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Dihydro-2*H*-thiopyran-3(4*H*)-one-1,1-dioxide – a new cyclic ketomethylenic reagent for the Dimroth-type 1,2,3-triazole synthesis

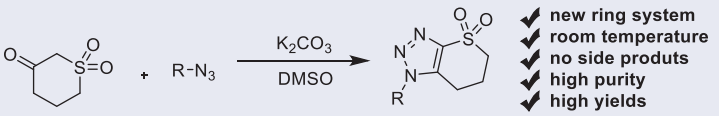
Nazariy T. Pokhodylo[a], Mykola A. Tupychak[a], and Vitalii A. Palchykov[b,c]

[a]Department of Organic Chemistry, Ivan Franko National University of Lviv, Lviv, Ukraine; [b]Research Institute of Chemistry and Geology, Oles Honchar Dnipro National University, Dnipro, Ukraine; [c]Department of Chemistry and Biochemistry, University of Texas at Dallas, Richardson, TX, USA

ABSTRACT

A series of 1,5,6,7-tetrahydrothiopyrano[2,3-*d*][1,2,3]triazole 4,4-dioxides, new triazole-based bicyclic ring system, were prepared via base-mediated click reaction of organic azides with the readily available dihydro-2*H*-thiopyran-3(4*H*)-one-1,1-dioxide. The reaction proceeded at room temperature in 5-12 h with catalysis by base-solvent system K_2CO_3/DMSO. High purity products were isolated by simple filtration and no formation of side products was observed. The key structure was confirmed by an X-ray study.

GRAPHICAL ABSTRACT



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Azide; click reaction; thiopyranone; 1,2,3-triazoles; sulfone

Introduction

The reaction of azides with activated ketomethylenic compounds is an efficient and convenient method for the preparation of 1*H*-1,2,3-triazole derivatives and, due to the introduction of protocols that meet the requirements of click chemistry, this type of reactions is currently in focus.[1] A large number of organic azides, including highly reactive electron-withdrawing azides such as unique perfluoroalkyl azides[2] or electron-deficient aromatic azides (azidofurazans,[3] 2-azidothiazoles,[4] 2-azidothiadiazole,[5] 2- and 4-azidopyrimidines,[6] 3-azido-1,2,4-triazine,[7] azido-1,3,5-triazines[8]), are used in the reaction due to new modified protocols. At the same time, new ketomethylenic compounds activated with the nitro,[2] sulfonyl,[9] phosphonate moiety[10] or electron-deficient aromatic ring[11] were applied in the Dimroth reaction in addition to the widely studied β-ketoesters, β-diketones and derivatives of cyanoacetic acid[12] enlarging the scope of reaction application.

CONTACT Nazariy T. Pokhodylo pokhodylo@gmail.com Department of Organic Chemistry, Ivan Franko National University of Lviv, Kyryla i Mefodiya St. 6, Lviv 79005, Ukraine

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While the Dimroth reaction is a well-researched subject area, some of its aspects (the recently discovered atypical attack of the azido group on the ester group instead of the keto group in β-ketoesters,[13] the regiocontrol of the reaction in case of asymmetric β-ketones, which is currently provided only when one of the diketone substituents is trifluoromethyl,[14] competing aromatization of intermediate triazolines,[10a] or the Regitz diazotransfer as side reaction[12]) are still studied insufficiently limiting a wide use of this reaction. Among the aforementioned reaction limitations, the competitive diazo transfer reaction is the most common and is always expected as a side process for cyclocondensation. The main reasons for the diazo transfer are: an anion asynchronous mechanism; high acidity of the methylene proton; high basicity of the internal nitrogen atom in intermediate triazine; low azide nucleophilicity (azides with an electron-withdrawing group); sterically hindered or conformationally restricted keto group.

In most cases, the side diazocompounds were found in the reactions of azides with cyclic β-diketones: dimedon, cyclohexanedione or 1,3-indandione, which had high CH-acidity and were conformationally restricted complicating an attack of azide on the carbonyl atom.[15] However, it was found that 6,7-dihydro-1*H*-benzo[*d*][1,2,3]triazole-4(5*H*)-ones could be obtained with high yields via cyclization of azides to substituted cyclohexane-1,3-diones using mild bases, such as triethylamine in catalytic amounts,[16] anhydrous magnesium carbonate in ethanol ($T = 20\,^{\circ}C$, 8 h),[3a] 1,1,3,3-tetramethylguanidine (TMG) in ethanol at 30 °C[17] or DBU in PEG-400 at 80 °C.[18] Other cyclic ketomethylenic compounds remain insufficiently studied. Ones of such reagents of practical interest is cyclic β-sulfoketone. It is noteworthy that 4-(arylsulfonyl)-1-aryl-5-methyl-1*H*-1,2,3-triazoles, namely 4-((4-(tert-butyl)phenyl)sulfonyl)-1-(2,5-dimethoxyphenyl)-5-methyl-1*H*-1,2,3-triazole, were found recently to be highly active pregnane X receptor modulators in the treatment of a disorder of uncontrolled cellular proliferation, such as cancer.[9d,e] Due to the concept of the lead-oriented synthesis and the increasing interest to conformationally restricted structures, ennobling of sulfonytriazole scaffold with $(CH_2)_n$-bridge might induce the biological activity of screening compounds. However, cyclic β-sulfoketones in the Dimroth-type reaction were not studied. Given the fact that the sulfonyl group is much larger than the keto group, it can create steric hindrance for the reaction to be realized as synchronous [3 + 2] cycloaddition and, as noted above, due to the significant CH-acidity of β-sulfoketone can lead to diazo transfer. Previously, β-sulfoketones have been commonly implemented in the Michael reaction. For example, dihydro-2*H*-thiopyran-3(4*H*)-one-1,1-dioxide has been used for creation of small libraries of new bicyclic systems, bearing a thiopyran-S,S-dioxide motif, via the base-catalyzed domino Knoevenagel–Michael-heterocyclization and demonstrated excellent reactivity as CH-acid.[19] Taking into account the above facts, cyclic β-sulfoketones were selected for the Dimroth-type 1,2,3-triazole synthesis as potential reagents for creating combinatorial libraries of new triazole derivatives and screening them for anticancer activity.[20]

Results and discussion

In this work, the cyclic ketones: dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide **1a**,[21] dihydrothiophen-3(2*H*)-one 1,1-dioxide **1b** and benzo[*e*][1,2]oxathiin-4(3*H*)-one 2,2-dioxide **1c**,[22] in which the sulfone group in structural $COCH_2SO_2$ moiety served as the

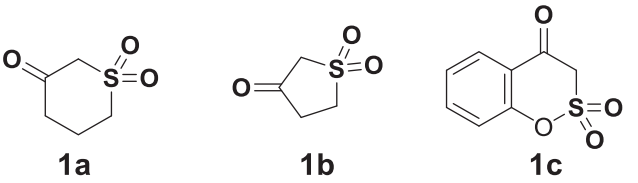
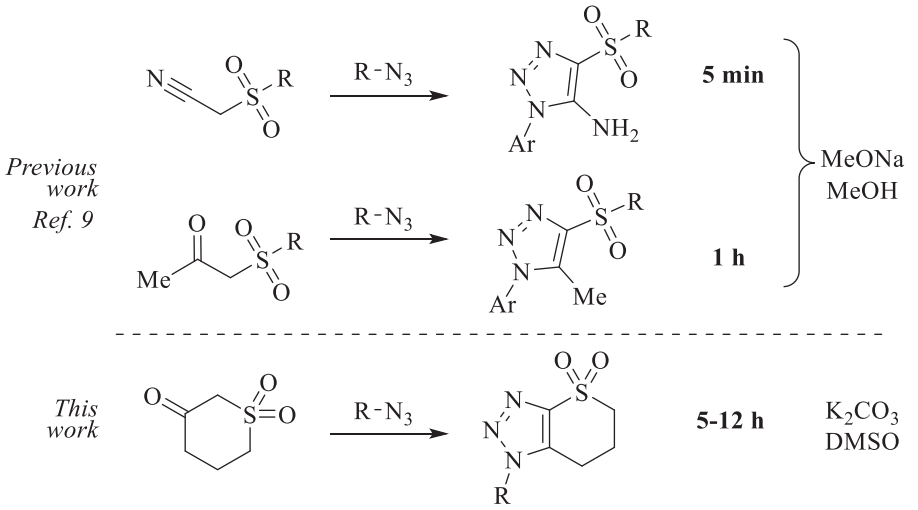


Figure 1. Selected cyclic β-sulfoketones.



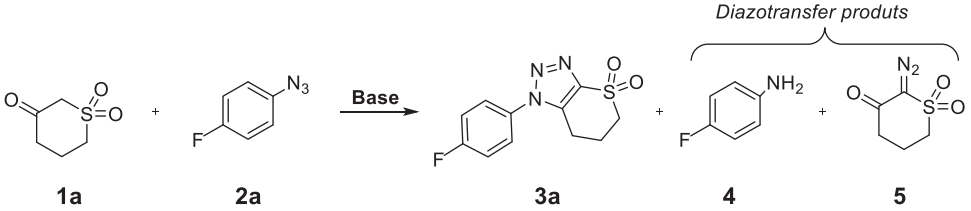
Scheme 1. Previously used and proposed reagents for 4-sulfonyl-1*H*-1,2,3-triazoles preparation

methylene group ketomethylenic activator (Figure 1), were studied in the Dimroth-type 1,2,3-triazole synthesis.

Previously, we have found that reactions of arylsulfoacetones and arylsulfoacetonitriles with azides rapidly occurred in the MeONa/MeOH and led to 4-sulfonyl-1*H*-1,2,3-triazoles in good or high yields at room temperature or after a brief heating and without the formation of side products (Scheme 1).[9a] Moreover, in case of sulfoacetonitrile, the reaction occurs at the time of mixing the reagents. Arylsulfoacetones reacts slower at room temperature. The conversion of azide to triazole ended within a few minutes at a heating or in 1 hour at room temperature depending on the substituent in arylazide.

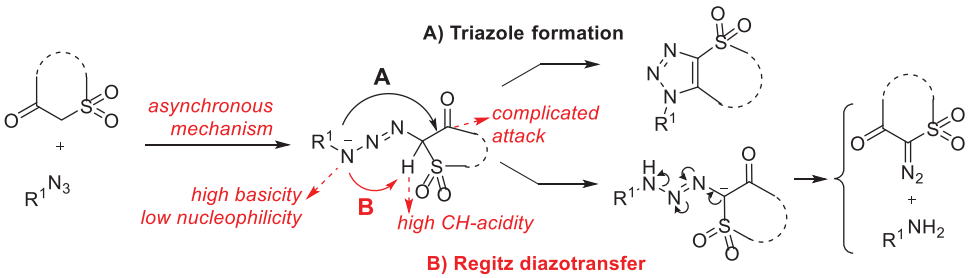
Based on the results of previous studies on base-mediated azides condensation reactions,[10a,13] the 4-fluorophenylazide **2** was selected for optimization studies for this cyclocondensation with dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide **1a** in five base-solvent system protocols (Table 1). All optimization experiments were performed at room temperature (approx. 20 °C) as required by click chemistry.[23] We found that the base-solvent system sufficiently affects the yields of triazole and side diazo transfer products formation. In MeONa/MeOH system, diazo transfer was indicated via formation of 4-flouroaniline **4** as the main reaction and no 1,2,3-triazole **3a** formation was observed. Tertiary amines, such as triethylamine in MeOH, led to the formation of 1,2,3-triazole **3a** with very low yield (up to 5%) after 12 h. Pyrrolidine/THF

Table 1. Optimization of the reaction conditions: effect of solvent and base.



Entry	Base/Solvent	Time, h	Triazole 3 yield, %[a,b]	Aniline 4 yield, %[a,b]
1	MeONa/MeOH	12	–	56
2	Et_3N/MeOH	12	5	–
3	Pyrrolidine/THF	12	29	–
4	DBU/THF	1	48	19
5	K_2CO_3/DMSO	7	87	–

[a]Isolated yields are given.
[b]Products determined by LC MS/APCI.



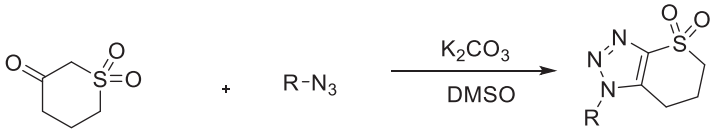
Scheme 2. Concurrent paths of triazole formation (A) vs. diazotransfer (B). Main factors.

demonstrated comparable catalytic activity to triethylamine providing the formation of triazole **3a** in 29% after 12 h. The 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) significantly increase the reaction and 48% of azide **2a** were converted into 1,2,3-triazole **3a** after 1 h, but more than 19% of 4-flouroaniline **4** were also found in the reaction medium. On the contrary, in the system of K_2CO_3/DMSO, the reaction of dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide **1a** occurs with the formation of triazole **3a** in high yield after 7 h. It is plausible to assume that K_2CO_3 acts not only as a base but also as a dehydrating agent accelerates the water elimination in intermediate triazoline creating what gives an advantage over other bases. It should be noted that the K_2CO_3/DMSO system was previously effective for electron-withdrawing azides[5] and sterically hindered azides.[24] On the other hand, the cyclic dihydrothiophen-3(2*H*)-one 1,1-dioxide **1b** and benzo[*e*][1,2]oxathiin-4(3*H*)-one 2,2-dioxide **1c** did not yield target triazoles under any of the tested for dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide **1a** conditions.

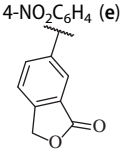
According to the reaction mechanism, probably, the limiting stage - the formation of a cyclic transition state in cases of strained conformations and low reacted aromatic ketone, becomes energetically unprofitable. The concurrent paths of the Dimroth and Regitz reactions can be represented by the following scheme (Scheme 2).

We used a wide range of azides **2** with substituents of different nature to validate the K_2CO_3/DMSO protocol. It was found that in all cases (Entry 1-7, Table 2) triazole **3**

Table 2. 1,5,6,7-Tetrahydrothiopyrano[2,3-*d*][1,2,3]triazole 4,4-dioxides.



1a **2a-g** **3a-g**

Entry	*R*	Time, h	Yield of 3, %[a]
1.	4-FC_6H_4 (**a**)	7	87
2.	3-ClC_6H_4 (**b**)	7	83
3.	3-$CF_3C_6H_4$ (**c**)	5	92
4.	3-$NO_2C_6H_4$ (**d**)	5	90
5.	4-$NO_2C_6H_4$ (**e**)	5	91
6.	 (**f**)	10	77
7.	Bn (**g**)	12	71

[a]Isolated yields are given.

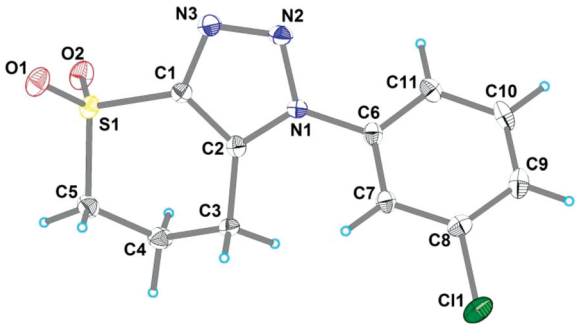


Figure 2. The molecular structure of 1-(3-chlorophenyl)-1,5,6,7-tetrahydrothiopyrano[2,3-*d*][1,2,3]triazole 4,4-dioxide **(3 b)** with displacement ellipsoids drawn at the 50% probability level. Selected bond distances: S1–C1 1.7439(18) Å, S1–C5 1.770(2) Å, S1–O1 1.4376(14) Å, S1–O2 1.4418(14) Å, C2–C3 1.489(3) Å, N1–C6 1.431(2) Å.

was the only product and no side products of the diazotransfer (4, 5) were observed. Moreover, the yield of triazoles from azides **2c–e** containing nitro and trifluoromethyl was the highest. The procedure was also tolerant to the furan ring in 6-azidoisobenzofuran-1(3*H*)-one **2f**,[25] but the triazole yield was slightly lower. The lowest yield was in case of benzyl azide **2g**, but no side products were isolated here.

The structure of compound **3b** was also proven by a single crystal X-ray diffraction analysis, the molecular drawing of which is shown in Figure 2. Single crystals of 1-(3-chlorophenyl)-1,5,6,7-tetrahydrothiopyrano[2,3-*d*][1,2,3]triazole 4,4-dioxide **(3b)** were obtained by slow dilution with water of the compound solution in DMSO. The compound **3b** crystallizes in the monoclinic space group $P2_1/c$ with one triazole molecule in the asymmetric unit. The 3-chlorophenyl and triazole rings are twisted relative to each other by 45.3(2)°. The tetrahydrothiopyran ring has a synclinal conformation relative to

the C3–C4 and C4–C5 bonds. The C2–C3–C4–C5 and C3–C4–C5–S1torsion angles are −53.6(2)° and 68.17(19)°, respectively.

Conclusion

Thus, it is shown that dihydro-2*H*-thiopyran-3(4*H*)-one-1,1-dioxide is a promising building block for the synthesis of triazole via the Dimroth reaction. Base solvent system K_2CO_3/DMSO allowed the annulation of triazole in a high yield which is an efficient route to new bicyclic thiopyrano[2,3-*d*][1,2,3]triazoles in one step and this is the first example of such a system. Results of the current study can be used both for the synthesis of polycyclic triazoles and evaluation of their biological activity.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on Varian Unity Plus 400 (400 and 101 MHz, respectively) and Bruker 170 Avance 500 (500 and 126 MHz, respectively) spectrometers in DMSO-d_6 solutions using TMS or the deuterated solvent as internal reference. Mass spectral analyses were performed using an Agilent 1100 series LC/MSD with API-ES/APCI mode (200 eV). Elemental analyses were accomplished using a Carlo Erba 1106 instrument. Melting points were determined on a Boetius melting point apparatus.

Synthesis of 1-aryl-1,5,6,7-tetrahydrothiopyrano[2,3-d][1,2,3]triazole 4,4-dioxide 3 (general procedure)

Potassium carbonate 2.8 g (0.02 mol) was added with vigorous stirring to a solution of azide **2** (0.01 mol) and dihydro-2*H*-thiopyran-3(4*H*)-one 1,1-dioxide **1** (1.5 g, 0.01 mol) in 5 mL of DMSO. The mixture was stirred at room temperature for 5-12 h (see Table 2) (the consumption of the starting azide was monitored by TLC) and diluted with 25 mL of water, and the precipitate was filtered off.

1-(4-Fluorophenyl)-1,5,6,7-tetrahydrothiopyrano[2,3-d][1,2,3]triazole 4,4-dioxide (3a)

Yield: 87% as a white solid; mp 238–239°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02–7.67 (m, 2H), 7.65–7.24 (m, 2H), 3.78–3.44 (m, 2H), 3.15–2.76 (m, 2H), 2.53–2.18 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 161.06 (d, $^1J_{C-F}$=257.9 Hz), 143.29 ($C_{triazole}$-4), 139.40 ($C_{triazole}$-5), 131.96 (C_{Ar}-1), 127.57 (d, $^3J_{C-F}$ = 9.0 Hz, 2xCH_{Ar}-2,6), 117.40 (d, $^2J_{C-F}$ = 22.7 Hz, 2xCH_{Ar}-3,5), 52.01 (CH_2), 21.45 (CH_2), 20.98 (CH_2); MS (*m/z*, APCI) 469.0 (M^+ + 1); Anal. calcd for $C_{11}H_{10}FN_3O_2S$: C, 49.43; H, 3.77; N, 15.72. Found: C, 49.49; H, 3.71; N, 15.78.

Single crystal X-ray diffraction study of compound 3 b

Diffraction data for compound **3b** were collected on an Agilent Gemini A four-circle diffractometer equipped with an Atlas CCD detector with MoK_α radiation (λ = 0.71073 Å). The collected diffraction data were processed with the CrysAlis PRO program.[26] The structure was solved by ShelXT and refined by least squares method

on F^2 by ShelXL software with the following graphical user interface of OLEX^2.[27] Atomic displacements for non-hydrogen atoms were refined using an anisotropic model. Hydrogen atoms were situated on geometrically calculated positions and refined as riding atoms with relative isotropic displacement parameters. The complete crystallographic dataset was deposited at the Cambridge Crystallographic Data Center (deposit CCDC 1983912).

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ORCID

Nazariy T. Pokhodylo http://orcid.org/0000-0001-8222-5008
Mykola A. Tupychak http://orcid.org/0000-0002-9880-0983
Vitalii A. Palchykov http://orcid.org/0000-0003-3748-4566

References

[1] Jalani, H. B.; Karagöz, A. C.; Tsogoeva, S. B. Synthesis of Substituted 1,2,3-Triazoles via Metal-Free Click Cycloaddition Reactions and Alternative Cyclization Methods. *Synthesis.* **2016**, *49*, 29–41. DOI: 10.1055/s-0036-1588904.

[2] Blastik, Z. E.; Klepetářová, B.; Beier, P. Enamine-Mediated Azide-Ketone [3 + 2] Cycloaddition of Azidoperfluoroalkanes. *Chemistry Select.* **2018**, *3*, 7045–7048. DOI: 10.1002/slct.201801344.

[3] (a) Batog, L. V.; Rozhkov, V. Y.; Struchkova, M. I. Azido-1,2,5-Oxadiazoles in Reactions with 1,3-Dicarbonyl Compounds. *Mendeleev Commun.* **2002**, *12*, 159–161. DOI: 10.1070/MC2002v012n04ABEH001589. (b) Olesen, P. H.; Sørensen, A. R.; Ursø, B.; Kurtzhals, P.; Bowler, A. N.; Ehrbar, U.; Hansen, B. F. Synthesis and in Vitro Characterization of 1-(4-Aminofurazan-3-yl)-5-Dialkylaminomethyl-*1H*-[1,2,3]Triazole-4-Carboxylic Acid Derivatives. A New Class of Selective GSK-3 Inhibitors. *J. Med. Chem.* **2003**, *46*, 3333–3341. DOI: 10.1021/jm021095d.

[4] Pokhodylo, N. T.; Savka, R. D.; Pidlypnyi, N. I.; Matiychuk, V. S.; Obushak, M. D. Synthesis of 2-Azido-1,3-Thiazoles as 1,2,3-Triazole Precursors. *Synth. Commun.* **2010**, *40*, 391–399. DOI: 10.1080/00397910902981274.

[5] Pokhodylo, N. T.; Shyyka, O. Y.; Savka, R. D.; Obushak, M. D. 2-Azido-1,3,4-Thiadiazoles, 2-Azido-1,3-Thiazoles, and Aryl Azides in the Synthesis of 1,2,3-Triazole-4-Carboxylic Acids and Their Derivatives. *Russ. J. Org. Chem.* **2018**, *54*, 1090–1099. DOI: 10.1134/S1070428018070205.

[6] Krivopalov, V. P.; Nikolaenkova, E. B.; Sedova, V. F.; Mamaev, V. P. Reaction of Aryl-Substituted Azidopyrimidines with 1,3-Dicarbonyl Compounds. *Chem. Heterocycl. Compd.* **1983**, *19*, 1116–1120. DOI: 10.1007/BF00505770.

[7] El-Khoshnieh, Y. O. Reactions of 1,2,4-Triazine Azides with α-Keto and α-Ester Phosphorus Ylides. Synthesis of Some New 1-Rtiazolo-1,2,3-Triazoles. *Heterocycl. Commun.* **1999**, *5*, 77–82. DOI: 10.1515/HC.1999.5.1.77.

[8] (a) Yan, Z.; Li, Y.; Ma, M. Solvent-Directed Click Reaction Between Active Methylene Compounds and Azido-1,3,5-Triazines. *Org. Lett.* **2019**, *21*, 7204–7208. DOI: 10.1021/acs.orglett.9b02089. (b) Azev, Y. A.; Loginova, I. P.; Guselnikova, O. L.; Shorshnev, S. V.; Rusinov, V. L.; Chupakhin, O. N. Reactions of Diazido Derivatives of s-Triazine with C-Nucleophiles. *Mendeleev Commun* **1994**, *4*, 104–107. DOI: 10.1070/MC1994v004n03ABEH000371. (c) Nikolaenkova, E. B.; Krivopalov, V. P. Synthesis of 4,6-Bis(1*H*-1,2,3-Triazolyl)Pyrimidines by the Reaction of 4,6-Diazido-2-(4-Methoxyphenyl)-Pyrimidine with Compounds Containing a Reactive Methylene Group. *Chem. Heterocycl. Compd.* **1997**, *33*, 968–972. DOI: 10.1007/BF02253171.

[9] (a) Pokhodylo, N. T.; Matiychuk, V. S.; Obushak, M. D. (Arylsulfonyl)Acetones and -Acetonitriles: New Activated Methylenic Building Blocks for Synthesis of 1,2,3-Triazoles. *Synthesis.* **2009**, *2009*, 2321–2323. DOI: 10.1055/s-0029-1216850. (b) Saraiva, M. T.; Costa, GaP.; Seus, N.; Schumacher, R. F.; Perin, G.; Paixão, M. W.; Luque, R.; Alves, D. Room-Temperature Organocatalytic Cycloaddition of Azides with *β*-Keto Sulfones: Toward Sulfonyl-1,2,3-Triazoles. *Org. Lett.* **2015**, *17*, 6206–6209. DOI: 10.1021/acs.orglett.5b03196. (c) Ramírez-Villalva, A.; González-Calderón, D.; Rojas-García, R. I.; González-Romero, C.; Tamaríz-Mascarúa, J.; Morales-Rodríguez, M.; Zavala-Segovia, N.; Fuentes-Benítes, A. Synthesis and Antifungal Activity of Novel Oxazolidin-2-One-Linked 1,2,3-Triazole Derivatives. *Med. Chem. Commun.* **2017**, *8*, 2258–2262. DOI: 10.1039/C7MD00442G. (d) Lin, W.; Wang, Y.-M.; Chai, S. C.; Lv, L.; Zheng, J.; Wu, J.; Zhang, Q.; Wang, Y. D.; Griffin, P. R.; Chen, T. SPA70 is a Potent Antagonist of Human Pregnane X Receptor. *Nat. Commun.* **2017**, *8*, 741. DOI: 10.1038/s41467-017-00780-5. (e) Chen, T.; Lin, W.; Wang, Y. 1,4,5-Substituted 1,2,3-Triazole Analogues as Antagonists of the Pregnane X Receptor. Patent US20190077770 A1, 2019.

[10] (a) Pokhodylo, N. T.; Shyyka, O. Y.; Goreshnik, E. A.; Obushak, M. D. 4-Phosphonated or 4-Free 1,2,3-Triazoles: What Controls the Dimroth Reaction of Arylazides with 2-Oxopropylphosphonates? *Chemistry Select.* **2020**, *5*, 260–264. DOI: 10.1002/slct.201904688. (b) González-Calderón, D.; Fuentes-Benítes, A.; Díaz-Torres, E.; González-González, C. A.; González-Romero, C. Azide–Enolate 1,3-Dipolar Cycloaddition as an Efficient Approach for the Synthesis of 1,5-Disubstituted 1,2,3-Triazoles from Alkyl/Aryl Azides and *β*-Ketophosphonates. *Eur. J. Org. Chem.* **2016**, *2016*, 668–672. DOI: 10.1002/ejoc.201501465.

[11] (a) L'Abbé, G.; Luyten, I.; Vercauteren, K.; Dehaen, W. Study of the Diazoimine/Triazole Equilibria for Substituted Oxazoles and Oxadiazoles. *Bull. Soc. Chim. Belges.* **2010**, *102*, 683–684. DOI: 10.1002/bscb.19931021010. (b) Pokhodylo, N. T.; Shyyka, O. Y. 1-(5-(R-Amino)-1,2,4-Thiadiazol-3-yl)Propan-2-Ones – Convenient Ketomethylenic Reagents for the Gewald and Dimroth Reactions. *J. Heterocyclic Chem.* **2014**, *51*, 1487–1490. DOI: 10.1002/jhet.1719. (c) Pokhodylo, N. T.; Matiychuk, V. S.; Obushak, M. D. Synthesis of the 1*H*-1,2,3-Triazole Derivatives by the Cyclization of Arylazides with 1-(1,3-Benzothiazol-2-yl)Acetone, 1,3-Benzothiazol-2-Ylacetonitrile and (4-Aryl-1,3-Thiazol-2-yl)Acetonitrile. *Chem. Heterocycl. Comp*. **2009**, *45*, 483–488. DOI: 10.1007/s10593-009-0287-6.

[12] (a) Krivopalov, V. P.; Shkurko, O. P. 1,2,3-Triazole and Its Derivatives. Development of Methods for the Formation of the Triazole Ring. *Russ. Chem. Rev.* **2005**, *74*, 339–379. DOI: 10.1070/RC2005v074n04ABEH00089. (b) Pokhodylo, N. T.; Matiychuk, V. S.; Obushak, M. D. Synthesis of Triazoles via Regioselective Reactions of Aryl Azides with Cyanoacetyl Pyrroles and Indoles. *Synthesis.* **2009**, *2009*, 1297–1300. DOI: 10.1055/s-0028-1087992.

[13] Pokhodylo, N. T.; Shyyka, O. Y.; Matiychuk, V. S.; Obushak, M. D.; Pavlyuk, V. V. A Novel Base-Solvent Controlled Chemoselective Azide Attack on an Ester Group versus

Keto in Alkyl 3-Substituted 3-Oxopropanoates: Mechanistic Insights. *ChemistrySelect*. **2017**, *2*, 5871–5876. DOI: 10.1002/slct.201700577.

[14] Rozin, Y. A.; Leban, J.; Dehaen, W.; Nenajdenko, V. G.; Muzalevskiy, V. M.; Eltsov, O. S.; Bakulev, V. A. Regioselective Synthesis of 5-Trifluoromethyl-1,2,3-Triazoles via CF_3-Directed Cyclization of 1-Trifluoromethyl-1,3-Dicarbonyl Compounds with Azides. *Tetrahedron*. **2012**, *68*, 614–618. DOI: 10.1016/j.tet.2011.10.110.

[15] Benati, L.; Montevecchi, P. C.; Spagnolo, P.; Foresti, E. Synthesis and Reactivity of 4-Acyl-5-Hydroxytriazolines Resulting from Thermal Reaction of Aryl and Tosyl Azides with 2-Substituted Indane-1,3-Diones. *J. Chem. Soc, Perkin Trans. 1*. **1992**, *1992*, 2845–2850. DOI: 10.1039/P19920002845.

[16] Gorup, A.; Kovačič, M.; Kranjc-Škraba, B.; Mihelčič, B.; Simonič, S.; Stanovnik, B.; Tišler, M. Reactions of Azidoazolopyridazines with 1,3-Dicarbonyl Compounds. *Tetrahedron*. **1974**, *30*, 2251–2255. DOI: 10.1016/S0040-4020(01)97366-1.

[17] Ahmadi, F.; Tisseh, Zeinab, N.; Dabiri, M.; Bazgir, A. Efficient TMG Catalyzed Synthesis of 1,2,3-Triazoles. *C. R. Chim*. **2013**, *16*, 1086–1090. DOI: 10.1016/j.crci.2013.05.006.

[18] Singh, H.; Khanna, G.; Khurana, J. M. DBU Catalyzed Metal Free Synthesis of Fused 1,2,3-Triazoles through [3 + 2] Cycloaddition of Aryl Azides with Activated Cyclic C-H Acids. *Tetrahedron Lett*. **2016**, *57*, 3075–3080. DOI: 10.1016/j.tetlet.2016.05.082.

[19] Palchykov, V. A.; Chabanenko, R. M.; Konshin, V. V.; Dotsenko, V. V.; Krivokolysko, S. G.; Chigorina, E. A.; Horak, Y. I.; Lytvyn, R. Z.; Vakhula, A. A.; Obushak, M. D.; et al. Dihydro-2*H*-Thiopyran-3(*4H*)-One-1,1-Dioxide – a Versatile Building Block for the Synthesis of New Thiopyran-Based Heterocyclic Systems. *New J. Chem*. **2018**, *42*, 1403–1412. DOI: 10.1039/C7NJ03846A.

[20] (a) Pokhodylo, N. T.; Shyyka, O. Y.; Matiychuk, V. S. Synthesis and Anticancer Activity Evaluation of New 1,2,3-Triazole-4-Carboxamide Derivatives. *Med. Chem. Res*. **2014**, *23*, 2426–2438. DOI: 10.1007/s00044-013-0841-8. (b) Shyyka, O. Y.; Pokhodylo, N. T.; Finiuk, N. S. Anticancer Activity Evaluation of Thieno[3,2-*e*][1,2,3]Triazolo[1,5-*a*]Pyrimidines and Thieno[2,3-*e*][1,2,3]Triazolo[1,5-*a*]Pyrimidine Derivatives. *Biopolym. Cell*. **2019**, *35*, 321–330. DOI: 10.7124/bc.000A0F. (c) Pokhodylo, N. T.; Shyyka, O. Y.; Matiychuk, V. S. Synthesis of 1,2,3-Triazole Derivatives and Evaluation of Their Anticancer Activity. *Sci. Pharm*. **2013**, *81*, 663–676. DOI: 10.3797/scipharm.1302-04.

[21] (a) Kozirev, E. K.; Palchykov, V. A. Thiopyran-3-One-1,1-Dioxides in the Synthesis of Heterocycles. *Chem Heterocycl Comp*. **2019**, *55*, 349–351. DOI: 10.1007/s10593-019-02463-z. (b) Chabanenko, R. M.; Mykolenko, S. Y.; Kozirev, E. K.; Palchykov, V. A. Multigram Scale Synthesis of 3,4- and 3,6-Dihydro-2*H*-Thiopyran 1,1-Dioxides and Features of Their NMR Spectral Behaviour. *Synth. Commun*. **2018**, *48*, 2198–2205. DOI: 10.1080/00397911.2018.1486427.

[22] Grygoriv, G. V.; Lega, D. A.; Chernykh, V. P.; Zaprutko, L.; Gzella, A. K.; Pawełczyk, A.; Shemchuk, L. A. 1,2-Benzoxathiin-4(*3H*)-One 2,2-Dioxide – New Enol Nucleophile in Three-Component Interaction with Benzaldehydes and Active Methylene Nitriles. *RSC Adv*. **2018**, *8*, 37295–37302. DOI: 10.1039/C8RA06801A.

[23] Xi, W.; Scott, T. F.; Kloxin, C. J.; Bowman, C. N. Click Chemistry in Materials Science. *Adv. Funct. Mater*. **2014**, *24*, 2572–2590. DOI: 10.1002/adfm.201302847.

[24] (a) Pokhodylo, N. T.; Obushak, M. D. A Convenient Synthesis of [1,2,3]Triazolo[1,5-a]Quinolone. *Russ. J. Org. Chem*. **2019**, *55*, 1241–1243. DOI: 10.1134/S107042801908027X. (b) Pokhodylo, N. T.; Shyyka, O. Y.; Obushak, M. D. Convenient Synthetic Path to Ethyl 1-Aryl-5-Formyl-1*H*-1,2,3-Triazole-4-Carboxylates and 1-Aryl-1,5-Dihydro-4*H*-[1,2,3]Triazolo[4,5-*d*]Pyridazin-4-Ones. *Chem. Heterocycl. Comp*. **2018**, *54*, 773–779. DOI: 10.1007/s10593-018-2348-1.

[25] Pokhodylo, N. T.; Matiychuk, V. S.; Obushak, M. D. Synthesis of Isothiocoumarin Derivatives. *Chem. Heterocycl. Comp*. **2010**, *46*, 140–145. DOI: 10.1007/s10593-010-0484-3.

[26] Agilent. CrysAlisPRO. *Oxford Diffraction/Agilent Technologies UK Ltd*, Yarnton, Oxfordshire, England, 2014.

[27] (a) Sheldrick, G. M. SHELXT – Integrated Space-Group and Crystal-Structure Determination. *Acta Crystallogr. A Found. Adv.* **2015**, *71*, 3–8. DOI: 10.1107/S2053273314026370. (b) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Crystallogr.* **2009**, *42*, 339–341. DOI: 10.1107/S0021889808042726.