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Synthesis of fused heterocycles from 2-aryl-5-(chlorosulfonyl)-1,3-oxazole-4-carboxylates and α-aminoazoles involving the Smiles rearrangement

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Reaction of methyl 2-aryl-5-(chlorosulfonyl)-1,3-oxazole-4-carboxylates with 1H-pyrazol-5-amines and 1H-1,2,4-triazol-5-amines proceeds with the participation of endocyclic aminoazole nitrogen atoms to yield products containing a primary amino group. Being treated by sodium hydride these products undergo a further transformation into the tricyclic compounds. It has been shown that the cyclocondensation pathway includes the Smiles rearrangement with extrusion of SO_2 followed by the elimination of MeOH. This reaction sequence is a convenient approach to the synthesis of new annulated [1,3]oxazolo[5,4-d]pyrimidine derivatives.

1. Introduction

Among a variety of pharmaceutically promising amides of azolesulfonic acids, oxazolesulfonyl amides seem to us particularly interesting. These species have the weakly aromatic oxazole ring capable to hydrolytic cleavage,[1] which may be important for bioactivity associated with the enzyme inhibition. Thus, 1,3-oxazole-5-sulfonyl amide **1** (**Fig. 1**) is known to be a rare dual cyclooxygenase-2/5-lipoxygenase inhibitor.[2]

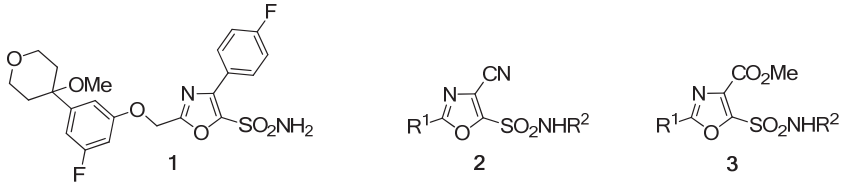

Fig. 1. Biologically active 1,3-oxazole-5-sulfonyl amides

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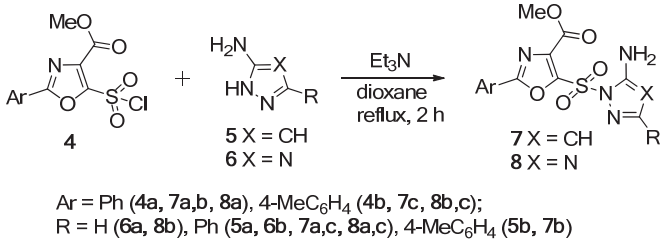
Other promising representatives of 1,3-oxazole-5-sulfonyl amides are those bearing a pronounced electron-withdrawing substituent at position C(4), in particular, compounds **2** and **3** obtained recently from the corresponding 1,5-oxazole 5-sulfonyl chlorides in our laboratory.[3,4] One of our research tasks was entering into the sulfonamide grouping of **2** and **3** an electron-deficient heterocyclic substituent R^2, which increases the acidity of the N—H linkage making a molecule to be easier delivered to the target enzyme like that in the case of the sulfanilamide drugs.[5] Recently we reported that the interaction of 4-cyano-1,3-oxazole-5-sulfonyl chlorides with 1*H*-pyrazol-5-amines and 1*H*-1,2,4-triazol-5-amine leads to unexpected substitution products, which, nevertheless, are useful for further heterocyclization.[6]

The aim of the present work was to investigate into products of interaction of 1,3-oxazole-5-sulfonyl chlorides having a methoxycarbonyl group at position C(4) with the aforementioned heterocyclic amines.

2. Results and Discussion

Methyl 2-aryl-5-(chlorosulfonyl)-1,3-oxazole-4-carboxylates **4** were treated with commercially available 1*H*-pyrazol-5-amines **5** and 1*H*-1,2,4-triazol-5-amines **6** in the conditions shown in **Scheme 1**.



Scheme 1. Synthesis of compounds **7** and **8**

Despite the fact that a very similar analogy was reported with this reaction,[6] its result requires careful consideration because both endo- and exocyclic aminoazole nitrogen atoms can take part. It is known, for example, that 3-metyl-1*H*-pyrazol-5-amine as well as 3-metyl-1*H*-1,2,4-triazol-5-amine react with aromatic sulfonyl chlorides to give mixtures of sulfonyl derivatives.[7,8] Nevertheless, the reaction of **4** with **5** and **6** in the presence of triethylamine proceeded quite regioselectively with 76-84% yield of *endo*-substitution products **7** and **8**. The fact that compounds **7** and **8** contain a primary amino group is confirmed by i) two characteristic IR absorption bands relevant to the asymmetric and symmetric N–H stretching from 3500-3200 cm^{-1}, ii) a two proton NMR singlet at 6.5 ppm (for **7**) and within 7.8-7.5 ppm (for **8**). X-ray crystal analysis of **7c** and **8b** was also carried out, which revealed their additional structural stabilization due to an intramolecular $NH_2\cdots O_2S$ hydrogen bond (**Fig. 2** and **Fig. 3**).

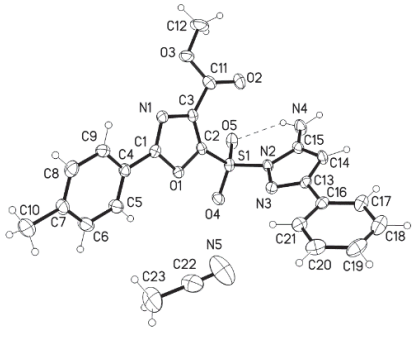


Fig. 2. ORTEP diagram of solvate **7c**·MeCN with 50% ellipsoids probability

In molecule **7c**, the 1,3-oxazole and the pyrazole ring mean planes make a dihedral angle of 80.60(9)°. Benzene ring C(4)-C(9) and the CO_2Me group are rotated relative to the 1,3-oxazole ring by 13.67(15) and 29.75(16)º, respectively. Intramolecular N(4)H···O(5) hydrogen bond was found with the following parameters N(4)–H 0.83(3) Å, N(4)···O(5) 2.807(3) Å, N(4)HO(5) 133(2)º.

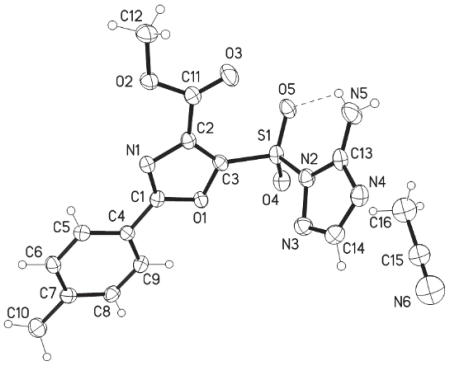
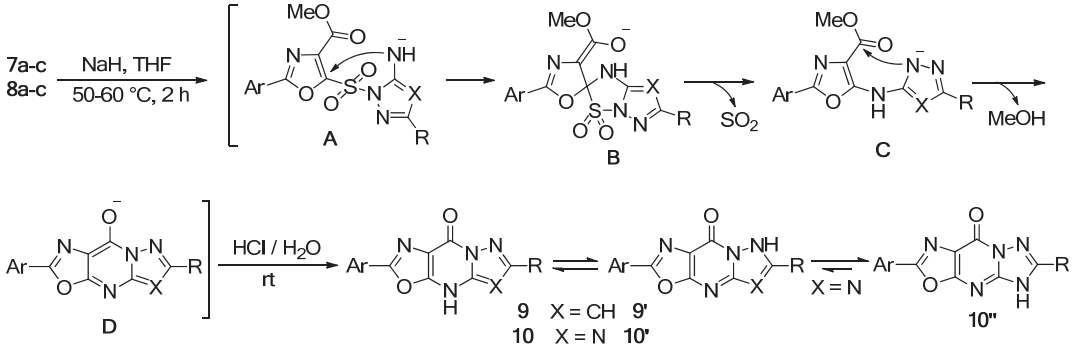


Fig. 3. ORTEP diagram of solvate **8b**·MeCN with 50 % ellipsoids probability

In molecule **8b**, the 1,3-oxazole and the triazole ring mean planes make a dihedral angle of 77.26(10)°. The benzene ring is almost coplanar with the 1,3-oxazole ring and the ester group is slightly rotated so that dihedral angles between the corresponding planes are 2.7 (1)º and 9.0 (1)º. Both intramolecular N(5)H···O(5) N(5)–H 0.85(5) Å, N(5)···O(5) 2.832(4) Å, N(5)HO(5) 127(4)º) and intermolecular N(5)H···N(4') hydrogen bonds were found in a crystal.

Our recent investigations showed that analogues of products **7** and **8** bearing a CN group instead of CO_2Me at C(4) of the 1,3-oxazole ring when treated by sodium hydride undergo a transformation into tricyclic compounds.[6] **Scheme 2** demonstrates how compounds **7** and **8** have been involved in a similar cyclocondensation to provide fused heterocycles **9** and **10**.



Scheme 2. Formation of compounds **9** and **10**

As for the mechanism, anion-intermediates **A-D** are conceived, from which sequence **A-C** is a new example of the N – S Smiles rearrangement with the sulfur dioxide extrusion.[9]

Products **9** and **10** were obtained in 60-75% yield and are very high melted and poorly soluble solids. Their structure was verified by the spectral data, among which it is worth mentioning the strong IR absorption in the region 1680-1720 cm^{-1} attributed to C=O bond vibration. This characteristic allows excluding the existence of **9** and **10** in the OH tautomer form in the solid state. However, they can exist in different NH tautomer forms (**9, 9'** and **10, 10', 10"**). X-ray diffraction study of compound **10c** showed that the [1,3]oxazolo[5,4-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-9(5*H*)-one structure **10"** takes place in a crystal (**Fig. 4**). We did not study the tautomerism in a solution. In the ^1H NMR spectra of **9**

and **10** dissolved in DMSO-d_6, the NH signal was not detected but multiplets analysis indicated the presence of the only tautomer.

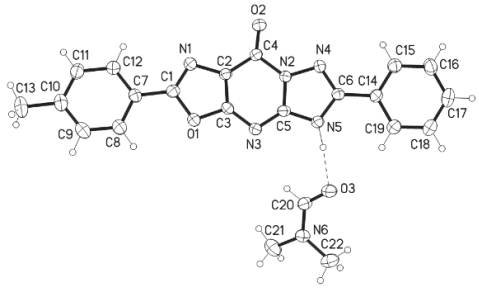
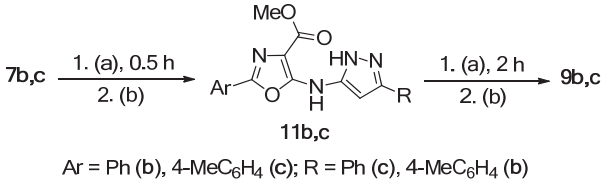


Fig. 4. ORTEP diagram of solvate **10c** DMF with 30% ellipsoids probability

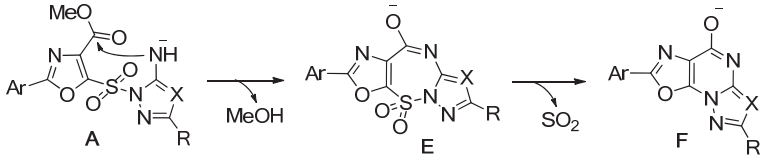
In compound **10c**, the tricyclic system O(1)N(1)-N(5)C(1)-C(6) is planar with Rms deviation of the fitted atoms equal to 0.0143. Hydrogen bond N(5)H···O(3) between molecule **10c** and a DMF solvate molecule was found in a crystal with the following parameters N(5)–H 1.00(3) Å, N(5)···O(3) 2.680(2) Å, N(5)HO(3) 168(2)º.

It should be noted that the elimination of MeOH is, apparently, a rate-determining stage of the transformation **A→D**. We found that if compounds **7b,c** are heated with NaH in THF for only 30 min, the Smiles rearrangement products **11b,c** are allowed to be isolated in 62-65% yield after acidifying the reaction mixture (**Scheme 3,** one of the two possible tautomers of **11** is shown). These later cyclize into **9b,c** on further heating with NaH in THF.



Scheme 3. Preparation of compounds **11** and their transformation into **9.** Reagents and conditions: (a) NaH, THF, 50-60 °C; (b) HCl / H_2O, rt.

This observation along with the above crystallographic evidence supports the cyclocondensation pathway shown in **Scheme 2** and doubts on the alternative possibility depicted in **Scheme 4**.



Scheme 4. An alternative cyclocondensation pathway

Theoretically anions **A** could eliminate MeOH to give 7 membered cyclic intermediates **E**. An analogy of this cyclization has been reported.[10] Anions **E** could undergo ring contraction to give anions **F**. The protonation of the latter could lead to the angular regioisomers of tricyclic compounds **8** and **9**, which in fact were not found during the experiment.

3. Conclusion

In conclusion, described in the article cyclocondensation reaction of esters **7** and **8** under the action of NaH the Smiles rearrangement with extrusion of SO_2 does occur followed by the elimination of MeOH. This reaction sequence is a convenient approach to the synthesis of new "*a*" annulated [1,3]oxazolo[5,4-*d*]pyrimidine derivatives.

Acknowledgements

We would like to thank **Enamine** Ltd for the material and technical support.

4. Experimental

4.1. Instruments, Reagents, and Methods

Melting points were determined on a Fisher-Johns apparatus. IR spectra were recorded on a Vertex-70 spectrometer from KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury 400 (400 and 100 MHz, respectively) and Bruker Avance DRX 500 (500 and 125 MHz, respectively) spectrometers in DMSO-d_6. ^{13}C NMR spectra were obtained for most new compounds, except for **9a-c** and **10a,b** because of their poor solubility. LC-MS analysis was performed on an Agilent 1200 Series system equipped with a diode array and a G6130A mass-spectrometer (atmospheric pressure electrospray ionization). Combustion elemental analysis was performed in the Institute of Bioorganic Chemistry and Petrochemistry analytical laboratory.

Crystallographic measurements were performed on a Bruker Smart Apex II diffractometer operating in the ω scan mode using Mo-K_α radiation with λ = 0.71078 Å. Structures were solved by direct methods and refined by the full-matrix least-squares technique in the anisotropic approximation for non-hydrogen atoms using the Bruker SHELXTL program package.[11] The carbon-linked hydrogen atoms were placed at calculated positions and refined as a "riding" model, the other hydrogen atoms were located in DF synthesis and refined isotropically. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC1834792, CCDC1834794, and CCDC1834796. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk).

Methyl 2-aryl-5-(chlorosulfonyl)-1,3-oxazole-4-carboxylates **4** were prepared according to the published method.[4] 1*H*-Pyrazol-5-amines **5** and 1*H*-1,2,4-triazol-5-amines **6** were supplied by Enamine Ltd, Kiev.

Compounds **9** have been arbitrarily named as [1,3]oxazolo[5,4-*d*]pyrazolo[1,5-*a*]pyrimidin-9(4*H*)-one tautomers but compounds **10** – as [1,3]oxazolo[5,4-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-9(5*H*)-one tautomers taking into account the X-ray analysis.

4.2. Experimental procedure and physical data for compounds 7 and 8

Compound **4** (4 mmol) was added to a solution of heterocyclic amine **5** or **6** (4 mmol) and Et_3N (4 mmol) in anhydrous dioxane (15 mL), this composition was refluxed for 2 h. The resulting mixture was cooled to 20–25 °C, the precipitate was filtered off, and the filtrate was evaporated in vacuum. The residue was triturated with water to give a crude product which was separated, recrystallized from MeCN, and dried at 70-80 °C.

*Methyl 5-((5-amino-3-phenyl-1H-pyrazol-1-yl)sulfonyl)-2-phenyl-1,3-oxazole-4-carboxylate (**7a**)*

Light yellow solid; 76% yield; mp 144-146 °C. IR, ν, cm^{-1}: 3444, 3304 (NH_2); 1731 (C=O). ^{1}H NMR (500 MHz), δ: 7.97 (d, J = 8.0 Hz, 2H, ArH), 7.74-7.57 (m, 5H, ArH), 7.40-7.39 (m, 3H, ArH), 6.55 (s, 2H, NH_2), 5.90 (s, 1H, CH), 3.93 (s, 3H, CH_3O). ^{13}C NMR (125 MHz), δ: 162.5, 159.5, 157.5, 154.2, 146.6, 135.7, 133.6, 131.6, 130.0, 129.2, 127.6, 126.5, 124.7, 85.9, 53.8. MS, *m/z*: 425 $[M+1]^+$. Anal. calcd for $C_{20}H_{16}N_4O_5S$: C, 56.60; H, 3.80; N, 13.20; S, 7.55. Found: C, 56.65; H, 3.86; N, 13.02; S, 7.61.

*Methyl 5-((5-amino-3-(4-methylphenyl)-1H-pyrazol-1-yl)sulfonyl)-2-phenyl-1,3-oxazole-4-carboxylate (**7b**)*

Colorless solid; 82% yield; mp 185-187 °C. IR, *v*, cm^{-1}: 3437, 3302 (NH_2); 1729 (C=O). ^1H NMR (500 MHz), *δ*: 7.97 (d, *J* = 7.0 Hz, 2H, ArH), 7.68-7.56 (m, 5H, ArH), 7.20 (d, *J* = 7.5 Hz, 2H, ArH), 6.52 (s, 2H, NH_2), 5.86 (s, 1H, CH), 3.93 (s, 3H, CH_3O), 2.29 (s, 3H, CH_3C). ^{13}C NMR (125 MHz), δ: 162.4, 159.5, 157.5, 154.2, 146.6, 139.6, 135.7, 133.5, 130.0, 129.7, 128.9, 127.6, 126.5, 124.7, 85.8, 53.8, 21.4. MS, *m/z*: 439 $[M+1]^+$. Anal. calcd for $C_{21}H_{18}N_4O_5S$: C, 57.53; H, 4.14; N, 12.78; S, 7.31. Found: C, 57.48; H, 4.16; N, 12.69; S, 7.22.

*Methyl 5-((5-amino-3-phenyl-1H-pyrazol-1-yl)sulfonyl)-2-(4-methylphenyl)-1,3-oxazole-4-carboxylate (**7c**)*

Light yellow solid; 84% yield; mp 150-152 °C. IR, *v*, cm^{-1}: 3496, 3392 (NH_2); 1725 (C=O). ^1H NMR (400 MHz), *δ*: 7.85 (d, *J* = 8.0 Hz, 2H, ArH), 7.71-7.69 (m, 2H, ArH), 7.39-7.37-(m, 5H, ArH), 6.53 (s, 2H, NH_2), 5.87 (s, 1H, CH), 3.90 (s, 3H, CH_3O), 2.37 (s, 3H, CH_3C). ^{13}C NMR (125 MHz), *δ*: 162.7, 159.6, 157.4, 154.2, 146.1, 144.0, 135.8, 131.7, 130.5, 130.0, 129.2, 127.6, 126.5, 121.9, 85.9, 53.7, 21.6. MS, *m/z*: 439 $[M+1]^+$. Anal. calcd for $C_{21}H_{18}N_4O_5S$: C, 57.53; H, 4.14; N, 12.78; S, 7.31. Found: C, 57.55; H, 4.15; N, 12.88; S, 7.31.

*Crystallographic data for compound **7c***

$C_{21}H_{18}N_4O_5S \cdot 0.5C_2H_3N$, *M* = 458.98. Crystal size ca 0.11x0.18x0.44 mm, triclinic, space group P-1, *a* = 9.253(4), *b* = 10.106(4), *c* = 12.259(3) Å, *α* = 93.040(8), *β* = 104.037(10), *γ* = 100.383(9)°, *V* = 1088.3(7) $Å^3$, *Z* = 2, d_c = 1.401 $g \cdot cm^{-3}$, *μ* = 0.193 $мм^{-1}$, *F*(000) = 478. Intensities were measured at 173K within $\theta_{max} \leq 25.5°$ (8851 reflections total, 4001 unique reflections, R_{merg} = 0.0417). The convergence was obtained at *R*1 = 0.0512, *wR*2 = 0.0931 for 2840 observed reflections with $I \geq 2\sigma(I)$ and at *R*1 = 0.0822, *wR*2 = 0.1025, GOF = 1.049 for 4001 independent reflections, 315 parameters, the maximum and minimum peaks on the final difference map correspond to 0.27 and – 0.459 e/$Å^3$.

*Methyl 5-((5-amino-3-phenyl-1H-1,2,4-triazol-1-yl)sulfonyl)-2-phenyl-1,3-oxazole-4-carboxylate (**8a**)*

Light yellow solid; 80% yield; mp 201-203 °C. IR, *v*, cm^{-1}: 3471, 3429, 3324, 3244 (NH_2); 1736 (C=O). ^1H NMR (500 MHz), *δ*: 8.02 (d, *J* = 7.5 Hz, 2H, ArH), 7.89-7.87 (m, 2H, ArH), 7.73 (s, 2H, NH_2), 7.68 (t, *J* = 7.5 Hz, 1H, ArH), 7.61 (t, *J* = 7.5 Hz, 2H, ArH), 7.48-7.42 (m, 3H, ArH), 3.92 (s, 3H, CH_3O). ^{13}C NMR (125 MHz), *δ*: 162.9, 162.3, 159.4, 158.9, 145.9, 136.3, 133.6, 131.1, 130.1, 129.6, 129.2, 127.8, 127.0, 124.7, 53.9. MS, *m/z*: 426 $[M+1]^+$. Anal. calcd for $C_{19}H_{15}N_5O_5S$: C, 53.64; H, 3.55; N, 16.46; S, 7.54. Found: C, 53.70; H, 3.55; N, 16.61; S, 7.52.

*Methyl 5-((5-amino-1H-1,2,4-triazol-1-yl)sulfonyl)-2-(4-methylphenyl)-1,3-oxazole-4-carboxylate (**8b**)*

Colorless solid; 84% yield; mp 172-175 °C. IR, *v*, cm^{-1}: 3461, 3395, 3302, 3227 (NH_2); 1737 (C=O). ^1H NMR (500 MHz), *δ*: 7.92 (d, *J* = 8.0 Hz, 2H, ArH), 7.73 (s, 1H, CH), 7.57 (s, 2H, NH_2), 7.44 (d, *J* = 8.0 Hz, 2H, ArH), 3.90 (s, 3H, CH_3O), 2.42 (s, 3H, CH_3C). ^{13}C NMR (125 MHz), *δ*: 163.2, 159.3, 158.2, 154.0, 145.5, 144.2, 136.2, 130.7, 127.8, 121.9, 53.8, 21.7. MS, *m/z*: 364 $[M+1]^+$. Anal. calcd for $C_{14}H_{13}N_5O_5S$: C, 46.28; H, 3.61; N, 19.27; S, 8.82. Found: C, 46.23; H, 3.59; N, 19.40; S, 8.86.

*Crystallographic data for compound **8b***

$C_{14}H_{13}N_5O_5S \cdot 0.5C_2H_3N$, *M* = 383.88. Crystal size ca 0.11x0.17x0.46mm, triclinic, space group P-1, *a* = 6.996(3), *b* = 8.646(3), *c* = 14.881(7) Å, *α* = 89.843(16), *β* = 80.885(13), *γ* = 71.778(10)°, *V* =

843.1(6) Å^3, $Z = 2$, $d_c = 1.512$ g·cm^{-3}, $\mu = 0.233$ мм$^{-1}$, $F(000) = 398$. Intensities were measured at 173K within $\theta_{max} \leq 27.8°$ (10099 reflections total, 3826 unique reflections, $R_{merg} = 0.0415$). The convergence was obtained at $R1 = 0.0549$, $wR2 = 0.1337$ for 2621 observed reflections with $I \geq 2\sigma(I)$ and at $R1 = 0.0919$, $wR2 = 0.1506$, GOF = 1.067 for 3826 independent reflections, 247 parameters, the maximum and minimum peaks on the final difference map correspond to 0.58 and – 0.49 e/Å^3.

*Methyl 5-((5-amino-3-phenyl-1H-1,2,4-triazol-1-yl)sulfonyl)-2-(4-methylphenyl)-1,3-oxazole-4-carboxylate (**8c**)*

Colorless solid; 82% yield; mp 197-199 °C. IR, ν, cm^{-1}: 3473, 3401, 3311, 3231 (NH_2); 1749 (C=O). ^{1}H NMR (500 MHz), δ: 7.91-7.87 (m, 4H, ArH), 7.72 (s, 2H, NH_2), 7.45-7.39 (m, 5H, ArH), 3.92 (s, 3H, CH_3O), 2.39 (s, 3H, CH_3C). ^{13}C NMR (125 MHz), δ: 163.1, 162.3, 159.4, 158.9, 145.5, 144.2, 136.3, 131.1, 130.6, 129.6, 129.2, 127.7, 127.0, 122.0, 53.8, 21.7. MS, *m/z*: 440 $[M+1]^+$. Anal. calcd for $C_{20}H_{17}N_5O_5S$: C, 54.66; H, 3.90; N, 15.94; S, 7.30. Found: C, 54.63; H, 3.87; N, 15.88; S, 7.25.

*4.3. Experimental procedure and physical data for compounds **9***

To a solution of compound **7** or **11** (1 mmol) in anhydrous THF (15 mL), 80 mg of 60% NaH (2 mmol) was added. The reaction mixture was stirred at 20-25 °C for 1 h then heated at 50-60 °C for 2 h, cooled to room temperature, diluted with water (20 mL), and acidified by the concd hydrochloric acid (0.2 mL). The precipitate formed was filtered off, recrystallized from DMF/MeCN (1:1), and dried at 70-80 °C to give the analytically pure product.

*2,6-Diphenyl[1,3]oxazolo[5,4-d]pyrazolo[1,5-a]pyrimidin-9(4H)-one (**9a**)*

Colorless solid; 67% yield; mp above 300 °C. IR, ν, cm^{-1}: 3400-2650 (NH, CH), 1689 (C=O). ^{1}H NMR (400 MHz), δ: 8.06-8.04 (m, 4H, ArH), 7.58-7.52 (m, 6H, ArH), 6.95 (s, 1H, CH). MS, *m/z*: 329 $[M+1]^+$. Anal. calcd for $C_{19}H_{12}N_4O_2$: C, 69.51; H, 3.68; N, 17.06. Found: C, 69.60; H, 3.66; N, 17.18.

*6-(4-Methylphenyl)-2-phenyl[1,3]oxazolo[5,4-d]pyrazolo[1,5-a]pyrimidin-9(4H)-one (**9b**)*

Colorless solid; 63% (from **7b**), 72% (from **11b**) yield; mp above 300 °C. IR, ν, cm^{-1}: 3295 (NH), 1689 (C=O). ^{1}H NMR (400 MHz), δ: 8.09-8.07 (m, 2H, ArH), 7.96-7.95 (m, 2H, ArH), 7.59 (s, 3H, ArH), 7.36-7.34 (m, 2H, ArH), 6.91 (s, 1H, CH), 2.39 (s, 3H, CH_3). MS, *m/z*: 343 $[M+1]^+$. Anal. calcd for $C_{20}H_{14}N_4O_2$: C, 70.17; H, 4.12; N, 16.36. Found: C, 70.11; H, 4.12; N, 16.31.

*2-(4-Methylphenyl)-6-phenyl[1,3]oxazolo[5,4-d]pyrazolo[1,5-a]pyrimidin-9(4H)-one (**9c**)*

Light yellow solid; 62% (from **7c**), 69% (from **11c**) yield; mp above 300 °C. IR, ν, cm^{-1}: 3321 (NH), 1684 (C=O). ^{1}H NMR (400 MHz), δ: 8.06-7.95 (m, 4H, ArH), 7.54-7.40 (m, 5H, ArH), 6.95 (s, 1H, CH), 2.41 (s, 3H, CH_3). MS, *m/z*: 343 $[M+1]^+$. Anal. calcd for $C_{20}H_{14}N_4O_2$: C, 70.17; H, 4.12; N, 16.36. Found: C, 70.20; H, 4.10; N, 16.23.

*4.4. Experimental procedure and physical data for compounds **10***

To a solution of compound **8** (1 mmol) in anhydrous THF (15 mL), 80 mg of 60% NaH (2 mmol) was added. The reaction mixture was stirred at 20-25 °C for 1 h then heated at 50-60 °C for 2 h, cooled to room temperature, diluted with water (20 mL), and acidified by the concd hydrochloric acid (0.2 mL). The precipitate formed was filtered off, recrystallized from DMF/MeCN (1:1), and dried at 70-80 °C to give the analytically pure product.

*2,6-Diphenyl[1,3]oxazolo[5,4-d][1,2,4]triazolo[1,5-a]pyrimidin-9(5H)-one (**10a**)*

Colorless solid; 70% yield; mp above 300 °C. IR, ν, cm^{-1}: 3290 (NH), 1684 (C=O). ^1H NMR (400 MHz), δ: 8.11-8.07 (m, 4H, ArH), 7.64-7.58 (m, 6H, ArH). MS, *m/z*: 330 $[M+1]^+$. Anal. calcd for $C_{18}H_{11}N_5O_2$: C, 65.65; H, 3.37; N, 21.27. Found: C, 65.70; H, 3.36; N, 21.41.

*2-(4-Methylphenyl)[1,3]oxazolo[5,4-d][1,2,4]triazolo[1,5-a]pyrimidin-9(5H)-one (**10b**)*

Colorless solid; 60% yield; mp above 300 °C. IR, ν, cm^{-1}: 3370-2640 (NH, CH), 1724 (C=O). ^1H NMR (400 MHz), δ: 8.86 (s, 1H, CH), 7.96 (d, J = 7.2 Hz, 2H, ArH), 7.40 (d, J = 7.2 Hz, 2H, ArH), 2.40 (s, 3H, CH_3). MS, *m/z*: 269 $[M+1]^+$. Anal. calcd for $C_{13}H_9N_5O_2$: C, 58.43; H, 3.39; N, 26.21. Found: C, 58.39; H, 3.38; N, 26.42.

*2-(4-Methylphenyl)-6-phenyl[1,3]oxazolo[5,4-d][1,2,4]triazolo[1,5-a]pyrimidin-9(5H)-one (**10c**)*

Colorless solid; 75% yield; mp above 300 °C. IR, ν, cm^{-1}: 3120-2550 (NH, CH), 1692 (C=O). ^1H NMR (400 MHz), δ: 8.12-8.10 (m, 2H, ArH), 7.97 (d, J = 7.6 Hz, 2H, ArH), 7.63 (s, 3H, ArH), 7.39 (d, J = 7.6 Hz, 2H, ArH), 2.40 (s, 3H, CH_3). ^{13}C NMR (100 MHz, 375 K), δ: 163.0, 161.7, 156.1, 151.0, 149.9, 149.4, 140.7, 131.2, 129.2, 128.6, 126.3, 125.8, 125.2, 123.4, 113.9, 20.5. MS, *m/z*: 330 $[M+1]^+$. Anal. calcd for $C_{19}H_{13}N_5O_2$: C, 66.47; H, 3.82; N, 20.40. Found: C, 66.50; H, 3.79; N, 20.28.

*Crystallographic data for compound **10c***

$C_{19}H_{17}N_5O_2 \cdot C_3H_7NO$, M = 416.44. Crystal size ca 0.13x0.25x0.31mm, triclinic, space group P-1, a = 7.606(3), b = 11.748(4), c = 12.175(4) Å, α = 93.747(10), β = 100.826(9), γ = 106.889(8)º, V = 1014.2(5) $Å^3$, Z = 2, d_c = 1.364 $g \cdot cm^{-3}$, μ = 0.095 $мм^{-1}$, $F(000)$ = 436. Intensities were measured at room temperature within $\theta_{max} \le 26.54°$ (14299 reflections total, 4184 unique reflections, R_{merg} = 0.061). The convergence was obtained at $R1$ = 0.053, $wR2$ = 0.105 for 2166 observed reflections with $I \ge 2\sigma(I)$ and at $R1$ = 0.1256, $wR2$ = 0.1318, GOF = 1.002 for 4184 independent reflections, 288 parameters, the maximum and minimum peaks on the final difference map correspond to 0.19 and – 0.19 e/$Å^3$.

*4.5. Experimental procedure and physical data for compounds **11***

To a solution of one of compounds **7b,c** (1 mmol) in anhydrous THF (15 mL), 80 mg of 60% NaH (2 mmol) was added. The reaction mixture was stirred at 20-25 °C for 1 h then heated at 50-60 °C for 30 min, cooled to room temperature, diluted with water (20 mL), and acidified by the concd hydrochloric acid (0.2 mL). The precipitated product was filtered off, recrystallized from MeCN, and dried at 70-80 °C.

*Methyl 5-((3-(4-methylphenyl)-1H-pyrazol-5-yl)amino)-2-phenyl-1,3-oxazole-4-carboxylate (**11b**)*

Colorless solid; 62% yield; mp 278-280 °C. IR, ν, cm^{-1}: 3295 (NH), 1689 (C=O). ^1H NMR (400 MHz), δ: 12.99 (s, 1H, NH), 9.37 (s, 1H, NH), 7.90 (d, J = 8.0 Hz, 2H, ArH), 7.69 (d, J = 8.4 Hz, 2H, ArH), 7.55-7.47 (m, 3H, ArH), 7.29 (d, J = 7.2 Hz, 2H, ArH), 6.70 (s, 1H, CH), 3.83 (s, 3H, CH_3O), 2.35 (s, 3H, CH_3C). ^{13}C NMR (125 MHz), δ: 162.5, 150.2, 130.1, 129.5, 129.2, 126.2, 125.2, 125.1, 105.9, 92.9, 51.0, 20.9. MS, *m/z*: 375 $[M+1]^+$. Anal. calcd for $C_{21}H_{18}N_4O_3$: C, 67.37; H, 4.85; N, 14.96. Found: C, 67.44; H, 4.91; N, 14.83.

*Methyl 2-(4-methylphenyl)-5-((3-phenyl-1H-pyrazol-5-yl)amino)-1,3-oxazole-4-carboxylate (**11c**)*

Colorless solid; 65% yield; mp 289-291 °C. IR, ν, cm^{-1}: 3321 (NH), 1677 (C=O). ^1H NMR (400 MHz), δ: 13.06 (s, 1H, **NH**), 9.38 (s, 1H, NH), 7.80-7.78 (m, 4H, ArH), 7.50-7.33 (m, 5H, ArH), 6.73 (s, 1H, CH), 3.82 (s, 3H, CH_3O), 2.36 (s, 3H, CH_3C). ^{13}C NMR (125 MHz), δ: 162.5, 155.0, 150.5,

139.9, 129.7, 129.0, 128.3, 125.2, 125.1, 123.6, 105.9, 93.1, 51.0, 21.0. MS, *m/z*: 375 $[M+1]^+$. Anal. calcd for $C_{21}H_{18}N_4O_3$: C, 67.37; H, 4.85; N, 14.96. Found: C, 67.40; H, 4.80; N, 14.81.

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