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SYNTHESIS OF SUBSTITUTED 1,3-DIHYDROPIROROLO[3,4-*F*]INDOL-2,5,7-TRIONS

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Abstract. *The paper concerns the development of the method for the preparation of functional isoindole-1,3-diones derivatives based on 5-nitro-4-phenacylphthalonitriles using Schmidt rearrangement.*

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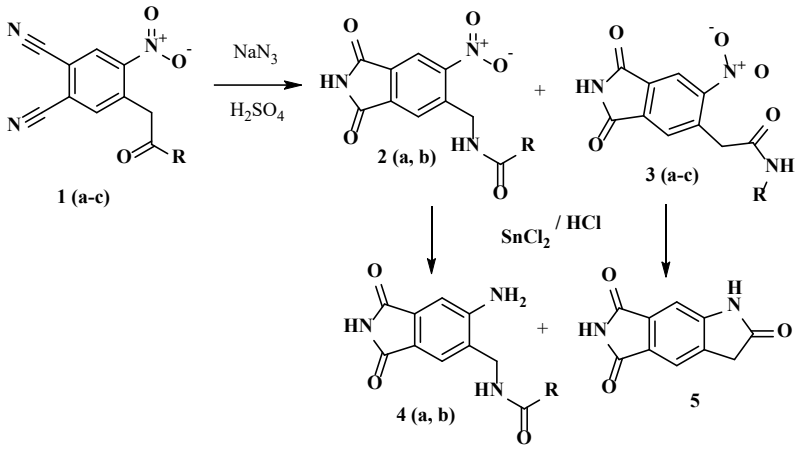
Introduction

The interaction of ketones of various structures with hydrogen acids is known as Schmidt's rearrangement. This reaction is widely used in organic synthesis [1] to produce a variety of amides, including isomers [2, 3], as well as analogues of natural products [4, 5]. However, its application to the rearrangement of ketones containing an isoindole-1,3-dione or phthalonitrile fragment is not described in the scientific literature. It is known that various substituted isoindole-1,3-diones or phthalimides can be used as drugs (thalidomide being the best known among them [6]), inhibitors of certain enzymes used for the treatment of various forms of cancer [7-9]. In addition, the use of these compounds to treat Alzheimer's disease [10] and various forms of depression [11] and the use as anti-inflammatory agents [12] are also known. In order to summarize the above, it can be concluded that nitrogen-containing heterocyclic systems of different structures still attract the attention of chemists [13-16].

The purpose of the study is development of the method for the synthesis of substituted amides containing the isoindole-1,3-dione fragment using Schmidt rearrangement in the presence of sulfuric acid and study the properties of the synthesized compounds. Earlier, we developed a method for the synthesis of similar amides using polyphosphoric acid (PPA) [17]. In terms of economics, replacing PPA with sulfuric acid is technologically more attractive as it reduces the cost of the target products.

Main body

For Schmidt rearrangement, ketones of different structures and sodium azide are often used in the presence of Bransted or Lewis acids [18], which sometimes act as solvents [1, 19] and promoters. In order to achieve our purpose, we proposed to use the previously synthesized 5-nitro-4-phenacylphthalonitriles [20] in the Schmidt reaction. The interaction of substrate **1 (a-c)** with twice the excess sodium azide in the presence of 80% H_2SO_4 was conducted at 90-100 °C for 3.5-5 hours. The non-selective Schmidt rearrangement of the carbonyl group and hydrolysis of two cyanogroups of 5-nitro-4-phenacylphthalonitriles to the corresponding isoindole-1,3-dions were proceeded simultaneously (so called *one-pot* reaction) (see Scheme below).



1 - **4**: **a** – R=C_6H_5; **b** – R=4-MeC_6H_4; **c** – R=4-$MeOC_6H_4$

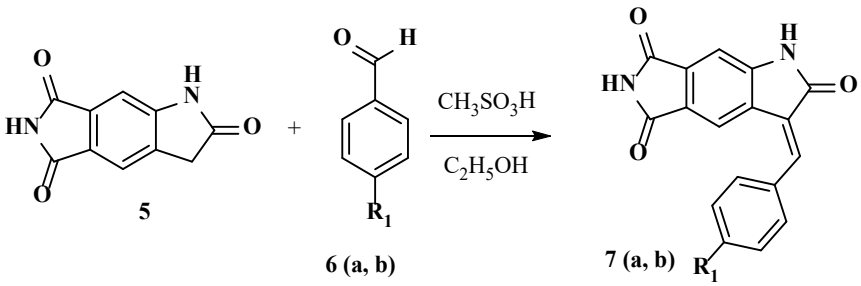
We found that when sulfuric acid was used as solvent, as in the reaction with PPA, a mixture of isomeric products **2 (a, b)** and **3 (a, b)** was formed. For substrate **1c** (R=4-$MeOC_6H_4$) the dominant formation of amide **3c** (over 95%) was observed. Varying the reaction temperature had no significant effect on the isomer ratio (determined from the characteristic signals of the amide protons in the ^{1}H NMR spectra). In addition, it should be noted that further hydrolysis of the isoindole-1,3-diones occurs when the reaction temperature rises above 100 °C, leading to the formation of dicarboxylic acids in yields up to 15%. Earlier we showed, that upon prolonged heating of 5-nitro-4-phenacylphthalonitrile **1 (a-c)** in sulfuric acid hydrolysis of cyanogroups proceeds with formation of corresponding dicarboxylic acids [21].

In general, the reaction considered can be divided into two: the first one is the hydrolysis of the cyanogroups of 5-nitro-4-phenacylphthalonitriles to the corresponding isoindole-1,3-dions; the second one is the Schmidt rearrangement of the resulting isoindole-1,3-dions under reaction conditions. It was found that the hydrolysis of cyanogroups is a slower step, so the above conditions were the most appropriate for the *one-pot* reaction.

The separation of the mixture of isomeric amides **2** and **3** was quite difficult. Nevertheless, after reduction of the above products by tin chloride according to the previously described procedure [20] the formation of amines **4 (a, b)** and pyrrolo[3,4-*f*]indole-2,5,7(1*H*,3*H*,6*H*)-trion **5** was observed. Thus, these compounds could be readily separated by recrystallization from alcohol, as structure **5** was slightly soluble in it. The formation of pyrroloindole **5** during the reduction of amides **3 (a-c)** can probably be explained by the fact that the reaction involves intramolecular transamination followed by the elimination of the aromatic amine.

The structure of synthesized compounds **2**, **3** and **4** was confirmed by NMR spectroscopy and mass spectrometry data and agreed with similar compounds synthesized by the method [17], the yields of these products also slightly differ from those obtained earlier.

Pyrrolo[3,4-*f*]indole-2,5,7-trion **5** was of most interest as a potential building-block for the creation of BAS, so its chemical properties were investigated using aldol-croton condensation with aromatic aldehydes under acid catalysis. The interaction of pyrroloindole **5** with compounds **6 (a, b)** was conducted in alcohol in the presence of catalytic amounts of methanesulfonic acid at 60-80 °C for 2.5-3.5 hours (see Scheme below). The reaction under study resulted by the formation of 3-substituted 1,3-dihydropyrrolo[3,4-*f*]indole-2,5,7-**trions 7** (a, b) as major products which, according to *1*H NMR spectroscopy, represented a mixture of ^{E}/*Z* isomers in the ratio 1:2.



6, 7: **a** – R=Cl; **b** – R=OMe

The structure of all the synthesized compounds was confirmed by combined NMR and mass spectrometry data. During the reduction of compounds **3 (a-c)**, the formation of pyrroloindoltrion **5** was observed in all cases with characteristic NH-proton signals in the region of 10.94 ppm and 11.09 ppm. Precise correlation of *E*/*Z* isomers of structures **7 (a, b)** was also made using the *NOESY* spectrum of compound **7a** (Fig. 1). For both isomers a cross-peak of 1-NH/8-H protons is observed, and for the *E*-isomer an additional cross-peak of 4-H/2'6'-H protons is observed. By literature review, such reactions often proceeded regioselectively to form a single *Z*-isomer [22, 23] or an *E*-isomer [24].

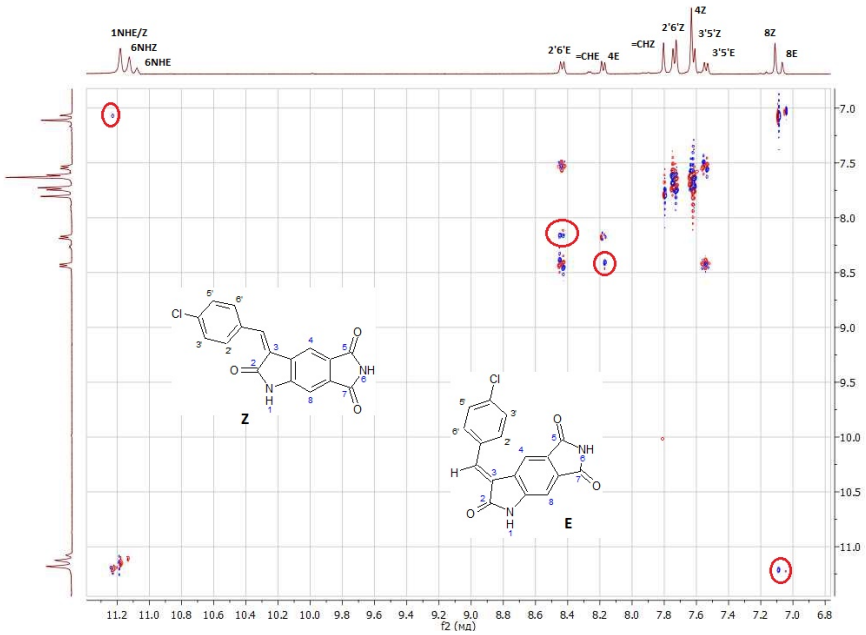


Fig. 1. Fragment of the *NOESY* spectrum of compound 7a

As a result of the study a method for the synthesis of substituted amides containing the isoindole-1,3-dione fragment using Schmidt rearrangement in the presence of sulfuric acid was developed and the properties of the synthesized compounds were studied.

Experimental part

IR spectra were recorded on a PerkinElmer Fourier RX-1 with a wavelength of 700-4000 cm^{-1}. The substances under analysis were in the form of a suspension in petrolatum liquidum.

NMR spectra were registered on the apparatus Bruker DRX-400 or Bruker DRX-500 for solutions in DMSO-d_6 at 30 °C. Solvent residual proton signals in ^1H NMR (δ_H= 2.50 ppm) or in ^{13}C (δ_C 39.5 ppm) were the reference for the chemical shift readout, tetramethylsilane signal was used as the marker.

Mass spectra were recorded using a FINNIGAN MAT.INCOS 50 chromato-mass spectrometer and a KratorMS-30 high-resolution mass spectrometer (England) at 70 eV ionization voltage and 100-220 °C temperature in the ionization chamber (N. D. Zelinsky Institute of Organic Chemistry Russian Academy of Sciences, Moscow).

Elemental analysis was conducted in the analytical laboratory of INEOS RAS (A.N. Nesmeyanov Institute of Organoelement Compounds of Russian Academy of Sciences, Moscow) on a PerkinElmer 2400.

The melting point was determined by Büchi M-560 melting point and boiling point apparatus.

Methodology for the synthesis of compounds 2 (a, b) and **3 (a-c)**

To the solution of 1 mmol of 5-nitro-4-phenacylphthalonitrile **1 (a-c)** in 3 ml of 80% H_2SO_4 was added 2 mmol NaN_3 in portions, the reaction mixture was stirred for 3.5-5 h at 90-100 °C. The reaction was monitored by Thin-Layer Chromatography (TLC) until the disappearing of stain of the starting component. After the reaction was completed, the mixture was cooled down to room temperature. The reaction mixture was separated into ice and the precipitate of product mixture 2 **(a, b)** and **3 (a-c)** was filtered off.

Methodology for the synthesis of 1,3-dihydropyrrolo[3,4-*f*]indole-2,5,7(6*H*)-trion 5

To the solution of 3 mmol $SnCl_2$ in 2 ml of concentrated HCl and 2 ml EtOH was added a mixture of 0.5 mmol of compounds **2/3**, the reaction mixture was stirred for 1-2 hours at 40-50 °C. The precipitate was filtered off on cooling. Then it was heated in 2-3 ml of alcohol until the boiling. The undissolved product was filtered off from the hot solution and compound **5** was obtained. Yield 67%, Tm 298–300 °C. Mass-spectrum, ν/sm^{-1}: 3237 (NH), 1770, 1725, 1706 (C=O), 1615 (Ar). Mass-spectrum (electron-impact (EI), 70 eV), *m*/*z* (*I*ratio (%)): 202 $[M]^+$ (38), 173 (19), 155 (12). NMR Spectrum ^1H (DMSO-d6, δ, ppm, *J*/Hz): 3.65 (s, 2H, 3-CH_2); 7.08 (s, 1H, 8-H); 7.62 (s, 1H, 4-H); 10.94 (s, 1H, 1-NH); 11.09 (br. s, 1H, 6-NH). NMR Spectrum ^{13}C (DMSO-d6, δ, ppm): 35.95, 102.81, 119.11, 125.37, 132.14, 133.30, 149.19, 168.98, 169.24, 176.08. Found (%): C, 59.18; H, 2.97; N, 13.82. $C_{10}H_6N_2O_3$. Calculated, (%): C, 59.41; H, 2.99; N, 13.86.

Methodology for the synthesis of compounds 7 (a, b)

To the solution of 1 mmol of compound **5** in alcohol was added 1.5 mmol of aldehyde **6 (a, b)** and 0.1 mmol of methanesulfonic acid, the reaction mixture was stirred at 60-80 °C for 2.5-3.5 hours. The precipitate of the compounds 7 **(a, b)** was filtered off on cooling.

(*E*)-3-(4-chlorobenzylidene)-1,3-[dihydropyrrolo] 3,4-*f*]indole -2,5,7(6*H*)-trion **7a:** NMR ^{1}H (DMSO-d6, δ, ppm, *J*/Hz): 7.07 (s, 1H, 8-H), 7.54 (d, 2H, 3'-H, 5'-H, *J*=8.1), 8.17 (s, 1H, 4-H), 8.19 (s, 1H, =CH), 8.43 (d, 2H, 2'-H, 6'-H, *J*=8.1), 11.08 (br. s, 1H, 8-NH), 11.18 (br. s, 1H, 1-NH).

(*Z*)-3-(4-)chlorobenzylidene-1,3-[dihydropyrrolo] 3,4-*f*]indole - 2,5,7(6*H*)- trion **7a:** NMR ^{1}H (DMSO-d6, δ, ppm, *J*/Hz): 7.11 (s, 1H, 8-H), 7.62 (d, 2H, 3'-H, 5'-H, *J*=8.1), 7.63 (s, 1H, =CH), 7.74 (d, 2H, 2'-H, 6'-H, *J*=8.1), 7.81 (s, 1H, 4-H), 11.12 (br. s, 1H, 8-NH), 11.18 (br. s, 1H, 1-NH).

Yield 83%, melting temperature (Tm) 387-388 °C. Mass-spectrum (EI, 70 eV), *m*/*z* (*I*ratio (%)): 326 $[M]^+$ (32), 324 $[M]^+$ (100), 225 (39), 213 (54), 190 (18), 163 (23), 109 (18), 44 (33).

(*E*)-3-(4-methoxybenzylidene)-1,3-dihydropyrrolo[3,4-*f*]indole-2,5,7(6*H*)-trion **7b:** NMR ^{1}H (DMSO-d6, δ, ppm, *J*/Hz): 3.88 (s, 3H, OMe), 7.09 (s, 1H, H-8), 7.15 (d, 2H, 3'-H, 5'-H, *J*=8.5), 7.78 (d, 2H, 2'-H, 6'-H, *J*=8.5), 7.88 (s, 1H, =CH), 8.24 (cs 1H, H-4), 11.10 (s, 1H, 8-NH), 11.18 (s, 1H, 1-NH).

(*Z*)-3-(4-methoxybenzylidene)-1,3-dihydropyrrolo[3,4-*f*]indole-2,5,7(6*H*)-trion **7b:** NMR ^{1}H (DMSO-d6, δ, ppm, *J*/Hz): 3.87 (s, 3H, OMe), 7.10 (s, 1H, H-8), 7.14 (d, 2H, 3'-H, 5'-H, *J*=8.5), 7.16 (s, 1H, =CH), 7.78 (d, 2H, 2'-H, 6'-H, *J*=8.5), 7.90 (s, 1H, H-4), 11.18 (s, 1H, 8-NH), 11.20 (s, 1H, 1-NH),

Yeild 76%, Tm 393-394 °C. Mass-spectrum (EI, 70 eV), *m*/*z* (*I*ratio (%)): 320 $[M]^+$ (100), 289 (15), 213 (48), 107 (18), 44 (33).

References

1. **Thigulla, Ya., Ranga, S., Ghosal, S., Subbalakshmi, J. & Bhattacharya, A.** (2017) One-Pot Two Step Nazarov-Schmidt Rearrangement for the Synthesis of Fused δ-Lactam Systems, *Chem. Select*, 2(30), pp. 9744-9750. DOI: 10.1002/slct.201701848 [online]. Available at: https://chemistry-europe.onlinelibrary.wiley.com/doi/10.1002/slct.201701848 (accessed on 13.01.2022).
2. **Bräse, S., Banert, K.** (Eds.) (2010) *Organic azides: syntheses and applications*. John Wiley & Sons. DOI: 10.1002/9780470682517 [online]. Available at: https://onlinelibrary.wiley.com/doi/10.1002/9780470682517.ch4 (accessed on 22.01.2022).
3. **Lang, S. & Murphy, J.A.** (2006) Azide rearrangements in electron-deficient systems, *Chem. Soc. Rev.*, 35(2), pp. 146-156. DOI: 10.1039/B505080D [online]. Available at: https://pubs.rsc.org/en/content/articlelanding/2006/cs/b505080d/unauth (accessed on 16.02.2022).
4. **Ding, S. L., Ji, Y., Su, Y., Li, R. & Gu, P.** (2019) Schmidt Reaction of ω-Azido Valeryl Chlorides Followed by Intermolecular Trapping of the Rearrangement Ions: Synthesis of Assoanine and Related Pyrrolophenanthridine Alkaloids, *J. Org. Chem.*, 84(4), pp. 2012-2021. DOI: 10.1021/acs.joc.8b03018 [online]. Available at: https://pubs.acs.org/doi/abs/10.1021/acs.joc.8b03018 (accessed on 03.05.2022).
5. **Nyfeler, E. & Renaud, Ph.** (2006) Intramolecular Schmidt Reaction: Applications in Natural Product Synthesis, *Chimia,* 60(5), pp. 276-284. DOI: 10.2533/000942906777674714 [online]. Available at: https://chimia.ch/chimia/article/view/2006_276/3453 (accessed on 01.03.2022).
6. **Zou, H., Zhou, L., Li, Y., Cui, Y., Zhong, H., Pan, Z., Yang, Zh. & Quan, J.** (2010) Benzo[*e*]isoindole-1,3-diones as potential inhibitors of glycogen synthase kinase-3 (GSK-3). Synthesis, kinase inhibitory activity,

zebrafish phenotype, and modeling of binding mode, *J. Med. Chem.*, 53(3), pp. 994-1003. DOI: 10.1021/jm9013373 [online]. Available at: https://pubs.acs.org/doi/abs/10.1021/jm9013373 (accessed on 03.02.2022).

7. **Figg, W.D., Raje, S., Bauer, K.S., Tompkins, A., Venzon, D., Bergan, R., Chen, A., Hamilton, M., Pluda, J. & Reed, E.** (2000) Pharmacokinetics of thalidomide in an elderly prostate cancer population, *J. Pharm. Sci*., 88(1), pp. 121-125. DOI: 10.1021/js980172i [online]. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1021/js980172i (accessed on 03.05.2022).
8. **Ouenadio, F., Walchshofer, N., Trentesaux, C., Barret, R. & Paris, J.** (2001) Synthesis and antiproliferative activity of [2-(phthaloylamino)alkyl]triphenyl phosphonium derivatives against K562 cell line, *Anti-Cancer Drugs*, 12(7), pp. 603-606. DOI: 10.1097/00001813-200108000-00007 [online]. Available at: https://journals.lww.com/anti-cancerdrugs/Abstract/2001/08000/Synthesis_and_antiproliferative_activity_of.7.aspx (accessed on 13.02.2022).
9. **Sansom, G.N., Kirk, N.S., Guise, C.P., Anderson, R.F., Smaill, J.B., Patterson, A.V. & Kelso, M.J.** (2019) Prototyping kinase inhibitor-cytotoxin anticancer mutual prodrugs activated by tumour hypoxia: A chemical proof of concept study, *Bioorg Med. Chem. Lett.*, 29(10), pp. 1215-1219. DOI: 10.1016/j.bmcl.2019.03.015 [online]. Available at: https://www.sciencedirect.com/science/article/pii/S0960894X19301441 (accessed on 11.05.2022).
10. **Lee, H.J., Lim, S.J., Oh, S.J., Moon, D.H., Kim, D.J., Tae, J. & Yoo, K.H.** (2008) Isoindol-1,3-dione and isoindol-1-one derivatives with high binding affinity to β-amyloid fibrils, *Bioorg. Med. Chem. Lett.,* 18(5), pp. 1628-1631. DOI: 10.1016/j.bmcl.2008.01.066 [online]. Available at: https://www.sciencedirect.com/science/article/pii/S0960894X08000838 (accessed on 04.01.2022).
11. **Chirkov, Z.V., Kabanova, M.V., Filimonov, S.I., Abramov, I.G., Petzer, A., Petzer, J.P., Firgang, S.I. & Suponitsky, K.Y.** (2015) Inhibition of monoamine oxidase by indole-5, 6-dicarbonitrile derivatives, *Bioorg. Med. Chem. Lett.*, 25(6), pp. 1206-1211. DOI: 10.1016/j.bmcl.2015.01.061 [online]. Available at: https://www.sciencedirect.com/science/article/pii/S0960894X15000827 (accessed on 03.05.2021).
12. **Meng, X.B., Han, D., Zhang, S.N., Guo, W., Cui, J.R. & Li, Z.J.** (2007) Synthesis and anti-inflammatory activity of N-phthalimidomethyl 2, 3-dideoxy-and 2, 3-unsaturated glycosides, *Carbohydr. Res.*, 342(9), pp. 1169-1174. DOI: 10.1016/j.carres.2007.03.009 [online]. Available at: https://www.sciencedirect.com/science/article/pii/S0008621507001334 (accessed on 03.12.2021).
13. **Kabanova, M.V., Makarova, E.S., Chirkova, Z.V., & Filimonov, S.I.** (2021) Simplified method for obtaining 3-bromindol-5,6-dicarbonitrils from 1-hydroxindol-5,6-dicarbonitriles, *From Chemistry Towards Technology Step-By-Step*, 2(1), pp. 111-115. DOI: 10.52957/27821900_2021_01_111 [online]. Available at: http://chemintech.ru/index.php/tor/2021tom2no1 (accessed on 08.02.2021).
14. **Abramov, I.G. & Karpov, R.Z.** (2020) Synthesis of 4-heterylamino-5-nitrophthalonitriles based on 4-bromo-5-nitrophthalonitrile, *From Chemistry Towards Technology Step-By-Step*, 1(1), pp. 62-67. DOI: 10.52957/27821900_2020_01_62 [online]. Available at: http://chemintech.ru/index.php/tor/2020tom1n1 (accessed on 03.05.2022).
15. **Kotov, A.D., Kunichkina, A.S. & Proskurina, I.K.** (2021) Transformation of 5-halogen-3-aril-2,1-benzisoxazoles into quinazolines, *From Chemistry Towards Technology Step-By-Step*, 2(4), pp. 81-84. DOI: 10.52957/27821900_2021_04_81 [online]. Available at: http://chemintech.ru/index.php/tor/2021-2-4 (accessed on 11.011.2021).
16. **Filimonov, S.I., Makarova, E.S., Chirkova, Z.V. & Kabanova, M.V.** (2022) Diastereomeric composition of the reaction of the formation of hexahydro-5*H*-CHOMENO[4,3-D]PYRIDIN-5-ONES, *From Chemistry Towards Technology Step-By-Step*, 3(1), pp. 131-138. DOI: 10.52957/27821900_2022_01_131 [online]. Available at: http://chemintech.ru/index.php/tor/2022tom3no1 (accessed on 03.03.2022).
17. **Slastikhina, P.V., Chirkova, Z.V., Kabanova, M.V., Abramov, I.G., Filimonov, S.I., Begunov, R.S. & Suponitsky, K.Y.** (2020) Synthesis of substituted isoindole-1,3-diones with an amide fragment using the Schmidt rearrangement, *Rus. Chem. Bull.*, 69, pp. 2378-2382. DOI: 10.1007/s11172-020-3027-9 [online]. Available at: https://link.springer.com/article/10.1007/s11172-020-3027-9#citeas (accessed on 23.05.2021).
18. **Desai, P., Schildknegt, K., Agrios, K.A., Mossman, C., Milligan, G.L. & Aube, J.** (2000) Reactions of alkyl azides and ketones as mediated by Lewis acids: Schmidt and Mannich reactions using azide precursors, *J. Am.*

Chem. Soc., 122(30), pp. 7226-7232. DOI: 10.1021/ja000490v [online]. Available at: https://pubs.acs.org/doi/abs/10.1021/ja000490v (accessed on 03.05.2022).

19. **Rokade, B.V., Prabhu, K.R.** (2012) Chemoselective Schmidt reaction mediated by triflic acid: selective synthesis of nitriles from aldehydes, *J. Org. Chem*., 77(12), pp. 5364-5370. DOI: 10.1021/jo3008258 [online]. Available at: https://pubs.acs.org/doi/abs/10.1021/jo3008258 (accessed on 13.05.2022).
20. **Filimonov, S.I., Chirkova, Z.V., Abramov, I.G., Firgang, S.I., Stashina, G.A., Strelenko, Y.A. & Suponitsky, K.Y.** (2012) Base-induced transformations of ortho-nitrobenzylketones: intramolecular displacement of nitro group versus nitro-nitrite rearrangement, *Tetrahedron*, 68(30), pp. 5991-5997. DOI: 10.1016/j.tet.2012.05.034 [online]. Available at: https://www.sciencedirect.com/science/article/pii/S0040402012007260 (accessed on 01.05.2022).
21. **Chirkova, Z.V., Kabanova, M.V., Filimonov, S.I., Abramov, I.G., Petzer, A., Petzer, J.P. & Suponitsky, K.Y.** (2016) An evaluation of synthetic indole derivatives as inhibitors of monoamine oxidase, *Bioorg. Med. Chem. Lett.*, 26(9), pp. 2214-2219. DOI: 10.1016/j.bmcl.2016.03.060 [online]. Available at: https://www.sciencedirect.com/science/article/pii/S0960894X16302803 (accessed on 10. 04.2022).
22. **Suthar, Sh.K., Aggarwal, V., Chauhan, M., Sharma, A., Bansal, S. & Sharma, M.** (2015) Molecular docking and biological evaluation of hydroxysubstituted (Z)-3-benzylideneindolin-2-one chalcones for the lead identification as tyrosinase inhibitors, *Med. Chem. Res.*, 24, pp. 1331–1341. DOI: 10.1007/s00044-014-1225-4 [online]. Available at: https://link.springer.com/article/10.1007/s00044-014-1225-4 (accessed on 11.05.2022).
23. **Maroju, S., Podila, N.K., Velupula, G., Chittimalla, S. & Pasad, T.R.** (2018) Synthesis and Characterization of New (Z)-5-((1 H-1, 2, 4-Triazol-1-yl)methyl)-3-arylideneindolin-2-ones, *J. Heterocycl. Chem.*, 56(1), pp. 153-157. DOI: 10.1002/jhet.3389 [online]. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1002/jhet.3389 (accessed on 03.05.2022).
24. **Tizzard, G.J., Coles, S.J., Edwards, M., Onyeabo, R.O., Allen, M. & Spencer, J.** (2013) Synthesis and solid-state characterisation of 4-substituted methylidene oxindoles, *Chem. Central J.*, 7(1), pp. 1-10. DOI: 10.1186/1752-153X-7-182 [online]. Available at: https://bmcchem.biomedcentral.com/articles/10.1186/1752-153X-7-182 (accessed on 15.05.2022).

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