 (3H, m, H Ar); 4.61 (1H, br. s, 11-CH); 3.70 (3H, br. s, OCH₃); 2.38 (2H, br. s, 13-CH₂); 2.05 (3H, s, 5-CH₃). ¹³C NMR spectrum, δ, ppm: 156.7 (C); 155.2 (C); 150.6 (2CH); 148.4 (C); 140.6 (C); 138.8 (C); 125.0 (C); 121.7 (CH); 121.5 (CH); 120.2 (2CH); 112.0 (CH); 83.3 (C); 55.7 (CH₃); 44.5 (CH); 32.3 (CH₂); 24.3 (CH₃). Found, %: C 64.30; H 4.90; N 20.59. C₁₈H₁₇N₅O₂. Calculated, %: C 64.47; H 5.11; N 20.88.

7-Ethoxy-5-methyl-2-(pyridin-4-yl)-11,12-dihydro-5,11-methano[1,2,4]triazolo[1,5-c][1,3,5]benzoxadiazocine (11w). Yield 58%, mp 273–274°C. ¹H NMR spectrum, δ, ppm (J, Hz): 8.64–8.55 (2H, m, H Ar); 8.40–8.32 (1H, m, NH); 7.81–7.74 (2H, m, H Ar); 6.92–6.79 (3H, m, H Ar); 4.60 (1H, br. s, 11-CH); 3.93 (2H, q, J = 6.9, OCH₂CH₃); 2.38 (2H, br. s, 13-CH₂); 2.05 (3H, s, 5-CH₃); 1.28 (3H, t, J = 6.6, OCH₂CH₃). ¹³C NMR spectrum, δ, ppm: 158.7 (C); 155.1 (C); 150.6 (2CH); 147.6 (C); 140.7 (C); 138.8 (C); 125.1 (C); 121.7 (CH); 121.5 (CH); 120.2 (2CH); 113.2 (CH); 83.3 (C); 64.1 (CH₂); 44.5 (CH); 32.3 (CH₂); 24.3 (CH₃); 15.1 (CH₃). Found, %: C 64.88; H 5.41; N 20.23. C₁₉H₁₉N₅O₂. Calculated, %: C 65.32; H 5.48; N 20.04.

Supplementary information file containing ¹H and ¹³C NMR spectral data of the obtained compounds **11a–w** is available at the journal website at <http://link.springer.com/journal/10593>.

The work was supported by Artvin Coruh University research project (BAP-2012.F19.02.24) and the Council of Higher Education of Turkey, Mevlana Exchange Program (MEV-2016-027).

References

- (a) Biginelli, P. *Gazz. Chim. Ital.* **1891**, *21*, 487. (b) Tron, G. C.; Minassi, A.; Appendino, G. *Eur. J. Org. Chem.* **2011**, 5541.
- (a) Kappe, C. O. *Tetrahedron* **1993**, *49*, 6937. (b) Suresh; Sandhu, J. S. *ARKIVOC* **2012**, (i), 66. (c) Heravi, M. M.; Asadi, S.; Lashkariani, B. M. *Mol. Diversity* **2013**, *17*, 389. (d) Barbero, M.; Cadamuro, S.; Dughera, S. *Green Chem.* **2017**, *19*, 1529.
- (a) Panda, S. S.; Khanna, P.; Khanna, L. *Curr. Org. Chem.* **2012**, *16*, 507. (b) Alvim, H. G. O.; Lima, T. B.; de Oliveira, A. L.; de Oliveira, H. C. B.; Silva, F. M.; Gozzo, F. C.; Souza, R. Y.; da Silva, W. A.; Neto, B. A. D. *J. Org. Chem.* **2014**, *79*, 3383.
- (a) Kappe, C. O. *Eur. J. Med. Chem.* **2000**, *35*, 1043. (b) Slobbe, P.; Ruijter, E.; Orru, R. V. A. *MedChemComm* **2012**, *3*, 1189. (c) de Fátima, Â.; Braga, T. C.; Neto, L. d. S.; Terra, B. S.; Oliveira, B. G. F.; da Silva, D. L.; Modolo, L. V. *J. Adv. Res.* **2015**, *6*, 363. (d) Sepehri, S.; Sanchez, H. P.; Fassih, A. *J. Pharm. Pharm. Sci.* **2015**, *18*, 1.
- (a) Dondoni, A.; Massi, A. *Acc. Chem. Res.* **2006**, *39*, 451. (b) Isambert, N.; Lavilla, R. *Chem.–Eur. J.* **2008**, *14*, 8444. (c) Wan, J.-P.; Liu, Y. *Synthesis* **2010**, 3943.
- (a) Svetlik, J.; Hanus, V.; Bella, J. *J. Chem. Res., Synop.* **1991**, 4. (b) Abbas, E. M. H.; Abdallah, S. M.; Abdoh, M. H.; Tawfik, H. A.; El-Hamouly, W. S. *Turk. J. Chem.* **2008**, *32*, 297. (c) Světlík, J.; Veizerová, L.; Kettmann, V. *Tetrahedron Lett.* **2008**, *49*, 3520. (d) El-Hamouly, W. S.; Tawfik, H. A.; Abbas, E. M. H. *Green Chem. Lett. Rev.* **2009**, *2*, 213. (e) Cheng, Q.; Wang, Q.; Xu, X.; Ruan, M.; Yao, H.; Yang, X. *J. Heterocycl. Chem.* **2010**, *47*, 624.
- (a) Chebanov, V. A.; Gura, K. A.; Desenko, S. M. *Top. Heterocycl. Chem.* **2010**, *23*, 41. (b) Chebanov, V. A.; Desenko, S. M. *Diversity-Oriented Synth.* **2012**, *1*, 43.
- (a) Svetlik, J.; Veizerová, L.; Mayer, T. U.; Catarinella, M. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4073. (b) Světlík, J.; Prónayová, N.; Švorc, L.; Frecer, V. *Tetrahedron* **2014**, *70*, 8354. (c) Tkachenko, V. V.; Muravyova, E. A.; Desenko, S. M.; Shishkin, O. V.; Shishkina, S. V.; Sysyov, D. O.; Müller, T. J. J.; Chebanov, V. A. *Beilstein J. Org. Chem.* **2014**, *10*, 3019. (d) Murlykina, M. V.; Sakhno, Y. I.; Desenko, S. M.; Shishkina, S. V.; Shishkin, O. V.; Sysyov, D. O.; Kornet, M. N.; Schols, D.; Goeman, J. L.; Van der Eycken, J.; Van der Eycken, E. V.; Chebanov, V. A. *Eur. J. Org. Chem.* **2015**, 4481. (e) Světlík, J.; Prónayová, N.; Frecer, V.; Cież, D. *Tetrahedron* **2016**, *72*, 7620.
- Sedash, Y. V.; Gorobets, N. Yu.; Chebanov, V. A.; Konovalova, I. S.; Shishkin, O. V.; Desenko, S. M. *RSC Adv.* **2012**, *2*, 6719.
- (a) Gorobets, N. Yu.; Sedash, Y. V.; Ostras, K. S.; Zaremba, O. V.; Shishkina, S. V.; Baumer, V. N.; Shishkin, O. V.; Kovalenko, S. M.; Desenko, S. M.; Van der Eycken, E. V. *Tetrahedron Lett.* **2010**, *51*, 2095. (b) Kondratiuk, M.; Gorobets, N. Yu.; Sedash, Y. V.; Gümüş, M. K.; Desenko, S. M. *Molbank* **2016**, *2016*, M898.
- Komykhov, S. A.; Bondarenko, A. A.; Musatov, V. I.; Diachkov, M. V.; Gorobets, N. Yu.; Desenko, S. M. *Chem. Heterocycl. Compd.* **2017**, *53*, 378. [*Khim. Geterotsikl. Soedin.* **2017**, *53*, 378.]
- Světlík, J.; Kettmann, V. *Tetrahedron Lett.* **2011**, *52*, 1062.
- Frolova, L. V.; Malik, I.; Uglinskii, P. Y.; Rogel', S.; Kornienko, A.; Magedov, I. V. *Tetrahedron Lett.* **2011**, *52*, 6643.
- Claridge, T. D. W.; Davies, S. G.; Polywka, M. E. C.; Roberts, P. M.; Russell, A. J.; Savory, E. D.; Smith, A. D. *Org. Lett.* **2008**, *10*, 5433.
- Chen, Q.; Jiang, L.-L.; Chen, C.-N.; Yang, G.-F. *J. Heterocycl. Chem.* **2009**, *46*, 139.
- (a) Kappe, C. O. *J. Org. Chem.* **1997**, *62*, 7201. (b) Alvim, H. G. O.; da Silva Júnior, E. N.; Neto, B. A. D. *RSC Adv.* **2014**, *4*, 54282.
- (a) Muravyova, E. A.; Desenko, S. M.; Rudenko, R. V.; Shishkina, S. V.; Shishkin, O. V.; Sen'ko, Y. V.; Vashchenko, E. V.; Chebanov, V. A. *Tetrahedron* **2011**, *67*, 9389. (b) Sakhno, Y. I.; Desenko, S. M.; Shishkina, S. V.; Shishkin, O. V.; Sysyov, D. O.; Groth, U.; Kappe, C. O.; Chebanov, V. A. *Tetrahedron* **2008**, *64*, 11041.
- Gümüş, M. K.; Gorobets, N. Yu.; Sedash, Y. V.; Shishkina, S. V.; Desenko, S. M. *Tetrahedron Lett.* **2017**, *58*, 3446.
- Cieplak, A. S. In *Structure Correlation*; Bürgi, H. B.; Dunitz, J. D., Eds.; Wiley-VCH: Weinheim, 2008, p. 205.
- Gilmore, K.; Alabugin, I. V. *Chem. Rev.* **2011**, *111*, 6513.
- Světlík, J.; Tureček, F.; Hanuš, V. *J. Chem. Soc., Perkin Trans. 1* **1987**, 563.